

Aus dem Max von Pettenkofer-Institut für Hygiene und Medizinische Mikrobiologie

Lehrstuhl: Bakteriologie

der Ludwig-Maximilians-Universität München

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*Analysis of Helicobacter pylori VacA-containing vacuoles  
and VacA intracellular trafficking*

Dissertation

zum Erwerb des Doktorgrades der Naturwissenschaften

an der Medizinischen Fakultät

der Ludwig-Maximilians-Universität München

vorgelegt von

Beate Kern

aus Schrobenhausen

2014

Gedruckt mit Genehmigung der Medizinischen Fakultät  
der Ludwig-Maximilians-Universität München

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Tag der mündlichen Prüfung: 03.06.2015

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Teile dieser Arbeit werden veröffentlicht:

Kern B., Jain U., Utsch C., Otto A., Busch B., Jiménez-Soto L.F., Becher D., Haas R.: Characterization of *Helicobacter pylori* VacA-containing vacuoles (VCVs), VacA intracellular trafficking and interference with calcium signalling in T-lymphocytes. *Cell Microbiol* 2015, doi: 10.1111/cmi.12474 (accepted)

Publikation im Promotionszeitraum, die nicht in der Arbeit enthalten ist:

Fischer W., Breithaupt U., Kern B., Smith S.I., Spicher C., Haas R.: A comprehensive analysis of *Helicobacter pylori* plasticity zones reveals that they are integrating conjugative elements with intermediate integration specificity. *BMC Genomics* 2014, 15:310

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## Summary

The human pathogen *Helicobacter pylori* colonizes half of the global population. Residing at the stomach epithelium, it contributes to the development of diseases like gastritis, duodenal and gastric ulcers, and gastric cancer. It has evolved a range of mechanisms to aid in colonization and persistence, manipulating the host immune response to avoid clearance. A major factor in this is the secreted vacuolating cytotoxin VacA which has a variety of effects on host cells. VacA is endocytosed and forms anion-selective channels in the endosome membrane, causing the compartment to swell. The resulting VacA-containing vacuoles (VCVs) can take up most of the cellular cytoplasm. Even though vacuolation is VacA's most prominent and namesake effect, the purpose of the vacuoles is still unknown.

VacA exerts influence on the host immune response in various ways, both pro- and anti-inflammatory. Most importantly, it disrupts calcium signaling in T-lymphocytes, inhibiting T-cell activation and proliferation and thereby suppressing the host immune response. Furthermore, VacA is transported to mitochondria, where it activates the mitochondrial apoptosis pathway. Within the cell, VacA has only been shown to localize to endocytic compartments/VCVs and mitochondria. Considering its diverse effects, however, the existence of other cellular sites of action seems plausible.

In this study, the VCV proteome was comprehensively analyzed for the first time in order to investigate VCV function. To this end, three different strategies for VCV purification from T-cells were devised and tested. Eventually, VCVs were successfully isolated via immunomagnetic separation, using a VacA-specific primary antibody and a secondary antibody coupled to magnetic beads. The purified vacuoles were then measured by mass spectrometry, revealing not only proteins of the endocytic system, but also proteins usually localized in other cellular compartments. This apparent recruitment of proteins involved in all kinds of cellular pathways indicates a central function of VCVs in VacA intoxication effects.

In a global evaluation, the VCV proteome exhibited an enrichment of proteins implicated in immune response, cell death, and cellular signaling; all of these are processes that VacA is known to influence. One of the individual proteins contained in the sample was STIM1, a calcium sensor normally residing in the endoplasmic reticulum (ER) that is important in store-operated calcium entry (SOCE). This corroborates the findings of a concurrent report, in which VacA severely influenced SOCE and colocalized with STIM1. A direct interaction of STIM1 with VacA was examined in a pull-down assay, but could be neither shown nor excluded.

Immunofluorescence experiments conducted in HeLa cells confirmed the presence of VacA in the ER and also found it to traffic to the Golgi apparatus, identifying these two cellular compartments as novel VacA target structures. The exact route of VacA transport remains unclear, but the involvement of both the ER and the Golgi suggests the possibility of retrograde trafficking, analogous to other bacterial toxins like shiga and cholera toxins.

In summary, the elucidation of the VCV proteome and the discovery of the ER and the Golgi apparatus as VacA target structures have generated intriguing starting points for future studies. The detection of many proteins implicated in VacA intoxication effects in the VCV proteome leads to the proposal of VCVs as signaling hubs that may coordinate the complex meshwork of VacA effects. Further investigation of individual proteins is expected to help greatly in illuminating this matter.

## Zusammenfassung

Etwa die Hälfte der Weltbevölkerung ist mit dem humanpathogenen Bakterium *Helicobacter pylori* infiziert. Es kolonisiert das Magenepithel und trägt dort zur Entstehung von Krankheiten wie Gastritis, Magen- und Zwölffingerdarmgeschwüren und Magenkrebs bei. Um erfolgreich zu kolonisieren und zu persistieren, hat *H. pylori* eine Reihe von Mechanismen entwickelt, die unter anderem die Immunantwort des Wirts manipulieren und so die Beseitigung durch das Immunsystem verhindern. Ein wichtiger Faktor hierbei ist das sekretierte vakuolisierende Zytotoxin (*vacuolating cytotoxin*) VacA, das vielfältige Auswirkungen auf Wirtszellen hat. Nach der Endozytose bildet VacA Anionenkanäle in der Endosomenmembran, was zum Anschwellen der Endosomen zu sogenannten VacA-beinhaltenden Vakuolen (*VacA-containing vacuoles*, VCVs) führt. Diese können fast das gesamte Zytoplasma einnehmen. Obwohl Vakuolisierung der markanteste und namensgebende Effekt von VacA ist, konnte die Funktion der Vakuolen bislang nicht geklärt werden.

VacA beeinflusst die Immunantwort des Wirts sowohl stimulierend als auch supprimierend. Am wichtigsten erscheint dabei, dass VacA den Calcium-Stoffwechsel in T-Lymphozyten stört, dadurch die T-Zell-Aktivierung und -Proliferation hemmt und so die Immunantwort unterdrückt. Des Weiteren wird VacA zu Mitochondrien transportiert, wo es den mitochondrialen Apoptoseweg aktiviert. Bisher wurde VacA nur dort und in endosomalen Kompartimenten/VCVs beobachtet. Angesichts der diversen Auswirkungen der VacA-Intoxikation liegt es jedoch nahe, dass das Toxin auch anderswo in der Zelle agiert.

Um die Funktion von VCVs herauszufinden, wurde in der vorliegenden Arbeit das VCV-Proteom erstmals umfassend charakterisiert. Zu diesem Zweck wurden drei Strategien für die VCV-Aufreinigung aus T-Zellen entworfen und getestet. Die erfolgreiche Isolation von VCVs erfolgte mittels einer immunomagnetischen Methode, bestehend aus einem VacA-spezifischen primären Antikörper und einem sekundären Antikörper, der an magnetische Kügelchen gebunden ist. Anschließend wurden die aufgereinigten Vakuolen massenspektrometrisch gemessen. In den analysierten Proben befanden sich nicht nur Proteine des endozytischen Systems, sondern auch Proteine, die normalerweise in anderen zellulären Kompartimenten lokalisiert sind. Diese Rekrutierung von Proteinen vieler zellulärer Vorgänge impliziert, dass VCVs in der VacA-Intoxikation eine zentrale Rolle spielen.

Eine allgemeine Untersuchung des VCV-Proteoms zeigte eine Anreicherung von Proteinen, die an Immunantwort, Zelltod und Signaltransduktion beteiligt sind; all dies sind Prozesse, die

VacA bekanntermaßen beeinflusst. Eines der in der Probe vorhandenen Proteine war STIM1, ein  $\text{Ca}^{2+}$ -Sensor, der sich gewöhnlich im endoplasmatischen Retikulum (ER) befindet und wesentlich für den speicherabhängigen Calciumeinstrom (*store-operated calcium entry*, SOCE) ist. Dies unterstützt die Ergebnisse einer gleichzeitig durchgeführten Studie, in der VacA SOCE beeinträchtigte und mit STIM1 kolokalisierte. Eine direkte Interaktion von STIM1 mit VacA wurde mit Hilfe von *pull-down* Experimenten analysiert, konnte aber weder nachgewiesen noch widerlegt werden.

Immunfluoreszenzversuche in HeLa-Zellen bestätigten die Anwesenheit von VacA im ER und zeigten es außerdem auch im Golgi-Apparat. Dadurch wurden ER und Golgi-Apparat als neue Zielstrukturen von VacA identifiziert. Der genaue Transportweg von VacA ist noch ungeklärt, doch die Beteiligung von ER und Golgi-Apparat deutet auf die Möglichkeit des retrograden Transports hin, analog zu anderen bakteriellen Toxinen wie Shiga oder Cholera Toxin.

Zusammenfassend liefern die Aufklärung des VCV-Proteoms und die Entdeckung von ER und Golgi-Apparat als VacA-Zielstrukturen interessante Startpunkte für zukünftige Studien. Da im VCV-Proteom viele Proteine aufgefunden wurden, die für VacA-Intoxikationseffekte von Bedeutung sind, ist es denkbar, dass VCVs als Signalplattformen das komplizierte Geflecht von VacA-Effekten koordinieren. Weiterführende Untersuchungen der einzelnen Proteine im VCV-Proteom könnten bei der Erforschung dieser Hypothese von großem Nutzen sein.

# 1 Introduction

The relationship between humans and *Helicobacter pylori* is a complex one. The human stomach is *H. pylori*'s ecological niche, and it has been for at least 60 000 years, when humans emigrated from Africa [1]. By contrast, it has only been thirty years since the discovery of *H. pylori* as a colonizer of the human stomach [2], which was thought to be sterile before. In these thirty years, *H. pylori* infection has been found to be a major factor in various gastric diseases like gastritis, gastric ulcers and gastric cancer [3,4], and antibiotic therapy is readily available [5]. But lately, more and more evidence is emerging for its beneficial role for the host - *H. pylori* infection may protect from inflammatory bowel disease and immune disorders like asthma [6–8]. Elucidation of this ambivalent relationship may therefore not only help treat and cure *H. pylori*-induced diseases, but also enable the constructive use of its favorable effects.

## 1.1 *H. pylori* Epidemiology

About half of the world's population is infected with this Gram-negative pathogen, with the prevalence varying between 20% in developed countries and 90% in some developing countries [9,10]. Infection always leads to a chronic gastritis that remains asymptomatic in most carriers [11]. About 10-20% of infected individuals develop symptoms ranging from peptic ulcer disease to atrophic gastritis to gastric adenocarcinoma [9]. The implication of *H. pylori* in carcinogenesis lead to its classification as a group 1 carcinogen by the World Health Organization in 1994 [12]. Infection usually happens in early childhood, is transmitted via the gastric-oral route within families [13,14], and persists for life if not eradicated with antibiotics [9]. Therapy is only administered in symptomatic patients or in individuals with an increased risk for gastric cancer. It consists of two antibiotics and a proton pump inhibitor and is about 80% effective, with the growing problem of resistant strains [5].

## 1.2 Overview of the Infection Process

*Helicobacter pylori* has evolved a variety of features that help the bacterium colonize and persist in the hostile environment of the human stomach. It is not an acidophile and can only survive for minutes in the acidic stomach lumen where the pH is as low as 2 [15]. For this reason, it

must quickly relocate to the mucus layer lining the gastric epithelial surface. The mucus is about 300  $\mu\text{m}$  thick and its pH increases gradually, reaching neutral conditions at the epithelium [16]. *H. pylori* employs chemotaxis to navigate towards the epithelium. Its namesake spiral shape and its flagella enable the bacterium to move through the mucus in a corkscrew-like motion [17]. A further aid in this process is the urease enzyme expressed by *H. pylori*: it permits the organism to buffer its microenvironment and periplasm [18], thereby resisting the acidic conditions and modifying the mucus texture, making it less gel-like and thus easier to penetrate [19]. A small number of bacterial cells has been detected inside of epithelial cells, but *H. pylori* is generally considered an extracellular pathogen [20]. Attachment to the epithelium is facilitated by several adhesins, the most well-researched among them being BabA and SabA. Both bind glycosylated blood group antigens [21,22]. When adherent, *H. pylori* uses a type IV secretion system to inject CagA, a protein encoded by the cytotoxin-associated gene A (*cagA*), into the host cell [23,24]. CagA has various effects on epithelial cells, altering cell signaling, cell polarity, extrusion, motility, and proliferation, and is heavily implicated in the development of cancer [4,25,26]. Another protein toxin of *H. pylori* and central to this work is the vacuolating cytotoxin VacA, which is secreted and then affects different host cell types in diverse ways, contributing to initial colonization and immune evasion, and thereby persistence [27]. Among other things, it can act on both pro- and anti-inflammatory pathways, modulating the host immune response. The complex interplay of CagA, VacA, and other factors to manipulate the host suggests that an escalation is usually avoided to prevent clearance by the host's immune system [14]. The effects of these two main *H. pylori* toxins on host cells, with particular focus on VacA, will be outlined in further detail below.

### 1.3 *H. pylori* Immune Evasion

In order to persist, *H. pylori* escapes, manipulates, and counteracts the host immune response, employing diverse strategies. Usually, bacteria are recognized by pattern recognition receptors on cells of the innate immune system, but *H. pylori* avoids this with modified pathogen-associated molecular patterns. Examples of this are modifications in flagellins and lipopolysaccharide [28,29], two bacterial components that are usually detected by the host. *H. pylori* also actively modulates the immune response by activating the adaptor protein Myd88, causing expression of the anti-inflammatory cytokine IL-10 [30]. The adaptive immune system produces antibodies against *H. pylori*, but these do not confer sufficient immunity, which is also

a problem in vaccination research [31]. In fact, antibodies and B-cells can be neglected in the immune response to *H. pylori* infection [32]. Macrophages are recruited to the site of infection and produce nitric oxide that is toxic to bacteria, but *H. pylori*-induced arginase II and ornithine decarboxylase also cause macrophage apoptosis [33,34]. Neutrophils infiltrate and release reactive oxygen species, which is simultaneously induced and combated by the *H. pylori* factor NapA [35]. Another instance where the bacterium actively interferes is the T-cell response. By acting on dendritic cells, *H. pylori* can cause the preferential development of regulatory T-cells ( $T_{reg}$ ) over immunostimulatory  $T_H1/T_H17$  cells, again downregulating the immune response [36]. These are just a few examples of how *H. pylori* avoids clearance by the host immune system. At the same time, a low level of inflammation is maintained, which may be necessary for persistence by providing nutrients for the bacteria [14,27,37]. This complex evasion and manipulation of innate and adaptive immune responses, together with its supply of virulence factors, enable *H. pylori* to establish an optimal niche for colonization.

## 1.4 The Vacuolating Cytotoxin VacA

### 1.4.1 Vacuolation

As is evident from its name, one effect of VacA on intoxicated cells is the induction of large cytoplasmic vesicles, also termed vacuoles [38,39]. Vacuolation has been observed in various types of cultured and primary cells [38,40,41]. Even though this effect was the first one to be noticed, and remains important as a convenient phenotype for assessing toxin activity and susceptibility, its purpose continues to be unknown. It is still unclear whether vacuolation is an effect in and of itself, or whether it is just a by-product of other processes.

In contrast to most other vacuole-inducing bacteria, vacuoles do not serve as the main site for survival or replication of *H. pylori*. Although it is capable of invading cells, it does so rarely [20], and vacuolation is purely a result of the VacA toxin, not the presence of bacteria.

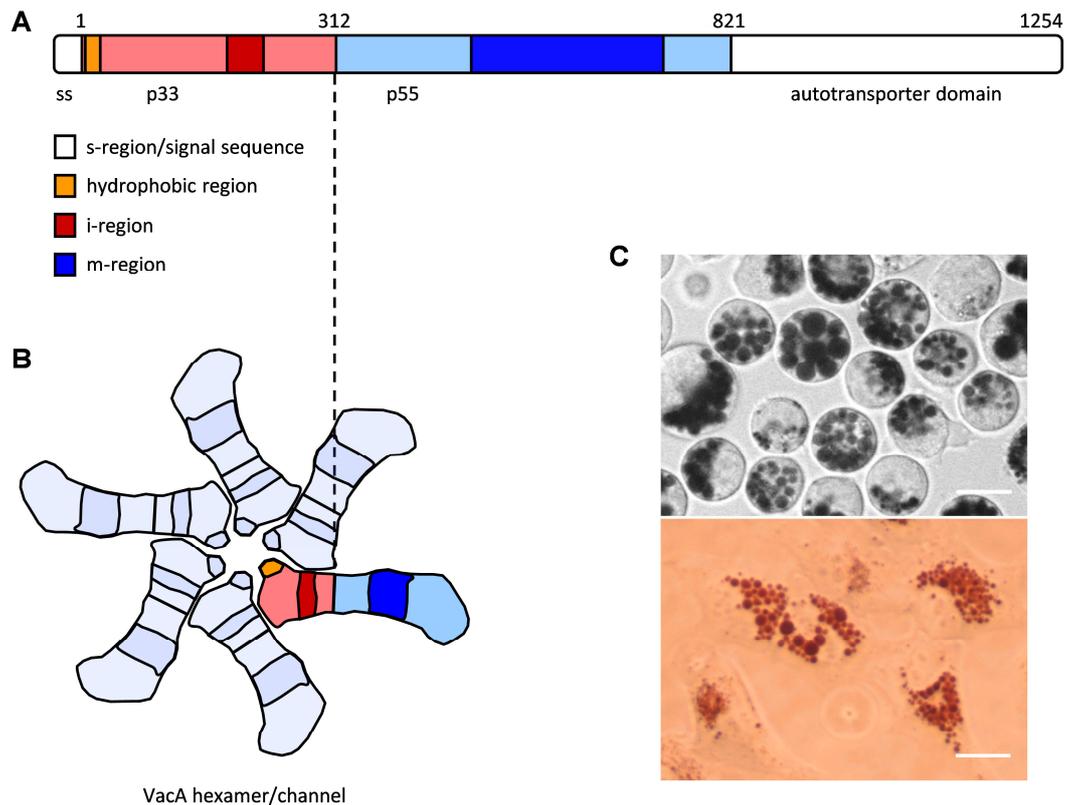
In the current model of the process of vacuole formation (reviewed in [27]), VacA binds to host cells, and during or after internalization, inserts into the membrane of the newly formed endocytic compartments. In these membranes, it oligomerizes to form anion-selective channels [42] that facilitate the influx of  $Cl^-$  ions, a process that the vacuolar ATPase (vATPase) compensates by importing protons. This results in a low luminal pH, which is balanced by the diffusion of membrane-permeable weak bases like ammonia into the endocytic compartments,

where they become protonated and therefore trapped. Finally, osmotic swelling leads to the expansion of the formerly small vesicles into vacuoles with a diameter of up to 5  $\mu\text{m}$  that can take up a large part of the cytoplasm (see Figure 1C). The membranes of these vacuoles carry markers of late endosomes and lysosomes like Rab7 and Lamp1 and 2 [43,44], and are therefore hypothesized to be a hybrid endo-lysosomal compartment [45], but VacA avoids lysosomal degradation [46]. Other proteins that can be found on vacuoles include Rac1 and syntaxin-7 [47,48]. Rab7 and Rac1 are both small GTPases. Rab7 plays an important role in vesicle transport, particularly in the late endocytic pathway, while Rac1 is implicated in actin cytoskeleton reorganization and intracellular signal transduction. Both have been shown to be required for VacA-induced vacuolation [49,47]. The same is the case for the aforementioned vATPase [50–52], but reports differ in the case of syntaxin-7 [53,48].

Regarding the question whether vacuolation is an intermediate step in VacA-induced processes or a by-product, some effects have been shown to be vacuolation-independent. For most effects, however, this has not been specifically investigated. A closer look at the vacuoles themselves may help answer this question.

### 1.4.2 VacA Protein Structure and Channel Formation

The protein toxin VacA is encoded by a chromosomal gene, *vacA*, which is carried by virtually all *H. pylori* isolates, suggesting an important role in colonization [27]. A 140 kDa protoxin is produced, comprising a signal sequence, a passenger domain, and an autotransporter domain (Figure 1A). Both the signal sequence and the autotransporter domain are cleaved during transport of the protein across the inner and outer bacterial membranes [55–57]. The resulting 95 kDa mature toxin molecules then self-assemble into high molecular weight, flower-shaped structures with six- or seven-fold symmetry (Figure 1B). While water-soluble two-layered dodecamers have been imaged in high resolution [58], membrane channels are probably single-layered hexameric structures with a diameter of about 30 nm [59–61]. Interestingly, when pre-formed oligomers are added to cells, they do not show vacuolating activity. Instead, they have to be 'activated' by acidic or basic pH, which causes dissociation into monomers [61,62]. This suggests that cell binding depends on the monomeric form of the toxin and has to happen before channel formation can occur.



**Figure 1: Structure of VacA and cellular vacuolation.**

(A) Signal sequence (also called s-region) and autotransporter domain are cleaved during VacA secretion. The remaining mature toxin consists of the p33 and p55 domain. The p33 domain contains the i-region and a hydrophobic stretch of about 30 aa, which is essential for channel formation. The p55 domain contains the m-region, which is implicated in cell binding specificity. Amino acid counts of *H. pylori* strain 60190 VacA are indicated at the top. (B) VacA channels comprise six monomers and are shaped like flowers, with the p33 domains making up the channel core and the p55 domains representing the petals. (A) and (B) modified from [54]. (C) VacA intoxication in the presence of weak bases causes the formation of large cytoplasmic vacuoles that take up most of the cytoplasm and can reach a diameter of up to 5  $\mu\text{m}$ . Vacuoles are acidic and can therefore be stained with neutral red. Top image, Jurkat E6-1 cells; bottom image, HeLa cells. Scale bars represent 10  $\mu\text{m}$ .

The mature VacA protein can be further subdivided into two domains termed p33 and p55 according to their approximate molecular weights (Figure 1A). The crystal structure of the p55 domain has been solved, showing secondary structural features characteristic for autotransporter passenger domains [63]. Structural information on the p33 domain is still lacking, but the p55 crystal structure in combination with multiple electron microscopy studies on VacA oligomers allows at least some inferences. VacA has been called sock-shaped, with the p55 domain being the heel and foot and the p33 domain representing the calf portion (see Figure 1B; [63]). To continue the analogies, in the flower-shaped oligomer or channel, p33 subunits make up the core, while p55 subunits form the petals. The two subunits have been assigned different functions over the years. The p33 domain was originally considered responsible for VacA channel formation and therefore vacuolation [64], consistent with its

position at the center of oligomeric structures. However, p55 was later also found to play a part in this [65]. On the other hand, p33 was observed to contribute to host cell binding [65], a function initially assigned to the p55 domain [66]. Apparently, the two domains' functions cannot easily be separated. Still, p33 is commonly considered the toxic subunit and p55 the cell binding subunit, analogously to AB toxin terminology. Proteolytic cleavage can naturally separate the two domains, but they remain non-covalently attached [56]. When the subunits are expressed independently and then mixed before addition to cells, the wild-type effect is preserved [67,68,65], and the biological significance of cleavage is not clear.

An interesting detail is the protein's only strongly hydrophobic region. It is contained within the first thirty amino acids of p33, and it is presumed to insert into membranes for channel formation [69]. A mutant version of VacA lacking this hydrophobic region (VacA $\Delta$ 6-27) forms channels considerably more slowly than the wild-type, and fails to induce vacuolation [70]. Recently, electron microscopy experiments have shown that oligomers containing VacA $\Delta$ 6-27 have organization defects at their core that may account for this [71]. The fact that mixed mutant/wild-type oligomers exhibit these defects, too, helps explain the dominant negative effect of the mutant that was observed early on [70]. This hydrophobic region contains three tandem repeats of a GXXXG motif characteristic for membrane dimerization domains, one of which (G14XXXG18) was found to be essential for channel formation and cytotoxicity [69,72].

### 1.4.3 Allelic Diversity of VacA

*H. pylori* are genetically extremely diverse, due at least in part to their natural DNA uptake competence, which facilitates horizontal gene transfer. This diversity is mirrored in VacA sequences. VacA does not show significant homology to any other known protein [39]. Three regions exhibit a particular allelic diversity: the N-terminal signal region (with s1 and s2 alleles), the intermediate region in the p33 domain (i1, i2, and possibly i3), and the mid-region in the p55 domain (m1 and m2) [73–75]. The s1, i1, and m1 alleles are associated with more severe diseases in humans (summarized in [76]) and the s1 and i1 alleles also correlate with the presence of CagA, which also means more severe disease outcomes [75]. The varying medical consequences have at least partially been explained by experimental findings. Different VacA variants affect different cell types in vitro, and a stretch of 148 amino acids within the m-region was found to determine cell type specificity through binding [40,77]. This agrees with earlier reports mentioned above that p55 mediates binding to host cells. The s2 allele has an additional hydrophilic segment at the N-terminus that the s1 allele lacks; these 12 amino acids seem to

prevent vacuolation by altering channel formation [78,79], concurring with the lowered toxicity of s2 VacA. The i-region was only discovered recently and has not been thoroughly studied on a molecular level, but seems to determine VacA toxicity specifically for T-cells [76]. Taken together, the molecular differences of distinct forms of VacA may explain the variance in strain pathogenicity, especially in combination with other virulence factors like CagA (see 1.5.3).

The VacA protein produced by the strain 60190 is somewhat of a standard in VacA research. It has s1/i1/m1 alleles, is highly toxic, and is produced in comparatively large amounts by the bacterium. The sequence details depicted in Figure 1 refer to this variant.

#### 1.4.4 VacA Internalization and Trafficking

A substantial amount of research has focused on VacA binding to host cells and its subsequent internalization, and even though much is now known about both processes, they are far from clear. Multiple studies have searched for the VacA receptor and have yielded different results. Cellular structures that bind VacA include phospho- and glycosphingolipids [80,81,60,82], sphingomyelin [83], and heparan sulphate [84]. Several protein receptors have also been found, some conferring cell-type specificity. The epidermal growth factor receptor (EGFR) was observed to mediate VacA uptake in HeLa cells [85]. Receptor protein-tyrosine phosphatases  $\alpha$  and  $\beta$  (RPTP $\alpha/\beta$ ) were also identified as receptors on kidney and stomach epithelium cells, respectively [62,86]. The  $\beta$ 1 integrin subunit CD29 acts as a complementary receptor on epithelial cells [87]. On T-cells, VacA is endocytosed via the  $\beta$ 2 integrin subunit CD18 [88], and most recently, VacA was reported to bind to multimerin-1 on platelet cells [89]. Additionally, VacA is known to bind the extracellular matrix protein fibronectin [90]. Whatever the receptor may be, there is consensus that VacA localizes to lipid rafts in the host cell membrane, which are necessary for internalization [91,92]. Since for example RPTP $\alpha/\beta$  usually reside outside lipid rafts, it has been speculated whether the VacA-receptor complex relocates to lipid rafts after VacA binding [93]. Glycosylphosphatidylinositol-anchored proteins (GPI-APs), a specific component of lipid rafts, also play a role in VacA internalization, although they are probably not an actual receptor [94,95]. VacA presumably does not induce its own uptake, but instead exploits a constitutive cellular pathway [96,88].

The VacA uptake process appears to be similar in epithelial cells and lymphocytes [97] and is dependent on temperature, energy, and actin, but independent of clathrin and dynamin [98,99,95,94,100]. One group of researchers specifically investigated the VacA-containing compartments shortly after uptake and found these compartments to lack common markers for

known types of endosomes. Also, uptake unusually was independent of most known endocytosis modulators. Due to the presence of the above mentioned GPI-APs, these compartments were therefore identified as a relatively new type of compartments called GEECs (GPI-AP-enriched early endosomal compartments) [96,101]. Most VacA is contained in GEECs approximately 10 min after uptake. Later on, the GPI-APs are transported to recycling endosomes, while VacA is sorted to the degradative pathway, arriving in early endosomes after about 30 min. By way of late endosomes, after 120 min it finally reaches the endo-lysosomal hybrid compartments that then become vacuoles (time points taken from [96,102]) (see Figure 2).

## **1.5 VacA-Induced Effects on Host Cells**

Generally, for many intoxication effects, the internalization of VacA seems to be required, but they may also be the result of signaling cascades triggered by VacA binding to receptors. The latter is most probably the case for rapid effects that occur before internalization can even be complete (30-60 min after intoxication) [27]. In some cases, however, the distinction between the two has not been established. This study's focus on VacA-induced vacuoles naturally puts an emphasis on internalization-dependent effects, but does not omit those caused purely by cell binding in order to give a thorough overview.

### **1.5.1 Mitochondrial Effects and Apoptosis**

Besides endosomal compartments, VacA is known to localize only to mitochondria. It first accumulates in endosomes and is later transported to the organelle [103–105], but how the toxin gets there is still a matter of debate. When it was discovered that VacA-containing endosomal compartments attract actin, which forms tails and is able to move the endosomes through the cytosol [102], a way of transport to mitochondria appeared to be found. However, how VacA is then translocated from the endosome to the mitochondria is still unclear. Membrane fusion and direct membrane-to-membrane transfer have both been speculated about, especially since endosomes and mitochondria come into very close physical contact upon VacA intoxication [106]. Emergence into the cytosol and subsequent uptake into mitochondria is also still a possibility [107]. In any case, targeting of VacA to mitochondria depends on the first 32 amino acids in the protein's N-terminus, the same stretch that is responsible for correct channel formation, and this seems to function analogously to a signal sequence [103,105]. The most

prominent effect of the VacA-mitochondria interaction is the induction of apoptosis. The molecular mechanism of this has not been fully clarified, but a current model integrating the available experimental evidence is as follows [108]: VacA is imported into the inner mitochondrial membrane (IMM) [105], where it forms channels. This leads to the influx of Cl<sup>-</sup> ions into the mitochondrial matrix and consequential loss of the mitochondrial membrane potential [109,104]. Mitochondria with a defect membrane potential recruit Drp1, which induces their fission and also the fragmentation of the mitochondrial network [110]. Alongside Drp1, the pro-apoptotic factor Bax is recruited to mitochondria via VacA-containing endosomes [106] and triggers the release of cytochrome c, eventually causing the cell to undergo apoptosis [103,111,112]. Localization of VacA to mitochondria can happen as early as 60 min after intoxication, but is most evident after at least 12 h and has been reported to precede the induction of both mitochondrial fission and apoptosis [106,110].

Mitochondrial effects of VacA and vacuolation are independent of each other, but both depend on VacA channel forming activity [111,106]. This was shown by using channel blocking substances, which abolished apoptotic effects [111]. The use of mutant VacA $\Delta$ 6-27 is not meaningful in this context, because the mutant protein also lacks the sequence necessary for mitochondrial import, causing it to accumulate in endosomes [106]. However, it has not been investigated whether the mitochondrial effects depend on VacA forming a channel in the IMM, or whether VacA needs to form a channel to escape from endosomes [113].

Apoptosis caused by *H. pylori* infection has been observed in epithelial cells and cells of the immune system, including T-, B-, and dendritic cells [112,114,115]. It has been argued to be a major reason for ulcer formation in the stomach, but this is unlikely since a parallel hyperproliferative response maintains epithelial integrity [116]. However, apoptosis of epithelium does lead to faster turnover of cells, possibly providing more nutrients for the bacteria and preventing cancer formation due to damaged cells, while apoptosis of immune cells helps suppress the immune response [108]. VacA-induced apoptosis may therefore be an important factor in persistence.

### 1.5.2 Immunomodulatory Effects

VacA effects on the host immune response are both pro- and anti-inflammatory. The clustering of endocytic compartments in response to VacA intoxication [44] may purely be a way of getting VacA to its destination, but such hijacking of host vesicular trafficking greatly disrupts natural cellular transport processes and could also explain some of the effects observed in

immune cells. In macrophages, VacA impairs vesicular maturation, leading to the formation of large vesicular compartments called megasomes. This may prevent efficient killing of phagocytosed bacteria [117] and therefore contribute to intracellular survival. In B-cells, VacA interferes with antigen presentation, likely also due to alterations in vesicular trafficking [118].

As mentioned before, *H. pylori* influences the host T-cell response, partly through VacA. Intoxication leads to a downregulation of IL-2 production, which is important for T-cell viability and proliferation [119–121]. VacA inhibits the Ca<sup>2+</sup>-calmodulin-dependent phosphatase calcineurin and, as a consequence of this, the nuclear translocation of the transcription factor NFAT, which controls IL-2 expression. In the T-cell line Jurkat, altered expression of 46 genes was observed following VacA intoxication [119]. VacA is also involved in skewing the T-cell response, causing the differentiation of naïve T-cells into T<sub>reg</sub> cells instead of immunostimulatory types of T-cells [36]. Fascinatingly, both T<sub>reg</sub> cells isolated from *H. pylori*-infected individuals and purified VacA can be used to prevent asthma in mice [7,8,122], again illustrating the complex relationship of the bacterium and its host.

### 1.5.3 CagA Effects and CagA-VacA Interplay

Unlike VacA, the cytotoxin-associated gene (*cag*) product CagA is not a secreted toxin, but is injected into the host cell via a type IV secretion system (T4SS) apparatus [24]. Both the toxin and the T4SS are encoded on the *cag* pathogenicity island (*cag* PAI), a 40-kb-sequence that was probably acquired through horizontal gene transfer [123]. The T4SS pilus and CagA itself interact with  $\beta$ 1 integrin on host cells [124,125]. After translocation of CagA into the host cell cytosol, it is phosphorylated by the host kinases Src and Abl [126,127]. CagA binds at least 20 known host cell proteins in either its phosphorylated or unphosphorylated form. One current hypothesis is that phosphorylated CagA acts like a masterkey, mimicking a phosphorylated host cell protein and thereby hijacking various cellular signaling pathways [128]. The most visually impressive effect of CagA intoxication is the so-called hummingbird phenotype, a distinctive cellular morphology characterized by cell elongation and cell scattering [128]. Other CagA effects are the disruption of cell-cell junctions, loss of cell polarity, changes in motility and proliferation, and the induction of a pro-inflammatory response, namely IL-8 expression (reviewed in [128,4,25]).

From an epidemiological point of view, the presence of the *cagA* gene in *H. pylori* strains infecting humans is associated with more severe forms of disease and cancer [129,130], and there seems to be a connection between CagA and VacA. *H. pylori* strains have been grouped

into two categories, where type I strains produce an active VacA and carry the *cag* PAI and type II strains produce a non-functional (mutated or truncated) VacA and lack the *cag* PAI. Type I strains cause more severe clinical outcomes [131], further highlighting the importance of both pathogenicity factors.

Interestingly, on a cellular level, CagA and VacA have some opposing effects. This starts with the two effects that were observed first for both toxins: cells that show VacA-induced vacuolation show less CagA-induced hummingbird cell morphology, and vice versa [132]. Even though vacuolation and hummingbird phenotype have no meaning *per se*, this illustrates on an easily comprehensible level that the two toxins counteract each other's effects in the cell. It has been observed that CagA activates and VacA downregulates the pleiotropic transcription factor NFAT [133,119,120]; similarly, VacA induces apoptosis, while CagA suppresses it, leading to its classification as an oncoprotein [26,134]. Moreover, CagA was shown to inhibit VacA uptake into cells and also to interfere with intracellular VacA trafficking, stopping VacA in GEECs and preventing its advancement into late endosomes and mitochondria [135,136], thereby controlling the apoptotic effects of VacA. This suggests that *H. pylori* may, via CagA, control the intracellular distribution of VacA and its resulting effects. Considering that VacA is a secreted toxin that can diffuse away from bacteria while physical contact between bacteria and host cells is necessary for CagA injection, an interesting possibility emerges: *H. pylori* may harness VacA-induced effects like apoptosis for initial colonization or to dispose of immune cells recruited to the site of infection [132,135,136,113]. At the same time, directly infected epithelial cells would be protected to avoid loss of bacterial attachment and to limit overall tissue damage.

In most instances where VacA and CagA exert influence on the same pathway, their effects seem to be antagonistic, but one example of a synergistic effect has also been reported. CagA promotes uptake and transcytosis of the iron transporter transferrin while VacA provokes mislocalization of transferrin to sites of bacterial attachment - the two toxins seem to collaborate to make iron available to *H. pylori* [37]. Another case of collaboration, albeit not on the same pathway, is that the disruption of the epithelial cell layer by CagA (and also VacA) may enable VacA to reach and affect immune cells in lower cell layers [137,138,108].

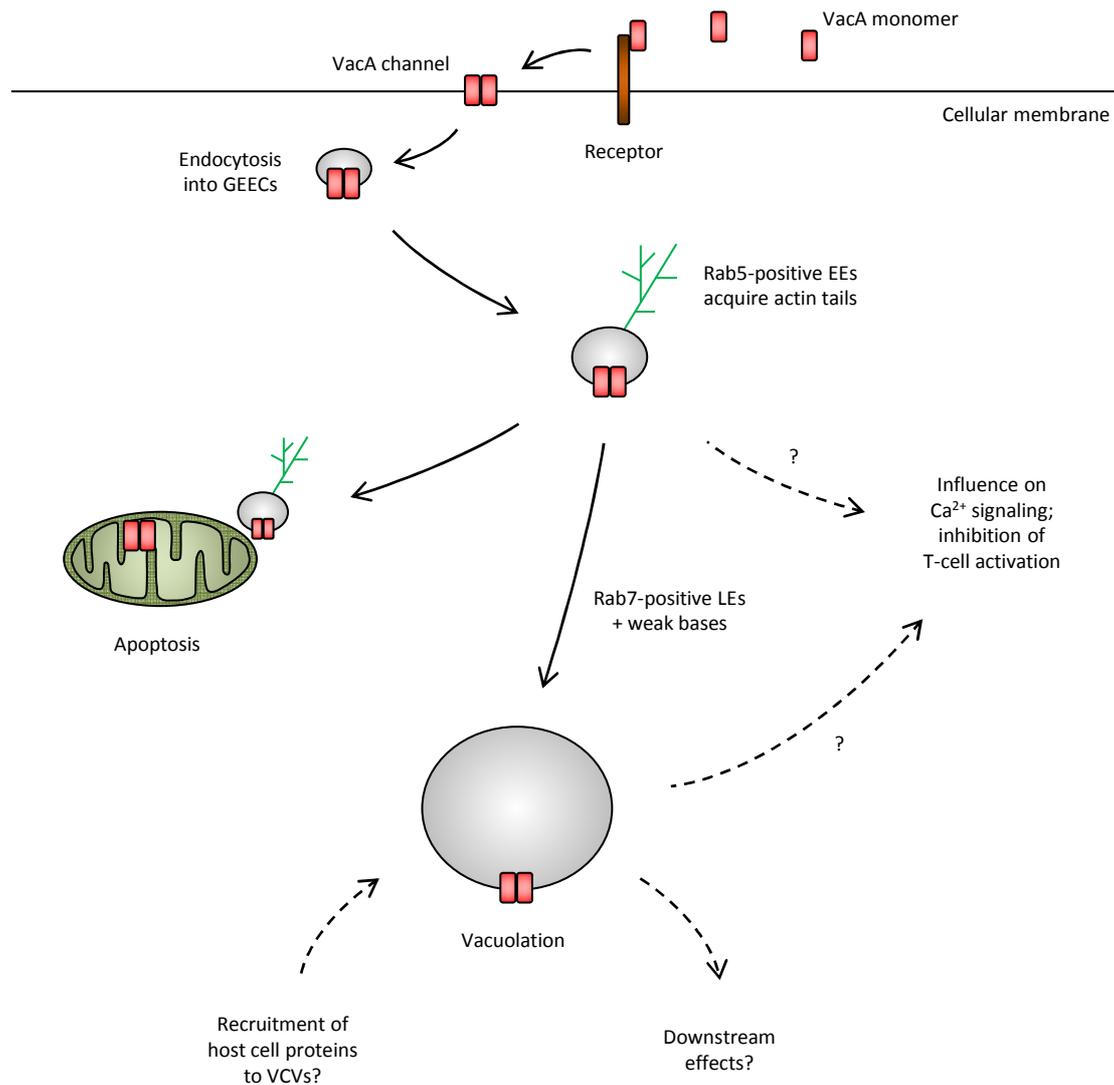
#### **1.5.4 VacA and Intracellular Calcium Signaling**

A role of VacA in intracellular Calcium ( $\text{Ca}^{2+}$ ) signaling has been suggested by several groups, but their results are somewhat contradictory. VacA was shown to cause a rapid, transient increase in cytosolic calcium concentrations in epithelial cells, leading to pepsinogen secretion

[139]. In another report, the intracellular  $\text{Ca}^{2+}$  concentration was found to oscillate as a response to VacA intoxication in mast cells, resulting in  $\text{TNF}\alpha$  transcription and granule secretion [140]. In both cases, the additional calcium was shown to come, at least in part, from intracellular stores. A third publication investigated the increase in cytosolic calcium concentrations following stimulation with the ionophore ionomycin in the Jurkat T-cell line and found that pre-incubation with VacA abrogated this increase [120]. As mentioned in 1.5.2, VacA blocks the proliferation of T-cells at the level of the  $\text{Ca}^{2+}$ -calmodulin-dependent phosphatase calcineurin [119–121]. Usually, during T-cell activation, intracellular calcium is abundant and binds calmodulin, enabling it to activate calcineurin. Calcineurin then dephosphorylates nuclear factor of activated T-cells (NFAT), exposing a nuclear localization sequence. This leads to translocation of NFAT into the nucleus, where it induces the expression of several genes important for T-cell activation, among them IL-2 (reviewed in [141]). What exactly VacA does to inhibit calcineurin is not clear. Some have suggested that VacA channels depolarize the T-cell cytoplasmic membrane, thereby disrupting calcium signaling altogether [120,121]. This hypothesis is supported by the fact that these effects depend on VacA channel forming activity. In conclusion, calcium signaling is essential in T-cell activation, and by disrupting such an important process, VacA can severely impact the host immune response. The molecular details of this, however, need to be further investigated.

### **1.5.5 VacA - A Multifunctional Mystery**

As is evident from all these examples, VacA intoxication has diverse consequences in host cells (see Figure 2). Channel formation has been proposed to be VacA's key mechanism as it is essential for those effects presumed to be most important, namely, vacuolation, induction of apoptosis, and inhibition of T-cell proliferation [92]. There are, however, other effects that are channel-independent, including degradation of epithelial growth factor (EGF), inhibition of procathepsin D maturation, clustering and redistribution of late endocytic compartments, and impaired antigen presentation [142,44,118]. For others, channel dependency has not been shown (all this is reviewed in [92]). It has also been speculated that all VacA-induced effects may in fact be attributed to the hijacking of the host vesicular trafficking system which may cause an extensive disruption of natural intracellular transport processes [113]. Also, importantly, for several effects, the site of VacA action inside the cell remains unclear. There are still many details to be learned to fully understand the complex array of VacA effects.



**Figure 2: VacA uptake, intracellular trafficking, and effects.**

This diagram shows a general overview of what happens after VacA encounters a host cell, starting at the top with VacA binding to the cell surface receptors and channel formation. VacA is endocytosed into GPI-AP-enriched early endosomal compartments (GEECs) and then transported to early endosomes (EE) carrying the EE marker Rab5. These associate with polymerized actin structures (depicted in green) that move them through the cytosol. VacA-containing endocytic compartments can be found in close proximity to mitochondria, where VacA inserts into the inner mitochondrial membrane (IMM) and induces apoptosis. Directed trafficking of VacA to other cellular organelles might also occur. Where VacA influences intracellular calcium signaling, for example, is unclear. Most VacA, however, accumulates in late endosomes (LE) carrying the LE marker Rab7. In the presence of weak bases, VacA causes the swelling of these compartments to easily visible, large vacuoles by forming a channel in the LE membrane. It is conceivable that VacA-containing vacuoles (VCVs) then proceed to recruit host cell proteins and in this fashion, or otherwise, cause the other known VacA effects.

## 1.6 Endosomes as Signaling Platforms

The endosomal network is conventionally viewed as a sorting and trafficking system. It is responsible for the transport of a wide variety of cargo from the cell surface to sites of degradation or recycling. Depending on the cargo, this implies an indispensable role of endosomes in such essential cellular processes as nutrient absorption and hormone-mediated signal transduction [143]. Moreover, a role of endosomes as signaling platforms is now recognized, assuming that signaling complexes are assembled on endocytic vesicles as a way of locally arranging all molecules necessary to trigger a specific signaling cascade [143–145]. The protein content of an endosome may therefore allow conclusions about the signaling pathway or network that the endosome is currently acting on. In the context of VacA intoxication, the presence of VacA on endocytic vesicles alters vesicular protein content [45], thereby possibly changing cellular signaling processes. The elucidation of the proteome of VacA-containing vacuoles (VCVs) could therefore provide information on signaling cascades influenced by VacA intoxication.

## 1.7 Aim of This Study

Even though a large amount of research done on *H. pylori* is concerned with VacA, it is still unclear whether the toxin's most prominent effect, cellular vacuolation, is an effect in and of itself, or just a by-product. Also, for some VacA effects, the cellular site of action is unknown. Integrating these two problems, a hypothesis is proposed: that VacA-containing vacuoles (VCVs) may function as a control center, constituting a platform for intracellular signaling to aid in VacA's multiple actions (see Figure 2). The idea that VCVs do in fact have a purpose is particularly supported by four experimental findings: a) VacA greatly alters vesicular trafficking [142,44,118]; b) VacA causes changes in the protein content of endocytic compartments in intoxicated cells [45], both indicating more than simple toxin endocytosis; c) VacA-containing vesicles acquire an actin tail that propels them through the cell cytoplasm [102]; and d) physical proximity of VacA-containing vesicles and mitochondria may explain how VacA reaches mitochondria [106], and may be how VacA gets to other, yet unknown, sites of action.

The aim of this work was therefore to isolate VCVs from VacA-intoxicated cells and investigate their proteome by mass spectrometric analysis. The types of proteins found on VCVs could help understand not only the purpose of VacA-induced vacuolation, but also elucidate more of the

cellular processes that VacA influences. These experiments were to be conducted in T-cells, which are an important target of VacA. Also, under physiological conditions, T-cells are not usually directly infected by *H. pylori*, so the antagonistic effects of CagA and other infection-related consequences do not have to be considered.

Additionally, the intracellular localization of VacA in intoxicated cells was to be investigated further (see Figure 2). This may lead to a better understanding of known VacA effects and the identification of possible new VacA target structures.



## 2 Materials and Methods

### 2.1 Materials

#### 2.1.1 Chemicals

Chemicals were generally purchased from Roth, Merck, or Sigma-Aldrich unless specified otherwise. Double-distilled water was purchased from Roth and used for PCR reactions, enzymatic digestions and other sensitive applications. Regular distilled water was used for other purposes like the preparation of buffers.

#### 2.1.2 Standard Buffers

Buffer	Ingredients
SDS sample buffer (2x)	100 mM Tris-HCl pH 6.8, 4% (w/v) SDS, 20% (v/v) glycerol, 10% (v/v) $\beta$ -mercaptoethanol, 0.2% (w/v) bromphenol blue
PBS	2.7 mM KCl, 138 mM NaCl, 1.5 mM $\text{KH}_2\text{PO}_4$ , 8 mM $\text{Na}_2\text{HPO}_4$
TBS	150 mM NaCl, 20 mM Tris-HCl, pH 7.5
HS	20 mM HEPES, 250 mM sucrose, 0.5 mM EGTA, pH 7.2

Commercially available, cell culture grade PBS (Dulbecco's PBS with calcium and magnesium, Gibco Invitrogen, Life Technologies) was used for all cell and vacuole related experiments, while self-prepared PBS was used for everything else.

An asterisk (\*) denotes the addition of protease inhibitors to a buffer at the following concentrations: 1 mM PMSF, 1 mM sodium vanadate, 1  $\mu\text{M}$  leupeptin, 1  $\mu\text{M}$  pepstatin.

#### 2.1.3 Bacterial Strains and Cell Lines

Internal ID	Properties/plasmid carried	Source/reference
<i>E. coli</i> strains		
DH5 $\alpha$	F- $\Phi$ 80d <i>lacZ</i> $\Delta$ M15 $\Delta$ ( <i>lacZYA-argF</i> ) U169 <i>deoR</i> <i>recA1</i> <i>endA1</i> <i>hsdR17</i> ( <i>rK</i> -, <i>mK</i> +) <i>phoA</i> <i>supE44</i> $\lambda$ - <i>thi-l</i> <i>gyr</i> A96 <i>relA1</i>	Invitrogen, Life Technologies
TOP10	F- <i>mcrA</i> $\Delta$ ( <i>mrr-hsdRMS-mcrBC</i> ) $\Phi$ 80 <i>lacZ</i> $\Delta$ M15 $\Delta$ <i>lacO</i> 74 <i>recA1</i> <i>ara</i> $\Delta$ 139 $\Delta$ ( <i>ara-leu</i> )7697 <i>galU</i> <i>galK</i> <i>rpsL</i> (StrR) <i>endA1</i> <i>nupG</i>	Invitrogen, Life Technologies

	Internal ID	Properties/plasmid carried	Source/reference
		F- <i>ompT hsdS<sub>B</sub></i> ( <i>r<sub>B</sub>-</i> , <i>m<sub>B</sub>-</i> ) <i>dcm gal λ</i> (DE3) pLysS Cm <sup>r</sup>	Stratagene
STIM1-ER	BK-E19	BL21DE3 pLysS pET28a(+)-ER-STIM1 (pBK5)	This work
STIM1-Cyt	BK-E21	BL21DE3 pLysS pET28a(+)-CT-STIM1 (pBK6)	This work
GFP	BK-E22	BL21DE3 pLysS pET28a(+)-GFP1-10 (pFS1)	F. Schindele;[146]
<b><i>H. pylori</i> strains</b>			
60190	BK-H6	Strain producing an <i>slil</i> m1 <i>VacA</i>	ATCC 49503
60190Δ6-27	BK-H11	Strain producing <i>slil</i> m1 <i>VacA</i> Δ6-27	[70]
P12	BK-H7	Clinical isolate strain	[147]
P12Δ <i>VacA</i>	BK-H8	Clinical isolate strain lacking <i>vacA</i>	W. Fischer
<b>Cell lines</b>			
HeLa		Human epithelial cell line	ATCC CCL-2
Jurkat E6-1		Human T-cell line	ATCC TIB-152
Jurkat E6-1 EGFP-Rab7		Human T-cell line stably expressing EGFP- Rab7	This work

#### 2.1.4 Growth Media, Supplements and Antibiotics

Item	Supplier
LB Broth base	Life Technologies
LB agar	Life Technologies
BB medium	Oxoid, Thermo Fisher Scientific
GC agar base	Oxoid, Thermo Fisher Scientific
RPMI medium	Life Technologies
DMEM medium	Life Technologies
FCS	Life Technologies
Calf serum (bovine serum)	Life Technologies
Horse serum	Life Technologies
Cholesterol	Gibco, Invitrogen
Ampicillin	Sigma-Aldrich
G418	PAA, GE Healthcare Life Sciences
Kanamycin	Sigma-Aldrich
Nystatin	Sigma-Aldrich
Penicillin / Streptomycin	Life Technologies
Trimethoprim	Sigma-Aldrich

### 2.1.5 Commercially Available Kits

Kit name	Supplier
Amaxa Cell Line Nucleofector Kit V	Lonza
QIAprep Spin Miniprep Kit	Qiagen
illustra GFX PCR DNA and Gel Band Purification Kit	GE Healthcare
Alexa Fluor 647 Monoclonal Antibody Labeling Kit	Invitrogen

### 2.1.6 Plasmids

Plasmid name	Properties	Source
pET28a(+)	<i>E. coli</i> expression vector with N- and C-terminal 6xHis-tags	Novagen
pBK5	pET28a(+)-ER-STIM1 (ER-luminal part of STIM1) with N- and C-terminal 6xHis-tags	This work
pBK6	pET28a(+)-CT-STIM1 (cytoplasmic part of STIM1) with N-terminal 6xHis-tag	This work
pEGFP-C1 Rab7A	Eukaryotic expression vector carrying an EGFP-Rab7 fusion protein and a G418 resistance cassette	X. Sewald

### 2.1.7 Oligonucleotides

Name	Sequence	Purpose and properties
BK11	TTC TCT ACA CTC TCT TTT TTT TTT TTT TTT-C <sub>6</sub> H <sub>12</sub> -NH <sub>2</sub>	Coupled to TurboBeads (see 2.2.17)
BK16	GAT <u>CGC GGC CGC</u> CTA CTT CTT AAG AGG CTT C	RP for the cytoplasmic part of STIM1; <u>NotI</u>
BK29	GAT <u>CGA ATT CTC</u> TGA GGA GTC CAC TG	FP for the ER-luminal part of STIM1; <u>EcoRI</u>
BK30	GAT <u>CGC GGC CGC</u> GCG AGT CAA GAG AGG A	RP for the ER-luminal part of STIM1; <u>NotI</u>
BK32	GAT <u>CGA ATT CCG</u> TTA CTC CAA GGA GCA C	FP for the cytoplasmic part of STIM1; <u>EcoRI</u>

All oligonucleotides used in this work were purchased from Biomers.net without modifications, except for BK11 which was modified with an amino linker at the 3' end to enable covalent coupling. Oligonucleotide sequences are written 5' → 3'. Restriction enzyme recognition sites are underlined. FP = forward primer, RP = reverse primer.

### 2.1.8 Enzymes and Proteins

Enzyme/protein	Source
Restriction enzymes	Roche Applied Science or Thermo Fisher Scientific
Trypsin-EDTA	Gibco, Invitrogen
T4 DNA ligase	Thermo Fisher Scientific
Ex Taq polymerase	Takara, Clontech
LA Taq polymerase	Takara, Clontech
VacA from <i>H. pylori</i> strain P76	Purified by I. Barwig

### 2.1.9 Antibodies and Antisera

Antibody/antiserum	Antigen	Origin	Supplier/reference
<b>Primary antibodies</b>			
$\alpha$ -VacA_rec (AK197)	Recombinant <i>H. pylori</i> P3 His-VacA aa 92-723	Rabbit	[147]
$\alpha$ -RecA (AK263)	Recombinant whole <i>H. pylori</i> P1 His-RecA	Rabbit	[148]
$\alpha$ -BabA (AK277)	Recombinant <i>H. pylori</i> 26695 His-BabA aa 123-431	Rabbit	[149]
$\alpha$ -VacA_nat (AK297)	Native whole <i>H. pylori</i> 60190 VacA	Rabbit	This work
Pre-immune serum	Taken from same animal as AK297	Rabbit	This work
$\alpha$ -Alexa488	Alexa488	Rabbit	Molecular Probes, Life Technologies (A-11094)
$\alpha$ -calnexin	Human calnexin peptide (aa 116-301)	Mouse	BD Biosciences (610524)
$\alpha$ -GFP	<i>Aequorea victoria</i> GFP (aa 3-17)	Rabbit	Sigma (G1544)
$\alpha$ -giantin	Human giantin peptide (aa 1-469)	Rabbit	Abcam (ab24586)
$\alpha$ -His	Polyhistidine-tag	Mouse	Antibodies Online (ABIN387699)
<b>Secondary antibodies</b>			
$\alpha$ -rabbit-POX	Rabbit IgG	Goat	Sigma-Aldrich (A0545)
$\alpha$ -mouse-POX	Mouse IgG	Goat	Sigma-Aldrich (A9917)
$\alpha$ -mouse-Alexa555	Mouse IgG	Goat	Molecular Probes, Life Technologies (A21422)
$\alpha$ -rabbit-Alexa555	Rabbit IgG	Goat	Molecular Probes, Life Technologies (A21428)

POX = horseradish peroxidase

## 2.2 Methods

### 2.2.1 *Escherichia coli* Methods

#### 2.2.1.1 Cultivation and Strain Maintenance

*E. coli* were grown either on LB agar plates (LB Agar, Life Technologies) at 37 °C for cloning and other routine experiments or in LB liquid medium (LB Broth Base, Life Technologies) at 200 rpm and 27 °C for protein expression; see table below for concentrations of relevant antibiotics. Culture stocks were generated by collecting the bacteria from agar plates with sterile cotton swabs, resuspending in LB liquid media supplemented with 20% glycerol, and freezing at -70 °C in cryogenic tubes (Nalgene, Thermo Fisher Scientific).

Antibiotic	Final concentration
Ampicillin	100 mg/l
Kanamycin	50 mg/l

#### 2.2.1.2 Preparation of Chemically Competent *E. coli*

*E. coli* DH5 $\alpha$  and BL21(DE3)pLysS were rendered chemically competent using the method of Hanahan 1983. Aliquots of 50  $\mu$ l were stored at -70 °C until further use. For higher transformation efficiencies, commercially obtained One Shot TOP10 competent cells (Invitrogen, Life Technologies) were used in some experiments.

#### 2.2.1.3 Transformation of Chemically Competent *E. coli*

Aliquots of all strains of chemically competent *E. coli* were thawed on ice, mixed with DNA (100-500 ng of a ligation reaction or 10-100 ng plasmid DNA) and incubated on ice for another 30 min, followed by a heat shock of 30-90 s at 42 °C. 1 ml warm LB medium was added to enable bacterial recovery (37 °C, 200 rpm, 1 h). Bacteria were then plated on selective LB agar plates containing the appropriate antibiotic for selection of transformants.

## 2.2.2 *Helicobacter pylori* Cultivation and Strain Maintenance

Serum agar plates for *H. pylori* were made from GC Agar Base (36 g/l, Oxoid, Thermo Fisher Scientific) and supplemented after autoclaving with horse serum, vitamin mix, nystatin and trimethoprim as detailed in the table below.

*H. pylori* were always cultivated at 37 °C under microaerobic conditions (5% O<sub>2</sub>, 10% CO<sub>2</sub>, 85% N<sub>2</sub>). Culture stocks were plated on serum agar plates and left to grow for 2-3 days. Cultures were then passaged onto fresh plates every day and at least once before experiments. From plates, they were transferred to liquid BB medium (Oxoid, Thermo Fisher Scientific) supplemented with cholesterol, nystatin and trimethoprim (respective concentrations see table) and agitated at 90 rpm. Culture stocks were generated by collecting the bacteria from agar plates with sterile cotton swabs, resuspending in BB medium supplemented with 20% glycerol and 10% FCS, and freezing at -70 °C in cryogenic tubes (Nalgene, Thermo Fisher Scientific).

Additive	Final concentration
Horse serum (Invitrogen)	8%
Vitamin mix (100 g/l a-D-glucose, 10 g/l L-glutamine, 26 g/l L-cysteine, 1.1 g/l L-cystine, 0.15 g/l L-arginine, 0.1 g/l cocarboxylase, 20 mg/l iron(III)nitrate, 3 mg/l thiamine, 13 mg/l p-aminobenzoic acid, 0.25 g/l NAD, 10 mg/l vitamin B12, 1 g/l adenine, 30 mg/l guanine, 0.5 g/l uracil)	1%
Nystatin	4400 U/l
Trimethoprim	5 mg/l
Cholesterol	1:250

## 2.2.3 Cell Culture

### 2.2.3.1 Cultivation and Cell Line Maintenance

All cell lines were maintained at 37 °C and 5% CO<sub>2</sub> with the appropriate media as indicated in the table below and subcultured every 2-3 days. Cell culture media, buffers and additives were obtained from Life Technologies unless otherwise stated. Generally, cells were grown in 75 cm<sup>2</sup> tissue culture flasks (BD Falcon) and in 6-, 12- and 24-well plates (tissue culture treated cell culture clusters, Costar, Corning Inc.). Culture stocks were prepared by centrifuging approximately 10<sup>7</sup> cells at 250 x g for 5 min and resuspending them in 4 ml freezing medium consisting of 50% culture medium, 45% FCS, and 5% DMSO. 1 ml aliquots were stored in

cryogenic tubes (Nalgene, Thermo Fisher Scientific) at -70 °C for at least 24 h and then transferred to liquid nitrogen tanks for long term storage.

Cell stocks taken from nitrogen storage were incubated at 37 °C until thawed, washed twice with prewarmed culture medium (centrifugation at 250 x g, 5 min) and then incubated and subcultured at least once before experiments. Jurkat E6-1 EGFP-Rab7 cells were cultured without antibiotic for one day after thawing for better recovery.

Adherent cells (HeLa) were detached from cell culture dishes by treatment with trypsin-EDTA for 3-5 min at 37 °C after a PBS wash step.

Cell line	Source	Medium
HeLa	ATCC CCL-2	DMEM with 10% FCS, 2mM glutamine
Jurkat E6-1	ATCC TIB-152	RPMI with 10% FCS
Jurkat E6-1 EGFP-Rab7	This work	RPMI with 10% FCS, 10 mM HEPES, 1 mM sodium pyruvate, 1 mg/ml G418 (PAA, GE Healthcare Life Sciences)

#### 2.2.3.2 Transfection of Jurkat E6-1 Cells

Jurkat E6-1 cells were transfected by electroporation using the Amaxa Cell Line Nucleofector Kit V and a Nucleofector I device (both Lonza) according to the manufacturer's recommendations for this cell line. RPMI medium for transfected cells was supplemented with additional additives (see 2.2.3.1)

Transfection efficiency was examined via microscopy (Leica TCS SP5) or flow cytometry (FACSCanto II, BD Biosciences).

#### 2.2.3.3 Production of a Stable Jurkat E6-1 EGFP-Rab7 Cell Line

Rab7 is a late endosomal marker known to line the membranes of VCVs [43]. A stable Jurkat E6-1 cell line expressing an EGFP-Rab7 fusion protein was created as a tool for better monitoring of the VCV isolation process. The plasmid pEGFP-C1 Rab7A codes for this fusion protein and a G418 resistance cassette.

In order to perform selection of transfected cells with G418, the antibiotic tolerance of untransfected wild-type Jurkat E6-1 cells was examined by treating cells with varying concentrations of G418 (0-1.4 mg/ml in steps of 0.2 mg/ml). A concentration of 1 mg/ml was chosen for selection and applied to cells 24-48 h after transfection. To enrich EGFP-Rab7 expressing cells, the mixed culture was subjected to cell sorting via flow cytometry. Ksenija

Jovanovic at the Institute for Immunology (Ludwig-Maximilians-Universität München) kindly did this with a FACSAria I. Since cell sorting took place in a non-sterile environment, a mixture of penicillin and streptomycin was added to the cells after sorting to avoid bacterial contamination (final concentrations 100 U/ml and 100µg/ml, respectively).

## 2.2.4 Cloning

### 2.2.4.1 Isolation of Plasmid DNA from *E. coli*

Plasmid DNA was prepared from *E. coli* using the QIAprep Spin Miniprep Kit (Qiagen) according to the manufacturer's instructions with the exception that bacteria were grown on plates and first resuspended in PBS before being centrifuged (1000 x g, 5 min) and then resuspended in P1. DNA was eluted with double-distilled water and DNA concentration in the eluate was measured with a NanoDrop ND-1000 spectrometer (PeqLab).

### 2.2.4.2 Restriction Digestion

Plasmid DNA and PCR amplicons were digested with restriction endonucleases obtained from Thermo Fisher Scientific or Roche Applied Science and the corresponding buffers following the manufacturers' recommendations. Approximately 100 ng DNA were used for restriction digestion analysis and up to 5 µg for preparative purposes, with 0.5-1 U/µl enzyme in the reaction and reaction times of 2-16 h.

### 2.2.4.3 Agarose Gel Electrophoresis

For both analytical and preparative purposes, DNA fragments were separated according to length on 1% agarose gels cast with and run in TAE buffer in horizontal agarose gel electrophoresis chambers (Bio-Rad). Agarose NEEO ultra-quality was purchased from Roth. DNA samples were mixed with 0.17-0.5 volumes of GEBS loading buffer before application to the gel. Gels were either stained with ethidium bromide (1 mg/l) and inspected under UV light or stained with methylene blue (0.1% (w/v)) and destained with water. Relevant DNA bands were excised with a scalpel and purified as detailed in 2.2.4.6.

**TAE buffer:** 40mM Tris, 20 mM acetic acid, 1 mM EDTA

**GEBS loading buffer:** 20% (w/v) glycerol, 50 mM EDTA, 0.05% (w/v) bromphenol blue, 0.5% sarkosyl

#### 2.2.4.4 Ligation

Vector and insert DNA were combined at a molar ratio of 1:3 to 1:7 in a total reaction volume of 10 µl containing 5 U of T4 DNA ligase (Thermo Fisher Scientific). The reaction was incubated at 4-20 °C for 4-24 h.

#### 2.2.4.5 Polymerase Chain Reaction (PCR)

For this work, DNA was amplified via Polymerase Chain Reaction (PCR) solely for preparative purposes with Ex Taq and LA Taq polymerases (Takara, Clontech). Generally, the manufacturer's protocols were followed. A standard annealing temperature of 54 °C was used. PCR amplicons were analyzed via agarose gel electrophoresis (see 2.2.4.3).

#### 2.2.4.6 Purification of DNA from Enzymatic Reactions and Agarose Gels

The illustra GFX PCR DNA and Gel Band Purification Kit (GE Healthcare) was used according to the manufacturer's instructions to extract DNA from enzymatic reactions (2.2.4.2, 2.2.4.5) or agarose gels (2.2.4.3). The DNA was eluted in double-distilled water.

#### 2.2.4.7 DNA Sequencing

Plasmids were sequenced by GATC Biotech AG to confirm the absence of problematic mutations. Sequence data was analyzed with CLC DNA Workbench 6 software.

#### 2.2.4.8 Cloning of Polyhistidine-Tagged STIM1 Fragments for Pull-Down Experiments

STIM1 fragments were amplified with specific primers (see table below) and subcloned into pET28a(+) (Novagen), introducing N-terminal polyhistidine-tags for easy purification and detection of the proteins. Restriction enzyme recognition sites are underlined.

Primer	Sequence	Properties
BK16	GAT <u>CGC GGC CGC</u> CTA CTT CTT AAG AGG CTT C	RP for the cytoplasmic part of STIM1; <u>NotI</u>
BK29	GAT <u>CGA ATT CTC</u> TGA GGA GTC CAC TG	FP for the ER-luminal part of STIM1; <u>EcoRI</u>
BK30	GAT <u>CGC GGC CGC</u> GCG AGT CAA GAG AGG A	RP for the ER-luminal part of STIM1; <u>NotI</u>
BK32	GAT <u>CGA ATT CCG</u> TTA CTC CAA GGA GCA C	FP for the cytoplasmic part of STIM1; <u>EcoRI</u>

## 2.2.5 Protein Biochemical Methods

### 2.2.5.1 SDS Polyacrylamide Gel Electrophoresis (SDS-PAGE)

Proteins were separated according to size via SDS polyacrylamide gel electrophoresis (SDS-PAGE). The size of the proteins of interest determined the polyacrylamide concentration of the separating gel (6-10%). Gel composition was taken from [150]. Gels were cast and run with a Mini-Protean III vertical gel electrophoresis system (Bio-Rad).

Protein samples were mixed with SDS sample buffer and boiled (10 min, 98 °C) before application to the gel. After electrophoresis, the proteins in the gels were either stained directly (see 2.2.5.3) or transferred to membranes and analyzed by immunoblotting (see 2.2.5.4 and 2.2.5.6, respectively).

**SDS-PAGE running buffer:** 5 mM Tris-HCl pH8.3, 50 mM glycerol, 0.02% SDS

**SDS sample buffer (2x):** 100 mM Tris-HCl pH 6.8, 4% (w/v) SDS, 20% (v/v) glycerol, 10% (v/v)  $\beta$ -mercaptoethanol, 0.2% (w/v) bromphenol blue

### 2.2.5.2 Preparation of Standardized Bacterial and Cell Lysates for SDS-PAGE

In order to be able to compare different bacterial and cell lysates on an SDS polyacrylamide gel or a Western Blot, the samples were prepared in a standardized manner. For bacteria, 1 ml of a bacterial suspension with an OD<sub>550</sub> of 0.2 (corresponding to approximately  $6 \times 10^7$  bacterial cells) was centrifuged at 1000 x g for 5 min. For mammalian cells,  $10^6$  cells were centrifuged at 425 x g for 5 min at 4 °C. The cell pellets were resuspended in 20  $\mu$ l RIPA buffer supplemented with protease inhibitors and mixed with 25  $\mu$ l SDS sample buffer before boiling (98 °C, 10 min). Usually, 5  $\mu$ l of bacterial and 3  $\mu$ l of mammalian cell lysates were used for SDS-PAGE.

**RIPA buffer:** 50 mM Tris-HCl pH 7.4, 125 mM NaCl, 1 mM EDTA, 1% NP-40, 6 mM sodium deoxycholate

### 2.2.5.3 Coomassie Staining of SDS Polyacrylamide Gels

In order to visualize proteins on SDS polyacrylamide gels directly, the gels were stained in a Coomassie solution (0.275% (w/v) Coomassie Brilliant Blue R250 (Biomol), 50% methanol, 10% acetic acid) and subsequently treated with destaining solution (10% methanol, 10% ethanol, 7.5% acetic acid) until all relevant bands were visible. Stained gels were photographed with a Bio-Rad ChemiDoc XRS.

#### 2.2.5.4 Transfer of Proteins from SDS Polyacrylamide Gels onto Membrane

For the purpose of immunostaining, proteins were transferred from SDS polyacrylamide gels onto membrane (Immun-Blot PVDF Membrane, Bio-Rad) using semi-dry blotting chambers (Biotec-Fischer). Gel and membrane were sandwiched between pieces of filter paper that had been soaked in anode I/II and cathode buffers on the anode/cathode side of gel and membrane, respectively. A current of 1.2 mA/cm<sup>2</sup> was applied for 60-70 min. After transfer, the membrane was either dried (1 h at 37 °C or over night at RT) or directly used for immunoblotting. Dried membrane was briefly reactivated with methanol before further use.

**Anode I buffer:** 300 mM Tris-HCl pH 10.4, 10% methanol

**Anode II buffer:** 25 mM Tris-HCl pH 10.4, 10% methanol

**Cathode buffer:** 25 mM Tris-HCl pH 9.6, 40 mM 6-amino caproic acid, 10% methanol

#### 2.2.5.5 Spotting of Protein Samples onto Membrane for Dot Blots

Purified protein samples were also spotted directly onto membrane without prior SDS-PAGE in order to keep the proteins' native conformation. To this end, PVDF membrane (Immun-Blot PVDF Membrane, Bio-Rad) was briefly activated in methanol and kept moistened with TBS. A self-made dot blot apparatus was used to immobilize the membrane and to administer samples (1-10 ng of protein mixed with 50-100 µl of TBS for better dispersal of sample within the well). Vacuum was applied to remove excess liquid and the membrane was subsequently used for immunoblotting.

#### 2.2.5.6 Immunoblotting (Western Blot)

Membranes were incubated in blocking solution (5% skim milk in TBS) for at least 1 h to saturate unspecific binding sites. Primary and secondary antibodies were applied as detailed in the table below. Primary antibodies were diluted in blocking solution and incubated for at least 1.5 h at RT (or for longer periods at 4 °C), while secondary antibodies were diluted in 1% skim milk in TBS and incubated for 45-60 min at RT. After antibody incubation steps, membranes were washed with TBS-T (TBS containing 0.075% Tween 20), usually three times for 7 min each. Addition of substrate (Immobilon Chemiluminescent HRP Substrate, Millipore) initiates a chemiluminescence reaction which is catalyzed by horseradish peroxidase (POX) bound to the secondary antibody. This reaction was detected with X-ray films (Fuji Medical X-Ray Films Super RX, Fujifilm) or via a Bio-Rad ChemiDoc XRS.

	Origin	Dilution
<b>Primary Antibodies (diluted in 1% skim milk in TBS)</b>		
$\alpha$ -VacA_rec (AK197)	Rabbit	1:2000
$\alpha$ -VacA_nat (AK297)	Rabbit	1:10 000
$\alpha$ -His	Mouse	1:10 000
$\alpha$ -calnexin	Mouse	1:2500
$\alpha$ -GFP	Rabbit	1:3000
<b>Secondary Antibodies (diluted in TBS-T)</b>		
$\alpha$ -mouse-POX	Goat	1:10 000
$\alpha$ -rabbit-POX	Goat	1:10 000

#### 2.2.5.7 Determination of Protein Concentration

A colorimetric assay was employed to measure the concentration of protein solutions, e.g. purified VacA. Varying dilutions of the protein solution of interest and a dilution series of BSA (0-0.6 mg/ml) were assayed with Protein Assay Dye Reagent Concentrate (Bio-Rad) according to the manufacturer's instructions. Absorbance at 595 nm was measured in 96-well plates (Costar EIA/RIA plate, flat well, medium binding, Corning) using a Tecan Sunrise microplate reader.

In some instances, most notably after labeling with Alexa dyes (see 2.2.5.9), samples were measured with the UV-VIS module of a NanoDrop ND-1000 spectrometer (PeqLab) because the label would have interfered with the colorimetric assay. In these cases, protein concentration was calculated using the relevant protein's specific extinction coefficient.

#### 2.2.5.8 Protein Precipitation for SDS-PAGE

To precipitate proteins, 450  $\mu$ l protein solution were successively mixed with 900  $\mu$ l methanol, 300  $\mu$ l chloroform, and 300  $\mu$ l water, with thorough mixing after each addition. Centrifugation (20 000 x g, 2 min) separated hydrophobic and hydrophilic phases, and the upper phase was removed. After addition of 1.5 ml methanol to the remaining liquid, the sample was mixed and centrifuged again for 5 min. All supernatant was discarded, and the precipitate was dried in a vacuum concentrator and resuspended in 1x SDS sample buffer. Agitation for 10-60 min ensured complete solution before boiling and analysis by SDS-PAGE and Western Blot (see 2.2.5.1, 2.2.5.4, and 2.2.5.6).

#### 2.2.5.9 Labeling of VacA with Alexa Dyes

Purified VacA was labeled with different Alexa fluorophores obtained from Invitrogen, using either the Alexa Fluor 647 Monoclonal Antibody Labeling Kit or individually bought Alexa Fluor carboxylic acid succinimidyl esters. The kit was used according to the manufacturer's instructions while the separate dyes were used following a modified protocol. The desiccated dye was resuspended in 100  $\mu$ l MeOH for aliquoting into four portions and re-dried in a vacuum concentrator. 112  $\mu$ g VacA were mixed with 50  $\mu$ l 1 M NaHCO<sub>3</sub> before adding PBS(-) to a total volume of 500  $\mu$ l. One portion of dye (250  $\mu$ g) per labeling reaction was solved in 20  $\mu$ l DMSO and added to the mix, which was then incubated at RT in the dark for 45 min under gentle agitation. To remove unbound dye, the sample was extensively dialyzed against PBS(-) at 4 °C (over night against 4 l and another 4 h against 1 l) in Slide-A-Lyzer dialysis cassettes (100K MWCO, Thermo Fisher Scientific). Protein concentration and degree of labeling were assessed using a NanoDrop ND-1000 spectrometer according to Invitrogen's instructions, and toxin activity was assayed via neutral red uptake (see 2.2.8)

**PBS(-):** 7.7 mM Na<sub>2</sub>HPO<sub>4</sub>, 2.5 mM NaH<sub>2</sub>PO<sub>4</sub>, 150 mM NaCl

#### 2.2.6 **Purification of VacA**

To produce large amounts of VacA, *H. pylori* was grown in sequential liquid cultures of 30-250 ml for total final culture volumes of about 1 l. These cultures typically had a final OD<sub>550</sub> of around 0.35 and were harvested by centrifugation (6000 x g, 20 min, 4 °C). All further steps were performed at 4 °C or on ice. The cell pellet was discarded and the supernatant, containing the secreted toxin, was sterile-filtrated (Nalgene Rapid-Flow Sterile Disposable Bottle Top Filters with PES Membrane, 0.45  $\mu$ m pore size, Thermo Fisher Scientific). VacA was precipitated by the slow addition of one volume of cold, saturated ammonium sulfate solution under continuous slow stirring. After 4-16 h of further stirring, the precipitate was sedimented by centrifugation (20 000 x g, 30 min, 4 °C) and thoroughly resuspended in a total volume of 30 ml cold PBS. Sample volume was reduced to 4 ml with a centrifugal filter unit (Amicon Ultra, Ultracel, 100K MWCO, Millipore) (4000 x g, 4 °C) to simplify gel filtration, which was carried out with a Sephacryl S300 16/60 column on an ÄKTAexplorer system (Amersham Biosciences, GE Healthcare Life Sciences), using a running buffer containing 100 mM NaCl and 50 mM NaPO<sub>4</sub> at pH 7.4. The resulting fractions were examined for purity via SDS-PAGE and Coomassie staining, pooled accordingly, and again concentrated by centrifugation to a final volume of about 1-1.5 ml. The final protein concentration was determined as described in 0 and usually

ranged between 0.4 and 1 mg/ml in a volume of 0.5-1.5 ml. For every preparation of VacA, the toxin's activity was tested in a vacuolation assay (see 2.2.8).

After purification, VacA is oligomerized and thus biologically inactive. Before all intoxication experiments, purified VacA was therefore acid-activated. This was done by adding 0.2 volumes of 0.3 M HCl, incubating at 37 °C for 20-30 min, and neutralizing with 0.2 volumes of 0.3 M NaOH.

### **2.2.7 Preparation of Concentrated Culture Supernatant (CCS)**

Concentrated *H. pylori* culture supernatant (CCS) was prepared as a faster and cheaper alternative to purified VacA for experiments that did not necessitate absolute purity of the toxin. To this end, liquid cultures were grown and subjected to ammonium sulfate precipitation as described in 2.2.6. The resuspended precipitate was then directly dialyzed against PBS (dialysis tubing purchased from Medicell) (over night against 5 l and another 4 h against 1 l). Vacuolating activity of CCS was also verified in a vacuolation assay (see 2.2.8) every time, and the volume of CCS to be used in experiments was adjusted so that its vacuolating activity equaled that of 1 µg/ml purified VacA. Contrary to purified VacA, CCS does not have to be acid-activated.

### **2.2.8 Vacuolation Assay**

Cytotoxic activity of newly prepared VacA or CCS, or activity of labeled VacA, was confirmed in a vacuolation assay. The fact that VacA-induced vacuoles can be stained with neutral red enables the quantification of toxin activity via neutral red uptake. This assay was performed on HeLa cells with a confluency of 70-90%, usually seeded one or two days before the experiment in 12-well tissue culture plates. VacA was acid-activated and added to cells to a final concentration of 1 µg/ml. In the case of CCS, different volumes were used (5-20 µl/ml) and compared to the last preparation of VacA. As a non-intoxicated control, one well was treated with 'acid-activated' water instead of VacA. After 4 h of incubation, NH<sub>4</sub>Cl was added to a final concentration of 2 mM to enlarge vacuoles (30-60 min). The cell medium was then replaced with RPMI supplemented with 10% FCS and 1:50 neutral red solution (0.4% in PBS, Merck). After another 10 min, the cells were washed twice with PBS containing 0.5% BSA. The neutral red taken up into vacuoles was then extracted with 70% ethanol/0.37% HCl and its absorbance was measured in a 96-well plate (Costar EIA/RIA plate, flat well, medium binding, Corning) at 534 nm (reference wavelength 405 nm) using a Tecan Sunrise microplate reader.

A simpler variation of this approach was also used to ensure successful intoxication in other experiments, e.g. before vacuole isolation (see 2.2.19). Here, neutral red was added directly to a small aliquot of intoxicated cells and vacuolation was confirmed via microscopy.

### 2.2.9 Vacuolation Time Course

In order to ensure ideal VCVs for vacuole isolation, vacuolation in Jurkat E6-1 cells was observed over time. Neutral red uptake was used as an indicator for both number and size of vacuoles, and a variation of the neutral red uptake vacuolation assay (2.2.8) was performed with Jurkat E6-1 cells for different periods of intoxication.  $2 \times 10^5$  cells were seeded in 1 ml medium in 12-well plates. For each time point (4, 8, 24h), one well was intoxicated with 20  $\mu$ l CCS (see 2.2.7), while another well was not.  $\text{NH}_4\text{Cl}$  was added to a final concentration of 2 mM to all wells at the time of intoxication. After 4, 8, and 24 h, neutral red solution was added directly to the cells (1:50), and another 10 min later, the cells were washed twice with PBS/0.5% BSA by centrifuging at 200 x g for 5 min. Neutral red was extracted from vacuoles with 70% ethanol/0.37% HCl and its absorbance was measured in a 96-well plate at 534 nm (reference wavelength 405 nm). The arithmetic mean of the absorbance of all non-intoxicated wells was used as a blank value to normalize the measurements of the intoxicated cells. A one way ANOVA was performed on the data, followed by a Kruskal-Wallis test and a comparison of all pairs of columns. The data was analyzed with GraphPad Prism 5.

### 2.2.10 Production of $\alpha$ -VacA\_nat

An antiserum was raised against purified, native VacA in a rabbit by Gramsch Laboratories according to their standardized protocol. Purified VacA (see 2.2.6) was injected on day one and 21 (75  $\mu$ g, in dorsum, neck and shoulder) and again on day 42, 49, and 56 (50  $\mu$ g, intramuscularly in the hind thigh). Serum was taken on day 63 (boost #1) and on day 70 (boost #2), stabilized with azide, and received from Gramsch Laboratories. The second boost was named AK297 ( $\alpha$ -VacA\_nat) and characterized for this work. Also, pre-immune serum of the same animal was used for comparison (see 2.2.11).

### 2.2.11 Vacuolation Inhibition Assay

It was investigated whether  $\alpha$ -VacA\_nat had the capacity to inhibit VacA-induced vacuolation through binding to VacA. To this end, a vacuolation assay was performed as in 2.2.8 but with

two added elements: one, heat-inactivation of complement proteins in antisera (56 °C, 30 min) parallel to VacA acid-activation, and two, incubation of (acid-activated) VacA with (heat-inactivated) sera to allow binding (30 min on ice). Prior to this experiment, the total protein content of all antisera was measured (2.2.5.7). For each antiserum, a volume equivalent to 600 µg protein was used to (potentially) inhibit 1 µg VacA.

Since neutral red uptake of unintoxicated cells varies considerably from one experiment to the next, absolute measured values cannot be used. Instead, an unintoxicated cell sample treated with NH<sub>4</sub>Cl served as a negative background control. Another sample intoxicated with VacA and treated with NH<sub>4</sub>Cl but without any antiserum served as a positive control that was set to 100%, while all other samples were expressed in relation. This was done for all three independent experiments separately. The data was analyzed with Graph Pad Prism 5.

### 2.2.12 Pull-Down Experiments

Pull-down experiments with the aim of investigating a possible interaction of VacA with STIM1 were performed in two directions for verification. For both directions, VacA was incubated with lysates of *E. coli* expressing STIM1 protein fragments. In the first approach, Ni-NTA agarose (Qiagen) was used to precipitate the His-tagged STIM1 fragments, while in the second, α-VacA<sub>nat</sub> and Protein G agarose (Roche Applied Science) were used to precipitate VacA.

To express the polyhistidine-tagged STIM1 fragments or controls, the relevant *E. coli* strains (BK-E19, 21, 22, 23) were grown at 27 °C and 200 rpm in LB medium supplemented with kanamycin until they reached an OD<sub>550</sub> of 0.5-0.6, at which point expression was induced by the addition of IPTG to a final concentration of 1 mM. Three hours later, the cultures were centrifuged (4000 x g, 20 min, 4 °C) and the bacterial pellet was resuspended in 1/50 volume lysis buffer (specified below). Samples were handled on ice from here onwards. Cells were lysed via sonication (Sonifier 250, Branson; 10-50% duty cycle, output control 5, three 20 s intervals followed by 20 s rest) and the lysate was centrifuged (15 000 x g, 30 min, 4 °C) to remove cell debris.

For the precipitation of 6xHis-tagged STIM1 fragments, PBS\* was used as lysis buffer. The debris-free lysate was mixed with acid-activated VacA at 10 µg/ml and one volume of Ni-NTA beads that had been washed with PBS twice (centrifugation at 500 x g, 5 min, 4 °C). Samples were incubated over night at 4 °C under gentle agitation. After three washes with PBS\*, the beads were resuspended in 1/2 volume of PBS\*, of which 10 µl (1/50 of the total sample) were applied to an SDS polyacrylamide gel for subsequent analysis via Western Blot.

For the precipitation of VacA, PBS\*/0.01% NP-40 was used as lysis buffer. After the removal of cell debris, the supernatant was incubated with acid-activated VacA at a final concentration of 4 µg/ml for one hour at 4 °C under gentle agitation to enable the STIM1 protein fragments to bind to VacA.  $\alpha$ -VacA\_nat was then added (1:100) to bind VacA (over night, 4 °C), and 1/10 volume Protein G agarose was incubated with the samples for another 2 h to bind the primary antibody. The agarose beads were washed three times with PBS\*/0.01% NP-40 (centrifugation at full speed, 30-60 s) and resuspended directly in 2/25 volumes 2x SDS sample buffer. 10 µl of this (1/5 of the total sample) were applied to an SDS polyacrylamide gel for subsequent analysis via Western Blot.

### 2.2.13 Immunostaining Experiments

To investigate the localization of VacA in intoxicated HeLa cells, cells were treated with Alexa-labeled VacA and subsequently stained for Golgi apparatus marker giantin and ER marker calnexin. Similarly, co-intoxication with VacA and cholera toxin subunit B (CTxB), both fluorescently labeled, was performed.

Also, to further characterize the new antibody  $\alpha$ -VacA\_nat, it was used to stain Alexa-labeled VacA in intoxicated HeLa cells. Using a secondary antibody labeled with a different fluorophore than the one coupled to VacA facilitated a direct comparison of the signals of the immunostain with that of labeled VacA.

50 000 cells were seeded onto untreated glass cover slips (Menzel-Gläser, 12 mm, Omnilab) in 24-well plates on the day before the experiment. Before intoxication, the cell medium was changed to ensure equal volumes of 500 µl in each well. 3 µl VacA-Alexa488 or 2 µl VacA-Alexa568 (all acid-activated) were applied per well; this had previously been titrated as the ideal volumes for these batches of labeled VacA. CTxB-Alexa555 (Molecular Probes, Life Technologies) was applied at a concentration of 1.6 µg/ml. Samples were kept in the dark as much as possible to avoid fluorophore bleaching and washed three times with PBS between treatments and antibody incubation steps. Intoxication was done for 4 h at 37 °C and 5% CO<sub>2</sub>, as usual, but all subsequent incubation steps were carried out at room temperature and normal atmosphere. Cells were fixed with PFA (4% in PBS, 20 min), followed by permeabilization with Triton X-100 (0.1% in PBS, 10 min) and a blocking step with blocking buffer (8% calf serum in PBS, 30 min). Cover slips were then sequentially incubated with 70 µl primary and secondary antibody solution on parafilm for 50-60 min. After a final wash, the cover slips were mounted

onto glass slides using VectaShield mounting medium (Vector Laboratories) supplemented with 1 µg/ml DAPI and fixed with nail polish.

	Origin	Dilution
<b>Primary antibodies (diluted in blocking buffer)</b>		
α-calnexin	Mouse	1:200
α-giantin	Rabbit	1:400
α-VacA_nat (AK297)	Rabbit	1:5000
<b>Secondary antibodies (diluted in blocking buffer)</b>		
α-mouse-Alexa555	Goat	1:1000
α-rabbit-Alexa555	Goat	1:1000

#### 2.2.14 Microscopy and Image Analysis

Microscopy samples (most importantly samples produced with the methods detailed in 2.2.13 and 2.2.19) were examined with a Leica TCS SP5 confocal microscope. Routine image processing was done with ImageJ 1.45h (National Institutes of Health) while Volocity 6.0.1 (Perkin Elmer) was used for colocalization analyses.

#### 2.2.15 Homogenization of Jurkat E6-1 Cells

For various purposes, most notably for all approaches of VCV isolation, Jurkat E6-1 cells were homogenized using a ball homogenizer (Isobiotec) and an exclusion size of 10 µm.

Cells were handled on ice for the entire procedure and washed twice with cold PBS before being centrifuged (250 x g, 5 min) and resuspended in PBS\* (exemplarily, 10<sup>7</sup> cells were washed with 2 x 10 ml and resuspended in 3 ml). The cell suspension was transferred to disposable 3 ml Luer Lok syringes (BD Biosciences) and passaged 9 times through the ball homogenizer, which had previously been washed with distilled water and flushed with PBS\*. The homogenate was cleared of intact cells and large debris particles by centrifugation (200 x g, 10 min, 4 °C) before being processed further.

#### 2.2.16 Sequential VCV Centrifugation

To analyze VCV sedimentation properties, Jurkat E6-1 EGFP Rab7 cells were treated with 1 µg/ml VacA and 2mM NH<sub>4</sub>Cl for 5 h. 1 ml homogenate was then sequentially centrifuged (10 min, 4 °C) at 200, 600, 1000, 3000, 6000, 10 000, 15 000, and 20 000 x g. The pellets of all

steps were resuspended and boiled in 50  $\mu$ l SDS sample buffer, 10  $\mu$ l of which were applied to an SDS polyacrylamide gel. Another 1 ml each of cell suspension and homogenate were centrifuged and treated as described above to serve as controls. All fractions were analyzed for the presence of VacA and EGFP-Rab7 by Western Blot.

## 2.2.17 TurboBeads Methods

### 2.2.17.1 Coating of TurboBeads

One approach for the isolation of VCVs was to couple VacA to nanoscale magnetic beads (Carboxyl coated TurboBeads, TurboBeads LLC) that would be endocytosed along with VacA. The vacuoles were then supposed to be extracted from cell homogenate via magnetic separation. According to the manufacturer, the beads have a mean diameter of 30 nm, an average weight of  $1.26 \times 10^{-16}$ g, and 7560 carboxy groups per bead. 70  $\mu$ g VacA and VacA-Alexa488 were coupled to 330  $\mu$ l TurboBeads (approximately 0.12  $\mu$ mol beads), aiming to couple one VacA molecule to one bead.

The manufacturer's protocol for the coupling of protein to the TurboBeads was modified slightly. Beads were subjected to an ultrasonic bath for a few minutes to dissipate aggregates and washed three times with PBS and twice with MES buffer before being resuspended in 1 volume MES buffer. To this were added 1 volume each of 52 mM CMC (1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride) (substituted for EDC, solved in MES buffer) and 87 mM NHS (solved in MES buffer). This mixture was incubated for 20 min at RT under agitation to activate carboxyl groups. Protein ligand was added and the coupling reaction was again incubated for 20-60 min, after which the beads were washed three times with PBS- $T_{\text{beads}}$  and resuspended in 1 volume saturation solution (10 mM ethanolamine, 0.05% sodium azide in PBS). Another 20 min incubation period followed to ensure saturation.

Seeking to minimize bead aggregation, ssDNA with a 3' aminolinker (TTC TCT ACA CTC TCT TTT TTT TTT TTT TTT- $C_6H_{12}-NH_2$ ) was used as a ligand instead of protein (Maye 2007). In this case, 20  $\mu$ l of ssDNA at 234  $\mu$ M were used with 20  $\mu$ l TurboBeads according to the protocol detailed above. Another experiment was done in which the ssDNA was added to the saturation solution with the 'ligand' being PBS.

**MES buffer:** 54 mM in  $H_2O$ , pH 5.5

**PBS- $T_{\text{beads}}$ :** 3.7 mM  $NaH_2PO_4$ , 18 mM  $Na_2HPO_4$ , 314 mM NaCl, 0.05% Tween 20, pH 7.4

### 2.2.17.2 Intoxication with TurboBeads for Microscopy

VacA TurboBeads were subjected to sonication (10 min) and acid-activation before addition to cells. 10  $\mu$ l of beads, corresponding to a theoretical 2.1  $\mu$ g VacA, were used to intoxicate  $1.5 \times 10^5$  Jurkat E6-1 cells in 1 ml culture medium. 40 min of incubation on ice were followed by another 200 min at 37 °C for a total of the usual 4 h before addition of  $\text{NH}_4\text{Cl}$  (30-60 min). Cells were then washed once with culture medium without FCS and centrifuged onto untreated glass cover slips (Menzel-Gläser, 12 mm, Omnilab). PFA was added to a final concentration of 15%. After 30 min incubation at RT, the cover slips were washed twice with PBS and once with distilled water and then mounted onto glass slides.

### 2.2.17.3 Intoxication of TurboBeads for Quenching Assay

$2.5 \times 10^5$  Jurkat E6-1 cells were seeded in a volume of 500  $\mu$ l in 24-well plates. VacA TurboBeads were again subjected to sonication (10 min) and acid-activation before addition to cells. 10  $\mu$ l beads were used per well, as were 0.5  $\mu$ g of VacA-Alexa488. Intoxication was carried out for 40 min at RT. After this, all samples were handled on ice and washed twice with cold PBS (centrifugation at 830 x g for 6 min). Cells were resuspended in 400  $\mu$ l PBS supplemented with 4 $\mu$ g  $\alpha$ -Alexa488 where appropriate, followed by 30 min of gentle agitation at 4 °C. Fluorophore internalization was then analyzed by flow cytometry (FACSCanto II, BD Biosciences).

### 2.2.18 **Vacuole Sorting by Flow Cytometry**

One approach to purify VCVs was to make use of different fluorescent labels and sort VCVs from homogenate via flow cytometry. The late endosomal marker Rab7 is known to line VCV membranes [43], so a cell line stably expressing an EGFP-Rab7 fusion protein (2.2.3.3) was intoxicated with Alexa647-labeled VacA. In this setting, VCVs (and only VCVs) should be positive for both EGFP and Alexa647 fluorophores and therefore could be unambiguously sorted via flow cytometry.

Cells were intoxicated with varying amounts of labeled, acid-activated VacA (depending on the labeling batch and its specific activity) and 2 mM  $\text{NH}_4\text{Cl}$  over night and homogenized as described above (2.2.15). The homogenate was sometimes centrifuged and resuspended in a smaller volume of PBS\* to increase VCV concentration; various centrifugation conditions were tried, for example 5000 x g, 15 min, 4 °C. Three different FACS devices were used with the generous help of Dr. Matthias Schiemann and Lynette Henkel at the Flow Cytometry Core Unit

of the Institute for Medical Microbiology, Immunology and Hygiene (Technische Universität München): a FACS Aria IIIu (BD Biosciences), an S3 Cell Sorter (Bio-Rad), and a MoFlo Legacy (Beckman Coulter). All of these are equipped with the standard laser setup and filters needed, but differ regarding nozzle diameter (70-100  $\mu\text{m}$ ), optical sensitivity, internal pressure and resulting shearing forces. Particles positive for both fluorophores were sorted into one tube, and particles positive for EGFP only were sorted into another. Sorted fractions were then analyzed by microscopy (Leica TCS SP5) and SDS-PAGE.

### 2.2.19 Isolation of VCVs by Immunomagnetic Separation

Generally, the protocol for the isolation of VCVs was adapted from [151] and modified as needed. For the purpose of mass spectrometric analysis of VCVs, eight 75  $\text{cm}^2$  flasks of cells (corresponding to approximately  $8 \times 10^7$  cells) were used. The following protocol describes this scale of experiment.

Jurkat E6-1 or Jurkat E6-1 EGFP-Rab7 cells were intoxicated with CCS or VacA (1  $\mu\text{g}/\text{ml}$ ) with simultaneous administration of  $\text{NH}_4\text{Cl}$  and incubated over night. Starting with homogenization (2.2.15), all steps were carried out on ice or at 4  $^\circ\text{C}$ . The homogenate was blocked with 2% calf serum (30 min) and then incubated with  $\alpha\text{-VacA}_{\text{nat}}$  (1:500, 1 h). A centrifugation step was done to remove primary antibody (3000 x g, 30 min) and the pellet was resuspended in 4 ml PBS\*. MACS Anti-Rabbit IgG MicroBeads (Miltenyi) were added at 1:15 and incubated once more for 30 min (all binding incubation steps were performed under gentle agitation). The beads were then applied to three MACS MS separation columns (Miltenyi) equilibrated with 0.5 ml PBS\*. After sample binding, the columns were washed twice with 0.5 ml PBS\* and elution was achieved by removing the column from the magnetic holder and pressing with the supplied piston.

Intact cells, homogenate, column flowthrough and eluate were examined by microscopy and SDS-PAGE to monitor the procedure. For microscopy, 200/200/33/13  $\mu\text{l}$  of the respective fraction were applied to an 8-well slide ( $\mu\text{-Slide}$  8 well ibiTreat microscopy chamber, Ibidi) in a total volume of at least 200  $\mu\text{l}$  per well, centrifuged (600 x g, 10 min, 4  $^\circ\text{C}$ ) and analyzed shortly thereafter. Proportions of the individual fractions were kept similar to facilitate comparison of samples with respect to VCV numbers. For SDS-PAGE, the same fractions (250/250/750/750  $\mu\text{l}$ , respectively) were processed by centrifugation (15 000 x g, 10 min, 4  $^\circ\text{C}$ ), resuspension in 50  $\mu\text{l}$  2x SDS sample buffer, and boiling. 20  $\mu\text{l}$  of each fraction were applied to SDS polyacrylamide gels. In this case, unequal proportions of the individual fractions were used to ensure that

protein would be visible in all samples after Coomassie staining for comparison of protein composition.

Finally, for analysis by mass spectrometry, 750 µl eluate were centrifuged (15 000 x g, 10 min, 4 °C) and the supernatant was removed. The sample was rapidly frozen in liquid nitrogen before being stored at -70 °C until it was shipped to the mass spectrometry facility on dry ice.

#### **2.2.20 Mass Spectrometry**

Mass spectrometric analysis of isolated vacuoles (see 2.2.19) was kindly done by Andreas Otto at the Institute for Microbiology of the Ernst-Moritz-Arndt-University Greifswald as detailed in [152]. Data base searching was adjusted according to the organism of vacuole origin, using the human UniProt data base.

#### **2.2.21 Mass Spectrometry Data Processing**

The results of the mass spectrometric tests were obtained in the form of Excel files with the names of proteins matching identified peptides and corresponding UniProt accession numbers. Protein information was retrieved from UniProt using these accession numbers, and analysis was restricted to reviewed (Swiss-Prot) entries. Proteins' subcellular location was taken directly from UniProt's Subcellular Location column, while information about proteins' biological process was extracted from the Gene Ontology (GO) column and the GO tree provided at the UniProt web page.

#### **2.2.22 Isolation of Endoplasmic Reticulum from Jurkat E6-1 Cells**

A protocol established by Jo-Ana Herweg (Department of Microbiology, Biozentrum der Universität Würzburg) was adapted in order to investigate whether VacA localizes to the endoplasmic reticulum (ER) of intoxicated cells.  $2 \times 10^7$  Jurkat E6-1 cells were seeded in a total volume of 20 ml (two 75 cm<sup>2</sup> flasks) and intoxicated with 3 µg/ml acid-activated VacA (see 2.2.6). After 4 h of incubation, the cells were washed twice with cold PBS and resuspended in a total of 5.5 ml of IEB\* before being homogenized with a ball homogenizer (see 2.2.15). All steps after this were performed on ice or at 4 °C. The homogenate was centrifuged three times, yielding three fractions: 1000 x g/10 min (pellet = nuclear fraction, NF), 12 000 x g/15 min (pellet = mitochondrial fraction, MF), and 540 000 x g/1 h (pellet = crude microsomal fraction, CF). MF and NF pellets were resuspended in 80 µl and the CF pellet was resuspended in 200 µl

2x SDS sample buffer. Part of the final supernatant (450  $\mu$ l) was subjected to protein precipitation (see 2.2.5.8) and the precipitate was solved in 120  $\mu$ l 1x SDS sample buffer. All samples were boiled and analyzed by SDS-PAGE and Western Blot (see 2.2.5.1, 2.2.5.4, and 2.2.5.6). Sample volumes applied to the SDS polyacrylamide gel were: 16  $\mu$ l NF/MF (representing 20% of the sample), 20 $\mu$ l CF (10%), 35 $\mu$ l supernatant (9.5%).

**IEB\***: 5 mM HEPES, 0.5 mM EGTA pH 8, 12.5 mM KCl, 125 mM sucrose, with added protease inhibitors



## 3 Results

### 3.1 VacA Purification and Labeling

The production of purified, active VacA was a necessary prerequisite for most of the experiments conducted for this work. *H. pylori* secretes the VacA precursor protein into the culture medium via a type Va autotransporter mechanism, after which it is cleaved to yield the 95 kDa mature toxin [55–57]. Its self-oligomerization into high molecular weight structures can be utilized for purification since it enables separation from other proteins by ammonium sulfate precipitation and subsequent gel filtration. After purification and before use in intoxication experiments, VacA has to be acid-activated. This dissociates the oligomers, and only monomers are biologically active [61,62].

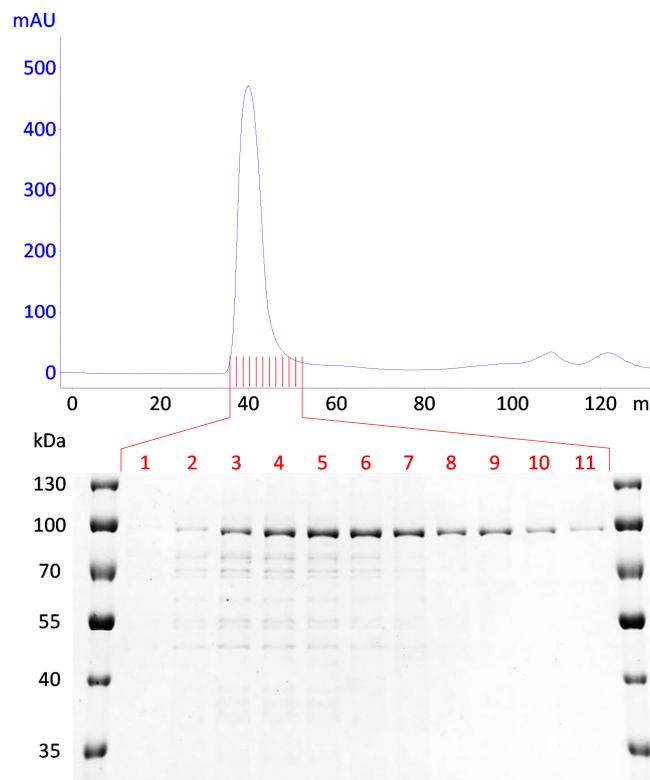
VacA was isolated from liquid culture supernatant of the *H. pylori* strain 60190, which produces large amounts of a highly toxic, s1m1i1 VacA. An isogenic strain producing an inactive mutant VacA was also used. This protein variant, VacA $\Delta$ 6-27, lacks the hydrophobic region responsible for channel formation. VacA was precipitated from the culture supernatant using ammonium sulfate and further purified by gel filtration on a Sephacryl S300 column (see 2.2.6).

Figure 3 shows the chromatogram of such a gel filtration. The absorption at 280 nm (blue line) was monitored as a measure of protein concentration. VacA can be seen to elute from the column starting at about 36 ml. Fractions (indicated in red) were collected until the peak had passed and then examined via SDS-PAGE/Coomassie staining for purity. VacA monomer bands can be seen at approx. 100 kDa (Figure 3, lower panel). Also visible are bands at lower molecular weights, assumed to be VacA degradation products or contaminants, but purity was sufficient for the purpose of this work. All fractions containing VacA of adequate purity were pooled and concentrated to a final concentration typically ranging between 0.4 and 1 mg/ml in a volume of 0.5-1.5 ml. Every batch of purified VacA was analyzed for toxin activity in a vacuolation assay (see 2.2.8) before being used in experiments. VacA $\Delta$ 6-27 did not cause cellular vacuolation (data not shown).

Small amounts of purified VacA were routinely labeled with fluorescent Alexa dyes (see 2.2.5.9). The concentration of labeled VacA was measured spectrometrically with a NanoDrop instrument to calculate the degree of labeling, which usually ranged between 0.1 and 1 Alexa molecule per VacA molecule. For every labeled batch, toxin activity was again examined in a vacuolation assay. Activity of labeled VacA was considerably lower than that of unlabeled VacA

## Results

(data not shown), and the amount of labeled VacA to be used in an experiment was increased accordingly so as to ensure appropriate vacuolating activity.



**Figure 3: VacA gel filtration.**

*H. pylori* 60190 culture supernatant was mixed with 50% ammonium sulfate and the precipitated proteins were subjected to gel filtration on a Sephacryl S300 column. The blue line represents protein eluting from the column, measured via the proteins' absorption at 280 nm (mAU = milli Absorbance Unit). The eluted fractions (indicated in red) were applied to a 10% SDS polyacrylamide gel and Coomassie stained. VacA bands can be seen just under 100 kDa. Fractions containing VacA at sufficient quantity and purity were then pooled and concentrated.

### 3.2 Characterization of $\alpha$ -VacA<sub>nat</sub>

Prior to this work,  $\alpha$ -VacA<sub>rec</sub>, an antiserum against a recombinantly expressed VacA fragment (aa 92-723), had been established [147]. Since  $\alpha$ -VacA<sub>rec</sub> was not sufficiently capable of recognizing native VacA in preliminary experiments conducted by U. Jain, a new antiserum was raised against native, purified toxin, here termed  $\alpha$ -VacA<sub>nat</sub>, with the aim of using it in applications like pull-down experiments or immunostaining. This serum was then characterized concerning its ability to recognize different forms of VacA in different settings.

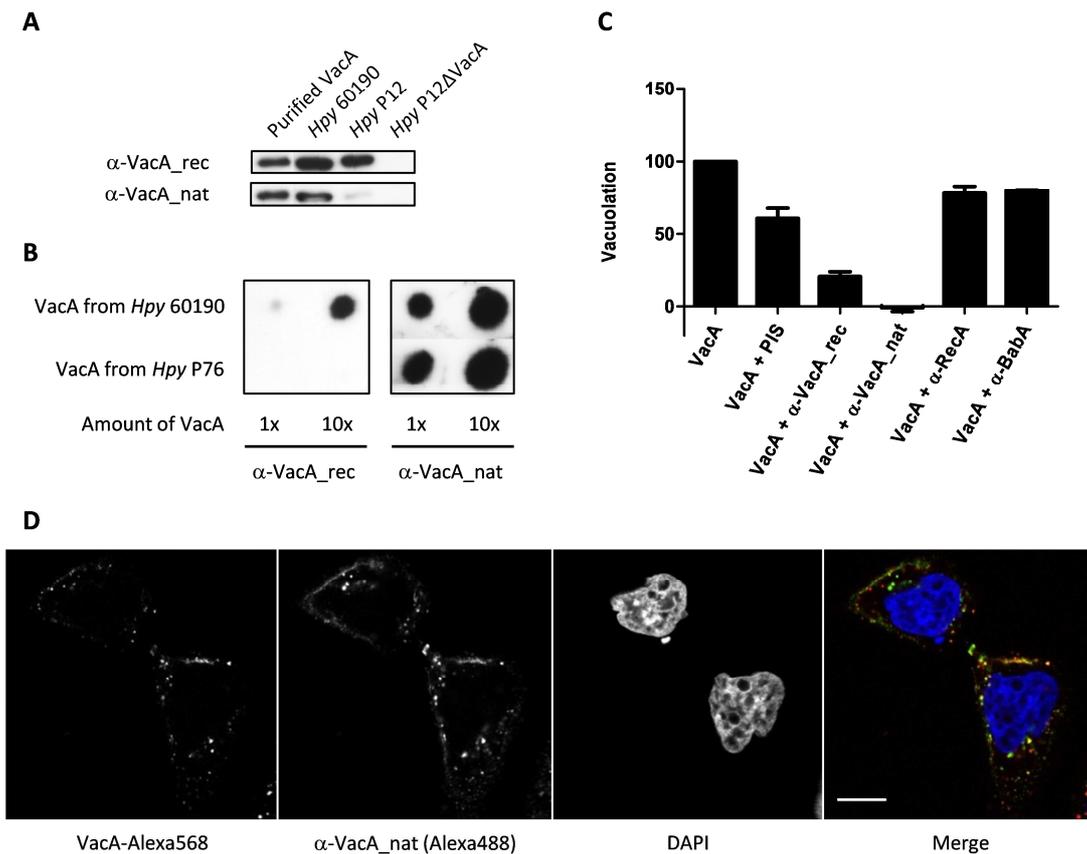
### 3.2.1 $\alpha$ -VacA<sub>nat</sub> in Immunoblotting

$\alpha$ -VacA<sub>nat</sub> was used in immunoblotting experiments to investigate its suitability for VacA detection under both native and denaturing conditions (Figure 4A and B). Purified VacA and lysates of different *H. pylori* strains were separated on an SDS polyacrylamide gel, denaturing all proteins, and transferred to PVDF membrane. The same membrane was sequentially probed with both VacA antisera, using  $\alpha$ -mouse-POX as a secondary antibody in both cases. Both sera clearly recognize both purified VacA from *H. pylori* strain 60190 and VacA in lysate of the same strain (Figure 4A). While  $\alpha$ -VacA<sub>rec</sub> also distinctly recognizes P12 VacA,  $\alpha$ -VacA<sub>nat</sub> does so only weakly. In another experiment, native conditions were maintained by spotting purified toxin directly onto membrane (Figure 4B). Subsequent probing with both antisera revealed that  $\alpha$ -VacA<sub>nat</sub> recognizes native VacA much better than  $\alpha$ -VacA<sub>rec</sub>, as expected. Purified VacA from strain P76 can serve as a proof of principle, since it is of the sli2m2 variety [87]. Its sequence differs substantially from that of VacA from strain 60190, which is categorized as sli1m1. This may explain why  $\alpha$ -VacA<sub>rec</sub> somewhat recognizes 60190 VacA but doesn't recognize P76 VacA. Some secondary structural properties of both VacA proteins, on the other hand, may be conserved, leading to  $\alpha$ -VacA<sub>nat</sub> recognizing both variants of the toxin under these conditions.

### 3.2.2 Inhibition of Vacuolation by Various Antisera

A functional assay was also devised to see whether  $\alpha$ -VacA<sub>nat</sub> binding to VacA interfered with VacA induced vacuolation (Figure 4C; see 2.2.11). The vacuolation assay routinely used to evaluate toxin activity was modified slightly, adding two steps before intoxication: inactivation of serum complement proteins in all antisera, and incubation of heat-inactivated antisera with acid-activated VacA to facilitate binding. After these steps, the VacA/antisera mixtures were added to HeLa cells, followed by the addition of NH<sub>4</sub>Cl four hours later to increase vacuole size for another 30-60 min. Subsequently, neutral red was added and taken up into vacuoles, which stain red due to their acidity. The neutral red was then extracted and its absorption was measured as an indicator of vacuolation. Five different sera were used:  $\alpha$ -VacA<sub>nat</sub> and pre-immune serum (PIS) from the same rabbit;  $\alpha$ -VacA<sub>rec</sub>;  $\alpha$ -RecA, directed against a cytoplasmic *H. pylori* protein; and  $\alpha$ -BabA, directed against an *H. pylori* outer membrane protein.  $\alpha$ -RecA and  $\alpha$ -BabA served as unspecific control sera. All sera's total protein content was measured in a Bradford assay and equivalent protein amounts of all sera were used in the experiment.

## Results



**Figure 4: Characterization of  $\alpha$ -VacA<sub>nat</sub>.**

(A) Lysates of different *H. pylori* strains as well as purified VacA from strain 60190 were analyzed by Western Blotting with  $\alpha$ -VacA<sub>rec</sub> and  $\alpha$ -VacA<sub>nat</sub> to compare the two antisera's ability to recognize different VacA variants (bands detected at approx. 100 kDa). (B) Purified VacA was spotted directly onto membrane to preserve its native conformation and subsequently analyzed by immunoblotting with both VacA antisera. (C) Various antisera, including those raised against VacA ( $\alpha$ -VacA<sub>rec</sub> and  $\alpha$ -VacA<sub>nat</sub>), were tested for their ability to inhibit VacA-induced vacuolation in HeLa cells. Pre-immune serum (PIS),  $\alpha$ -RecA and  $\alpha$ -Baba were used as unspecific controls. All sera were heat-inactivated to reduce complement effects and incubated with acid-activated VacA before intoxication. Vacuolation was measured via neutral red uptake after 4 h of intoxication and 1 h of NH<sub>4</sub>Cl treatment. All values were normalized to untreated cells and uninhibited vacuolation was set to 100%. Error bars represent standard errors of the mean of three independent experiments. (D) HeLa cells were intoxicated with VacA-Alexa568 for 4 h and subsequently stained with  $\alpha$ -VacA<sub>nat</sub> (and a secondary antibody labeled with Alexa488) so that both signals could be compared directly. Samples were analyzed by confocal microscopy. Scale bar represents 10  $\mu$ m.

Figure 4C shows a complete inhibition of vacuolation by  $\alpha$ -VacA<sub>nat</sub>, indicating that binding of  $\alpha$ -VacA<sub>nat</sub> to VacA prior to intoxication interferes with either VacA binding to cells or VacA channel formation.  $\alpha$ -VacA<sub>rec</sub> also has a strong inhibiting effect, suggesting in accordance with Dot Blot data (Figure 4B) that  $\alpha$ -VacA<sub>rec</sub> is also capable of recognizing native VacA to a certain extent. The control sera, and even pre-immune serum, still show a weak inhibition that can be attributed to serum proteins or other unspecific effects.

To conclude,  $\alpha$ -VacA<sub>nat</sub> was able to completely prevent VacA-induced vacuolation in this setting. Its inhibitory effect was dose-dependent (data not shown).

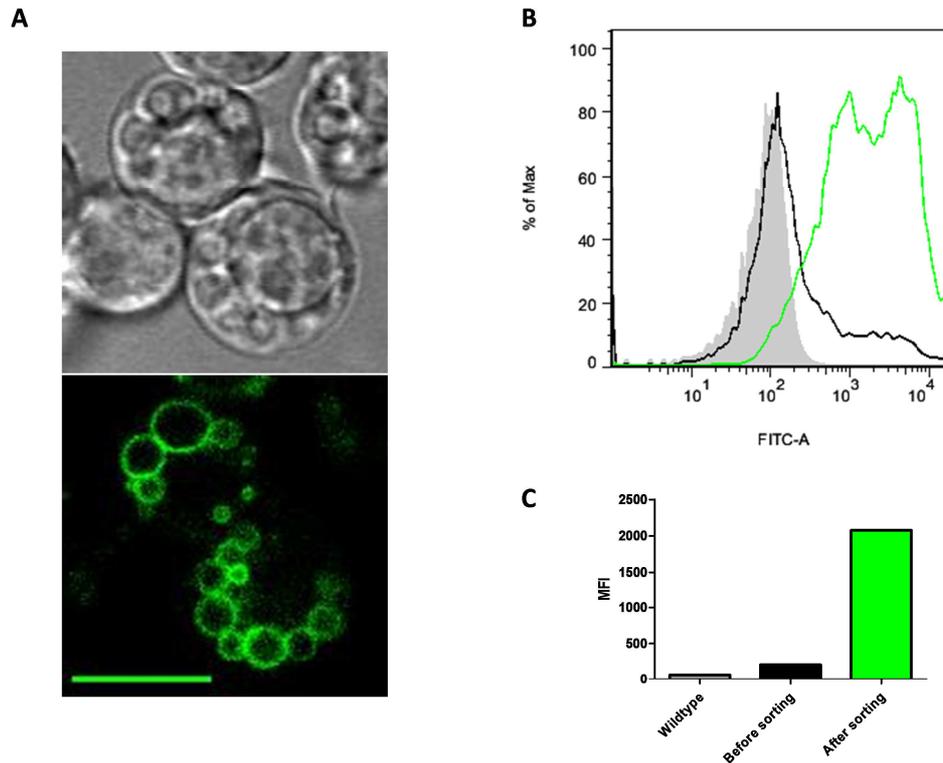
### 3.2.3 $\alpha$ -VacA\_nat in Immunostaining Experiments

To analyze  $\alpha$ -VacA\_nat's ability to recognize VacA after uptake into cells, it was used in immunostaining experiments. HeLa cells were intoxicated with acid-activated VacA-Alexa568, fixed, permeabilized and additionally stained with  $\alpha$ -VacA\_nat and a secondary antibody coupled to Alexa488 (Figure 4D) (see 2.2.13). The choice of two different fluorophores in the same sample permitted a direct comparison of the signals of labeled VacA and the VacA stain. They can be seen to overlap for the most part, but the stain signal was usually stronger and not as regionally restricted. The fact that the stain gave a more widely distributed signal is not due to unspecific staining, which was confirmed by the relevant unintoxicated control sample (data not shown). Instead, it is likely that not every VacA molecule was labeled with enough Alexa molecules to be detectable, whereas an antibody stain always entails an amplification of signal. Importantly, it can be concluded that  $\alpha$ -VacA\_nat does recognize VacA in this setting.

### 3.3 Stable Cell Line Jurkat E6-1 EGFP-Rab7

With the objective to isolate VCVs from cell lysate, a way to monitor VCV distribution in samples over the course of the isolation process became necessary. Microscopy was chosen as a fast and reliable method. Rab7 is a late endosomal marker known to localize to VCV membranes [43], and fluorescently tagged Rab7 can conveniently serve as a VCV marker. A plasmid coding for an EGFP-Rab7 fusion protein and a G418 resistance cassette was transfected into Jurkat E6-1 cells and transformants were selected by the addition of 1 mg/ml G418 to the cell culture medium (see 2.2.3.3).

Transfection efficiency was checked via confocal microscopy and flow cytometry. Figure 5A shows a micrograph of Jurkat E6-1 cells expressing EGFP-Rab7; vacuoles are clearly visible in both the brightfield and the green channel images. As the initial transfection efficiency was low (approx. 10%), EGFP-Rab7 expressing cells were enriched by flow cytometry cell sorting (Figure 5B and C). The mean fluorescence intensity, measured as an indicator of transfection efficiency, was increased by a whole order of magnitude after sorting. The thusly created cell line stably expressing the VCV marker EGFP-Rab7 was a suitable tool for VCV isolation.



**Figure 5: Creation of the stable cell line Jurkat E6-1 EGFP-Rab7.**

Rab7 is a late endosomal marker known to line VCV membranes. (A) Jurkat E6-1 EGFP-Rab7 cells exhibiting vacuolation after intoxication with VacA and treatment with NH<sub>4</sub>Cl for at least 4 h / 1 h, respectively. VCVs can be seen in the brightfield image (top) and labeled with EGFP-Rab7 in the green channel (bottom). Scale bar represents 10  $\mu$ m. (B) Expression of EGFP-Rab7 in stably transfected Jurkat E6-1 cells was evaluated by flow cytometry. The gray area represents wild-type (untransfected) Jurkat E6-1 cells. The stable cell line was subjected to cell sorting and analyzed before (black line) and afterwards (green line), clearly showing an enrichment in EGFP-Rab7 expressing cells. (C) The bar graph shows mean fluorescence intensity (MFI) (geometric mean) calculated from the measurements obtained in (B). Both (B) and (C) illustrate one representative experiment.

### 3.4 VCV Isolation

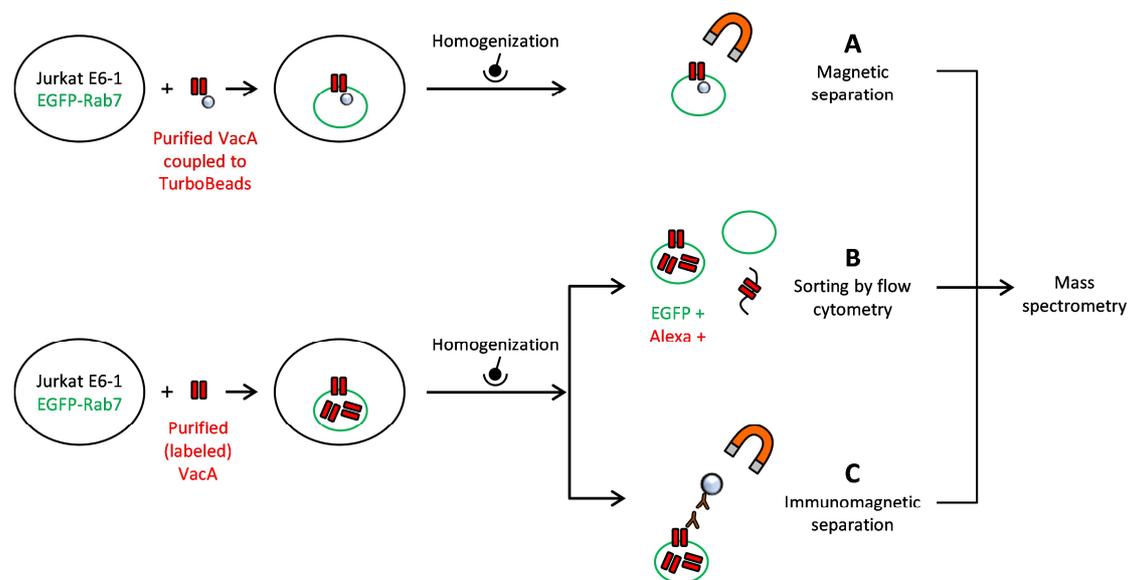
#### 3.4.1 Strategies

Three different strategies for the isolation of VCVs from cell lysate were considered over the course of this work and are depicted in Figure 6. They rely on different characteristics of VCVs, and while an overview is presented at this point, they will be discussed in detail in the following sections.

Strategy A (see 3.4.3) employs nanoscale magnetic beads of about the size of a VacA hexamer. After covalent coupling to VacA, these beads were to be internalized into cells along with VacA and then separated from cell homogenate with a magnet. Strategy B (see 3.4.4) utilizes the VCV

marker EGFP-Rab7 described in 3.3 and the fact that VacA can be fluorescently labeled with Alexa dyes (see 2.2.5.9). VCVs were then to be sorted from homogenate via flow cytometry, being the only particles carrying both fluorophores. In strategy C (see 3.4.5), the antiserum raised against native VacA,  $\alpha$ -VacA\_nat, was to be used to bind VacA integrated into VCV membranes. Using a secondary antibody directed against  $\alpha$ -VacA\_nat coupled to magnetic beads, VCVs were to be pulled out of the homogenate.

The ultimate goal of all these strategies was to isolate enough VCVs to be able to analyze their proteome by mass spectrometry (MS). The MS method used for this purpose has a minimal detection limit of about 100 ng, which is the same amount that can be visualized in one single band on an SDS polyacrylamide gel stained with Coomassie Brilliant Blue. SDS-PAGE and Coomassie staining were therefore used to assess total protein content of isolation samples. The VCV proteome was then expected to shed light on the possible functions of VCVs.



**Figure 6: Three different strategies for VCV isolation.**

Strategy A: Nanoscale magnetic TurboBeads coupled to VacA were to be internalized by intoxicated cells and then used to magnetically separate VCVs from homogenate. Strategy B: Cells expressing the GFP-labeled VCV marker Rab7 were to be intoxicated with Alexa-labeled VacA, resulting in VCVs carrying both fluorescent labels. These were then to be sorted from homogenate via flow cytometry. Strategy C: A primary antibody directed against VacA was to be used to bind to VacA inserted into the VCV membrane. A secondary antibody coupled to magnetic beads was then to be employed to separate VCVs from homogenate.

### 3.4.2 General Optimization Steps

Independent of the VCV isolation strategy, the conditions for preparing the starting material - meaning the cell homogenate containing VCVs - had to be optimized. After finding the ideal conditions, the strategies could be tested to find the most suitable one.

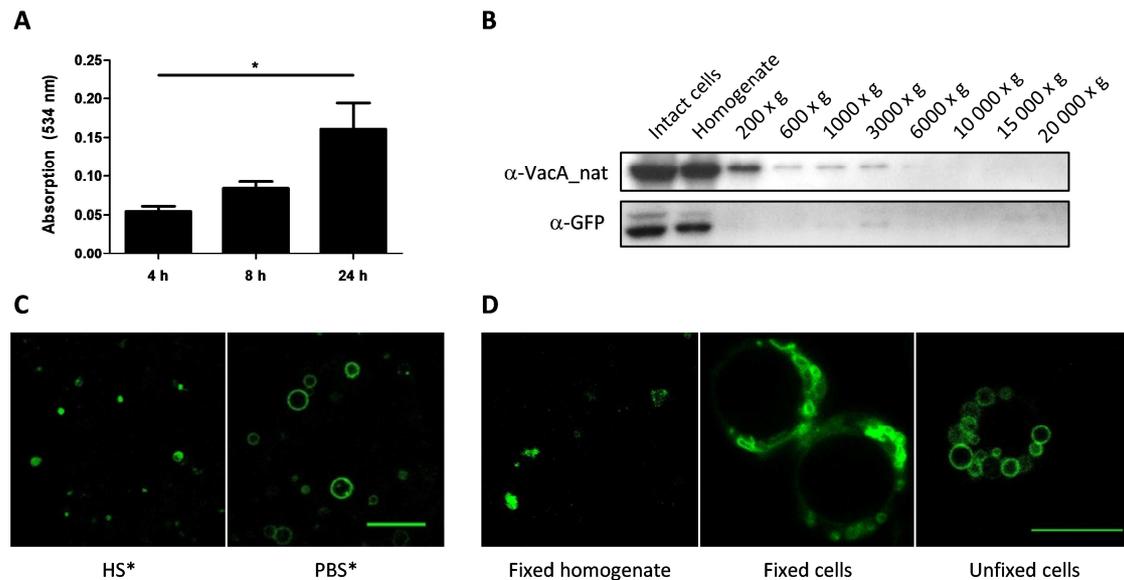
#### 3.4.2.1 Dependence of Vacuolation on Intoxication Period

Since the VCV purification process was to be monitored by microscopy, it was assumed that it would be easiest to isolate VCVs when they are large and numerous. To this end, different periods of intoxication were evaluated for degree of vacuolation (Figure 7A; see 2.2.9). Jurkat E6-1 cells were intoxicated with 1 µg/ml VacA and NH<sub>4</sub>Cl (to osmotically increase VCV size) and incubated for 4, 8, and 24 h. Longer periods were not tested for fear of cell damage. As in other vacuolation assays (see 2.2.8), neutral red uptake was measured as an indicator of vacuole size and/or number. For every time point, a sample of unintoxicated (but NH<sub>4</sub>Cl treated) cells was also measured. In contrast to HeLa cells, neutral red uptake of unintoxicated Jurkat cells varies little from one experiment to the next, so absolute values can be used, and normalization was done differently. The arithmetic mean of all measured values of unintoxicated cells was calculated and subtracted from the measured values of intoxicated cells. Vacuolation was observed to be time-dependent, with the difference between 4 h and 24 h being statistically significant ( $p < 0.05$ , Kruskal-Wallis and Dunn's multiple comparison tests). Intoxication for VCV isolation was therefore always performed over night.

#### 3.4.2.2 VCV Sedimentation Properties

All VCV isolation strategies necessitate the sedimentation of cell homogenate and VCVs by centrifugation. Therefore, VCV sedimentation properties were systematically investigated in a sequential centrifugation experiment (see Figure 7B; see 2.2.16). Jurkat E6-1 EGFP-Rab7 cells were intoxicated with VacA and treated with NH<sub>4</sub>Cl in parallel before homogenization. Homogenate was then sequentially centrifuged at 200, 600, 1000, 3000, 6000, 10 000, 15 000, and 20 000 x g. The pellets of all steps were then analyzed by Western Blot for the presence of VacA and EGFP. Cell suspension and homogenate served as controls for total VacA/EGFP-Rab7 content. While clearly not all VacA/EGFP-Rab7 sediments together with VCVs, both were detected in some of the fractions. VacA, which is expected to occur not just in VCVs but also in other cellular compartments and bound to plasma membrane, could be found in all fractions up

to 6000 x g. Most of EGFP-Rab7, on the other hand, was expected to be localized in VCVs, based on previous microscopy observations (see for example Figure 5A). It was detected most prominently in the 3000 x g fraction. Since this fraction was also positive for VacA, it was therefore concluded to contain the majority of VCVs. This experiment was monitored by microscopy in parallel, detecting only EGFP-Rab7, not VacA, and confirming this conclusion (data not shown).



**Figure 7: Optimization of VCV isolation conditions.**

(A) As an indicator for vacuolation over time, neutral red uptake was measured in Jurkat E6-1 cells after 4, 8, and 24 h of intoxication with VacA and parallel treatment with  $\text{NH}_4\text{Cl}$ . Measurements were normalized to unintoxicated cells. The graph was compiled with data obtained in three independent experiments. Error bars represent standard errors of the mean. \* =  $p < 0.05$  (Kruskal-Wallis and Dunn's multiple comparison tests). (B) To investigate VCV sedimentation properties, Jurkat E6-1 EGFP-Rab7 cells were intoxicated with VacA and treated with  $\text{NH}_4\text{Cl}$  (both 5 h) before homogenization. 1 ml homogenate was then sequentially centrifuged. One fifth of centrifugation pellets was loaded onto an SDS polyacrylamide gel and subsequently analyzed for the presence of VacA and EGFP-Rab7 by Western Blotting. (C) Different buffers were tested for homogenization of intoxicated,  $\text{NH}_4\text{Cl}$  treated Jurkat E6-1 EGFP-Rab7 cells. VCVs are clearly in a better condition in PBS\*. The asterisk denotes addition of protease inhibitors to the buffer. (D) Various fixation methods were tested for both homogenized and intact intoxicated cells. Samples fixed with PFA for 10 min at RT are shown as representative examples. Scale bars in (C) and (D) represent 10  $\mu\text{m}$ .

### 3.4.2.3 Homogenization and Fixation Conditions

The idea to isolate VCVs originally stemmed from a cooperation with the group of Hubert Hilbi, who have established a protocol to isolate *Legionella*-containing vacuoles from cells infected with *Legionella pneumophila* [151]. Some of the conditions detailed in their protocol were used as initial starting points for this work, including the homogenization buffer, HS\* (20 mM

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HEPES, 250 mM sucrose, 0.5 mM EGTA, pH 7.2; with added protease inhibitors). However, this turned out to not be ideal for the purpose of isolating VCVs, as it did not preserve vacuole shape in homogenate (see Figure 7C), making it difficult to identify VCVs in the later steps of the isolation process. PBS\* (also supplemented with protease inhibitors) was found to fulfill this requirement. HS buffer seems to have the wrong osmotic pressure, leading to a collapse of VCVs, which is in agreement with the fact that it was developed for vacuoles containing whole bacteria unlike VCVs.

Fixation presented similar problems since vacuole shape was not retained in either intact cells or homogenate, but vacuole shape was a necessary identifying feature of VCVs alongside EGFP fluorescence. Various fixation reagents were tested at different concentrations and conditions, but none proved successful. Among the reagents tested were glutaraldehyde, cyclohexylamine, methanol, ethanol, PFA with and without sucrose, PFA in HEPES, and commercially available CellFIX (BD Biosciences). Cells fixed with 0.5% PFA and homogenate fixed with 3% PFA for 10 min at RT are shown in Figure 7D as an example. During fixation, VCVs lost their characteristic round shape and shrank in size, making non-ambiguous identification impossible. The fact that fixation turned out to be unfeasible was especially problematic as it eliminated the possibility of validating the presence of specific proteins on isolated VCVs by immunostaining, as done in [151]. All monitoring of VCV isolation was henceforth performed with unfixed samples in 8-well slides.

### 3.4.3 Strategy A: TurboBeads Strategy

The first strategy for VCV isolation was based on nanoscale magnetic beads (Carboxyl coated TurboBeads, TurboBeads LLC). These beads have a mean particle size of 30 nm, about the same size as a VacA hexamer (see Figure 8A; [61]). Uptake of VacA coupled to beads was expected to happen normally, undisturbed by the extremely small beads. After intoxication and cell homogenization, the bead-containing VCVs were to be extracted from homogenate via magnetic separation.

#### 3.4.3.1 TurboBead Uptake

For detection purposes, VacA was labeled with Alexa488 before being coupled to beads. Bead uptake into Jurkat E6-1 cells was investigated using two methods: confocal microscopy and flow cytometry (see 2.2.17.2 and 2.2.17.3). For the first, cells were intoxicated with VacA-Alexa488 coupled to TurboBeads for 40 min at 4 °C to minimize particle movement and therefore bead

aggregation (see 3.4.3.2) followed by 200 min at 37 °C to allow for complete internalization. Cells were fixed with 15% PFA and analyzed by confocal microscopy (see Figure 8B). Images were processed with ImageJ, using the Orthogonal View function to visualize XZ and YZ 'side views' of the stack of images taken. This made it easier to determine whether a particle was fully internalized, like the one shown in Figure 8B at the center of the crosshairs. Internalized particles were observed and appeared similar to internalized VacA-Alexa488 without beads (data not shown).

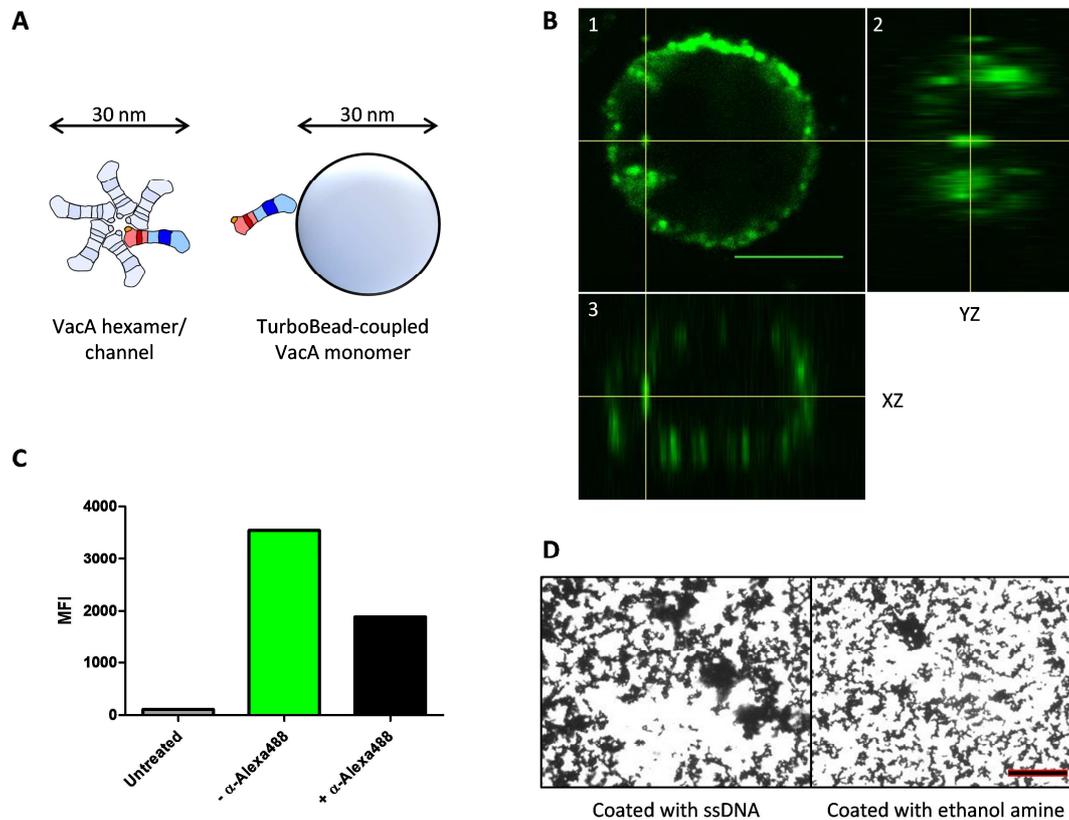
To verify this, a fluorescence quenching assay was performed (see Figure 8C). Jurkat E6-1 cells were intoxicated with VacA-Alexa488 coupled to TurboBeads for 40 min, which is enough time for VacA internalization to happen, according to previous research [88]. Cells were then incubated with  $\alpha$ -Alexa488 to quench external fluorescence, leaving only internalized fluorophore molecules to be detected by flow cytometry. Figure 8C displays mean fluorescence intensity measurements (MFI; geometric mean) for cells treated as described above (black bar), untreated cells (gray), and cells intoxicated with VacA-Alexa488 but not incubated with  $\alpha$ -Alexa488 as a positive control (green). About half of the fluorescence was quenched with  $\alpha$ -Alexa488, meaning that the other half was internalized. VacA-Alexa488 not coupled to TurboBeads showed the same pattern (data not shown). Results from both methods, flow cytometry and confocal microscopy, agree that VacA-coupled TurboBeads are internalized into Jurkat E6-1 cells.

#### 3.4.3.2 TurboBead Aggregation

While bead internalization data looked promising, bead aggregation was a problem that occurred in all TurboBeads experiments. In order to minimize aggregation and to keep bead uptake into cells as natural as possible, different buffers and various substances for coating the beads were tested (see 2.2.17.1). The initial choice for bead coating was  $\text{NH}_4\text{Cl}$ , since it is small, chemically inert, non-toxic, and does not trigger any cellular uptake pathways. Also, it has the amino group necessary for coupling to the carboxyl coated TurboBeads. Another substance recommended by the TurboBeads manufacturer was ethanol amine. As a last approach, the beads were coated with ssDNA, as steric repulsion by non-complementary DNA can facilitate nanoparticle dispersion (Maye 2007). Buffers tested for TurboBead resuspension include PBS, cell culture medium (RPMI supplemented with 10% FCS) since it would have been present in an intoxication setting anyway, and HES buffer (Voluven 6%, Fresenius Kabi) as recommended by the TurboBeads manufacturer. However, none of these attempts yielded satisfactory results

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(Figure 8D). Considering the likely possibility of bead aggregates influencing the natural VacA uptake pathway, and the low vacuolating activity of bead-coupled VacA (data not shown), this VCV isolation strategy was abandoned.



**Figure 8: TurboBeads strategy, internalization, and aggregation.**

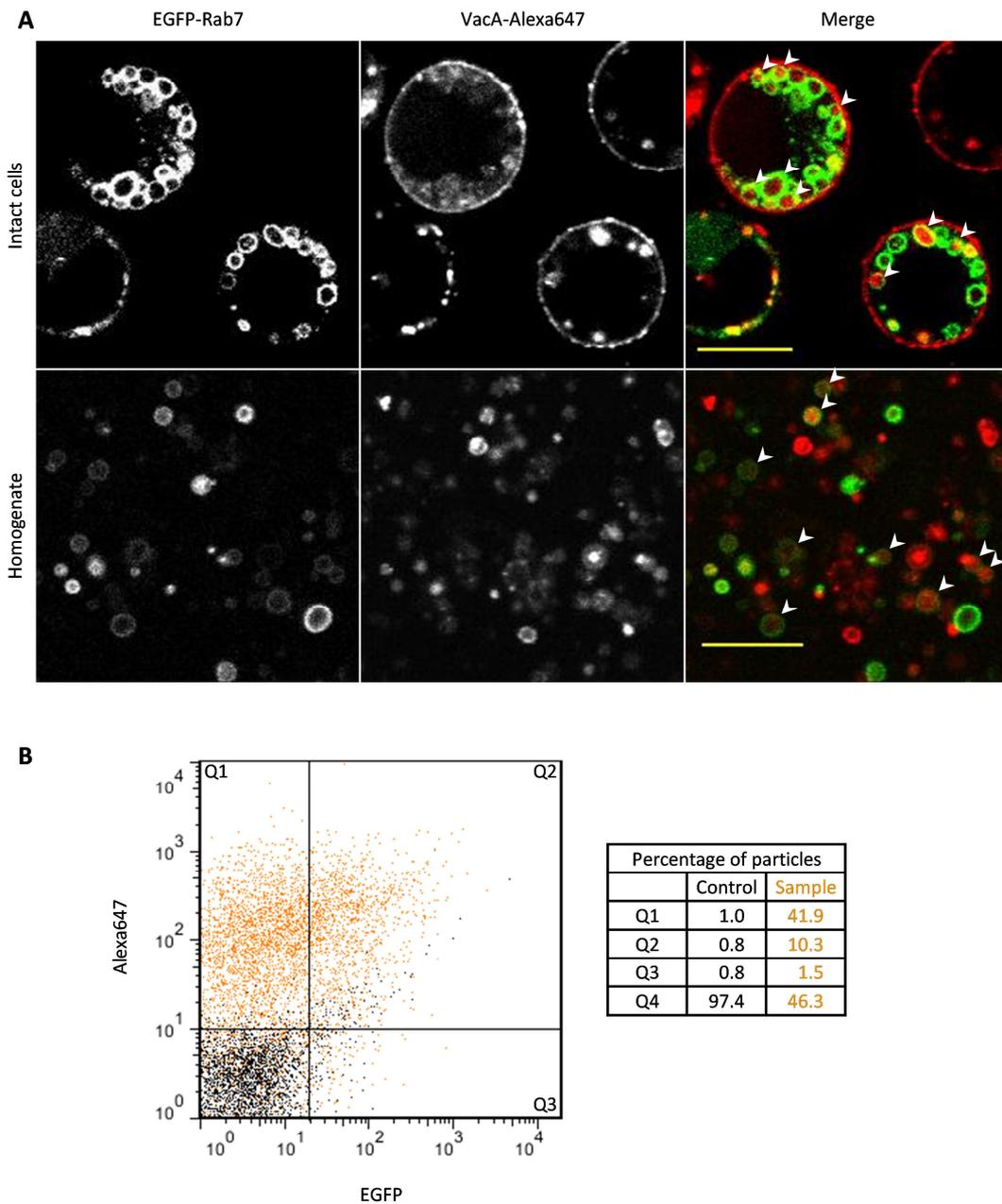
(A) Size comparison of VacA and TurboBead. TurboBeads have a diameter similar to that of VacA hexamers. VacA structure adapted from [54]. (B and C) TurboBead uptake was investigated via confocal microscopy and flow cytometry. (B) Jurkat E6-1 cells were treated with TurboBead-coupled VacA-Alexa488 (40 min at 4 °C followed by 200 min at 37 °C) and fixed. Shown here is a cell recorded on a stack of 12 slices at intervals of 9.57 μm. Panel 1 shows the regular ('top') view of slice 7 while panels 2 and 3 show YZ and XZ projections of the whole stack ('side views'), respectively, computed with the Orthogonal View function of ImageJ. An internalized particle can be seen at the center of the crosshairs. Scale bar represents 5 μm. (C) Jurkat E6-1 cells were treated with TurboBead-coupled VacA-Alexa488 for 40 min, then incubated with α-Alexa488 to quench external fluorescence. Subsequent analysis by flow cytometry revealed internalization of about 50% of the total fluorescence, compared to the unquenched control (not treated with α-Alexa488). The bar graph shows mean fluorescence intensity (MFI) measurements (geometric mean) from one representative experiment. (D) TurboBeads were coated with various substances and resuspended in various buffers to minimize aggregation. As examples, beads coated with ssDNA and ethanol amine resuspended in RPMI supplemented with 10% FCS are shown in a light microscopy image. Dark shapes are bead aggregates. Scale bar represents 200 μm.

### 3.4.4 Strategy B: VCV Sorting by Flow Cytometry

The second approach to isolate VCVs was to sort them from homogenate on the basis of their fluorescence properties. The stable cell line Jurkat E6-1 EGFP-Rab7 provided one fluorescent VCV marker, while labeling of VacA with Alexa dyes provided another. In Jurkat E6-1 EGFP-Rab7 cells intoxicated with Alexa-labeled VacA, the only particles positive for both fluorophores were expected to be VCVs, and sorting was assumed to yield a highly pure VCV preparation. Sorting experiments were conducted in collaboration with flow cytometry experts Dr. Matthias Schiemann and Lynette Henkel at the Flow Cytometry Core Unit of the Institute for Medical Microbiology, Immunology and Hygiene (Technische Universität München).

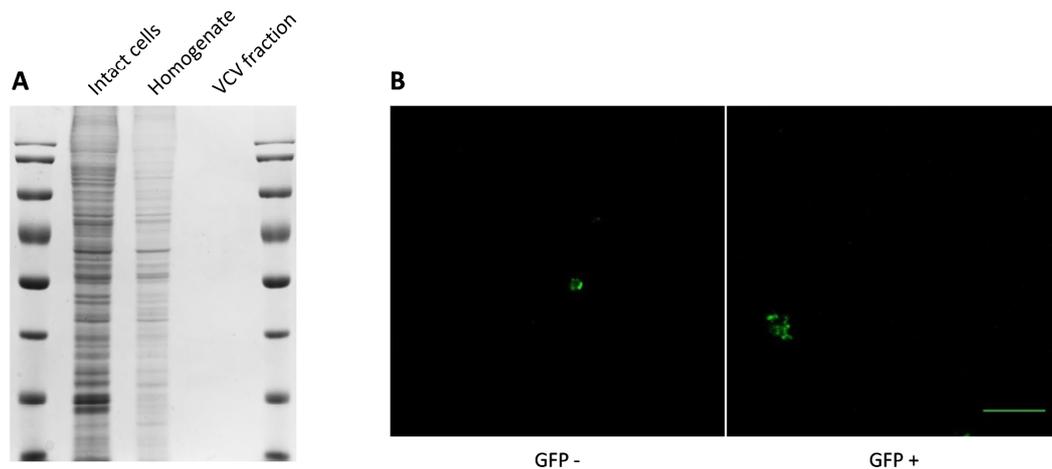
To assess the quality of the starting material, Jurkat E6-1 EGFP-Rab7 cells were intoxicated with VacA-Alexa647 and treated with  $\text{NH}_4\text{Cl}$  (both over night) and subjected to confocal microscopy before and after homogenization (see Figure 9A; details see 2.2.18). As expected, EGFP-Rab7 could be seen to line VCV membranes as before (see 3.3), while VacA-Alexa647 was found mainly in the VCV lumen. The homogenate contained numerous particles carrying both fluorophores (pointed out by white arrowheads in the rightmost images of Figure 9A) and was therefore deemed suitable for sorting. Control homogenates of Jurkat E6-1 cells not expressing EGFP-Rab7 and of cells intoxicated with unlabeled VacA were also imaged to confirm the absence of double positive particles (data not shown).

To determine which particles to sort, Jurkat E6-1 cells not expressing EGFP-Rab7 were intoxicated with unlabeled VacA, homogenized, and used as a negative control. A comparison of both homogenates analyzed with a FACSaria IIIu is shown in Figure 9B; the non-fluorescent negative control is depicted in black, the sample containing both EGFP and Alexa647 in orange. After selecting particles for the correct size according to their forward and sideward scattering properties, their fluorescence characteristics were inspected and positivity for both fluorophores was defined in relation to the negative control. The graph clearly shows that the sorting sample contains particles with much stronger fluorescence than the control in both channels, and the table details the percentages of particles registered in the respective quadrants. Double positive particles (quadrant 2) were then sorted and examined by microscopy and SDS-PAGE/Coomassie staining. In all cases, even though the sorting process itself seemed to work, the sorted fraction was found to contain nothing at all (Figure 10A), or no particles recognizable as VCVs.



**Figure 9: VCV homogenate prepared for flow cytometry sorting.**

(A) Jurkat E6-1 EGFP-Rab7 cells were intoxicated with VacA-Alexa647 and treated with  $\text{NH}_4\text{Cl}$  (both over night) before homogenization. Aliquots of intact cells and homogenate were examined by confocal microscopy for VCVs positive for both EGFP and Alexa647 (highlighted by white arrowheads) as a prerequisite for VCV sorting by flow cytometry. Scale bars represent 10  $\mu\text{m}$ . (B) Cells were treated with VacA and  $\text{NH}_4\text{Cl}$  over night and homogenized, and the homogenate was subjected to flow cytometry. Jurkat E6-1 cells not expressing EGFP-Rab7 were intoxicated with unlabeled VacA as a negative control (black); Jurkat E6-1 EGFP-Rab7 cells were intoxicated with VacA-Alexa647 (orange; compare bottom row in (A)). Particles in quadrant 2 were defined as VCVs, being positive for both EGFP and Alexa647, and were sorted. The table shows particle counts (%) of all quadrants; quadrant numbering as indicated in the graph. Representative sorting experiment performed on a FACSAria IIIu.



**Figure 10: Analysis of VCV fractions sorted by flow cytometry.**

(A) Homogenate of Jurkat E6-1 EGFP-Rab7 cells treated with VacA-Alexa647 was subjected to flow cytometry. Particles positive for both GFP and Alexa647 were sorted, but could not be detected by SDS-PAGE/Coomassie staining. (B) Homogenate of Jurkat E6-1 EGFP-Rab7 cells treated with unlabeled VacA was subjected to flow cytometry. In this experiment, particles were sorted into two fractions depending on the presence or absence of GFP. Small numbers of fluorescent particles were later found in both fractions. Scale bar represents 10  $\mu\text{m}$ .

Because the use of labeled VacA somewhat limited the amount of starting material for this experiment, but to find out whether vacuole sorting is at all possible, another sorting attempt was made with large amounts of homogenate from Jurkat E6-1 EGFP-Rab7 cells intoxicated with unlabeled VacA. Here, all particles were sorted into two fractions, GFP positive and GFP negative. Both fractions were again examined by microscopy, and both were found to contain very few apparently fluorescent particles with no clear vacuole shape (Figure 10B), which were concluded to be unspecific. It seems that the vacuoles generally are not stable enough to be sorted, but it is not clear what exactly happens to them. Various sorting devices were tried, specifically a FACSAria IIIu (BD Biosciences), an S3 Cell Sorter (Bio-Rad), and a MoFlo Legacy (Beckman Coulter). These differ in nozzle diameter (70-100  $\mu\text{m}$ ), optical sensitivity, internal pressure and resulting shearing forces, but none of them solved the problem. These circumstances do not allow the definite identification of VCVs in a sorted fraction and VCV sorting by flow cytometry was therefore rejected as a method for VCV purification.

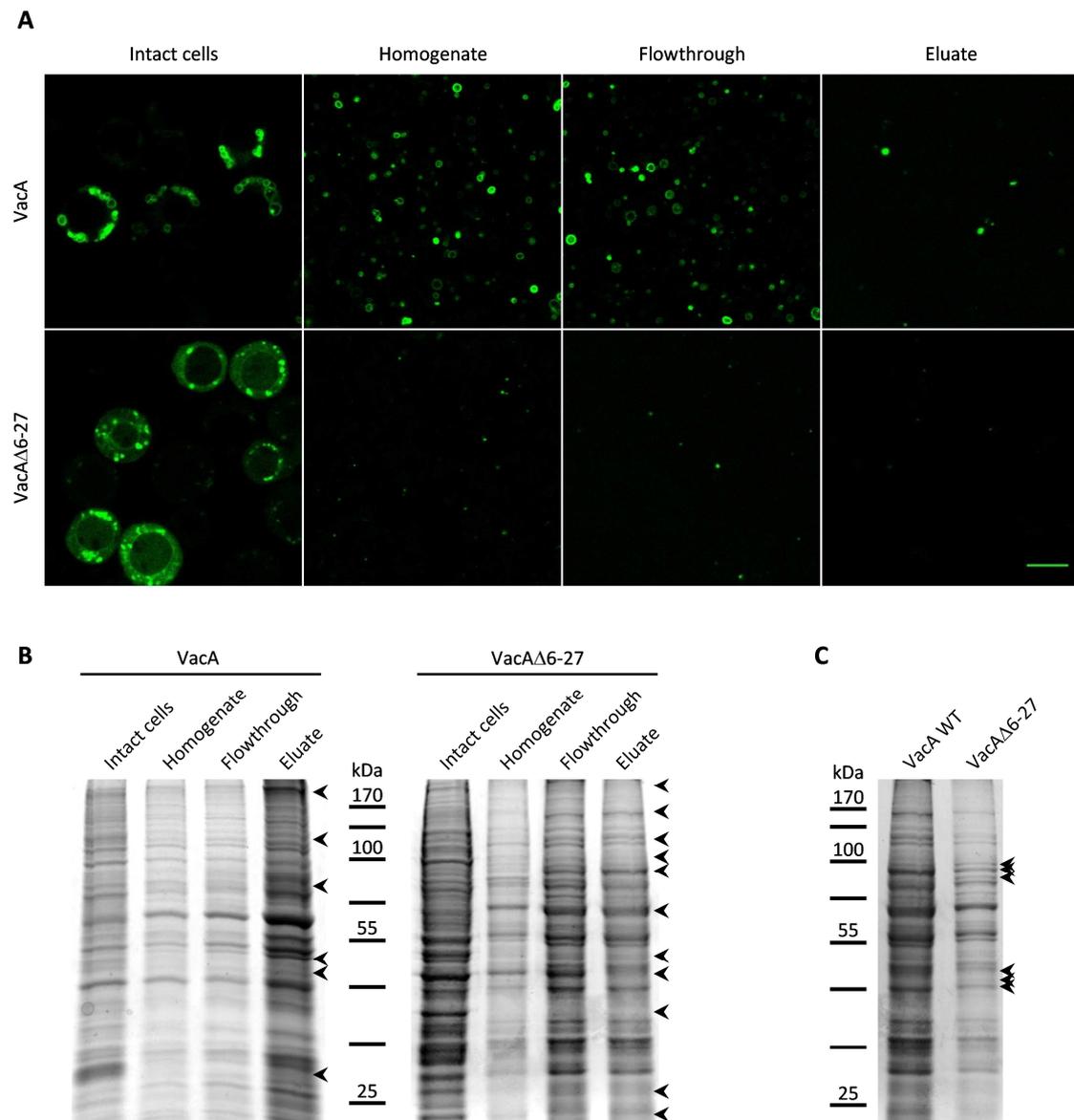
### 3.4.5 Strategy C: Immunomagnetic Purification of VCVs

Strategy C was finally chosen for VCV purification (see 3.4.1). As mentioned before, it was adapted from a protocol published by Hilbi and coworkers for the isolation of *Legionella*-containing vacuoles from cells infected with *Legionella pneumophila* [151]. It relies on a primary antibody that recognizes a vacuole membrane component, which was established in  $\alpha$ -

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VacA<sub>nat</sub>. A secondary antibody coupled to magnetic beads is then used in combination with magnetic columns to separate vacuoles from cell homogenate (see 2.2.19). The subsequent density gradient centrifugation as described in [151] to further enrich the vacuoles was unsuitable for this application because the gradient substance also caused vacuole collapse (data not shown), similar to the fixation reagents and homogenization buffers other than PBS (see Figure 7C and D).

To be specific, Jurkat E6-1 cells were treated with 1 µg/ml VacA, wild-type or mutant ( $\Delta 6-27$ ), and NH<sub>4</sub>Cl over night. After homogenization, the homogenate was cleared of cell debris, blocked with calf serum and incubated with  $\alpha$ -VacA<sub>nat</sub>. Centrifugation to remove unbound antibody was followed by incubation with secondary antibody coupled to magnetic beads. The sample was applied to pre-equilibrated magnetic separation columns and eluted after two wash steps. The VCV isolation process was monitored by confocal microscopy and SDS-PAGE/Coomassie staining of cells before homogenization ('intact cells'), homogenate after clearance ('homogenate'), material that had not bound to the magnetic column ('flowthrough'), and eluate (Figure 11). Fluorescent, round particles resembling vacuoles were found in all fractions when cells were treated with wild-type VacA, but not when cells were treated with VacA $\Delta 6-27$  (Figure 11A). This was to be expected, as VacA $\Delta 6-27$  is still able to bind to cells, but does not readily form membrane channels and therefore has no vacuolating activity [70]. Some non-fluorescent material is purified for both variants of VacA (brightfield images not shown), which is assumed to be mostly plasma membrane with VacA bound to it. This also explains the proteins visible in eluate of VacA $\Delta 6-27$  treated sample when applied to SDS polyacrylamide gels (Figure 11B and C). Cells treated with VacA $\Delta 6-27$  serve as a valuable background control for mass spectrometric analysis, as non-specific, non-VCV material is purified and can then be distinguished from VCV-specific proteins in the wild-type sample. For these reasons, wild-type and VacA $\Delta 6-27$  eluted VCV fractions can be seen to have a largely congruent protein composition in a direct comparison (Figure 11C). However, both eluates' composition differs enough from that of intact cells to indicate enrichment of VacA-bound material or VCVs.



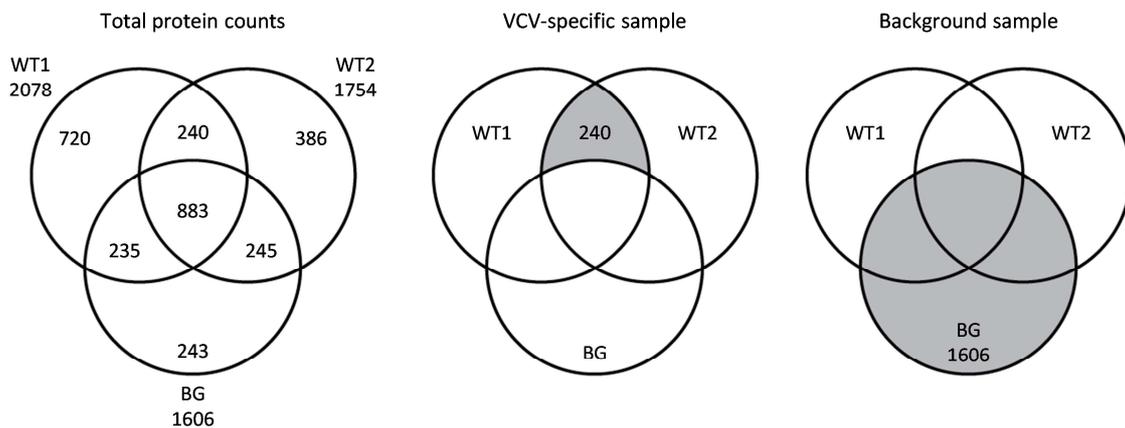
**Figure 11: Monitoring the VCV isolation process.**

Aliquots were taken at different stages of the isolation process for monitoring: before homogenization ('intact cells'), after clearing of the homogenate ('homogenate'), material that did not bind to the magnetic column ('flowthrough'), and eluate. (A) Equal portions of each step were loaded into an 8-well slide and checked for vacuolation and number of VCVs by confocal microscopy. Intoxication with the inactive mutant VacA (VacAΔ6-27) caused no vacuolation and resulted in no (fluorescent) VCVs being purified. Upper row, wild-type VacA treated cells; lower row, VacAΔ6-27 treated cells. Scale bar represents 10  $\mu$ m. (B and C) VCV isolation fractions were also analyzed by SDS-PAGE/Coomassie staining. (B) Protein composition of the individual fractions can be seen to differ. Arrowheads highlight the most prominent differences between eluate and the respective intact cells fractions. (C) Direct comparison of eluted VCVs of cells treated with VacA WT and VacAΔ6-27. The most noticeable differences in protein composition between the two lanes are again indicated by arrowheads.

### 3.5 Mass Spectrometry Results

Mass spectrometric experiments were conducted by Dr. Andreas Otto at the Institute for Microbiology of the Ernst-Moritz-Arndt-University Greifswald as detailed in [152] (see 2.2.20 and 2.2.21). Three VCV preparations were measured, two obtained from cells treated with wild-type VacA (WT1/2) and one from cells treated with VacA $\Delta$ 6-27 (BG, background). VacA $\Delta$ 6-27 is able to oligomerize, but does not form active membrane channels. Even though it binds to cells and is internalized, it does not cause vacuolation [70]. Analysis of mass spectrometry samples yielded lists of proteins identified with a probability of at least 96.3%. The accession numbers associated with these proteins were entered into the UniProt database and their information retrieved, but only reviewed entries were considered to ensure high reliability of information ([www.uniprot.org](http://www.uniprot.org)).

Two subsets were analyzed in detail and compared: the background sample, representing proteins purified in the presence of mutant VacA $\Delta$ 6-27 but in the absence of VCVs (1606 proteins), and the VCV-specific subset of proteins detected in both wild-type samples, but not in the background sample (240 proteins) (Figure 12). Full lists of proteins can be found in the appendix (see Table 2 for VCV-specific proteins, Table 3 for WT1 proteins, Table 4 for WT2 proteins, and Table 5 for background proteins).



**Figure 12: Mass spectrometry data sets.**

These Venn diagrams illustrate protein hits obtained for the three VCV preparations, two from wild-type VacA treated cells (WT1/2) and one from cells treated with VacA $\Delta$ 6-27 (background, BG). The diagram on the left shows counts of total proteins in all samples and subsets. Center diagram: proteins found in both wild-type samples, but not in the background sample, are expected to be VCV-specific. Right hand diagram: total background proteins. All numbers are reviewed UniProt entries only. Circles are not to scale.

The subset of proteins detected in both wild-type VCV preparations, but not in the background sample, was chosen for two reasons. Firstly, proteins found in the background sample are those that are unspecifically co-purified with this method and those that are purified with VacA $\Delta$ 6-27 associated with cell parts other than VCVs, for example plasma membrane. Proteins found in the wild-type samples but not found in the background sample can therefore be assumed to be specific for VCVs. Secondly, proteins found in both wild-type samples are more reliably specific than those found in only one. A comparison of this subset with the total background sample consequently provides an insight into what kind of proteins are enriched in VCVs.

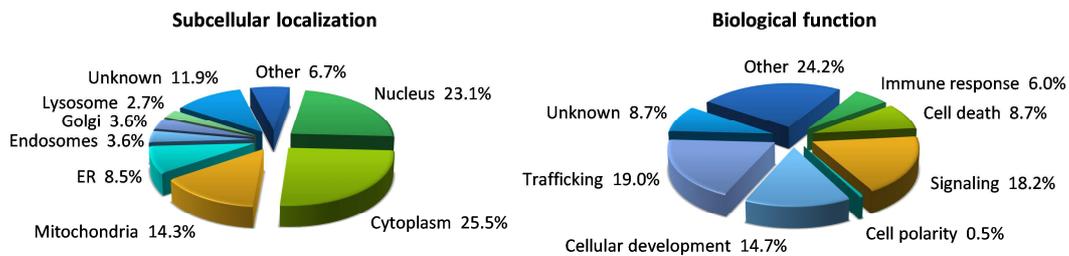
Using the information provided by UniProt, the proteins included in these two subsets were investigated more closely regarding their subcellular location and biological function. A graphic representation comparing the two subsets is shown in the upper part of Figure 11, while the same information is provided in a table format in the lower part with the most important items highlighted in red. With regard to subcellular localization, the biggest differences between VCV-specific and background sample concern nuclear and mitochondrial proteins. The VCV-specific subset contains 23.1% proteins usually localized to the nucleus; the background sample contains only 14.9%. For mitochondrial proteins, the ratio is reversed, with 14.3% in the VCV-specific subset and 21.4% in the background sample. There are also notable differences in the other categories, showing an enrichment of endosomal and lysosomal proteins in VCVs (1.4- and 2-fold, respectively). Golgi proteins, on the other hand, are decreased in the VCV-specific subset compared to the background (3.6% compared to 5.7%) Looking at the biological function of the proteins, VCVs exhibit an enrichment of proteins involved in immune response (6.0% compared to 3.2%), cell death (8.7% compared to 5.6%), and signaling (18.2% compared to 12.9%).

Looking at individual proteins, it is more reasonable to consider the complete wild-type samples without subtracting the background. Background subtraction can lead to the loss of proteins that are known to locate to VCVs, if they are present in the background sample also. This can be illustrated by the example of Rab7. As mentioned before, it is a late endosomal marker known to be present on VCV membranes [43], and an EGFP-Rab7 fusion protein was used as a fluorescent marker to monitor VCV purification. Its presence in the VCV preparations was confirmed by microscopy (Figure 11A), and in accordance with this, Rab7 was detected by MS in both wild-type samples. It was not found during microscopic investigation of the background sample but was still detected there by MS, a fact that can be attributed to this method's much higher sensitivity. This means, however, that even though Rab7 is clearly present on purified VCVs, it does not appear in the VCV-specific protein subset. The same is true for almost all

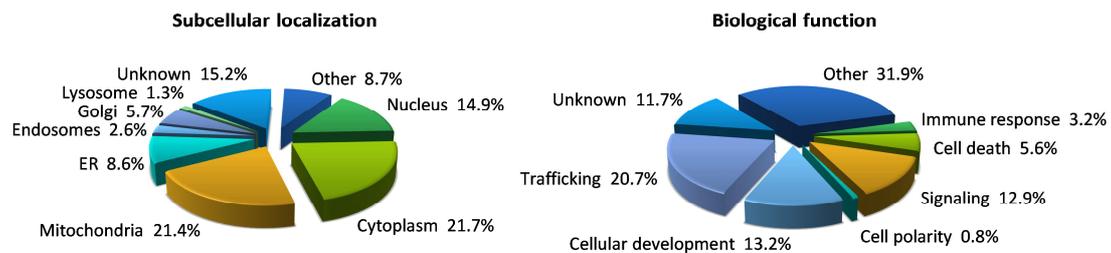
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other proteins known to locate to VCVs, including lysosomal markers Lamp1 and 2 [44,45] (Lamp2 is also known as Lgp110), the vacuolar ATPase [52], and the membrane fusion regulators Syntaxin-7 and Vamp7 [48,27,153]. All of these were found in all three samples (see Table 1).

### A VCV-specific set (240 proteins)



### B Total background (1606 proteins)



	Subcellular localization		Biological function	
	VCV-specific	Background	VCV-specific	Background
Nucleus	23.1%	14.9%	Immune response	6.0%
Cytoplasm	25.5%	21.7%	Cell death	8.7%
Mitochondria	14.3%	21.4%	Signaling	18.2%
ER	8.5%	8.6%	Cell polarity	0.5%
Endosomes	3.6%	2.6%	Cellular development	14.7%
Golgi	3.6%	5.7%	Trafficking	19.0%
Lysosome	2.7%	1.3%	Unknown	8.7%
Unknown	11.9%	15.2%	Other	24.2%
Other	6.7%	8.7%		

**Figure 13: Graphic and numerical display of the composition of VCV-specific and background subsets.**

The composition of the two relevant protein subsets regarding subcellular localization and biological function is visualized in pie charts and listed in the table for clarity. Notable differences are highlighted in red in the table.

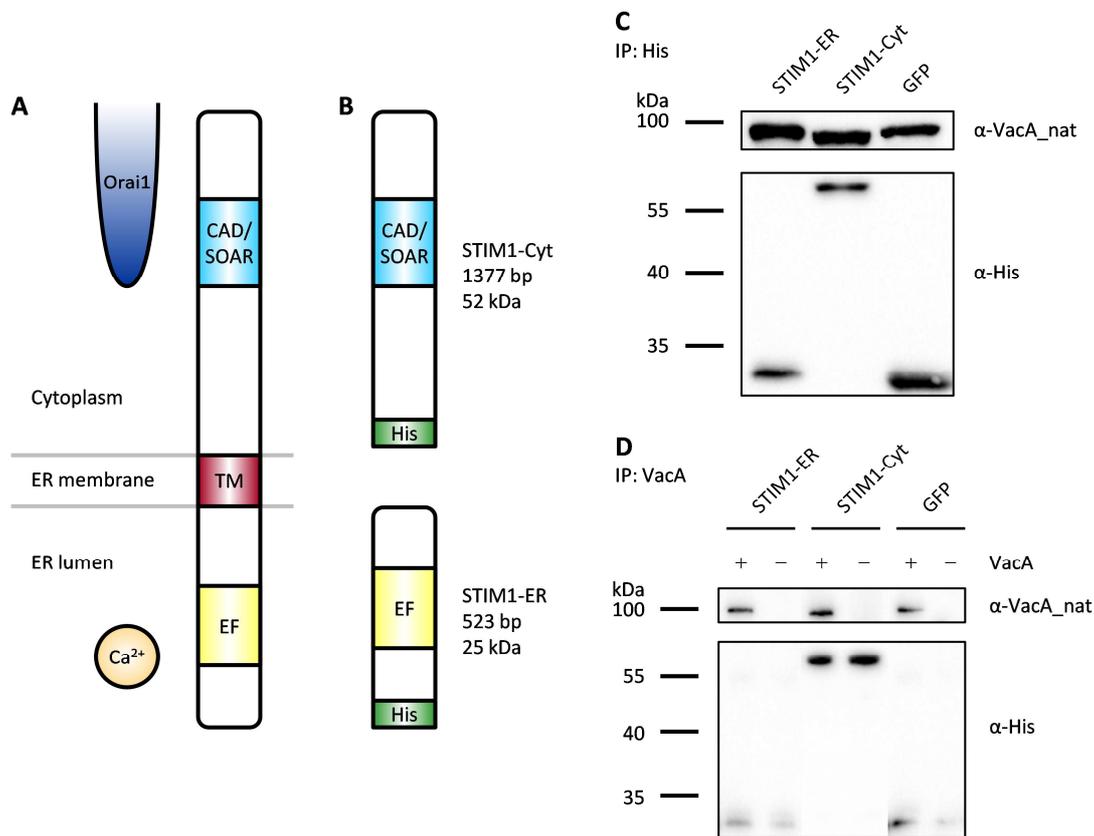
Two proteins known to occur in VCVs were not found in all fractions. The first is Rac1, a protein involved in actin cytoskeleton reorganization and intracellular signal transduction [47], which was detected in only one of the wild-type samples and in the background sample. The

second is  $\beta$ -glucosaminidase, an LE/lysosomal enzyme [45] that was found in none of the samples. Overall, the presence of almost all expected VCV-associated proteins in the wild-type samples validates the VCV purification method to a large extent. However, the above examples also illustrate that for some analyses, the background sample does not serve its purpose perfectly. The MS results lists were also scanned for host cell proteins known to be influenced by VacA or necessary for VacA-induced effects. Some of these were found in the VCV-specific sample, among them Cdc42, which is important for VacA uptake [96], Bak, a pro-apoptotic protein activated during VacA intoxication [154], the ER marker calnexin, and Drp1, a mitochondrial fission protein recruited and activated by VacA [110]. Others that were found in only one wild-type sample, or also in the background sample, include several members of the protein kinase C (PKC) family and Phosphoinositide-3 kinase (PI-3-K), which regulate T-cell activation, tubulin, and the small GTPase Rac1. PKCs, tubulin, and Rac1 are all known to play a role in VacA uptake [97,96]. Further analysis of MS measured samples can yield interesting targets for further investigation, as exemplified in the next section.

### 3.6 Investigation of Possible Interactions of VacA with STIM1

Previous work showed localization of VacA to the ER and an influence of VacA on intracellular calcium signaling in T-cells, where it disrupts store-operated calcium entry (SOCE) [155]. A closer look at ER proteins in the VCV-specific protein subset revealed the presence of classic ER markers calnexin and Sec61, indicating that ER was not generally co-purified unspecifically. Also found there were stromal interaction molecule 1 (STIM1) and the Inositol 1,4,5-trisphosphate receptor type 3 (ITPR3), both of which play an essential part in calcium signaling. Stimulation of a T-cell through the T-cell receptor results in calcium efflux from the ER into the cytosol via ITPR3. STIM1 senses the ER luminal  $\text{Ca}^{2+}$  concentration, and in the event of low calcium initiates calcium influx from the extracellular milieu through activation of Orai1, a SOCE channel [156]. The presence of STIM1 and ITPR3 in the VCV-specific subset provides additional evidence of an involvement of VacA in calcium signaling. Due to its role in SOCE, STIM1 seemed a likely candidate for VacA to interact with if VacA is transported to the ER and interferes with calcium signaling there. STIM1 (Figure 14) possesses an ER luminal EF hand domain, a helix-loop-helix motif common in calcium binding proteins which enables STIM1 to sense the ER luminal  $\text{Ca}^{2+}$  concentration [156]. Another important feature is a region termed CAD ( $\text{Ca}^{2+}$  release-activated  $\text{Ca}^{2+}$  activation domain, [157]) or SOAR (STIM-Orai activating

region, [158]), necessary for STIM1's interaction with and activation of the SOCE channel Orai1. As both the EF hand and the CAD/SOAR region seem plausible sites for VacA to bind when interfering with SOCE, potential interactions of VacA with STIM1 were investigated via pull-down experiments (see 2.2.12).



**Figure 14: Investigation of a possible VacA-STIM1 interaction.**

(A) Schematic representation of STIM1 residing in the ER membrane. The cytoplasmic part of STIM1 contains a domain called CAD/SOAR, which interacts with and activates Orai1, a calcium channel protein in the plasma membrane. The ER luminal part of STIM1 includes a calcium sensing EF hand domain. (B) For pull-down experiments, the cytoplasmic and ER luminal parts of STIM1 were expressed separately, omitting the transmembrane domain (TM). STIM1-Cyt and STIM1-ER were both tagged with a polyhistidine peptide and expressed in *E. coli*. (C and D) Lysates of *E. coli* expressing His-tagged STIM1 fragments were incubated with purified VacA or 'acid-activated' water (negative control samples in D) for pull-down experiments. (C) His-tagged bait proteins (His-STIM1-ER, His-STIM1-Cyt, His-GFP) were precipitated with Ni-NTA agarose and subsequently detected via Western Blotting at approx. 30, 60, and 30 kDa, respectively. VacA was unspecifically co-precipitated in all three samples, including the negative control sample which contained His-GFP instead of any STIM1 domains. (D) When the pull-down experiment was performed in the other direction, samples without VacA were used as additional negative controls. VacA was precipitated using the  $\alpha$ -VacA<sub>nat</sub> antibody and Protein G agarose. Irrespective of the presence or absence of VacA as bait, all three prey proteins were co-precipitated unspecifically. IP = immunoprecipitation (denotes protein that was specifically precipitated).

Previous attempts to immunoprecipitate native STIM1 from cell lysate had been unsuccessful (U. Jain, personal communication), presumably due to its transmembrane domain being difficult to solubilize. For this reason, a different approach was devised to express STIM1 recombinantly, separated into its cytoplasmic and ER luminal parts and omitting the transmembrane domain (Figure 14A and B). The ER luminal part contains the EF hand domain, while the cytoplasmic part contains the CAD/SOAR region. Both parts were cloned into pET28a(+), equipping them with polyhistidine-tags for easier purification and detection. An identically tagged truncated GFP (GFP1-10; [146]) expressed from the same plasmid backbone was used as a control for unspecific interactions. Lysates of *E. coli* expressing the 6xHis-tagged proteins were incubated with VacA to allow protein interactions to develop. Interactions were tested in both directions. First, the 6xHis-tagged proteins were used as bait, precipitating them with Ni-NTA agarose and then testing for co-precipitated VacA in a Western Blot (Figure 14C). VacA was detected in all three samples, indicating an unspecific interaction. Reciprocally, VacA was precipitated as bait with  $\alpha$ -VacA<sub>nat</sub> and Protein G agarose. Samples without VacA were handled the same way and served as additional negative controls. After the pull-down, the 6xHis-tagged proteins were detected via Western Blot (see Figure 14D). For each 6xHis-tagged protein (STIM1-ER, STIM1-Cyt, GFP), the signal in the  $\alpha$ -His blot is of comparative strength in samples with and without VacA, again suggesting unspecific interactions. In conclusion, interactions of VacA and the two parts of STIM1 could be neither shown nor refuted in this assay.

### 3.7 VacA Localization in Intoxicated Cells

#### 3.7.1 Colocalization of VacA with ER and Golgi Apparatus Markers and CTxB

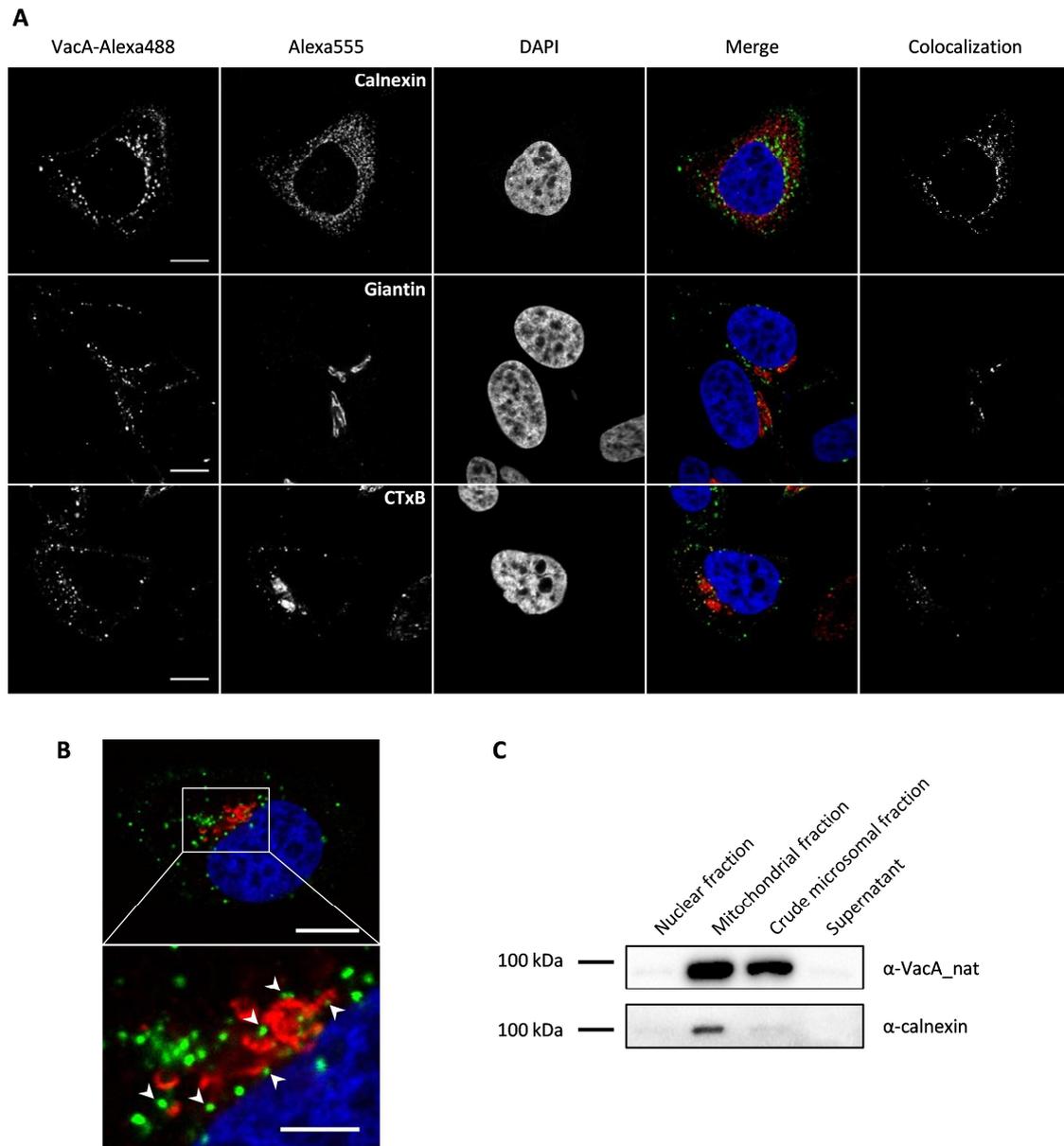
Late trafficking of VacA inside intoxicated cells is not very well-researched. VacA is taken up into endocytic compartments that were shown to be GEECs (GIP-AP-enriched early endosomal compartments, [96]) and is then routed through early and late endosomes, finally reaching compartments carrying both endosomal and lysosomal markers [45,44], but avoiding degradation [46]. After four hours, VacA is found in vesicles scattered throughout the cytosol (Figure 15A, first column), which become enlarged VCVs in the presence of weak bases [159]. VacA is also known to localize to mitochondria, more specifically to the inner mitochondrial membrane [103–105], and it may to be transported there via VCVs [106]. However, a

localization of VacA to other intracellular compartments has not yet been reported. Evidence of VacA involvement in intracellular calcium signaling suggested a possible trafficking of VacA to the ER, which was investigated in immunostaining experiments (see 2.2.13). HeLa cells were intoxicated with VacA-Alexa488, fixed, permeabilized, and stained for the ER marker calnexin or the Golgi apparatus marker giantin. In a similar setup, cells were intoxicated simultaneously with Alexa-labeled cholera toxin subunit B (CTxB-Alexa555). Although its uptake differs from that of VacA [96,160], CTxB is transported via the retrograde endocytic pathway to the Golgi [161], and might therefore provide an interesting comparison. DAPI staining of cell nuclei served as a general indicator of cell health. The results are shown in Figure 15A. In all three instances, VacA and the marker protein exhibit partial colocalization, suggesting that at least part of the internalized VacA localizes to the ER and the Golgi apparatus, respectively. Colocalization of VacA and CTxB not only in the large area representing the Golgi implies similarities in the transport of both toxins, but this may only be the case for CTxB that has not yet reached its final destination.

Interestingly, a substantial amount of VacA was found to localize in compartments closely associated with the Golgi apparatus (Figure 15B). These compartments may represent VacA being transported to or from the Golgi, possibly on its way to the ER via retrograde trafficking.

### 3.7.2 Isolation of Endoplasmic Reticulum

Another approach to verify whether VacA indeed localizes to the ER was to purify ER from VacA-intoxicated cells. Jurkat E6-1 cells were intoxicated with VacA for 4 h, homogenized, and subjected to sequential centrifugation (see 2.2.22). This resulted in a nuclear fraction, a mitochondrial fraction, and a crude microsomal fraction expected to contain the ER. All fractions were analyzed for the presence of VacA and the ER marker calnexin by immunoblotting (Figure 15C). Calnexin was found mostly in the mitochondrial fraction, indicating that the protocol needs to be optimized for this specific purpose. However, mitochondria and the ER are known to associate (reviewed in [162]), and the presence of VacA in both the mitochondrial and crude microsomal fractions supports the notion that at least some toxin localizes to the ER.



**Figure 15: VacA localization in intoxicated cells.**

(A) Localization of VacA in HeLa cells was examined after 4 h of intoxication in comparison to ER marker calnexin, Golgi apparatus marker giantin, and cholera toxin subunit B (CTxB). Colocalization was observed in all three cases to varying degrees (last column of images). Images were obtained with a confocal microscope. Scale bars represent 10  $\mu\text{m}$ . (B) This panel shows a detailed view of the Golgi apparatus (red) and numerous VacA signals (green) in close association. White arrowheads identify putative Golgi-associated vesicles. Scale bars represent 10  $\mu\text{m}$  in overview image and 5  $\mu\text{m}$  in close-up. (C) Jurkat E6-1 cells were intoxicated with VacA (4 h) and subjected to an ER purification protocol. Fractions were analyzed by Western Blotting for the presence of VacA and calnexin. For nuclear and mitochondrial fractions, 20% of the total sample were applied to the gel, but only 10% of the crude microsomal fraction and 9.5% of the supernatant, due to volume constraints.



## 4 Discussion

The namesake cellular effect of intoxication with *Helicobacter pylori* vacuolating cytotoxin VacA is the formation of large cytoplasmic vacuoles [38,39]. Until now, the function of these vacuoles is not known. They arise from endocytic vesicles containing VacA channels in their limiting membrane, which allow the influx of chloride ions, causing acidification and subsequent osmotic swelling of the vesicles [27]. VacA also exerts a variety of other effects on intoxicated cells, including the induction of apoptosis, the inhibition of T-cell activation and proliferation, and interference with intracellular calcium signaling (see sections 1.5.1, 1.5.2, and 1.5.4 for details). All of these depend on VacA channel forming activity [92]. Whether vacuolation is only a by-product of VacA channel formation, or whether it is its own effect, remains to be elucidated. In this study, VacA-containing vacuoles (VCVs) were isolated and their proteome was analyzed by mass spectrometry. This revealed information about the vacuoles' specific protein content and may help understand their purpose. Another part of this study further investigated VacA involvement in calcium signaling. Moreover, additional possible cellular target structures of VacA, besides vacuoles and mitochondria, were investigated.

### 4.1 VCV Isolation Strategies and Tools

The bulk of research investigating pathogen-induced vacuoles naturally focuses on vacuoles containing the pathogen. In those cases, purification methods often rely on density gradient centrifugation to separate pathogen-containing vacuoles (PCVs) from other cellular organelles. The difficulty in this technique is to overcome the similarity of PCVs and other organelles regarding their density, often requiring multiple centrifugation steps. This can be addressed by adding an immunological step to specifically target vacuoles, as done by the group of Hubert Hilbi for the isolation of *Legionella*-containing vacuoles [151]. Another challenge is the fact that PCVs interact with other organelles, leading to PCV preparations with considerable impurities [163]. The purity of isolated fractions is commonly monitored by electron microscopy, a method that was not available for this study but which may help evaluate VCV preparations in future experiments.

Other researchers have published PCV proteomes containing anywhere between 140 to 2400 proteins. The large differences in numbers can be attributed to the varying species of pathogens

and of host cells used for the isolation experiments, and importantly, the sensitivity of the MS technology. A comparison of protein numbers between different systems is therefore not advisable (all this is reviewed in [164]).

In this study, three different strategies were devised for VCV purification. Strategy A consisted of nanoscale magnetic beads called TurboBeads coupled to VacA monomers (see 3.4.2.3). After uptake of bead-bound VacA and vacuolation, the cells were to be homogenized and the vacuoles isolated with the help of a magnet. The main reason why this strategy was abandoned was the tendency of the beads to aggregate, preventing natural uptake (see Figure 8D). This problem was approached by using several different coating substances, but could not be solved. Other researchers have noted it to be an effect of the high specific surface energy of nanoparticles, making their use in biological settings difficult [165]. Recently, the TurboBeads manufacturer released new, polyethylene glycol (PEG) coated beads, specifically recommended for biomedical applications. These may be helpful in future experiments.

Strategy B was to sort VCVs from cell homogenate via flow cytometry (see 3.4.4). A cell line stably transfected to produce the fluorescent VCV marker EGFP-Rab7 [43] (see below) and intoxication with Alexa-labeled VacA provided the necessary characteristics for sorting, since only VCVs were expected to carry both EGFP and Alexa fluorophores. However, VCVs are apparently not stable enough to withstand the physical strain of flow cytometry (see Figure 10), even though the sorting conditions were adjusted to make the process as gentle as possible. This strategy was expected to yield VCV preparations with the highest purity and is still worth pursuing for similar applications.

VCVs were eventually successfully purified immunomagnetically, adapting strategy C from a protocol published by the group of Hubert Hilbi for the isolation of *Legionella*-containing vacuoles (LCVs) [151]. To this end, two indispensable tools were established. The first is a polyclonal antiserum which was shown to recognize VacA in its native conformation by native immunoblotting, functional inhibition of VacA-induced vacuolation, and immunostaining in this study (see section 3.2 and Figure 4). It was also used in pull-down experiments investigating possible protein-protein interactions of VacA (see 3.6). The antiserum was conclusively shown to be suitable for VCV purification. The second tool is the Jurkat T-cell line Jurkat E6-1 EGFP-Rab7, which stably expresses an EGFP-Rab7 fusion protein (see 3.3). Rab7 is a late endosomal protein that lines VCV membranes [43] and it served as a VCV marker to monitor the vacuole purification process (see Figure 5 and Figure 11). This way, it was possible to follow the distribution of VCVs through the successive steps of purification. In conclusion, these two tools laid the foundation for immunomagnetic VCV isolation.

The immunomagnetic method for VCV purification has one considerable flaw in that VacA is not exclusively situated on the VCV membrane, but is also for example still bound to the cytoplasmic membrane (see Figure 9A). This is in contrast to the original *Legionella* protocol, which uses a bacterial effector protein exclusively present on the LCV membrane as target. An appropriate control consisting of cells treated with mutant VacA was used to address this factor. This mutant VacA $\Delta$ 6-27 lacks 22 aa in its N-terminus which are necessary for proper channel formation and therefore vacuolation, although cellular uptake still happens [70]. Treatment of cells with this mutant toxin and their subjection to the VCV isolation protocol was expected to yield a purified fraction containing regular endocytic vesicles unaltered by VacA channel activity, and of course the aforementioned cytoplasmic membrane and other cell parts binding VacA. It was also expected to contain proteins unspecifically purified by the method, for instance proteins or cell parts that bind to the magnetic beads. This sample served as a valuable background control for the mass spectrometric analysis of VCVs (see 3.5).

## 4.2 The VCV Proteome

One past publication has reported an attempt to characterize the protein composition of VacA-containing vesicles by purifying them [45]. This publication, like this study, reasoned that determining the vacuolar protein content would help to find intracellular targets of VacA and to understand the details of VacA intoxication. The researchers showed that VacA intoxication causes a redistribution of markers of the endocytic network, specifically the recruitment to VCVs of the late endosomal marker Rab7 and the lysosomal marker Lamp2 and the absence of the late endosomal marker CI-M6PR. This was the first indication of VCVs being endo-lysosomal hybrid compartments. Due to the methods used, however, the analysis was constricted to checking for the presence of individual proteins. The present study for the first time performed a comprehensive investigation of the total VCV proteome by mass spectrometric (MS) analysis, seeking to find not only proteins that can be expected on an endocytic compartment, but various proteins involved in VacA intoxication effects.

### 4.2.1 VCV Analysis by MS - Strengths and Weaknesses

Two biological replicates of purified VCVs resulting from intoxication with wild-type VacA were measured. The results showed high variations between samples, with the first (WT1) returning 2078 protein hits and the second (WT2) returning 1754 (see Figure 12). The two

samples overlapped for 1123 proteins, clearly showing success, but also hinting that the analysis has to be performed several times, and only proteins found every time should be regarded as definite hits. The numbers are comparable to the results reported for *Legionella*-containing vacuoles (LCVs) purified with the same method, and analyzed on the same mass spectrometry platform. Around 1000-2000 host and *Legionella* proteins were identified, occurring once, twice, or in all three preparations that were examined [166,152]. As a background control for VCV purification, cells were treated with inactive mutant VacA $\Delta$ 6-27, which still binds to cells and is internalized, but does not cause vacuolation [70]. Subjecting this sample to the VCV isolation protocol should purify anything that unspecifically co-purifies with this method and any VacA-carrying cellular compartments that aren't vacuoles, for instance plasma membrane. The background sample contained 1606 proteins, indicating that the purity of the isolated VCV fraction is suboptimal. The researchers working on LCVs did not report the performance of a similar control experiment, precluding a direct comparison of preparation purity. However, subtraction of the proteins found in the background sample from the wild-type protein sets solves this problem. Considering only the proteins found in both wild-type samples (1123) and subtracting those found also in the background sample (883) leaves 240 proteins in the VCV-specific subset which was used for further interpretation (see Figure 12).

It has to be noted that this method is not quantitative and therefore does not permit inferences about the amount of any particular protein present in a sample. Also, there was no possibility to validate protein hits. The original protocol [151] intends immunofluorescence staining to confirm the presence of individual proteins on isolated, fixed vacuoles. This setup allows looking for colocalization of a target protein with the vacuole membrane marker, in the case of this study, EGFP-Rab7. Unfortunately, due to problems with fixation, this could not be done in intact VacA-intoxicated cells or isolated VCVs (see 3.4.2.3 and Figure 7D). None of the fixation reagents and protocols that were tried could preserve VCV membrane shape, eliminating an important characteristic for the identification of VCVs. Other methods, for example immunoblotting, do not facilitate the distinction between proteins present on the vacuole membrane, within the vacuole lumen, or elsewhere in the sample. However, a method of validation is needed to verify individual hits. One possibility to do this is to use different cells for immunostaining experiments, for instance adherent cells like HeLa cells, which can be fixed in a vacuolated state, with VCVs retaining their shape (data not shown). This then of course precludes the analysis of processes specific to T-cells. Another possibility is the transfection of T-cells with plasmids coding for target proteins fused to a fluorescent protein. This is more laborious but would have the added bonus of allowing the microscopic analysis of unfixed cells.

The presence of a protein in a VCV preparation of course assumes the presence of the respective protein on VCVs. However, another possibility that has to be considered is the co-purification of compartments that VacA has already been transported to prior to cell homogenization. Since trafficking of VacA to mitochondria depends on its first 32 amino acids [103,105], the use of VacA $\Delta$ 6-27 eliminates the co-purification of mitochondria in the background control sample. In the wild-type sample, mitochondria may be co-purified, and proteins localized to mitochondria could then appear in the VCV-specific subset. In the case of possible trafficking of VacA to other, yet unknown, cellular compartments, co-purification (and detection after background subtraction) would again depend on whether the VacA N-terminus acts as a targeting sequence in each particular case. Even though the presence of a protein in a VCV preparation does not guarantee its presence on VCVs, it nevertheless provides valuable information on VacA-induced cellular processes.

#### 4.2.2 Individual Proteins Found on VCVs

Table 1 shows a list of proteins whose presence in the three MS samples is of special interest. This includes: proteins that localize to VCVs; proteins that explicitly do not localize to VCVs; proteins that are required for VacA effects; proteins that are known not to be required for VacA effects; and other proteins of significance.

All but two proteins that are known to localize to VCVs were found in all MS samples: the small GTPase (and purification tool) Rab7 [43], the lysosomal markers Lamp1 and 2 (Lamp2 is also known as Lgp110) [44,45], the vacuolar ATPase (vATPase) [52], and the membrane fusion regulators Syntaxin-7 and Vamp7 [48,27,153]. The two exceptions are Rac1, a signal transductor [47], which was found in only one wild-type and the background sample, and  $\beta$ -glucosaminidase, an LE/lysosomal enzyme [45], which was not found at all. Rab7, vATPase, Vamp7, and Rac1 are also necessary for vacuolation [49,51,50,153,47]. The fact that virtually all proteins which are definitely known to be contained in VCVs were found in the MS measurements validates the isolation technique. The most notable exception,  $\beta$ -glucosaminidase, was only reported to reside in VCVs in a single study that used baby hamster kidney cells, which could explain the disagreement. Also, most proteins known not to localize to VCVs were not detected (these proteins are marked with the comment "not on VCVs" in Table 1), showing that VCVs were successfully enriched with this method.

The MS results were also scanned for individual proteins involved in VacA cell binding and internalization. Several protein receptors for VacA have previously been identified on different

cell types, including EGFR, RPTP $\alpha/\beta$ , CD18, CD29, and Multimerin-1 [85,62,86,88,87,89]. None of these were detected in the wild-type VCV samples. In T-cells, specifically, CD18 is known to mediate internalization as part of the lymphocyte function-associated antigen 1 (LFA-1) [88]. Its absence can be explained by the following findings: LFA-1 is recycled back to the plasma membrane in Rab11-positive structures, whereas VCVs never carry Rab11 [160]. This suggests that after joint uptake, LFA-1 (and thus CD18) and VacA part ways. It is unknown when exactly this happens, but since cells were treated with VacA over night before VCV isolation, it is quite possible that differential sorting of LFA-1 and VacA has already occurred at the point of cell homogenization.

VacA uptake is known to be independent of endocytic regulators clathrin, dynamin, and caveolin [94,96]. While dynamin and caveolin were not detected in any MS samples, clathrin was found in all three, indicating a possible unspecific co-purification. Interestingly, flotillin-2, a protein that forms microdomains in the plasma membrane and associates with lipid rafts, was detected in the VCV-specific subset. It is not clear whether flotillins actively participate in a distinct type of endocytosis, or if they are cargo, but they are required for the uptake and intracellular trafficking of cholera toxin [167–169]. An implication of flotillin-2 in VacA intoxication is especially intriguing, since VacA and cholera toxin uptake are thought to differ [96,160]. On the other hand, if VacA $\Delta$ 6-27 is indeed internalized just like wild-type VacA as the literature suggests [70], the absence of flotillin-2 in the background control sample raises the question where and when exactly VacA and VacA $\Delta$ 6-27 transport start to differ.

The cytoskeletal component actin is necessary for VacA uptake and known to polymerize at early endosomes containing VacA, moving them through the cytoplasm [95,102]. Even though no association of actin with late endosomes (including VCVs) could previously be shown via microscopy [102], this does not eliminate the possibility. Cytoplasmic actin was detected in the VCV-specific subset, strongly suggesting that VCVs still associate with actin to move through the cell. CD2AP, which was shown to bridge actin structures and endocytic vesicles [102], was not found in any of the MS samples. Its function could however simply be fulfilled by a different docking protein.

Other proteins involved in endocytic processes that have been investigated with regard to VacA uptake include: tubulin; the small GTPases Cdc42, Arf6, and RhoA; the RhoA-regulated kinases ROCK and MLCK; several members of the protein kinase C family (PKC); the protease calpain; and phosphoinositide 3-kinase (PI3K). Of these, calpain, PKC, and Cdc42 are required for VacA uptake [160,96]. All three were detected in at least one wild-type sample; Cdc42 is even in the VCV-specific subset. Again, as in the case of flotillin-2, the exact differences of VacA and

VacA $\Delta$ 6-27 uptake and transport need to be clarified. The others were found to have no influence on VacA internalization [160,96]. Some of the aforementioned proteins were not detected by MS at all (ROCK, MLCK), while another was found in all samples (RhoA), all in agreement with the fact that these proteins don't play a role in VCV formation. Of interest are PI3K and Arf6, both of which occur in one wild-type sample, but not in the background. This suggests a possible VCV specificity that needs to be verified in future experiments. Although PI3K is not required for VacA uptake, its inhibition resulted in a slight reduction in VacA internalization [160]. Both PI3K and Arf6 play a role in intracellular trafficking [170,171], which makes them appealing possible targets for VacA.

Regarding VacA-induced apoptosis, the mass spectrometry results reveal two out of three known mitochondrial effector proteins in the VCV-specific sample. The dynamin-related protein Drp1 and the multi-domain pro-apoptotic factors Bak and Bax are activated by VacA intoxication, leading to mitochondrial fission and cytochrome c release via two separate mechanisms, and eventually, to apoptosis [110,106]. Bax is recruited to mitochondria via early endosomes containing VacA, but was not found in late endosomes [106], consistent with its absence in MS samples. VacA also causes mitochondrial recruitment of Drp1, and the presence of Drp1 in the VCV-specific protein subset suggests that this may also happen via VacA-containing vesicles. Bak, however, is naturally already located in mitochondria, and its endosomal localization was not observed by Calore and coworkers [106]. It is conceivable that their methods were not as sensitive as mass spectrometry, or that the investigated time points differed, as Bak was detected in the VCV-specific subset, clearly showing its presence on VCVs and making it an intriguing candidate for further inspection. Another regulator of mitochondrial fission, MTFR1 [172], was found in the VCV-specific subset, further substantiating the connection between VacA intoxication, mitochondrial fission, and the mitochondrial apoptosis pathway.

As previous reports and research conducted during the course of this study demonstrated an influence of VacA on intracellular calcium signaling [139,120,140,119,155], the MS results lists were also scanned for proteins involved in this process. Calcineurin, a phosphatase important in T-cell activation and reported to be inhibited during VacA intoxication [119,120], was not detected in any of the samples. This is unsurprising because it is a cytoplasmic protein, and a direct interaction with VacA was never shown. Two very interesting proteins found in the VCV-specific subset are STIM1 and ITPR3. Both usually locate to the ER and are essential in T-cell calcium signaling (reviewed in [141,156]). Their significance will be discussed in detail in

section 4.3, but the discovery of these two proteins in the VCV-specific subset further corroborates VacA's role in calcium signaling.

**Table 1: List of individual proteins of interest and their presence in wild-type or background MS samples.**

This table groups proteins that have been investigated regarding in four VacA-related aspects: presence in/on VCVs and involvement in vacuolation; VacA binding to cells and internalization; VacA effects on mitochondria and Ca<sup>2+</sup> signaling; and colocalization or direct interaction with VacA. Detection of each protein in WT1, WT2, and BG MS samples is indicated with + (present) or – (absent). Proteins detected in the VCV-specific subset are shaded red, while possibly VCV-specific proteins (detected in one WT sample but not in the BG sample) are shaded orange. Proteins that occurred in all samples are highlighted in blue, and proteins found unspecifically or not at all are highlighted in green.

Protein	Function	Comment	Reference	WT1	WT2	BG
<b>VCV localization and vacuolation</b>						
Lamp1	Lysosomal marker	On VCVs	[44]	+	+	+
Lamp2 (Lgp110)	Lysosomal protein	On VCVs	[45]	+	+	+
Syntaxin7	SNARE	On VCVs	[27]	+	+	+
Rab7	Small GTPase; LE marker	On VCVs; necessary for vacuolation; necessary for redistribution of LE compartments	[43,49,44]	+	+	+
V-ATPase	Vacuolar ATPase	On VCVs; necessary for vacuolation	[52,51,50]	+	+	+
Vamp7	SNARE	On VCVs; necessary for vacuolation; interacts with syntaxin7 more when VacA present	[153]	+	+	+
Rac1	Small GTPase	On VCVs, necessary for vacuolation; necessary for VacA uptake	[47,160,96]	+	–	+
β-glucosaminidase	Lysosomal and LE marker	In VCVs	[45]	–	–	–
Cathepsin B	Lysosomal marker	Not on VCVs	[45]	–	–	–
CI-M6PR	Trans-Golgi and LE marker	Not on VCVs	[45]	–	+	–
Caveolin	Lipid raft endocytic marker	Not on VCVs	[96]	–	–	–
Rab5	Small GTPase; EE marker	Not on late VCVs but on early compartments (after GEECs)	[96]	+	+	+
Rab9	Small GTPase; LE-Golgi transport	Not influenced by VacA-induced endosomal redistribution	[173,44]	–	+	+
<b>VacA binding to cells and VacA uptake</b>						
EGFR	Receptor	VacA receptor on HeLa cells	[85]	–	–	–
RPTPα	Receptor	VacA receptor on kidney cells	[62]	–	–	–
RPTPβ	Receptor	VacA receptor on stomach cells	[86]	–	–	–
CD18	Integrin β <sub>2</sub>	VacA receptor on T-cells	[88]	–	–	+
CD29	Integrin β <sub>1</sub>	Complemental VacA receptor on epithelial cells	[87]	–	–	+
Multimerin-1	Unclear	VacA receptor on platelet cells	[89]	–	–	–
Actin	Cytoskeleton	Necessary for VacA uptake and endosome tails	[160,95,102]	+	+	–
Calpain	Protease	Necessary for LFA-1 clustering and VacA uptake	[160]	+	–	–
PKC (various)	T-cell activation	Necessary for VacA uptake	[160]	+	+	+

Protein	Function	Comment	Reference	WT1	WT2	BG
Cdc42	Small GTPase	Necessary for VacA uptake	[160,96]	+	+	-
CD2AP	Cytoskeleton	Required for VacA transfer from GEECs to EE	[102]	-	-	-
Tubulin	Cytoskeleton	Not necessary for VacA uptake	[160]	+	+	+
Clathrin	Clathrin-dependent endocytosis	Not necessary for VacA uptake	[160,94]	+	+	+
Dynamin	Clathrin-dependent endocytosis	Not necessary for VacA uptake	[160,94]	-	-	-
PI3K	T-cell activation	Not necessary for VacA uptake (small effect)	[160]	-	+	-
RhoA	Small GTPase; cytoskeletal dynamics	Not necessary for VacA uptake	[160]	+	+	+
ROCK	RhoA-regulated kinase	Not necessary for VacA uptake	[160]	-	-	-
MLCK	RhoA-regulated kinase	Not necessary for VacA uptake	[160]	-	-	-
Arf6	Small GTPase	Not necessary for VacA uptake	[96]	+	-	-
<b>Mitochondrial and Ca<sup>2+</sup> signaling effects</b>						
Drp1	Mitochondrial fission	Recruited and activated by VacA	[110]	+	+	-
MTRF1 (CHPPR)	Mitochondrial fission			+	+	-
Bax	Apoptosis	Activated by VacA; recruited to mitochondria via VacA-EE	[154,106]	-	-	-
Bak	Apoptosis	Activated by VacA	[154]	+	+	-
Calcineurin	Ca <sup>2+</sup> -dependent phosphatase	VacA blocks T-cell proliferation here	[119]	-	-	-
Orai1	SOCE channel	VacA does not colocalize with Orai1	[155]	-	-	-
STIM1	SOCE sensor	VacA blocks STIM1 clustering; VacA colocalizes with STIM1	[155]	+	+	-
ITPR3 (IP3R)	ER Ca <sup>2+</sup> channel			+	+	-
<b>Colocalization or interaction with VacA</b>						
Sec61 $\alpha$	ER protein translocator	VacA colocalizes with Sec61	[155]	+	+	-
Calnexin	ER marker	Partial colocalization with VacA	This study	+	+	-
Giantin (GOLGB1)	Golgi marker	Partial colocalization with VacA	This study	+	+	+
Rack1 (GNB2L1)	Signaling protein, interacts with PKC and SRC kinases	Interacts with VacA in Y2H and pull-downs	[174]	+	+	+
Fibronectin	Extracellular matrix, binds to integrins	interacts with VacA in vitro	[90]	-	-	+
Vip54	Putative filament	interacts with VacA in Y2H and pull-downs	[175]	-	-	-
<b>Vacuole-mitochondria contact (vCLAMPs) in yeast</b>						
Vps39 (Vam6)	Vacuolar fusion; vCLAMP formation		[176-178]	+	+	-
Vam7 (SNAP25 homolog)	Vacuolar fusion		[179,177]	-	-	-
Mnr2	Mg <sup>2+</sup> transporter; localizes to vCLAMP		[180,177]	-	-	-
Pho91	Phosphate transporter; localizes to vCLAMP		[181,177]	-	-	-
Ypt7	Small GTPase; vCLAMP formation		[178]	-	-	-

Three proteins were reported to interact with VacA directly in biochemical assays *in vitro*: the receptor for activated C kinase 1 Rack1 [174]; the extracellular matrix component fibronectin [90]; and a putative filament protein termed Vip54 [175].

Rack1, also known as GNB2L1, interacts with multiple cellular targets, including PKC and Src kinases and the integrin subunits CD18 and CD29 [182–184]. Its additional capacity to bind VacA is thus especially intriguing. It was detected in all three MS samples, possibly implying unspecific co-purification, but in the light of its proven interaction with VacA, this seems unlikely. GNB2L1 modifies both PKC and Src activity, activating the first and inhibiting the latter [182,183]. Albeit indirectly, this connects VacA with CagA phosphorylation by these two kinases. GNB2L1 interaction with CD18 and CD29, on the other hand, is interesting because both are known receptors for VacA. Upon VacA binding to the extracellular integrin domains, GNB2L1 may trigger intracellular signaling cascades that cause VacA effects. It is however unclear at which point GNB2L1 and VacA interact with each other, since they should be located at opposing sides of the cellular or endocytic membrane. Cytoplasmic localization of VacA via outer membrane vesicle delivery [185,186] or after endosome escape may be a way for the two proteins to come into direct contact. The same is true for the phosphatase calcineurin mentioned above.

Fibronectin was unsurprisingly not found in the wild-type VCV preparations. It is part of the extracellular matrix and therefore not expected to occur inside cells in significant amounts. Even though it directly binds VacA [90], this interaction would likely take place outside of cells, not in the context of VCVs.

Vip54 is a novel protein assumed to be an intermediate filament component on the basis of its structural characteristics and its interaction and co-distribution with known filament proteins [175]. The investigators suggest that it may mediate interactions between cytoskeletal filaments and VacA-containing endocytic compartments, but could not show the presence of Vip54 on VCVs. In accordance with this, it was also not detected in any of the MS samples. The hypothesis of VCV-filament interaction is compelling, but cannot be supported by the present evidence. Nevertheless, the interaction may occur at different points in time, or it may get lost during the physically rigorous process of VCV isolation.

The two individual proteins that remain to be discussed are the Golgi apparatus marker giantin and the ER marker calnexin. Both showed partial colocalization with VacA in intoxicated HeLa cells in immunofluorescence experiments (see 3.7.1). Colocalization may stem from three occurrences: trafficking of VacA to the respective compartment; recruitment of the marker proteins to VCVs; or very close physical contact of Golgi or ER with VCVs beyond microscopic

resolution. VacA trafficking to the Golgi apparatus or the ER will be discussed in a later section, but the latter two may also explain the presence of the marker proteins in VCV preparations. Both calnexin and giantin were detected in the wild-type MS samples. Calnexin is even contained in the VCV-specific protein subset, indicating either its presence in VCVs or VacA-induced co-purification of calnexin-carrying compartments alongside VCVs. Both of these incidents would suggest a connection between VacA/VCVs and the ER that has not been shown so far, and which will also be discussed later in the context of VacA trafficking. Giantin, on the other hand, was also found in the background sample. This means that, although unspecific co-purification cannot be ruled out, giantin may be present on VCVs. Alternatively, VacA $\Delta$ 6-27, although vacuolation-inactive, may still be transported to the Golgi and lead to the isolation of Golgi-derived compartments in the background control. Given the close proximity of VacA-containing vesicles to the Golgi apparatus observed via immunofluorescence (Figure 15B), a co-purification of Golgi-derived compartments also in wild-type samples is conceivable. Whether this happens in a VacA-dependent manner has to be investigated in future experiments. Surprisingly, the share of Golgi proteins was reduced in the VCV-specific sample compared to the background (see Figure 13). However, immunostaining experiments and VCV isolation were conducted after different periods of intoxication (4 h vs 16 h), leaving ample time for transport processes to occur, which could explain the seemingly low amount of Golgi proteins in VCVs.

#### 4.2.3 The VCV Proteome Decoded by Subcellular Localization and Biological Function

When looking at the general composition of the VCV-specific protein subset in comparison with the background sample (see Figure 13), the largest differences can be seen for nuclear and mitochondrial proteins. Nuclear proteins are enriched in the VCV-specific subset (23.1% compared to 14.9% in the background sample). A recruitment of nuclear proteins to VCVs is imaginable, but unlikely to happen in such large numbers. This is more likely to be a side-effect of the method. The disruption of nuclei during homogenization leads to the presence of sticky DNA in the sample, as was observed in the isolation process (data not shown). This DNA may then co-purify with VCVs but not with the smaller particles in the background sample, bringing along DNA-bound nuclear proteins. Using DNase during homogenization may help minimize this problem in future experiments. The reduction of mitochondrial proteins (14.3% compared to 21.4%) may be explained by a similar unspecific effect. Originally, an enrichment of mitochondrial proteins in the VCV-specific sample was anticipated, since VacA localizes to

mitochondria, and VCVs have been speculated to transport it there directly and/or interact with mitochondria [103–106].

Considering that VacA is known to alter vesicular trafficking and to change the protein content of endocytic compartments [142,44,118,45], the increase of endo- and lysosomal and signaling proteins in VCVs is as expected. The same is true for the enrichment in proteins involved in immune processes and cell death, since VacA greatly modulates the host immune response and induces apoptosis [107,108].

#### 4.2.4 Interorganellar Crosstalk between VCVs and Mitochondria/ER

Recent research, mostly conducted in yeast, has illuminated the importance of organelle-organelle contact sites for the transport of substances. Mitochondria are not connected to cellular metabolism via vesicular transport, but instead rely on direct contact with the ER for phospholipid and  $\text{Ca}^{2+}$  transport through so-called **ER-mitochondria encounter structures** (ERMES) (reviewed in [187]). Earlier this year, an additional contact site termed vCLAMP (**vacuole and mitochondria patch**) was identified, connecting mitochondria with vacuoles, the yeast lysosomal compartment [178,177]. vCLAMPs and ERMES were found to be reciprocally regulated, implying that each can restore loss of the other, and only loss of both caused lethal deficiencies in phospholipid transport. Establishment of vCLAMPs depends on Vps39, a component of the yeast vacuolar fusion process, and Ypt7, a small GTPase. The authors of these studies speculate that such contact sites may be conserved in higher eukaryotes, and Vps39 was indeed detected in the VCV-specific protein subset. While this may imply the formation of a VCV-mitochondria contact site, Ypt7 was absent in all MS samples. Also not detected were three other proteins reported to be present in vCLAMPs: Mnr2, a  $\text{Mg}^{2+}$  transporter, Pho91, a phosphate transporter, and Vam7, another vacuolar fusion contributor. VacA-containing vesicles and mitochondria have been shown to juxtapose [106], but whether this close proximity is used to form transport channels analogous to those found in yeast remains elusive. Further studies are needed to investigate putative contact sites, which can be expected to have a protein composition at least slightly different from vCLAMPs.

Similar contact sites have also been observed in cells infected with chlamydial organisms and *Legionella* [188–190]. These pathogens establish a replicative vacuole that associates closely with the ER, for example to obtain lipids necessary for bacterial growth. In the case of *Legionella*, fusion of ER vesicles with the bacterial vacuole has been reported [190]. Therefore, such contact

sites may not only serve in lipid or ion transport, but may be involved in the translocation of VacA from VCVs to mitochondria or the ER.

#### **4.2.5 VCVs as Multifunctional Platforms**

In general, the information obtained from VCV purification agrees with the literature. The sheer number of non-endocytic proteins detected specifically in VCVs strongly supports the hypothesis of VCVs having a purpose. Their identity as signaling hubs needs to be confirmed with experiments validating the presence of individual proteins on or in VCVs. An investigation of 'obvious' signaling regulators like members of the Rab superfamily [191] on VCVs proved difficult. Even though many Rab proteins were found, most are present on various compartments of the endo-membrane system and were therefore not detected specifically on VCVs. Besides signaling, some researchers are now suggesting an even bigger function for endosomes as assembly sites for molecular machinery. This has been described for instance for cytokinesis, where the abscission machinery that physically separates dividing cells is accumulated at the site of action by endocytic and secretory vesicles [143]. Observations like this have also been made for cell migration and polarity. This has led to the proposal of endosomes as specialized multi-purpose platforms, able to coordinate in space and time all the molecular actors necessary to execute such complex cellular processes [143]. If we turn this around, the proteins carried by an endocytic vesicle may offer information on the vesicle's purpose. Taken further, the protein cargo of an endocytic vesicle or a subpopulation of vesicles could therefore allow conclusions on what is happening in a cell at a given time point. In this light, the VCV proteome should be investigated from all points of view, since it could potentially give insight into all VacA-induced cellular processes. A comparison of the VCV proteome after different periods of intoxication and after intoxication with different VacA variants could also provide valuable information on this question. Proteome data confirmed by several measurements and an improved bioinformatic evaluation approach are necessary to assist in this endeavour.

### **4.3 Influence of VacA on Store-Operated Calcium Entry (SOCE)**

VacA has been reported to influence intracellular calcium signaling, severely disrupting T-cell activation and proliferation [139,120,140,119]. A possible intermediate in these processes is the  $\text{Ca}^{2+}$ -calmodulin-dependent phosphatase calcineurin [119,120], which needs sustained high intracellular calcium levels in order to function properly [141]. During the course of the present

study, the VacA-induced inhibition of ionophore-stimulated  $\text{Ca}^{2+}$  influx shown by Boncristiano and coworkers [120] was confirmed [155]. Additionally, a connection of this phenomenon with store-operated calcium entry (SOCE) was revealed. SOCE is defined as the influx of calcium into the cytosol from the extracellular milieu caused by the depletion of intracellular calcium stores, for instance the endoplasmic reticulum (ER). A main actor in this process, especially in T-cells, is the stromal interaction molecule STIM1, which localizes to the ER membrane and senses the calcium concentration in the ER lumen (see Figure 14A). Upon calcium depletion, STIM1 clusters in so-called puncta and relocates to ER-plasma membrane junctions. There, it interacts with and activates the plasma membrane-situated SOCE channel Orai1, which then opens to let  $\text{Ca}^{2+}$  into the cytosol (reviewed in [156]). The expression of both STIM1 and Orai1 is upregulated during T-cell activation [192], confirming their substantial role in this process. VacA was shown to colocalize with STIM1 and to interfere with STIM1 clustering in immunofluorescence experiments, clearly implicating VacA in SOCE inhibition [155]. This also for the first time demonstrated a possible localization of VacA to the ER. In contrast to the studies mentioned before, mutant VacA deficient in channel forming activity (VacA $\Delta$ 6-27) also showed an effect on cytoplasmic calcium concentrations, albeit less pronounced than the wild-type. Since SOCE-induced high intracellular calcium levels are required for calcineurin activity, an interference of VacA with SOCE offers a new possible explanation for calcineurin inhibition. At this point, it is not clear whether VacA effects on calcium signaling are really due to VacA channels as has been suggested [120,121], and if so, whether these channels are located in the plasma membrane or in the membrane of a cellular compartment like VacA-induced vacuoles or even the ER. Alternatively, SOCE effects may be the result of an interaction of monomeric VacA with STIM1. Irrespective of whether VacA needs to be present as a functional channel or not, the finding that the toxin is apparently transported to the ER needs to be addressed and will be discussed in the context of this present study's results in section 4.4.

The study that discovered VacA's involvement in SOCE and VacA-STIM1 colocalization also investigated a possible direct protein-protein interaction between VacA and STIM1 [155]. An interaction observed in a yeast two-hybrid (Y2H) screen was later refuted, leading to re-assessment via pull-down experiments in the present study (see 3.6). For these experiments, STIM1 was recombinantly expressed in *E. coli* in two separate parts, the cytoplasmic half and the ER luminal half. The cytoplasmic half included the CAD/SOAR domain that interacts with and activates the SOCE channel Orai1, and the ER luminal half contained the  $\text{Ca}^{2+}$ -sensing EF hand domain (see Figure 14A and B). The central transmembrane domain of STIM1 was omitted. Preceding experiments attempted but failed to precipitate STIM1 from lysate of VacA-

intoxicated kidney epithelium (HEK-293) cells, presumably because of the transmembrane domain being difficult to solubilize (U. Jain, personal communication). The two recombinantly expressed STIM1 parts were separately tested for VacA binding, but an interaction could neither be shown nor excluded. An interaction seems very likely considering VacA's colocalization with ER-situated STIM1 and its inhibition of STIM1 clustering, so several options remain to be investigated. Firstly, the interaction may be too weak to be detected with the techniques used so far. Secondly, the experimental environment, particularly the recombinant expression of STIM1 in *E. coli*, may be too different from physiological conditions to facilitate binding. This includes the possibility that the interaction may not be direct, but mediated by additional binding partners in a larger protein complex that are not present in this artificial setting. Thirdly, the interacting section of STIM1 may actually be the transmembrane domain itself. Since VacA is capable of inserting into membranes to form channels, this seems plausible. Many of these problems could be solved by pull-down experiments with VacA-intoxicated cells, but as mentioned before, this had been unsuccessful. A recent publication detailed a possible protocol for this purpose [193]. In this report, STIM1 was precipitated from both HEK-293 and Jurkat cells, revealing an interaction with thrombospondins, a family of matricellular proteins. The discovered interaction was reportedly robust, and it is not certain whether VacA and STIM1 bind as strongly. There are, of course, other methods to examine the interactions of membrane proteins, but many of them are not suitable for testing a protein like VacA. Expression of VacA in mammalian cells is difficult due to its cytotoxicity, and can also not guarantee its natural localization. This rules out experiments like mammalian membrane two-hybrid [194]. On the other hand, tagging VacA with larger fusion proteins, as would be required for techniques like fluorescence resonance energy transfer (FRET), is difficult in *H. pylori*, and might also compromise VacA activity. In these rather complex circumstances where the two proteins of interest come from two different kingdoms of life, and one of them is a cytotoxin, an experimental set-up like the HEK-293/Jurkat cell pull-down described by Duquette and coworkers [193] seems the most applicable.

Another interesting aspect in this is the link between mitochondria and cellular calcium homeostasis. Mitochondria can act as calcium buffers, taking up calcium from the cytosol if levels are high. This is the case especially at the immunological synapse and close to the ER. Ca<sup>2+</sup> release from the ER, for example during T-cell activation, leads to high local concentrations around release sites, deactivating release channels like ITPR3 as an act of self-regulation. By taking up some of this calcium, mitochondria can prolong calcium release from the ER, and reduce the amount of cytosolic calcium that is available for transport back into the ER. Together,

these effects result in a stronger activation of SOCE and a greater overall mobilization of calcium (all this is reviewed in [141]). Derogating mitochondrial buffering capacities is therefore an additional way to disrupt cellular calcium signaling and T-cell activation. This can be brought about by a reduction of the mitochondrial transmembrane potential, since this is the driving force behind mitochondrial  $\text{Ca}^{2+}$  uptake. VacA has been shown to do exactly that (Kimura 1999, Willhite 2004). Mitochondrial depolarization also diminishes STIM1 relocation to puncta at ER-plasma membrane junctions (Singaravelu 2011), which is necessary for Orai1 activation and therefore SOCE. For these reasons, it is conceivable that VacA influence on SOCE happens via binding to STIM1 or via the depolarization of mitochondria, or both. This further highlights the complexity and intricacy of the connections between mitochondrial function, calcium signaling, and VacA intoxication.

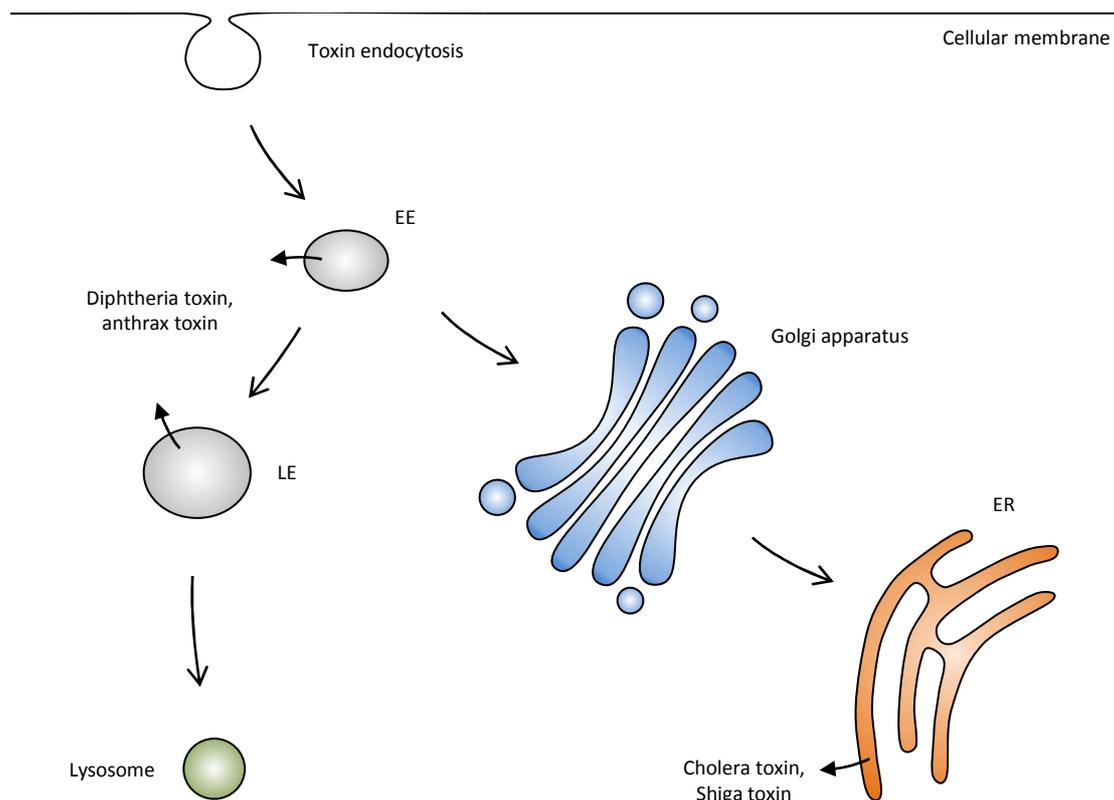
#### **4.4 VacA Partially Localizes to the ER and the Golgi Apparatus**

Immunofluorescence staining experiments were conducted in HeLa cells to analyze intracellular trafficking of VacA. Even though a substantial amount of research has focused on VacA trafficking, only a few basic points are clear (see Figure 2 and Figure 17). Shortly after endocytosis, VacA can be found in GPI-AP-enriched early endosomal compartments (GEECs), from where it is transported to Rab5-positive early endosomes and later Rab7-positive late endosomes (Gauthier 2005). After about four hours, VacA-containing compartments are distributed throughout the cytoplasm and carry endo- and lysosomal markers (Molinari 1997, Li 2004). These compartments then enlarge to become vacuoles. Whether VacA goes anywhere from here is unknown. Earlier VacA-containing vesicles acquire actin tails that confer mobility (Gauthier 2007) and come into close physical contact with mitochondria (Calore 2010), but it was not conclusively shown that this is VacA's mode of transportation. VacA does reach the inner mitochondrial membrane thanks to its hydrophobic N-terminus, which acts like a targeting sequence [103,105]. Prior to the present study, no other cellular target structures of VacA had been reported. Recently, VacA localization to the ER was shown via colocalization with STIM1 and the ER-membrane protein transporter Sec61 in immunofluorescence experiments (Jain 2013). This was confirmed in the present study by demonstrating a partial colocalization of VacA with the ER marker calnexin after four hours of intoxication (see 3.7.1 and Figure 15A). Both VacA and calnexin can be seen in vesicles scattered throughout the cytosol, with VacA being more prominent near the nucleus (Figure 15A, first row). Similarly, a

partial colocalization of VacA with the Golgi apparatus marker giantin showed for the first time that some VacA is trafficked to the Golgi (Figure 15A, second row). Since an effect of VacA on SOCE has been shown, the ER is likely to be an actual target structure of VacA. The Golgi apparatus, however, is completely uncharted territory in the context of VacA intoxication. Whether VacA localization to the Golgi has direct effects, or whether this organelle is only a transit point on the way to other destinations (see 4.5), awaits investigation. *Pseudomonas* exotoxin, for example, is activated in the Golgi apparatus, and bacterial LPS may affect cellular signaling by causing the disruption of vesicular trafficking after it accumulates in the Golgi apparatus [195,196]. But in the case of most other bacterial toxins, the Golgi is only a stop to be passed on the way to the ER, and finally, the cytoplasm.

#### 4.5 Is VacA Transported in a Retrograde Manner?

VacA has repeatedly been analyzed in comparison with classical bacterial AB toxins regarding uptake and intracellular trafficking [96,160]. AB toxins are targeted to the host cell cytosol and can reach it via two routes: one, by endosome escape, and two, via the retrograde pathway (see Figure 16) (reviewed in [197]). Escape from endosomes is usually triggered by low endosomal pH, which causes a conformational change in the toxin and its translocation across the endosomal membrane. The paradigm for this is diphtheria toxin secreted by *Corynebacterium diphtheriae* [198]. Retrograde trafficking is more complex (for a review see [197]). After endocytosis into early endosomes, the toxins are transported to the Golgi apparatus and from there to the ER, following the usual trafficking route of proteins in reverse. In a process called retro-translocation, the toxins then exploit endogenous protein transporters to cross the ER membrane into the cytosol. A direct transport of toxins from endosomes to the ER, without passing through the Golgi, has been observed, but has not entered the scientific consensus [199]. Some of these toxins, most famously Shiga toxin (released by *Shigella dysenteriae* and some *E. coli*) and cholera toxin (*Vibrio cholerae*), are very well-studied and can be used as tools to investigate the trafficking of new proteins of interest. Even though VacA is unlikely to be targeted to the host cell cytoplasm, it has been compared to AB toxins due to its structure [92]. AB toxins possess a B subunit responsible for cell binding and intracellular transport, and an A subunit conferring toxic activity [197]. In VacA, A and B subunits superficially correspond to the p33 and p55 domains, respectively, but the distinction between toxic and binding subunits is not as clear as it is for AB toxins (see 1.4.2).



**Figure 16: Internalization and trafficking of bacterial toxins.**

Bacterial toxins can reach their target, the host cell cytoplasm, via two routes: First, by escape from early or late endosomes (EE/LE) (diphtheria toxin, anthrax toxin), or second, by retrograde transport. In the latter case, toxins are transported through the Golgi apparatus and to the ER, from where they are retro-translocated into the cytoplasm (cholera toxin, Shiga toxin). Arrows with filled arrowheads symbolize translocation of toxins across membranes. Reviewed in [197].

The cell binding subunit B of cholera toxin (CTxB) was used in this study in co-intoxication experiments with VacA to gain insight into VacA trafficking pathways (see 3.7.1 and Figure 15A). Although the final destination of the toxic A subunit of cholera toxin is the ER, the subunits dissociate in the Golgi and the bulk of CTxB molecules persist there [200]. CTxB can therefore serve as a marker for retrograde trafficking up to the Golgi. The intracellular localization of both VacA and CTxB in co-intoxicated cells was analyzed by immunofluorescence in HeLa cells and compared (Figure 15A, third row). The two toxins are taken up by different mechanisms [96,160], but it is still possible that they reach the same endosome and are then both trafficked to the Golgi from there [201]. Again, the two proteins exhibited partial colocalization. The majority of CTxB localized to the Golgi apparatus close to the nucleus, where some punctiform VacA signals were also detected. This confirms the results obtained with VacA/giantin colocalization. Interestingly, the two toxins also colocalized in spots distinct from the Golgi, implying that they travel along the same route at least to some extent.

Whether these spots represent toxin on the way to the Golgi, to the ER, or to a third location needs to be explored.

Strikingly, the ER membrane protein transporter Sec61 was found specifically in the VCV proteome. It is discussed as the possible transporter system responsible for cholera toxin retro-translocation from the ER to the cytosol [202] and may therefore also be a candidate for a potential VacA retro-translocation. Further corroborating this possibility, Sec61 exhibited a limited colocalization with VacA in another study [155]. An additional intriguing detail are the VacA-containing compartments closely associated with the Golgi apparatus that were observed in the giantin colocalization experiments (Figure 15B). This resembles the juxtaposition of VacA-containing vesicles with mitochondria observed by Calore and coworkers [106]. VacA translocation from VCVs into mitochondria could happen via membrane fusion or direct membrane-to-membrane transfer, and the same is true for translocation to the Golgi. But again, it is not clear whether these compartments contain VacA on its way to or from the Golgi. A compelling possibility to examine in the future is whether VacA reaches the ER directly, without using the common route through the Golgi apparatus. Direct transport from endosomes to the ER seems unlikely, but remains possible [199]. Endosomes have been shown to form contact sites with the ER, especially as they mature [203]. This may facilitate the translocation of VacA as discussed for mitochondria and Golgi earlier. If this is the case, the Golgi apparatus and the ER may be two separate target structures of VacA (see Figure 17).

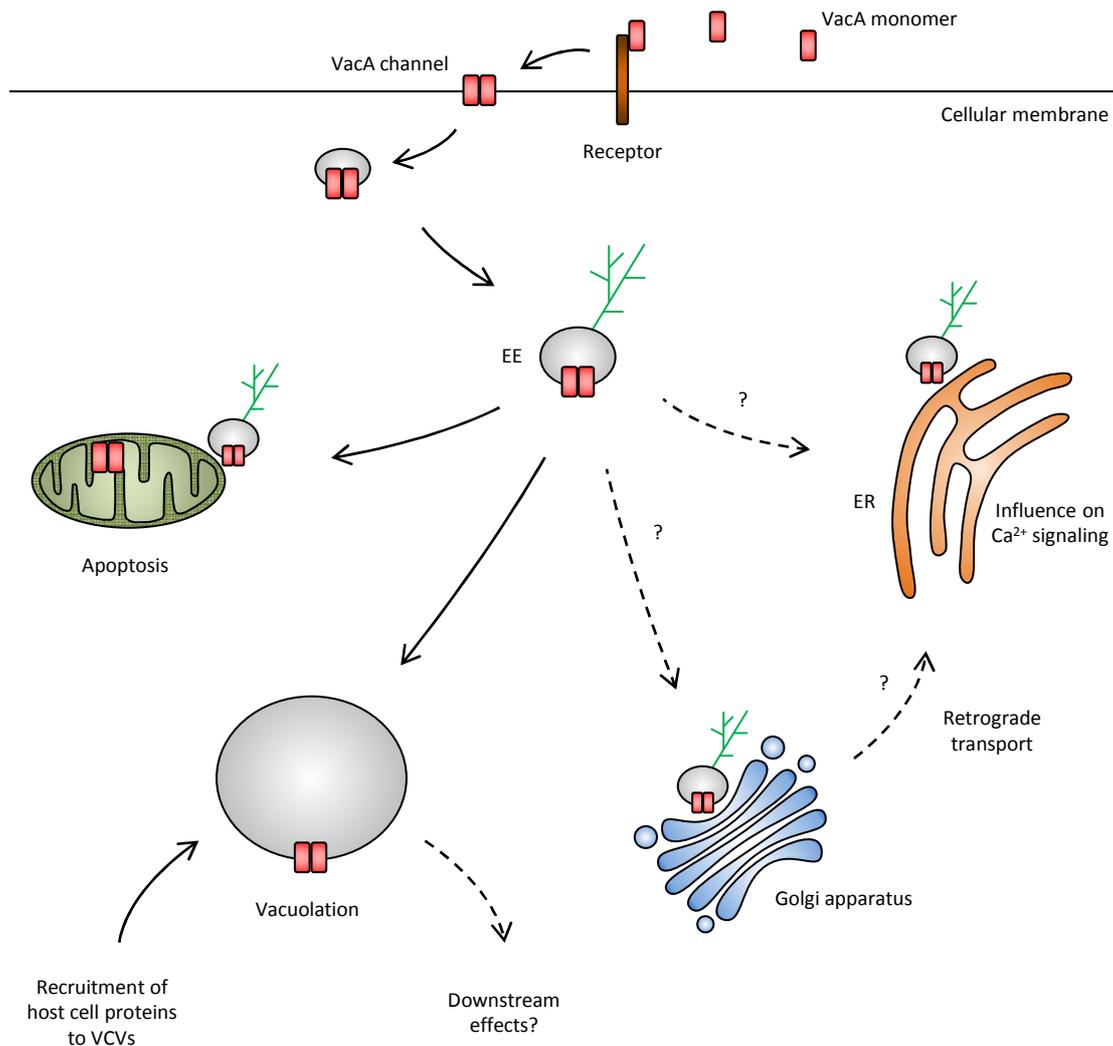
By investigating only one time point, this study focused on identifying novel VacA target structures. To fully elucidate VacA trafficking, different time points need to be analyzed, for instance using markers for different known trafficking pathways or time points. Preliminary experiments were conducted using the *Legionella* effector protein and inhibitor of retrograde trafficking RidL [204], but its presence did not seem to influence VacA localization (data not shown). This result is tentative and may be due to the small amounts of VacA that are potentially transported in a retrograde manner. Rab9, a small GTPase responsible for the transport between late endosomes and the Golgi [173], was detected by MS in one VCV preparation (see Table 1), supplying some evidence for retrograde transport.

Retrograde toxin trafficking is mediated by the transport of the respective toxin receptors. These receptors are often lipids, like the ganglioside GM1 in the case of cholera toxin [205]. VacA is known to bind many different receptor structures (see 1.4.3), including glycosphingolipids, a component of gangliosides [82]. This may account for its transport to the Golgi and the ER. Similarly, the wide variety of VacA receptors and their specific trafficking routes may explain VacA's multiple cellular targets. One way to find out whether this is the case is to use different

VacA allelic variants in experiments similar to the ones conducted for this study. The cell binding or receptor specificity conferred mostly by the p55 domain/the m-region (see 1.4.2 and 1.4.3) should then lead to a differing cellular distribution of different VacA variants. Moreover, VacA binding to different receptors may result in their crosslinking and the combinatorial activation of several internalization or signaling pathways [27].

The observation that VacA does indeed localize to the ER supports the idea that it influences intracellular calcium signaling from there (see 4.3). Interesting questions that need to be addressed are whether VacA does this as a monomeric toxin or as a hexameric channel, and whether it indeed interacts with STIM1 or instead forms pores in the ER membrane. One possibility to approach these questions is to conduct (cryo-)electron microscopy studies similar to those that gave great insight into VacA channel structure [61,58,71], but imaging fragments of intoxicated cells or their organelles instead of artificial membranes. Another possibility is stimulated emission depletion (STED) fluorescence microscopy, which brings the microscopic resolution down to 20 nm [206]. While this may not be sufficient to resolve VacA channel structure, it may still be precise enough to distinguish between VacA monomers and hexamers. To this end, it may be necessary to label VacA p33 and p55 with different fluorophores. This can be accomplished by expressing them separately in *E. coli* and mixing them to restore VacA activity before cell intoxication [65].

Performing the colocalization immunofluorescence experiments with mutant VacA $\Delta$ 6-27 as a control could be illuminating in two respects: First, it could give some hints as to whether channel formation is essential for VacA trafficking. Second, the VacA N-terminus acts as a targeting sequence for the transport to mitochondria [103,105]. There is evidence that some targeting sequences can facilitate so-called dual targeting to more than one cellular compartment [207], and it is conceivable that this is also the case for VacA. Analyzing the trafficking of mutant VacA lacking this sequence may therefore shed light on transport processes to various compartments. Isolation of ER, Golgi apparatus, or other organelles as tested briefly during this study (see 3.7.2), may also be useful to complement immunofluorescence experiments.



**Figure 17: VacA uptake, intracellular trafficking, and effects, continued.**

This diagram again presents what is known about VacA internalization and intracellular transport, as shown in Figure 2, integrated with the findings of this study. VacA is taken up into early endosomes (EE) which acquire an actin tail (depicted in green) that drives them through the cytoplasm. This may facilitate VacA transport to mitochondria, and possibly, the ER and the Golgi apparatus, where VacA was shown to localize for the first time. In which order VacA travels through these compartments and vacuoles is still unclear. The VCV proteome showed an enrichment in certain cellular proteins, supporting the notion of a VCV purpose.

## 4.6 Conclusion and Outlook

The present study attempted for the first time a comprehensive analysis of the complete proteome of VacA-containing vacuoles to find out whether VCVs are only a by-product of VacA intoxication, or whether they have a purpose. The evident existence of a VCV proteome which consists not only of endosomal proteins clearly indicates a purpose for VCVs, and the exact nature of this purpose is an intriguing subject for further study. An important part of this

will be the validation of the presence of individual proteins on VCVs with special focus on VCVs as putative signaling platforms. Numerous proteins involved in known VacA intoxication effects were detected in VCV preparations, and their validation will strengthen the connections between VacA effects and their underlying cellular pathways. Of particular interest are proteins that are implicated in cellular calcium homeostasis (including STIM1 and ITPR3), the mitochondrial apoptotic pathway (including Drp1 and Bak), and intracellular signaling and trafficking processes (including Rack1/GNB2L1 and Rab superfamily proteins), which may all contribute to immune modulation by VacA. VCV proteome analysis may therefore also prove to be a valuable tool to interconnect existing knowledge about VacA and its effects.

Additionally, the Golgi apparatus and the ER were identified as novel VacA target structures. The retrograde pathway is an obvious candidate for VacA transport to these compartments, analogous to the trafficking of other bacterial toxins. However, other routes, including direct endosome-ER transport, cannot yet be dismissed. In general, there are many details of VacA trafficking left to discover (see Figure 17). This encompasses the potential dependence of VacA transport on its N-terminus, and the matter of sequence: is VacA transported to all other compartments, including VCVs, from early endosomes? Or are vacuoles an intermediate step not only with regard to VacA function, but also with regard to transport? Also, which effects are caused by the trafficking of VacA to the Golgi and the ER? Does the toxin persist there, or is the cytoplasm its final target? And which effects are instead caused by the recruitment of cellular proteins to VCVs? All of these questions provide extensive potential for future investigations.

## 5 List of Abbreviations

\* Denotes the addition of protease inhibitors to a buffer

$\alpha$ -	Anti-
$\Delta$	Delta ( <i>deletion</i> )
6xHis-tag	Polyhistidine-tag
aa	Amino acid(s)
BB	Brucella broth
BSA	Bovine serum albumin
CMC	N-cyclohexyl-N'-(2-morpholinoethyl) carbodiimide metho-p-toluenesulfonate
CTxB	Cholera toxin subunit B
DAPI	4',6-diamidino-2-phenylindole
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
dNTP	Deoxyribonucleotide
EDC	1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
EDTA	Ethylenediaminetetraacetic acid
EGFP	Enhanced green fluorescent protein
ER	Endoplasmic reticulum
FACS	Fluorescence-activated cell sorting
FCS	Fetal calf serum
FP	Forward primer
g	Gravitational force
G418	Geneticin
GEBS	Glycerol EDTA bromphenol blue sarkosyl buffer
GFP	Green fluorescent protein
His	Histidine; polyhistidine-tag
Hpy	<i>Helicobacter pylori</i>
ID	Identifier
IEB	Isotonic extraction buffer
IgG	Immunoglobulin G
IL	Interleukin

## List of Abbreviations

IPTG	Isopropyl-1-thio- $\beta$ -D-galactopyranoside
kDa	Kilodalton
LB	Luria-Bertani/lysogeny broth
MES	2-(4-morpholino)ethanesulphonic acid hydrate
MWCO	Molecular weight cut-off
NHS	N-hydroxysuccinimide
NP-40	Nonyl-phenoxy polyethoxy ethanol
OD <sub>550</sub>	Optical density at a wavelength of 550 nm
PBS	Phosphate-buffered saline
PCR	Polymerase chain reaction
PFA	Paraformaldehyde
PMSF	Phenylmethylsulfonyl fluoride
POX	Horseradish peroxidase
PVDF	Polyvinylidene fluoride
RIPA	Radioimmunoprecipitation assay buffer
RP	Reverse primer
rpm	Rotations per minute
RT	Room temperature
SDS	Sodium dodecyl sulfate / sodium lauryl sulfate
SDS-PAGE	SDS polyacrylamide gel electrophoresis
ssDNA	Single-stranded DNA
TAE	Tris base acetic acid EDTA buffer
TBS	Tris-buffered saline
TCR	T-cell receptor
Tris	Tris(hydroxymethyl)aminomethane
U	Enzyme unit
VacA	Vacuolating cytotoxin A
VCV	VacA-containing vacuole
WT	Wild-type
Y2H	Yeast two-hybrid

## 6 Appendix

### 6.1 VCV-specific proteins

**Table 2: Proteins contained in the VCV-specific subset of mass spectrometry measurements (see 3.5). Listed are gene names, protein names, and UniProt accession numbers.**

Gene	Protein name	Accession
ACAA2	3-ketoacyl-CoA thiolase, mitochondrial	P42765
ACADSB	Short/branched chain specific acyl-CoA dehydrogenase, mitochondrial	P45954
ACO2	Aconitate hydratase, mitochondrial	Q99798
ACTB	Actin, cytoplasmic 1	P60709
ACTG1	Actin, cytoplasmic 2	P63261
ACTN1	Alpha-actinin-1	P12814
ADCK3	Chaperone activity of bc1 complex-like, mitochondrial	Q8NI60
AGPAT5	1-acyl-sn-glycerol-3-phosphate acyltransferase epsilon	Q9NUQ2
ALDOA	Fructose-bisphosphate aldolase A	P04075
ALOX5AP	Arachidonate 5-lipoxygenase-activating protein	P20292
ANP32E	Acidic leucine-rich nuclear phosphoprotein 32 family member E	Q9BTT0
ANXA11	Annexin A11	P50995
ARHGDIB	Rho GDP-dissociation inhibitor 2	P52566
ATP1B3	Sodium/potassium-transporting ATPase subunit beta-3	P54709
ATP5F1	ATP synthase F(0) complex subunit B1, mitochondrial	P24539
ATP6AP2	Renin receptor	O75787
ATP6V1C1	V-type proton ATPase subunit C 1	P21283
ATP6V1E1	V-type proton ATPase subunit E 1	P36543
B3GAT3	Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3	O94766
BAG2	BAG family molecular chaperone regulator 2	O95816
BAG6	Large proline-rich protein BAG6	P46379
BAK1	Bcl-2 homologous antagonist/killer	Q16611
BCAP31	B-cell receptor-associated protein 31	P51572

Gene	Protein name	Accession
BDH1	D-beta-hydroxybutyrate dehydrogenase, mitochondrial	Q02338
BLVRA	Biliverdin reductase A	P53004
BPHL	Valacyclovir hydrolase	Q86WA6
C17orf62	Uncharacterized protein C17orf62	Q9BQA9
C4A	Complement C4-A	P0C0L4
CALCOCO2	Calcium-binding and coiled-coil domain-containing protein 2	Q13137
CAPRIN1	Caprin-1	Q14444
CAPZA2	F-actin-capping protein subunit alpha-2	P47755
CBX5	Chromobox protein homolog 5	P45973
CCT3	T-complex protein 1 subunit gamma	P49368
CCT4	T-complex protein 1 subunit delta	P50991
CCT5	T-complex protein 1 subunit epsilon	P48643
CD3E	T-cell surface glycoprotein CD3 epsilon chain	P07766
CDK5	Cyclin-dependent kinase 5	Q00535
CDKAL1	Threonylcarbamoyladenine tRNA methyltransferase	Q5VV42
CHCHD2	Coiled-coil-helix-coiled-coil-helix domain-containing protein 2, mitochondrial	Q9Y6H1
CHCHD2P9	Putative coiled-coil-helix-coiled-coil-helix domain-containing protein CHCHD2P9, mitochondrial	Q5T1J5
CHID1	Chitinase domain-containing protein 1	Q9BWS9
CMPK1	UMP-CMP kinase	P30085
COX5B	Cytochrome c oxidase subunit 5B, mitochondrial	P10606
CPT1A	Carnitine O-palmitoyltransferase 1, liver isoform	P50416
CTNNA1	Catenin alpha-1	P35221
DDAH2	N(G),N(G)-dimethylarginine dimethylaminohydrolase 2	O95865
DDX39A	ATP-dependent RNA helicase DDX39A	O00148
DHCR24	Delta(24)-sterol reductase	Q15392
DHCR7	7-dehydrocholesterol reductase	Q9UBM7
DHTKD1	Probable 2-oxoglutarate dehydrogenase E1 component DHKTD1, mitochondrial	Q96HY7
DHX15	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15	O43143
DNAJA2	DnaJ homolog subfamily A member 2	O60884
DNAJB6	DnaJ homolog subfamily B member 6	O75190
ECI2	Enoyl-CoA delta isomerase 2, mitochondrial	O75521
EEF1D	Elongation factor 1-delta	P29692
EIF3C	Eukaryotic translation initiation factor 3 subunit C	Q99613
EIF3CL	Eukaryotic translation initiation factor 3 subunit C-like protein	B5ME19
EIF6	Eukaryotic translation initiation factor 6	P56537
ELMO1	Engulfment and cell motility protein 1	Q92556
EMC4	ER membrane protein complex subunit 4	Q5J8M3

Gene	Protein name	Accession
EMC7	ER membrane protein complex subunit 7	Q9NPA0
EMC8	ER membrane protein complex subunit 8	O43402
EPHX1	Epoxide hydrolase 1	P07099
ERLEC1	Endoplasmic reticulum lectin 1	Q96DZ1
ETFB	Electron transfer flavoprotein subunit beta	P38117
FASTKD2	FAST kinase domain-containing protein 2	Q9NYY8
FH	Fumarate hydratase, mitochondrial	P07954
FKBP11	Peptidyl-prolyl cis-trans isomerase FKBP11	Q9NYL4
FLG2	Filaggrin-2	Q5D862
FLOT2	Flotillin-2	Q14254
GAA	Lysosomal alpha-glucosidase	P10253
GABARAPL2	Gamma-aminobutyric acid receptor-associated protein-like 2	P60520
GADD45GIP1	Growth arrest and DNA damage-inducible proteins-interacting protein 1	Q8TAE8
GBAS	Protein NipSnap homolog 2	O75323
GTPBP6	Putative GTP-binding protein 6	O43824
H2AFV	Histone H2A.V	Q71UI9
H2AFZ	Histone H2A.Z	P0C0S5
H6PD	GDH/6PGL endoplasmic bifunctional protein	O95479
HAGH	Hydroxyacylglutathione hydrolase, mitochondrial	Q16775
HEXB	Beta-hexosaminidase subunit beta	P07686
HIST1H1D	Histone H1.3	P16402
HIST1H2AC	Histone H2A type 1-C	Q93077
HK1	Hexokinase-1	P19367
HLA-E	HLA class I histocompatibility antigen, alpha chain E	P13747
HNRNPA2B1	Heterogeneous nuclear ribonucleoproteins A2/B1	P22626
HNRNPA3	Heterogeneous nuclear ribonucleoprotein A3	P51991
HNRNPH3	Heterogeneous nuclear ribonucleoprotein H3	P31942
HRNR	Hornerin	Q86YZ3
HSPA1A	Heat shock 70 kDa protein 1A/1B	P08107
IDE	Insulin-degrading enzyme	P14735
IMPDH2	Inosine-5'-monophosphate dehydrogenase 2	P12268
ITGA4	Integrin alpha-4	P13612
ITGA5	Integrin alpha-5	P08648
ITPR3	Inositol 1,4,5-trisphosphate receptor type 3	Q14573
KHSRP	Far upstream element-binding protein 2	Q92945
KIDINS220	Kinase D-interacting substrate of 220 kDa	Q9ULH0
KIF5B	Kinesin-1 heavy chain	P33176
KRT6C	Keratin, type II cytoskeletal 6C	P48668
LAPTM5	Lysosomal-associated transmembrane protein 5	Q13571

Gene	Protein name	Accession
LDLR	Low-density lipoprotein receptor	P01130
LMNB2	Lamin-B2	Q03252
LRPAP1	Alpha-2-macroglobulin receptor-associated protein	P30533
LRRC8A	Volume-regulated anion channel subunit LRRC8A	Q8IWT6
LSM12	Protein LSM12 homolog	Q3MHD2
LYPLAL1	Lysophospholipase-like protein 1	Q5VWZ2
LYRM7	Complex III assembly factor LYRM7	Q5U5X0
MACROD1	O-acetyl-ADP-ribose deacetylase MACROD1	Q9BQ69
MAN2B1	Lysosomal alpha-mannosidase	O00754
MANF	Mesencephalic astrocyte-derived neurotrophic factor	P55145
MAP2K2	Dual specificity mitogen-activated protein kinase kinase 2	P36507
MCEE	Methylmalonyl-CoA epimerase, mitochondrial	Q96PE7
MCM3	DNA replication licensing factor MCM3	P25205
MESDC2	LDLR chaperone MESD	Q14696
MOB1A	MOB kinase activator 1A	Q9H8S9
MOB1B	MOB kinase activator 1B	Q7L9L4
MRPL53	39S ribosomal protein L53, mitochondrial	Q96EL3
MRPS30	28S ribosomal protein S30, mitochondrial	Q9NP92
MRPS33	28S ribosomal protein S33, mitochondrial	Q9Y291
MTFR1	Mitochondrial fission regulator 1	Q15390
MTPN	Myotrophin	P58546
MYBBP1A	Myb-binding protein 1A	Q9BQG0
NAA50	N-alpha-acetyltransferase 50	Q9GZZ1
NARS2	Probable asparagine--tRNA ligase, mitochondrial	Q96159
NCL	Nucleolin	P19338
NDUFAF6	NADH dehydrogenase	Q330K2
NDUFS1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	P28331
NDUFV1	NADH dehydrogenase [ubiquinone] flavoprotein 1, mitochondrial	P49821
NIPSNAP3A	Protein NipSnap homolog 3A	Q9UFN0
NLRX1	NLR family member X1	Q86UT6
NNT	NAD(P) transhydrogenase, mitochondrial	Q13423
NOP56	Nucleolar protein 56	O00567
NT5DC2	5'-nucleotidase domain-containing protein 2	Q9H857
NUDT21	Cleavage and polyadenylation specificity factor subunit 5	O43809
NUDT8	Nucleoside diphosphate-linked moiety X motif 8, mitochondrial	Q8WV74
NUP160	Nuclear pore complex protein Nup160	Q12769
NUP188	Nucleoporin NUP188 homolog	Q5SRE5
NUP93	Nuclear pore complex protein Nup93	Q8N1F7
ORMDL1	ORM1-like protein 1	Q9P0S3

Gene	Protein name	Accession
OSBPL11	Oxysterol-binding protein-related protein 11	Q9BXB4
OSBPL9	Oxysterol-binding protein-related protein 9	Q96SU4
OSGEPL1	Probable tRNA N6-adenosine threonylcarbamoyltransferase, mitochondrial	Q9H4B0
PAFAH1B1	Platelet-activating factor acetylhydrolase IB subunit alpha	P43034
PAICS	Multifunctional protein ADE2	P22234
PARK7	Protein DJ-1	Q99497
PBXIP1	Pre-B-cell leukemia transcription factor-interacting protein 1	Q96AQ6
PDCD11	Protein RRP5 homolog	Q14690
PDIA3	Protein disulfide-isomerase A3	P30101
PDK1	[Pyruvate dehydrogenase	Q15118
PLOD1	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1	Q02809
PML	Protein PML	P29590
POLDIP3	Polymerase delta-interacting protein 3	Q9BY77
POLR2A	DNA-directed RNA polymerase II subunit RPB1	P24928
POLR2B	DNA-directed RNA polymerase II subunit RPB2	P30876
PIIH	Peptidyl-prolyl cis-trans isomerase H	O43447
PPP2R2A	Serine/threonine-protein phosphatase 2A 55 kDa regulatory subunit B alpha isoform	P63151
PSAP	Prosaposin	P07602
PSMA1	Proteasome subunit alpha type-1	P25786
PSMB1	Proteasome subunit beta type-1	P20618
PSMC5	26S protease regulatory subunit 8	P62195
PTDSS1	Phosphatidylserine synthase 1	P48651
PTPLAD1	Very-long-chain (3R)-3-hydroxyacyl-[acyl-carrier protein] dehydratase 3	Q9P035
PTPN11	Tyrosine-protein phosphatase non-receptor type 11	Q06124
PWP2	Periodic tryptophan protein 2 homolog	Q15269
PXMP2	Peroxisomal membrane protein 2	Q9NR77
PYCR1	Pyrroline-5-carboxylate reductase 1, mitochondrial	P32322
RAB22A	Ras-related protein Rab-22A	Q9UL26
RAB33B	Ras-related protein Rab-33B	Q9H082
RAB4B	Ras-related protein Rab-4B	P61018
RAB5A	Ras-related protein Rab-5A	P20339
RAN	GTP-binding nuclear protein Ran	P62826
RANBP1	Ran-specific GTPase-activating protein	P43487
RARS	Arginine--tRNA ligase, cytoplasmic	P54136
RBBP4	Histone-binding protein RBBP4	Q09028
RBM25	RNA-binding protein 25	P49756
RFK	Riboflavin kinase	Q969G6
RHOG	Rho-related GTP-binding protein RhoG	P84095

Gene	Protein name	Accession
RMDN1	Regulator of microtubule dynamics protein 1	Q96DB5
RPL10	60S ribosomal protein L10	P27635
RPL13A	60S ribosomal protein L13a	P40429
RPL23	60S ribosomal protein L23	P62829
RPL4	60S ribosomal protein L4	P36578
RPS19BP1	Active regulator of SIRT1	Q86WX3
RPS5	40S ribosomal protein S5	P46782
RRAS2	Ras-related protein R-Ras2	P62070
RTN4IP1	Reticulon-4-interacting protein 1, mitochondrial	Q8WVV3
SAFB	Scaffold attachment factor B1	Q15424
SCD	Acyl-CoA desaturase	O00767
SEC61A1	Protein transport protein Sec61 subunit alpha isoform 1	P61619
SF3A2	Splicing factor 3A subunit 2	Q15428
SFPQ	Splicing factor, proline- and glutamine-rich	P23246
SIGMAR1	Sigma non-opioid intracellular receptor 1	Q99720
SIRT3	NAD-dependent protein deacetylase sirtuin-3, mitochondrial	Q9NTG7
SIT1	Signaling threshold-regulating transmembrane adapter 1	Q9Y3P8
SLC12A2	Solute carrier family 12 member 2	P55011
SLC1A4	Neutral amino acid transporter A	P43007
SLC25A40	Solute carrier family 25 member 40	Q8TBP6
SLC25A5	ADP/ATP translocase 2	P05141
SLTM	SAFB-like transcription modulator	Q9NWH9
SMARCA4	Transcription activator BRG1	P51532
SMC1A	Structural maintenance of chromosomes protein 1A	Q14683
SMC3	Structural maintenance of chromosomes protein 3	Q9UQE7
SNRPD1	Small nuclear ribonucleoprotein Sm D1	P62314
SNRPN	Small nuclear ribonucleoprotein-associated protein N	P63162
SOD1	Superoxide dismutase [Cu-Zn]	P00441
SOD2	Superoxide dismutase [Mn], mitochondrial	P04179
SQLE	Squalene monooxygenase	Q14534
SRPK1	SRSF protein kinase 1	Q96SB4
STIM1	Stromal interaction molecule 1	Q13586
STRAP	Serine-threonine kinase receptor-associated protein	Q9Y3F4
STX17	Syntaxin-17	P56962
SYPL1	Synaptophysin-like protein 1	Q16563
TLN1	Talin-1	Q9Y490
TMED7	Transmembrane emp24 domain-containing protein 7	Q9Y3B3
TMEM126B	Complex I assembly factor TMEM126B, mitochondrial	Q8IUX1
TMEM173	Stimulator of interferon genes protein	Q86WV6

Gene	Protein name	Accession
TMEM230	Transmembrane protein 230	Q96A57
TMEM59	Transmembrane protein 59	Q9BXS4
TMUB2	Transmembrane and ubiquitin-like domain-containing protein 2	Q71RG4
TMX2	Thioredoxin-related transmembrane protein 2	Q9Y320
TMX3	Protein disulfide-isomerase TMX3	Q96JJ7
TMX4	Thioredoxin-related transmembrane protein 4	Q9H1E5
TOMM70A	Mitochondrial import receptor subunit TOM70	O94826
TRIM28	Transcription intermediary factor 1-beta	Q13263
TSM	Elongation factor Ts, mitochondrial	P43897
TSG101	Tumor susceptibility gene 101 protein	Q99816
TSN	Translin	Q15631
UBE4A	Ubiquitin conjugation factor E4 A	Q14139
UCHL5	Ubiquitin carboxyl-terminal hydrolase isozyme L5	Q9Y5K5
UFSP2	Ufm1-specific protease 2	Q9NUQ7
UPF1	Regulator of nonsense transcripts 1	Q92900
USP10	Ubiquitin carboxyl-terminal hydrolase 10	Q14694
VARS	Valine--tRNA ligase	P26640
VAV1	Proto-oncogene vav	P15498
VPS39	Vam6/Vps39-like protein	Q96JC1
WDR3	WD repeat-containing protein 3	Q9UNX4
WDR36	WD repeat-containing protein 36	Q8NI36
XRCC6	X-ray repair cross-complementing protein 6	P12956
YME1L1	ATP-dependent zinc metalloprotease YME1L1	Q96TA2
YWHAG	14-3-3 protein gamma	P61981
ZC3H11A	Zinc finger CCCH domain-containing protein 11A	O75152

## 6.2 Wild-type sample 1 (WT1) proteins

**Table 3: Proteins contained in the wild-type 1 VCV preparation (WT1) measured by mass spectrometry (see 3.5). Listed are gene names, protein names, and UniProt accession numbers.**

Gene	Protein name	Accession
AAAS	Aladin	P36639
AARS2	Alanine--tRNA ligase, mitochondrial	Q8NHG7
AASDHPPT	L-aminoadipate-semialdehyde dehydrogenase-phosphopantetheinyl transferase	Q9BRR6
AASS	Alpha-aminoadipic semialdehyde synthase, mitochondrial	P54619
AATF	Protein AATF	Q9UDR5
ABAT	4-aminobutyrate aminotransferase, mitochondrial	P06744
ABCB10	ATP-binding cassette sub-family B member 10, mitochondrial	Q9NUT2
ABCB7	ATP-binding cassette sub-family B member 7, mitochondrial	Q5VST6
ABCB8	ATP-binding cassette sub-family B member 8, mitochondrial	O75027
ABCC1	Multidrug resistance-associated protein 1	Q6IN84
ABCD3	ATP-binding cassette sub-family D member 3	Q9NRK6
ABCE1	ATP-binding cassette sub-family E member 1	Q8NE71
ABCF1	ATP-binding cassette sub-family F member 1	P28288
ABHD10	Mycophenolic acid acyl-glucuronide esterase, mitochondrial	Q8N2K0
ABHD11	Alpha/beta hydrolase domain-containing protein 11	Q9NUJ1
ABHD12	Monoacylglycerol lipase ABHD12	P61221
ABHD16A	Abhydrolase domain-containing protein 16A	Q8NFV4
ABHD17B	Alpha/beta hydrolase domain-containing protein 17B	Q9NY61
ACAA1	3-ketoacyl-CoA thiolase, peroxisomal	Q8WUY1
ACAA2	3-ketoacyl-CoA thiolase, mitochondrial	P24752
ACAD10	Acyl-CoA dehydrogenase family member 10	P49748
ACAD8	Isobutyryl-CoA dehydrogenase, mitochondrial	O95870
ACAD9	Acyl-CoA dehydrogenase family member 9, mitochondrial	Q9UKU7
ACADM	Medium-chain specific acyl-CoA dehydrogenase, mitochondrial	Q9H845

Gene	Protein name	Accession
ACADS	Short-chain specific acyl-CoA dehydrogenase, mitochondrial	P11310
ACADSB	Short/branched chain specific acyl-CoA dehydrogenase, mitochondrial	Q6JQN1
ACADVL	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial	P16219
ACAT1	Acetyl-CoA acetyltransferase, mitochondrial	P09110
ACBD3	Golgi resident protein GCP60	Q96CW5
ACIN1	Apoptotic chromatin condensation inducer in the nucleus	P45954
ACN9	Protein ACN9 homolog, mitochondrial	O96019
ACO2	Aconitate hydratase, mitochondrial	O00767
ACOT13	Acyl-coenzyme A thioesterase 13	Q9NRP4
ACOT7	Cytosolic acyl coenzyme A thioester hydrolase	Q6Y288
ACOX1	Peroxisomal acyl-coenzyme A oxidase 1	Q99798
ACP1	Low molecular weight phosphotyrosine protein phosphatase	P62136
ACSF3	Acyl-CoA synthetase family member 3, mitochondrial	Q9NUB1
ACSL1	Long-chain-fatty-acid--CoA ligase 1	Q4G176
ACSS1	Acetyl-coenzyme A synthetase 2-like, mitochondrial	O14561
ACTB	Actin, cytoplasmic 1	P33121
ACTG1	Actin, cytoplasmic 2	P60709
ACTL6A	Actin-like protein 6A	Q9UKV3
ACTN1	Alpha-actinin-1	P63261
ACTN4	Alpha-actinin-4	P12814
ACTR1A	Alpha-centractin	O43707
ACTR2	Actin-related protein 2	Q86WX3
ACTR3	Actin-related protein 3	P61160
ADAM10	Disintegrin and metalloproteinase domain-containing protein 10	P61163
ADCK3	Chaperone activity of bc1 complex-like, mitochondrial	O00116
ADCK4	AarF domain-containing protein kinase 4	Q8NI60
ADPGK	ADP-dependent glucokinase	Q96D53
ADPRHL2	Poly(ADP-ribose) glycohydrolase ARH3	Q92974
AEBP1	Adipocyte enhancer-binding protein 1	P10109
AGK	Acylglycerol kinase, mitochondrial	P06280
AGPAT1	1-acyl-sn-glycerol-3-phosphate acyltransferase alpha	Q9UG56
AGPAT5	1-acyl-sn-glycerol-3-phosphate acyltransferase epsilon	Q99943
AGPS	Alkylldihydroxyacetonephosphate synthase, peroxisomal	O14672
AHCY	Adenosylhomocysteinase	Q43865
AHCYL1	Putative adenosylhomocysteinase 2	O15424
AHSA1	Activator of 90 kDa heat shock protein ATPase homolog 1	Q53H12
AIFM1	Apoptosis-inducing factor 1, mitochondrial	O95433
AIMP1	Aminoacyl tRNA synthase complex-interacting multifunctional protein 1	O95831
AK2	Adenylate kinase 2, mitochondrial	Q01813

Gene	Protein name	Accession
AK3	GTP:AMP phosphotransferase AK3, mitochondrial	P54819
AKR7A2	Aflatoxin B1 aldehyde reductase member 2	Q9NX46
ALAS1	5-aminolevulinate synthase, nonspecific, mitochondrial	Q9H583
ALB	Serum albumin	P20292
ALDH18A1	Delta-1-pyrroline-5-carboxylate synthase	Q96C36
ALDH3A2	Fatty aldehyde dehydrogenase	Q9NWT8
ALDH4A1	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial	P51648
ALDH5A1	Succinate-semialdehyde dehydrogenase, mitochondrial	Q13242
ALDH6A1	Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial	Q8N4V1
ALDOA	Fructose-bisphosphate aldolase A	P02768
ALG1	Chitobiosyldiphosphodolichol beta-mannosyltransferase	Q9NP73
ALG13	Putative bifunctional UDP-N-acetylglucosamine transferase and deubiquitinase ALG13	P04075
ALG5	Dolichyl-phosphate beta-glucosyltransferase	Q9BT22
ALKBH7	Alpha-ketoglutarate-dependent dioxygenase alkB homolog 7, mitochondrial	Q9Y673
ALOX5AP	Arachidonate 5-lipoxygenase-activating protein	P30038
ALYREF	THO complex subunit 4	Q8NI27
ANKLE2	Ankyrin repeat and LEM domain-containing protein 2	Q9BTT0
ANO6	Anoctamin-6	O14744
ANP32E	Acidic leucine-rich nuclear phosphoprotein 32 family member E	P30533
ANXA11	Annexin A11	P01008
ANXA2	Annexin A2	P50995
ANXA6	Annexin A6	P07355
APIB1	AP-1 complex subunit beta-1	P08133
APIG1	AP-1 complex subunit gamma-1	Q10567
AP1M1	AP-1 complex subunit mu-1	O43747
AP1S1	AP-1 complex subunit sigma-1A	Q9BXS5
AP2A1	AP-2 complex subunit alpha-1	P61966
AP2A2	AP-2 complex subunit alpha-2	O95782
AP2B1	AP-2 complex subunit beta	O94973
AP2M1	AP-2 complex subunit mu	P63010
AP2S1	AP-2 complex subunit sigma	Q96CW1
APMAP	Adipocyte plasma membrane-associated protein	P50583
APOA1BP	NAD(P)H-hydrate epimerase	P22307
APOL2	Apolipoprotein L2	Q9HDC9
APOO	Apolipoprotein O	Q6UXV4
APOOL	Apolipoprotein O-like	Q9BQE5
APRT	Adenine phosphoribosyltransferase	Q9BUR5
ARCN1	Coatmer subunit delta	P53618

Gene	Protein name	Accession
ARF1	ADP-ribosylation factor 1	P07741
ARF3	ADP-ribosylation factor 3	P84077
ARF4	ADP-ribosylation factor 4	P61204
ARF5	ADP-ribosylation factor 5	P18085
ARF6	ADP-ribosylation factor 6	P84085
ARG2	Arginase-2, mitochondrial	P62330
ARHGAP15	Rho GTPase-activating protein 15	Q15382
ARHGDI1	Rho GDP-dissociation inhibitor 2	P50395
ARHGEF2	Rho guanine nucleotide exchange factor 2	P78540
ARL2	ADP-ribosylation factor-like protein 2	O43488
ARL3	ADP-ribosylation factor-like protein 3	P36404
ARL8B	ADP-ribosylation factor-like protein 8B	P36405
ARMC1	Armadillo repeat-containing protein 1	Q8N2F6
ARMC10	Armadillo repeat-containing protein 10	Q9NVJ2
ARMCX3	Armadillo repeat-containing X-linked protein 3	Q9NVT9
ARPC3	Actin-related protein 2/3 complex subunit 3	P61158
ARPC4	Actin-related protein 2/3 complex subunit 4	O15145
ASAH1	Acid ceramidase	P59998
ASF1A	Histone chaperone ASF1A	Q13510
ASNA1	ATPase ASNA1	Q9Y294
ASPH	Aspartyl/asparaginyl beta-hydroxylase	O43681
ATAD1	ATPase family AAA domain-containing protein 1	P24539
ATAD3A	ATPase family AAA domain-containing protein 3A	Q8NBU5
ATAD3B	ATPase family AAA domain-containing protein 3B	Q9NVI7
ATG3	Ubiquitin-like-conjugating enzyme ATG3	Q5T9A4
ATIC	Bifunctional purine biosynthesis protein PURH	P22234
ATL2	Atlastin-2	Q9NT62
ATL3	Atlastin-3	Q8NHH9
ATP13A1	Probable cation-transporting ATPase 13A1	Q12797
ATP1A1	Sodium/potassium-transporting ATPase subunit alpha-1	Q9HD20
ATP1A3	Sodium/potassium-transporting ATPase subunit alpha-3	P05023
ATP1B3	Sodium/potassium-transporting ATPase subunit beta-3	P13637
ATP2A2	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2	P54709
ATP2A3	Sarcoplasmic/endoplasmic reticulum calcium ATPase 3	P16615
ATP2B4	Plasma membrane calcium-transporting ATPase 4	Q93084
ATP5A1	ATP synthase subunit alpha, mitochondrial	O75964
ATP5B	ATP synthase subunit beta, mitochondrial	P25705
ATP5D	ATP synthase subunit delta, mitochondrial	P06576
ATP5F1	ATP synthase F(0) complex subunit B1, mitochondrial	Q9NW81

Gene	Protein name	Accession
ATP5H	ATP synthase subunit d, mitochondrial	Q6DD88
ATP5L	ATP synthase subunit g, mitochondrial	Q99766
ATP5O	ATP synthase subunit O, mitochondrial	Q8N5M1
ATP5S	ATP synthase subunit s, mitochondrial	O75947
ATP5SL	ATP synthase subunit s-like protein	P23634
ATP6AP2	Renin receptor	Q96HR9
ATP6V0A2	V-type proton ATPase 116 kDa subunit a isoform 2	Q9H9H4
ATP6V0D1	V-type proton ATPase subunit d 1	Q9UBK9
ATP6V1A	V-type proton ATPase catalytic subunit A	Q99536
ATP6V1B2	V-type proton ATPase subunit B, brain isoform	P38606
ATP6V1C1	V-type proton ATPase subunit C 1	P21281
ATP6V1D	V-type proton ATPase subunit D	P21283
ATP6V1E1	V-type proton ATPase subunit E 1	Q9Y5K8
ATP6V1F	V-type proton ATPase subunit F	P36543
ATP6V1G1	V-type proton ATPase subunit G 1	Q16864
ATP6V1H	V-type proton ATPase subunit H	O75348
ATPAF1	ATP synthase mitochondrial F1 complex assembly factor 1	P30049
ATPAF2	ATP synthase mitochondrial F1 complex assembly factor 2	Q5TC12
ATXN10	Ataxin-10	P48047
AUH	Methylglutaconyl-CoA hydratase, mitochondrial	Q9UBB4
AUP1	Ancient ubiquitous protein 1	Q13825
AURKAIP1	Aurora kinase A-interacting protein	Q16352
AZI1	5-azacytidine-induced protein 1	Q9Y679
B3GALT1	Beta-1,3-glucosyltransferase	O94766
B3GAT3	Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3	Q9BXX5
BAG2	BAG family molecular chaperone regulator 2	O75531
BAG5	BAG family molecular chaperone regulator 5	O95816
BAG6	Large proline-rich protein BAG6	Q9UL15
BAK1	Bcl-2 homologous antagonist/killer	P46379
BANF1	Barrier-to-autointegration factor	O00154
BAZ1B	Tyrosine-protein kinase BAZ1B	P35613
BCAP31	B-cell receptor-associated protein 31	Q16611
BCAS2	Pre-mRNA-splicing factor SPF27	P61009
BCAT2	Branched-chain-amino-acid aminotransferase, mitochondrial	Q9UIG0
BCCIP	BRCA2 and CDKN1A-interacting protein	O15382
BCKDHA	2-oxoisovalerate dehydrogenase subunit alpha, mitochondrial	P11182
BCKDK	[3-methyl-2-oxobutanoate dehydrogenase [lipoamide]] kinase, mitochondrial	Q9P287
BCL2	Apoptosis regulator Bcl-2	O14874
BCL2L1	Bcl-2-like protein 1	Q9UPN4

Gene	Protein name	Accession
BCL2L13	Bcl-2-like protein 13	Q07817
BCS1L	Mitochondrial chaperone BCS1	P10415
BDH1	D-beta-hydroxybutyrate dehydrogenase, mitochondrial	Q9Y276
BET1L	BET1-like protein	Q02338
BID	BH3-interacting domain death agonist	Q9NYM9
BIRC5	Baculoviral IAP repeat-containing protein 5	Q96LW7
BLOC1S1	Biogenesis of lysosome-related organelles complex 1 subunit 1	O15392
BLVRA	Biliverdin reductase A	P55957
BMP2K	BMP-2-inducible protein kinase	P78537
BMS1	Ribosome biogenesis protein BMS1 homolog	Q9NSY1
BNIP1	Vesicle transport protein SEC20	Q9UBV2
BOLA1	BolA-like protein 1	Q14692
BPHL	Valacyclovir hydrolase	Q53HL2
BPNT1	3'(2),5'-bisphosphate nucleotidase 1	Q86WA6
BRI3BP	BRI3-binding protein	Q5VTR2
BRX1	Ribosome biogenesis protein BRX1 homolog	Q8WY22
BSG	Basigin	P51572
BST2	Bone marrow stromal antigen 2	Q8TDN6
BTN2A1	Butyrophilin subfamily 2 member A1	Q10589
BUD31	Protein BUD31 homolog	Q7KYR7
BYSL	Bystin	P41223
BZW1	Basic leucine zipper and W2 domain-containing protein 1	Q13895
BZW2	Basic leucine zipper and W2 domain-containing protein 2	Q7L1Q6
C10orf35	Uncharacterized protein C10orf35	Q8N5K1
C12orf10	UPF0160 protein MYG1, mitochondrial	Q99417
C15orf40	UPF0235 protein C15orf40	Q7Z7A1
C15orf61	Uncharacterized protein C15orf61	Q8WUR7
C16orf58	UPF0420 protein C16orf58	P09669
C16orf80	UPF0468 protein C16orf80	Q96GQ5
C17orf62	Uncharacterized protein C17orf62	Q9H3G5
C19orf10	UPF0556 protein C19orf10	Q5TZA2
C19orf52	Uncharacterized protein C19orf52	Q969H8
C1orf21	Uncharacterized protein C1orf21	Q6UB35
C1QBP	Complement component 1 Q subcomponent-binding protein, mitochondrial	Q9Y6E2
C21orf33	ES1 protein homolog, mitochondrial	Q9BS26
C2orf43	UPF0554 protein C2orf43	P52907
C2orf47	Uncharacterized protein C2orf47, mitochondrial	Q9H6V9
C3	Complement C3	A6NNL5
C3orf33	Protein C3orf33	P45973

Gene	Protein name	Accession
C3orf58	Deleted in autism protein 1	Q08211
C4A	Complement C4-A	P01024
C6orf120	UPF0669 protein C6orf120	O15182
C6orf203	Uncharacterized protein C6orf203	Q7Z4R8
C7orf50	Uncharacterized protein C7orf50	Q9P0P8
C8orf82	UPF0598 protein C8orf82	Q9BRJ6
C9	Complement component C9	P0C0L4
C9orf114	Uncharacterized protein C9orf114	Q9NPF2
C9orf89	Bcl10-interacting CARD protein	P53004
CACYBP	Calcyclin-binding protein	P00167
CAD	CAD protein	P11498
CALCOCO2	Calcium-binding and coiled-coil domain-containing protein 2	Q9BRK5
CALM1	Calmodulin	Q13112
CALR	Calreticulin	P62158
CAMLG	Calcium signal-modulating cyclophilin ligand	P27824
CAND1	Cullin-associated NEDD8-dissociated protein 1	P07384
CANX	Calnexin	P27797
CAP1	Adenylyl cyclase-associated protein 1	Q86VP6
CAPG	Macrophage-capping protein	Q01518
CAPN1	Calpain-1 catalytic subunit	P49069
CAPRN1	Caprin-1	P40121
CAPZA1	F-actin-capping protein subunit alpha-1	P08311
CARHSP1	Calcium-regulated heat stable protein 1	Q96BS2
CARS2	Probable cysteine--tRNA ligase, mitochondrial	Q5JTZ9
CAT	Catalase	Q13948
CBR4	Carbonyl reductase family member 4	O75976
CBX3	Chromobox protein homolog 3	Q8N4T8
CBX5	Chromobox protein homolog 5	Q13185
CCAR2	Cell cycle and apoptosis regulator protein 2	Q9GZT6
CCBL2	Kynurenine--oxoglutarate transaminase 3	P22694
CCDC115	Coiled-coil domain-containing protein 115	Q6P1S2
CCDC127	Coiled-coil domain-containing protein 127	Q96NT0
CCDC134	Coiled-coil domain-containing protein 134	Q96BQ5
CCDC167	Coiled-coil domain-containing protein 167	Q9H6E4
CCDC47	Coiled-coil domain-containing protein 47	Q8N163
CCDC51	Coiled-coil domain-containing protein 51	Q96A33
CCDC58	Coiled-coil domain-containing protein 58	Q96ER9
CCDC59	Thyroid transcription factor 1-associated protein 26	P37802
CCDC90B	Coiled-coil domain-containing protein 90B, mitochondrial	Q9NV96

Gene	Protein name	Accession
CCNK	Cyclin-K	P53701
CCNY	Cyclin-Y	O75909
CCSMST1	Protein CCSMST1	P41240
CCT2	T-complex protein 1 subunit beta	P17987
CCT3	T-complex protein 1 subunit gamma	P48643
CCT4	T-complex protein 1 subunit delta	P78371
CCT5	T-complex protein 1 subunit epsilon	P50991
CCT6A	T-complex protein 1 subunit zeta	P50990
CCT7	T-complex protein 1 subunit eta	P49368
CCT8	T-complex protein 1 subunit theta	Q99832
CD1C	T-cell surface glycoprotein CD1c	Q8ND76
CD2	T-cell surface antigen CD2	P29017
CD247	T-cell surface glycoprotein CD3 zeta chain	P09693
CD3D	T-cell surface glycoprotein CD3 delta chain	P06729
CD3E	T-cell surface glycoprotein CD3 epsilon chain	P04234
CD3G	T-cell surface glycoprotein CD3 gamma chain	P07766
CD47	Leukocyte surface antigen CD47	P20963
CD48	CD48 antigen	Q08722
CD5	T-cell surface glycoprotein CD5	P09326
CD82	CD82 antigen	P06127
CD84	SLAM family member 5	P63208
CD97	CD97 antigen	P27701
CDC37	Hsp90 co-chaperone Cdc37	P48960
CDC42	Cell division control protein 42 homolog	Q16543
CDC5L	Cell division cycle 5-like protein	P60953
CDCA8	Borealin	Q9Y3E2
CDH2	Cadherin-2	P43155
CDIPT	CDP-diacylglycerol--inositol 3-phosphatidyltransferase	Q99459
CDK1	Cyclin-dependent kinase 1	O14735
CDK2	Cyclin-dependent kinase 2	P06493
CDK5	Cyclin-dependent kinase 5	P24941
CDK5RAP2	CDK5 regulatory subunit-associated protein 2	Q96D05
CDK5RAP3	CDK5 regulatory subunit-associated protein 3	Q96SN8
CDK6	Cyclin-dependent kinase 6	Q00535
CDK9	Cyclin-dependent kinase 9	Q00534
CDKAL1	Threonylcarbamoyladenosine tRNA methylthiotransferase	P50750
CDKN2AIP	CDKN2A-interacting protein	Q14444
CECR5	Cat eye syndrome critical region protein 5	O94986
CENPM	Centromere protein M	Q9BXW7

Gene	Protein name	Accession
CENPV	Centromere protein V	Q9NSP4
CEP135	Centrosomal protein of 135 kDa	Q9Y6A4
CEP152	Centrosomal protein of 152 kDa	Q5VV42
CEP250	Centrosome-associated protein CEP250	Q6UW02
CEP41	Centrosomal protein of 41 kDa	Q7Z7K6
CEP57	Centrosomal protein of 57 kDa	Q9BYV8
CEP72	Centrosomal protein of 72 kDa	Q86XR8
CETN3	Centrin-3	Q9P209
CFL1	Cofilin-1	Q96BR5
CHAF1B	Chromatin assembly factor 1 subunit B	Q5T440
CHCHD1	Coiled-coil-helix-coiled-coil-helix domain-containing protein 1	P10809
CHCHD2	Coiled-coil-helix-coiled-coil-helix domain-containing protein 2, mitochondrial	Q96BP2
CHCHD2P9	Putative coiled-coil-helix-coiled-coil-helix domain-containing protein CHCHD2P9, mitochondrial	Q9BRQ6
CHCHD3	Coiled-coil-helix-coiled-coil-helix domain-containing protein 3, mitochondrial	Q9Y6H1
CHCHD4	Mitochondrial intermembrane space import and assembly protein 40	Q5JRA6
CHCHD6	Coiled-coil-helix-coiled-coil-helix domain-containing protein 6, mitochondrial	Q9NX63
CHD1	Chromodomain-helicase-DNA-binding protein 1	Q5T1J5
CHI3L2	Chitinase-3-like protein 2	P61604
CHMP2A	Charged multivesicular body protein 2a	O14646
CHP1	Calcineurin B homologous protein 1	O43633
CHST11	Carbohydrate sulfotransferase 11	Q9Y2V2
CIB1	Calcium and integrin-binding protein 1	Q9Y375
CISD1	CDGSH iron-sulfur domain-containing protein 1	Q99828
CISD2	CDGSH iron-sulfur domain-containing protein 2	Q9NZ45
CIT	Citron Rho-interacting kinase	P35221
CKAP4	Cytoskeleton-associated protein 4	Q96JB5
CKAP5	Cytoskeleton-associated protein 5	Q07065
CLIC1	Chloride intracellular channel protein 1	Q00610
CLINT1	Clathrin interactor 1	P29320
CLPB	Caseinolytic peptidase B protein homolog	O00299
CLPP	ATP-dependent Clp protease proteolytic subunit, mitochondrial	Q9H078
CLPX	ATP-dependent Clp protease ATP-binding subunit clpX-like, mitochondrial	Q16740
CLTC	Clathrin heavy chain 1	Q14008
CLYBL	Citrate lyase subunit beta-like protein, mitochondrial	O76031
CMAS	N-acetylneuraminidase cytidylyltransferase	Q9UMX5
CMPK1	UMP-CMP kinase	Q13303
CMPK2	UMP-CMP kinase 2, mitochondrial	Q9UJS0
CNNM3	Metal transporter CNNM3	P09543

Gene	Protein name	Accession
CNOT1	CCR4-NOT transcription complex subunit 1	Q9UKZ1
CNOT11	CCR4-NOT transcription complex subunit 11	Q8NE01
CNOT7	CCR4-NOT transcription complex subunit 7	A5YKK6
CNP	2',3'-cyclic-nucleotide 3'-phosphodiesterase	Q5EBM0
CNPY3	Protein canopy homolog 3	Q9UIV1
CNTRL	Centriolin	Q9BT09
COA1	Cytochrome c oxidase assembly factor 1 homolog	P02748
COA3	Cytochrome c oxidase assembly factor 3 homolog, mitochondrial	Q9GZY4
COA6	Cytochrome c oxidase assembly factor 6 homolog	Q9Y2R0
COA7	Cytochrome c oxidase assembly factor 7	Q5JTJ3
COLGALT1	Procollagen galactosyltransferase 1	P09211
COMMD2	COMM domain-containing protein 2	P23528
COPA	Coatomer subunit alpha	Q86X83
COPB1	Coatomer subunit beta	P35606
COPB2	Coatomer subunit beta'	P53621
COPG1	Coatomer subunit gamma-1	P48444
COPS4	COP9 signalosome complex subunit 4	Q4G010
COPS8	COP9 signalosome complex subunit 8	Q9BT78
COPZ1	Coatomer subunit zeta-1	Q9Y678
COQ3	Hexaprenyldihydroxybenzoate methyltransferase, mitochondrial	P61923
COQ5	2-methoxy-6-polyprenyl-1,4-benzoquinol methylase, mitochondrial	Q9NZJ6
COQ6	Ubiquinone biosynthesis monoxygenase COQ6	Q5HYK3
COQ7	Ubiquinone biosynthesis protein COQ7 homolog	Q9Y2Z9
COQ9	Ubiquinone biosynthesis protein COQ9, mitochondrial	Q99807
CORO1A	Coronin-1A	O75208
COTL1	Coactosin-like protein	P31146
COX11	Cytochrome c oxidase assembly protein COX11, mitochondrial	Q14019
COX15	Cytochrome c oxidase assembly protein COX15 homolog	Q9Y6N1
COX16	Cytochrome c oxidase assembly protein COX16 homolog, mitochondrial	Q7KZN9
COX18	Mitochondrial inner membrane protein COX18	Q9P0S2
COX4I1	Cytochrome c oxidase subunit 4 isoform 1, mitochondrial	Q8N8Q8
COX5A	Cytochrome c oxidase subunit 5A, mitochondrial	P13073
COX5B	Cytochrome c oxidase subunit 5B, mitochondrial	P20674
COX6B1	Cytochrome c oxidase subunit 6B1	Q9HCG8
COX6C	Cytochrome c oxidase subunit 6C	P10606
COX7A2	Cytochrome c oxidase subunit 7A2, mitochondrial	P14854
CPD	Carboxypeptidase D	Q8WWC4
CPNE3	Copine-3	Q9BV73
CPOX	Oxygen-dependent coproporphyrinogen-III oxidase, mitochondrial	P13196

Gene	Protein name	Accession
CPSF2	Cleavage and polyadenylation specificity factor subunit 2	O75131
CPT1A	Carnitine O-palmitoyltransferase 1, liver isoform	O43809
CPT2	Carnitine O-palmitoyltransferase 2, mitochondrial	P50416
CPVL	Probable serine carboxypeptidase CPVL	P23786
CRAT	Carnitine O-acetyltransferase	Q13137
CROCC	Rootletin	Q9BQA9
CRYZ	Quinone oxidoreductase	Q5XKP0
CSDE1	Cold shock domain-containing protein E1	Q9BSF4
CSEIL	Exportin-2	O14980
CSK	Tyrosine-protein kinase CSK	Q8NEV1
CSNK1A1	Casein kinase I isoform alpha	O75600
CSNK1G3	Casein kinase I isoform gamma-3	P48729
CSNK2A1	Casein kinase II subunit alpha	O75534
CSNK2A2	Casein kinase II subunit alpha'	P68400
CSNK2A3	Casein kinase II subunit alpha 3	P19784
CTAGE5	cTAGE family member 5	Q99627
CTNNA1	Catenin alpha-1	O15320
CTPS1	CTP synthase 1	Q02127
CTSA	Lysosomal protective protein	P24666
CTSC	Dipeptidyl peptidase 1	P04040
CTSD	Cathepsin D	P53634
CTSG	Cathepsin G	P07339
CUL4A	Cullin-4A	O14578
CUTA	Protein CutA	Q13619
CUX1	Protein CASP	Q9NXV6
CWC22	Pre-mRNA-splicing factor CWC22 homolog	O60888
CYB5A	Cytochrome b5	O43169
CYB5B	Cytochrome b5 type B	P08574
CYB5R1	NADH-cytochrome b5 reductase 1	Q8WUY8
CYB5R3	NADH-cytochrome b5 reductase 3	Q9UHQ9
CYC1	Cytochrome c1, heme protein, mitochondrial	P14406
CYCS	Cytochrome c	Q9HB71
CYP20A1	Cytochrome P450 20A1	Q66GS9
D2HGDH	D-2-hydroxyglutarate dehydrogenase, mitochondrial	P99999
DAAMI	Disheveled-associated activator of morphogenesis 1	Q9NRG7
DAD1	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit DAD1	Q9Y4D1
DAP3	28S ribosomal protein S29, mitochondrial	Q9Y2Q9
DARS	Aspartate--tRNA ligase, cytoplasmic	Q9HA77
DARS2	Aspartate--tRNA ligase, mitochondrial	P14868

Gene	Protein name	Accession
DBN1	Drebrin	Q5T2R2
DBT	Lipoamide acyltransferase component of branched-chain alpha-keto acid dehydrogenase complex, mitochondrial	Q56VL3
DCAKD	Dephospho-CoA kinase domain-containing protein	Q13409
DCD	Dermcidin	Q8WVC6
DCK	Deoxycytidine kinase	P81605
DCTN3	Dynactin subunit 3	O95822
DCXR	L-xylulose reductase	O75935
DDAH2	N(G),N(G)-dimethylarginine dimethylaminohydrolase 2	Q7Z4W1
DDRGK1	DDRGK domain-containing protein 1	O95865
DDX10	Probable ATP-dependent RNA helicase DDX10	Q96HY6
DDX18	ATP-dependent RNA helicase DDX18	Q13206
DDX21	Nucleolar RNA helicase 2	Q9NVP1
DDX23	Probable ATP-dependent RNA helicase DDX23	Q9NUL7
DDX24	ATP-dependent RNA helicase DDX24	Q9BUQ8
DDX27	Probable ATP-dependent RNA helicase DDX27	Q9GZR7
DDX28	Probable ATP-dependent RNA helicase DDX28	Q9NR30
DDX39A	ATP-dependent RNA helicase DDX39A	P33316
DDX3X	ATP-dependent RNA helicase DDX3X	Q96GQ7
DDX47	Probable ATP-dependent RNA helicase DDX47	O00571
DDX5	Probable ATP-dependent RNA helicase DDX5	Q9NY93
DDX50	ATP-dependent RNA helicase DDX50	Q9H0S4
DDX51	ATP-dependent RNA helicase DDX51	Q9BQ39
DDX54	ATP-dependent RNA helicase DDX54	Q8N8A6
DDX56	Probable ATP-dependent RNA helicase DDX56	Q8TDD1
DDX6	Probable ATP-dependent RNA helicase DDX6	P17844
DECR1	2,4-dienoyl-CoA reductase, mitochondrial	Q9NUI1
DECR2	Peroxisomal 2,4-dienoyl-CoA reductase	P26196
DEF6	Differentially expressed in FDCP 6 homolog	Q16698
DEK	Protein DEK	Q9HBB1
DESI2	Desumoylating isopeptidase 2	P35659
DHCR24	Delta(24)-sterol reductase	Q92506
DHCR7	7-dehydrocholesterol reductase	Q15392
DHFR	Dihydrofolate reductase	P63172
DHODH	Dihydroorotate dehydrogenase	P27708
DHRS4	Dehydrogenase/reductase SDR family member 4	P09417
DHRS7	Dehydrogenase/reductase SDR family member 7	Q9BTZ2
DHRS7B	Dehydrogenase/reductase SDR family member 7B	P55039
DHTKD1	Probable 2-oxoglutarate dehydrogenase E1 component DHKTD1,	Q9Y394

Gene	Protein name	Accession
	mitochondrial	
DHX15	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15	Q96HY7
DHX16	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX16	O43143
DHX30	Putative ATP-dependent RNA helicase DHX30	O60231
DHX9	ATP-dependent RNA helicase A	Q7L2E3
DIAPH1	Protein diaphanous homolog 1	Q8NDZ4
DKC1	H/ACA ribonucleoprotein complex subunit 4	Q96LL9
DLAT	Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex, mitochondrial	P36957
DLD	Dihydrolipoyl dehydrogenase, mitochondrial	O60832
DLG1	Disks large homolog 1	P09622
DLST	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex, mitochondrial	Q02218
DMAP1	DNA methyltransferase 1-associated protein 1	Q86YH6
DNAJA1	DnaJ homolog subfamily A member 1	Q9NPF5
DNAJA2	DnaJ homolog subfamily A member 2	P31689
DNAJA3	DnaJ homolog subfamily A member 3, mitochondrial	O60884
DNAJB1	DnaJ homolog subfamily B member 1	Q96EY1
DNAJB11	DnaJ homolog subfamily B member 11	O60610
DNAJB12	DnaJ homolog subfamily B member 12	Q9UBS4
DNAJB6	DnaJ homolog subfamily B member 6	P25685
DNAJC10	DnaJ homolog subfamily C member 10	Q9NXW2
DNAJC11	DnaJ homolog subfamily C member 11	Q8IXB1
DNAJC13	DnaJ homolog subfamily C member 13	Q9NVH1
DNAJC15	DnaJ homolog subfamily C member 15	O75165
DNAJC16	DnaJ homolog subfamily C member 16	Q9Y5T4
DNAJC19	Mitochondrial import inner membrane translocase subunit TIM14	Q9Y5L4
DNAJC3	DnaJ homolog subfamily C member 3	O75190
DNAJC30	DnaJ homolog subfamily C member 30	Q9Y2G8
DNAJC5	DnaJ homolog subfamily C member 5	Q13217
DNAJC7	DnaJ homolog subfamily C member 7	Q9H3Z4
DNAJC9	DnaJ homolog subfamily C member 9	Q99615
DNLZ	DNL-type zinc finger protein	Q8WXX5
DNMT1	DNA	Q5SXM8
DNTTIP2	Deoxynucleotidyltransferase terminal-interacting protein 2	P40227
DOCK2	Dedicator of cytokinesis protein 2	P26358
DOLPP1	Dolichyldiphosphatase 1	Q92608
DPF2	Zinc finger protein ubi-d4	Q96D71
DPM1	Dolichol-phosphate mannosyltransferase subunit 1	Q86YN1

Gene	Protein name	Accession
DRG1	Developmentally-regulated GTP-binding protein 1	Q16643
DRG2	Developmentally-regulated GTP-binding protein 2	Q9Y295
DSG1	Desmoglein-1	Q6IAN0
DSTN	Destrin	Q9BSY9
DTYMK	Thymidylate kinase	Q9NSB2
DUT	Deoxyuridine 5'-triphosphate nucleotidohydrolase, mitochondrial	Q02413
DYNC1H1	Cytoplasmic dynein 1 heavy chain 1	O00148
DYNC1H2	Cytoplasmic dynein 1 intermediate chain 2	P61803
DYNLT1	Dynein light chain Tctex-type 1	Q14204
EARS2	Probable glutamate--tRNA ligase, mitochondrial	Q6PI48
EBAG9	Receptor-binding cancer antigen expressed on SiSo cells	P49792
EBNA1BP2	Probable rRNA-processing protein EBP2	Q9HAF1
EBP	3-beta-hydroxysteroid-Delta(8),Delta(7)-isomerase	Q99848
ECH1	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	Q15125
ECHDC1	Ethylmalonyl-CoA decarboxylase	P55084
ECHS1	Enoyl-CoA hydratase, mitochondrial	Q9NXT5
ECI2	Enoyl-CoA delta isomerase 2, mitochondrial	P30084
ECSIT	Evolutionarily conserved signaling intermediate in Toll pathway, mitochondrial	O75521
EDC4	Enhancer of mRNA-decapping protein 4	Q9BQ95
EDEM3	ER degradation-enhancing alpha-mannosidase-like protein 3	Q6P2E9
EEF1D	Elongation factor 1-delta	Q7L9B9
EEF1E1	Eukaryotic translation elongation factor 1 epsilon-1	Q68D91
EEF1G	Elongation factor 1-gamma	P29692
EEF2	Elongation factor 2	P26641
EEPD1	Endonuclease/exonuclease/phosphatase family domain-containing protein 1	Q9BZQ6
EFR3A	Protein EFR3 homolog A	P13639
EFTUD2	116 kDa U5 small nuclear ribonucleoprotein component	O75643
EHD1	EH domain-containing protein 1	P49411
EIF1AX	Eukaryotic translation initiation factor 1A, X-chromosomal	Q13907
EIF1AY	Eukaryotic translation initiation factor 1A, Y-chromosomal	P47813
EIF2S1	Eukaryotic translation initiation factor 2 subunit 1	O14602
EIF2S2	Eukaryotic translation initiation factor 2 subunit 2	O00425
EIF3A	Eukaryotic translation initiation factor 3 subunit A	Q9H4M9
EIF3G	Eukaryotic translation initiation factor 3 subunit G	Q14152
EIF3I	Eukaryotic translation initiation factor 3 subunit I	O75821
EIF3K	Eukaryotic translation initiation factor 3 subunit K	Q13347
EIF3L	Eukaryotic translation initiation factor 3 subunit L	Q9UBQ5
EIF3M	Eukaryotic translation initiation factor 3 subunit M	Q9Y262
EIF4A1	Eukaryotic initiation factor 4A-1	Q9H2K0

Gene	Protein name	Accession
EIF4A2	Eukaryotic initiation factor 4A-II	P60842
EIF4A3	Eukaryotic initiation factor 4A-III	Q14240
EIF4G1	Eukaryotic translation initiation factor 4 gamma 1	P38919
EIF5A	Eukaryotic translation initiation factor 5A-1	Q04637
EIF6	Eukaryotic translation initiation factor 6	P63241
ELAC2	Zinc phosphodiesterase ELAC protein 2	Q63HN8
ELAVL1	ELAV-like protein 1	Q7L2H7
ELMO1	Engulfment and cell motility protein 1	Q15717
EMB	Embigin	Q00013
EMC1	ER membrane protein complex subunit 1	Q6PCB8
EMC2	ER membrane protein complex subunit 2	Q8N766
EMC3	ER membrane protein complex subunit 3	Q15006
EMC4	ER membrane protein complex subunit 4	Q9P0I2
EMC6	ER membrane protein complex subunit 6	Q5J8M3
EMC7	ER membrane protein complex subunit 7	Q9BV81
EMC8	ER membrane protein complex subunit 8	Q9NPA0
EMD	Emerin	O43402
ENDOD1	Endonuclease domain-containing 1 protein	P50402
ENO1	Alpha-enolase	O94919
ENPP4	Bis(5'-adenosyl)-triphosphatase ENPP4	P14625
EPB41L5	Band 4.1-like protein 5	P00374
EPHA3	Ephrin type-A receptor 3	Q9UBC2
EPHX1	Epoxide hydrolase 1	P19367
EPRS	Bifunctional glutamate/proline--tRNA ligase	Q5JPH6
EPS15L1	Epidermal growth factor receptor substrate 15-like 1	Q9Y6X5
ERAL1	GTPase Era, mitochondrial	Q14677
ERAP1	Endoplasmic reticulum aminopeptidase 1	O75616
ERAP2	Endoplasmic reticulum aminopeptidase 2	Q9NZ08
ERBB2IP	Protein LAP2	P42166
ERGIC1	Endoplasmic reticulum-Golgi intermediate compartment protein 1	Q14534
ERGIC2	Endoplasmic reticulum-Golgi intermediate compartment protein 2	P48449
ERGIC3	Endoplasmic reticulum-Golgi intermediate compartment protein 3	Q96RQ1
ERH	Enhancer of rudimentary homolog	Q9Y282
ERLEC1	Endoplasmic reticulum lectin 1	P84090
ERLIN2	Erlin-2	Q96DZ1
ERO1L	ERO1-like protein alpha	O94905
ERP29	Endoplasmic reticulum resident protein 29	Q96HE7
ERP44	Endoplasmic reticulum resident protein 44	P30040
ESD	S-formylglutathione hydrolase	P30042

Gene	Protein name	Accession
ESYT1	Extended synaptotagmin-1	P10768
ETF A	Electron transfer flavoprotein subunit alpha, mitochondrial	Q9BSJ8
ETF B	Electron transfer flavoprotein subunit beta	P13804
ETFDH	Electron transfer flavoprotein-ubiquinone oxidoreductase, mitochondrial	P38117
ETHE1	Persulfide dioxygenase ETHE1, mitochondrial	Q16134
EXD2	Exonuclease 3'-5' domain-containing protein 2	Q95571
EXOC1	Exocyst complex component 1	Q9NVH0
EXOC4	Exocyst complex component 4	Q9NV70
EXOSC10	Exosome component 10	Q9NPD3
EXOSC2	Exosome complex component RRP4	Q96A65
EXOSC4	Exosome complex component RRP41	Q13868
EZR	Ezrin	Q01780
F5	Coagulation factor V	Q9NUQ9
FABP5	Fatty acid-binding protein, epidermal	Q8IVS2
FADS2	Fatty acid desaturase 2	Q8NFF5
FAF2	FAS-associated factor 2	Q95864
FAHD1	Acylpyruvase FAHD1, mitochondrial	Q96GK7
FAHD2A	Fumarylacetoacetate hydrolase domain-containing protein 2A	Q96CS3
FAM120A	Constitutive coactivator of PPAR-gamma-like protein 1	P15311
FAM134C	Protein FAM134C	Q9NZB2
FAM136A	Protein FAM136A	Q86VR2
FAM162A	Protein FAM162A	Q96C01
FAM20B	Glycosaminoglycan xylosylkinase	O75695
FAM213A	Redox-regulatory protein FAM213A	Q96A26
FAM3C	Protein FAM3C	Q7L8L6
FAM49B	Protein FAM49B	Q9BRX8
FAM96B	Mitotic spindle-associated MMXD complex subunit MIP18	Q9UNW1
FAM98B	Protein FAM98B	P12259
FAR1	Fatty acyl-CoA reductase 1	O75844
FARS2	Phenylalanine--tRNA ligase, mitochondrial	Q9NSD9
FARSB	Phenylalanine--tRNA ligase beta subunit	Q9HCS7
FAS	Tumor necrosis factor receptor superfamily member 6	Q92973
FASN	Fatty acid synthase	Q92520
FASTKD1	FAST kinase domain-containing protein 1	Q6P587
FASTKD2	FAST kinase domain-containing protein 2	Q53R41
FASTKD5	FAST kinase domain-containing protein 5	Q9NYY8
FBL	rRNA 2'-O-methyltransferase fibrillar	P49327
FDFT1	Squalene synthase	P22087
FDPS	Farnesyl pyrophosphate synthase	Q05932

Gene	Protein name	Accession
FDX1	Adrenodoxin, mitochondrial	P12236
FDXR	NADPH:adrenodoxin oxidoreductase, mitochondrial	Q9NRN7
FECH	Ferrochelatase, mitochondrial	P36551
FEN1	Flap endonuclease 1	P37268
FERMT3	Fermitin family homolog 3	Q14146
FGFR1OP2	FGFR1 oncogene partner 2	P39748
FH	Fumarate hydratase, mitochondrial	Q92945
FIS1	Mitochondrial fission 1 protein	P02751
FKBP11	Peptidyl-prolyl cis-trans isomerase FKBP11	Q9Y3D6
FKBP2	Peptidyl-prolyl cis-trans isomerase FKBP2	Q9NYL4
FKBP4	Peptidyl-prolyl cis-trans isomerase FKBP4	P26885
FKBP8	Peptidyl-prolyl cis-trans isomerase FKBP8	Q02790
FLAD1	FAD synthase	Q8WVX9
FLG	Filaggrin	Q5D862
FLG2	Filaggrin-2	Q9NVK5
FLNB	Filamin-B	Q15007
FLOT1	Flotillin-1	O75369
FLOT2	Flotillin-2	O75955
FMNL1	Formin-like protein 1	Q14254
FN1	Fibronectin	P20930
FOXRED1	FAD-dependent oxidoreductase domain-containing protein 1	P51114
FPGS	Folypolyglutamate synthase, mitochondrial	Q96DP5
FRG1	Protein FRG1	Q16595
FTH1	Ferritin heavy chain	Q14331
FTL	Ferritin light chain	P02794
FTSJ2	Putative ribosomal RNA methyltransferase 2	Q96E11
FTSJ3	pre-rRNA processing protein FTSJ3	Q8NB90
FUNDC1	FUN14 domain-containing protein 1	Q9BWH2
FUNDC2	FUN14 domain-containing protein 2	P07954
FXN	Frataxin, mitochondrial	P14324
FXR1	Fragile X mental retardation syndrome-related protein 1	Q81VP5
G3BP1	Ras GTPase-activating protein-binding protein 1	Q96CU9
G3BP2	Ras GTPase-activating protein-binding protein 2	Q13283
GAA	Lysosomal alpha-glucosidase	Q9UHA4
GABARAPL2	Gamma-aminobutyric acid receptor-associated protein-like 2	P63244
GADD45GIP1	Growth arrest and DNA damage-inducible proteins-interacting protein 1	P04406
GALK1	Galactokinase	P80404
GALNT1	Polypeptide N-acetylgalactosaminyltransferase 1	P51570
GALNT2	Polypeptide N-acetylgalactosaminyltransferase 2	Q10472

Gene	Protein name	Accession
GALNT7	N-acetylgalactosaminyltransferase 7	Q10471
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase	Q9UN86
GARI	H/ACA ribonucleoprotein complex subunit 1	Q86SF2
GARS	Glycine--tRNA ligase	O95363
GATAD2A	Transcriptional repressor p66-alpha	P54886
GBAS	Protein NipSnap homolog 2	Q9BPW8
GCAT	2-amino-3-ketobutyrate coenzyme A ligase, mitochondrial	Q6YP21
GCDH	Glutaryl-CoA dehydrogenase, mitochondrial	P60520
GDAP1	Ganglioside-induced differentiation-associated protein 1	Q9H3P7
GDE1	Glycerophosphodiester phosphodiesterase 1	Q8TB36
GDI2	Rab GDP dissociation inhibitor beta	Q9NZC3
GFER	FAD-linked sulfhydryl oxidase ALR	Q9BT30
GFM2	Ribosome-releasing factor 2, mitochondrial	Q9P2E9
GFPT1	Glutamine--fructose-6-phosphate aminotransferase [isomerizing] 1	P06396
GGH	Gamma-glutamyl hydrolase	Q06210
GIGYF2	PERQ amino acid-rich with GYF domain-containing protein 2	Q96RR1
GIMAP1	GTPase IMAP family member 1	Q9H936
GK	Glycerol kinase	P04921
GLA	Alpha-galactosidase A	Q8IUX7
GLG1	Golgi apparatus protein 1	P00390
GLRX3	Glutaredoxin-3	P32189
GLRX5	Glutaredoxin-related protein 5, mitochondrial	O76003
GLS	Glutaminase kidney isoform, mitochondrial	Q86SX6
GLUD1	Glutamate dehydrogenase 1, mitochondrial	Q9UBM7
GLYR1	Putative oxidoreductase GLYR1	O94925
GMFB	Glia maturation factor beta	Q49A26
GMFG	Glia maturation factor gamma	P60983
GNA13	Guanine nucleotide-binding protein subunit alpha-13	O60234
GNA15	Guanine nucleotide-binding protein subunit alpha-15	Q14344
GNAI2	Guanine nucleotide-binding protein G(i) subunit alpha-2	P30679
GNAI3	Guanine nucleotide-binding protein G(k) subunit alpha	P04899
GNAQ	Guanine nucleotide-binding protein G(q) subunit alpha	P08754
GNAS	Guanine nucleotide-binding protein G(s) subunit alpha isoforms XLas	P50148
GNAS	Guanine nucleotide-binding protein G(s) subunit alpha isoforms short	Q5JWF2
GNB1	Guanine nucleotide-binding protein G(l)/G(s)/G(t) subunit beta-1	O75879
GNB2L1	Guanine nucleotide-binding protein subunit beta-2-like 1	P62873
GNPAT	Dihydroxyacetone phosphate acyltransferase	P63092
GOLGA2	Golgin subfamily A member 2	O15228
GOLGA3	Golgin subfamily A member 3	Q08379

Gene	Protein name	Accession
GOLGA5	Golgin subfamily A member 5	Q08378
GOLGA7	Golgin subfamily A member 7	Q8TBA6
GOLGB1	Golgin subfamily B member 1	Q7Z5G4
GOPC	Golgi-associated PDZ and coiled-coil motif-containing protein	Q86XS8
GPD1L	Glycerol-3-phosphate dehydrogenase 1-like protein	Q9HD26
GPI	Glucose-6-phosphate isomerase	Q95479
GPSM3	G-protein-signaling modulator 3	Q92643
GPX1	Glutathione peroxidase 1	Q9Y4H4
GRAMD1A	GRAM domain-containing protein 1A	P62993
GRAMD4	GRAM domain-containing protein 4	P07203
GRB2	Growth factor receptor-bound protein 2	Q6IC98
GRPEL1	GrpE protein homolog 1, mitochondrial	P11021
GRPEL2	GrpE protein homolog 2, mitochondrial	Q9HAV7
GRSF1	G-rich sequence factor 1	Q8TAA5
GSN	Gelsolin	P52566
GSR	Glutathione reductase, mitochondrial	Q12849
GSTK1	Glutathione S-transferase kappa 1	Q92896
GSTM1	Glutathione S-transferase Mu 1	Q9Y2Q3
GSTM3	Glutathione S-transferase Mu 3	P09488
GSTO1	Glutathione S-transferase omega-1	P21266
GSTP1	Glutathione S-transferase P	P78417
GTF3C3	General transcription factor 3C polypeptide 3	P55072
GTPBP10	GTP-binding protein 10	Q969Y2
GTPBP3	tRNA modification GTPase GTPBP3, mitochondrial	O43824
GTPBP4	Nucleolar GTP-binding protein 1	Q8WTT2
GTPBP6	Putative GTP-binding protein 6	Q8NBJ5
GUF1	Translation factor GUF1, mitochondrial	P11166
GXYLT1	Glucoside xylosyltransferase 1	Q8N442
GYPC	Glycophorin-C	Q8WWP7
H1FX	Histone H1x	P16401
H2AFV	Histone H2A.V	Q8IUE6
H2AFX	Histone H2AX	Q71U19
H2AFY	Core histone macro-H2A.1	P16104
H6PD	GDH/6PGL endoplasmic bifunctional protein	Q8TAE8
HACL1	2-hydroxyacyl-CoA lyase 1	Q9P035
HADH	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial	Q99714
HADHA	Trifunctional enzyme subunit alpha, mitochondrial	Q13011
HADHB	Trifunctional enzyme subunit beta, mitochondrial	P40939
HARS2	Probable histidine--tRNA ligase, mitochondrial	P41250

Gene	Protein name	Accession
HAUS1	HAUS augmin-like complex subunit 1	Q9UJ83
HAUS3	HAUS augmin-like complex subunit 3	Q9H6D7
HAUS4	HAUS augmin-like complex subunit 4	Q96CS2
HAUS7	HAUS augmin-like complex subunit 7	Q68CZ6
HAX1	HCLS1-associated protein X-1	Q99871
HBA1;	Hemoglobin subunit alpha	O00165
HBB	Hemoglobin subunit beta	P69905
HBD	Hemoglobin subunit delta	P68871
HCCS	Cytochrome c-type heme lyase	Q4VC31
HDDC2	HD domain-containing protein 2	Q16836
HDHD3	Haloacid dehalogenase-like hydrolase domain-containing protein 3	Q7Z4H3
HEATR1	HEAT repeat-containing protein 1	Q9BSH5
HEXB	Beta-hexosaminidase subunit beta	P22830
HIBADH	3-hydroxyisobutyrate dehydrogenase, mitochondrial	P63151
HIBCH	3-hydroxyisobutyryl-CoA hydrolase, mitochondrial	Q07686
HIGD1A	HIG1 domain family member 1A, mitochondrial	P6NVY1
HIGD2A	HIG1 domain family member 2A, mitochondrial	Q9Y241
HINT3	Histidine triad nucleotide-binding protein 3	Q9BW72
HIST1H1B	Histone H1.5	P16402
HIST1H1C	Histone H1.2	Q4G148
HIST1H1D	Histone H1.3	P16403
HIST1H2AC	Histone H2A type 1-C	Q92522
HIST1H2AG	Histone H2A type 1	Q99878
HIST1H2AH	Histone H2A type 1-H	Q93077
HIST1H2AJ	Histone H2A type 1-J	Q96KK5
HIST1H2BB	Histone H2B type 1-B	O75367
HIST1H2BC	Histone H2B type 1-C/E/F/G/I	P33778
HIST1H2BD	Histone H2B type 1-D	P62807
HIST1H2BH	Histone H2B type 1-H	P58876
HIST1H3A	Histone H3.1	Q93079
HIST1H4A	Histone H4	P68431
HIST2H2AB	Histone H2A type 2-B	P0C0S8
HK1	Hexokinase-1	O43464
HLA-A	HLA class I histocompatibility antigen, A-3 alpha chain	P63104
HLA-A	HLA class I histocompatibility antigen, A-25 alpha chain	P04439
HLA-A	HLA class I histocompatibility antigen, A-26 alpha chain	P04439
HLA-B	HLA class I histocompatibility antigen, B-8 alpha chain	P04439
HLA-E	HLA class I histocompatibility antigen, alpha chain E	Q9NQE9
HMGA1	High mobility group protein HMG-I/HMG-Y	P13747

Gene	Protein name	Accession
HNRNPA0	Heterogeneous nuclear ribonucleoprotein A0	Q9BQ52
HNRNPA1	Heterogeneous nuclear ribonucleoprotein A1	Q13151
HNRNPA2B1	Heterogeneous nuclear ribonucleoproteins A2/B1	P09651
HNRNPA3	Heterogeneous nuclear ribonucleoprotein A3	P22626
HNRNPC	Heterogeneous nuclear ribonucleoproteins C1/C2	P31942
HNRNPD	Heterogeneous nuclear ribonucleoprotein D0	P07910
HNRNPF	Heterogeneous nuclear ribonucleoprotein F	Q14103
HNRNPH1	Heterogeneous nuclear ribonucleoprotein H	P17096
HNRNPH3	Heterogeneous nuclear ribonucleoprotein H3	Q9BUJ2
HNRNPL	Heterogeneous nuclear ribonucleoprotein L	P52597
HNRNPM	Heterogeneous nuclear ribonucleoprotein M	P14866
HNRNPR	Heterogeneous nuclear ribonucleoprotein R	P52272
HNRNPUL1	Heterogeneous nuclear ribonucleoprotein U-like protein 1	P31943
HP1BP3	Heterochromatin protein 1-binding protein 3	Q86YZ3
HPCAL1	Hippocalcin-like protein 1	Q9NZL4
HRAS	GTPase HRas	Q14644
HRNR	Hornerin	O43390
HRSP12	Ribonuclease UK114	Q9NYU2
HS2ST1	Heparan sulfate 2-O-sulfotransferase 1	Q92598
HSCB	Iron-sulfur cluster co-chaperone protein HscB, mitochondrial	P08238
HSD17B10	3-hydroxyacyl-CoA dehydrogenase type-2	P02042
HSD17B11	Estradiol 17-beta-dehydrogenase 11	P60981
HSD17B12	Estradiol 17-beta-dehydrogenase 12	Q8NBQ5
HSD17B4	Peroxisomal multifunctional enzyme type 2	Q53GQ0
HSD17B7	3-keto-steroid reductase	P51659
HSD17B8	Estradiol 17-beta-dehydrogenase 8	P56937
HSDL2	Hydroxysteroid dehydrogenase-like protein 2	Q8IWL3
HSP90AA1	Heat shock protein HSP 90-alpha	Q7LGA3
HSP90AB1	Heat shock protein HSP 90-beta	P07900
HSP90B1	Endoplasmic	P06733
HSPA13	Heat shock 70 kDa protein 13	Q6YN16
HSPA1A	Heat shock 70 kDa protein 1A/1B	P48723
HSPA4	Heat shock 70 kDa protein 4	P08107
HSPA5	78 kDa glucose-regulated protein	Q96CP6
HSPA8	Heat shock cognate 71 kDa protein	P34932
HSPBP1	Hsp70-binding protein 1	Q5SSJ5
HSPD1	60 kDa heat shock protein, mitochondrial	Q15782
HSPE1	10 kDa heat shock protein, mitochondrial	Q6P1X6
HSPH1	Heat shock protein 105 kDa	P37235

Gene	Protein name	Accession
HTRA2	Serine protease HTRA2, mitochondrial	P11142
HYOU1	Hypoxia up-regulated protein 1	P07099
IARS2	Isoleucine--tRNA ligase, mitochondrial	P49590
IBA57	Putative transferase CAF17, mitochondrial	P19022
ICAM2	Intercellular adhesion molecule 2	Q9H2X8
ICT1	Peptidyl-tRNA hydrolase ICT1, mitochondrial	P13598
IDE	Insulin-degrading enzyme	Q14197
IDH2	Isocitrate dehydrogenase [NADP], mitochondrial	P51553
IDH3A	Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial	P14735
IDH3B	Isocitrate dehydrogenase [NAD] subunit beta, mitochondrial	P50213
IDH3G	Isocitrate dehydrogenase [NAD] subunit gamma, mitochondrial	O43837
IDI1	Isopentenyl-diphosphate Delta-isomerase 1	P48735
IFI27L2	Interferon alpha-inducible protein 27-like protein 2	Q9Y4L1
IGF2BP1	Insulin-like growth factor 2 mRNA-binding protein 1	P05198
IGF2BP3	Insulin-like growth factor 2 mRNA-binding protein 3	Q9NZI8
IGLL1	Immunoglobulin lambda-like polypeptide 1	P56537
IGSF8	Immunoglobulin superfamily member 8	P15814
IKBIP	Inhibitor of nuclear factor kappa-B kinase-interacting protein	Q969P0
IKZF1	DNA-binding protein Ikaros	Q70UQ0
IKZF2	Zinc finger protein Helios	Q13422
IL2RG	Cytokine receptor common subunit gamma	Q9UKS7
ILF2	Interleukin enhancer-binding factor 2	P31785
ILVBL	Acetolactate synthase-like protein	Q12905
IMMP1L	Mitochondrial inner membrane protease subunit 1	Q16891
IMMP2L	Mitochondrial inner membrane protease subunit 2	Q96LU5
IMMT	Mitochondrial inner membrane protein	P12268
IMP3	U3 small nucleolar ribonucleoprotein protein IMP3	Q96T52
IMPAD1	Inositol monophosphatase 3	Q9NV31
IMPDH2	Inosine-5'-monophosphate dehydrogenase 2	Q14974
INA	Alpha-internexin	Q12904
INPP5K	Inositol polyphosphate 5-phosphatase K	Q9NX62
IPO5	Importin-5	Q9BT40
IQGAP1	Ras GTPase-activating-like protein IQGAP1	Q15181
ISCA1	Iron-sulfur cluster assembly 1 homolog, mitochondrial	P46940
ISCA2	Iron-sulfur cluster assembly 2 homolog, mitochondrial	Q9BUE6
ISCU	Iron-sulfur cluster assembly enzyme ISCU, mitochondrial	Q86U28
ISG15	Ubiquitin-like protein ISG15	Q9H1K1
ISOC1	Isochorismatase domain-containing protein 1	P05161
ISOC2	Isochorismatase domain-containing protein 2, mitochondrial	Q96CN7

Gene	Protein name	Accession
ISY1	Pre-mRNA-splicing factor ISY1 homolog	Q96AB3
ITFG3	Protein ITFG3	P05556
ITGA4	Integrin alpha-4	Q9ULR0
ITGA5	Integrin alpha-5	P13612
ITGAL	Integrin alpha-L	P08648
ITGB1	Integrin beta-1	P20701
ITK	Tyrosine-protein kinase ITK/TSK	Q9H0X4
ITM2B	Integral membrane protein 2B	Q08881
ITM2C	Integral membrane protein 2C	Q9Y287
ITPA	Inosine triphosphate pyrophosphatase	Q9NQX7
ITPR2	Inositol 1,4,5-trisphosphate receptor type 2	Q9BY32
ITPR3	Inositol 1,4,5-trisphosphate receptor type 3	Q14571
JAGN1	Protein jagunal homolog 1	Q14573
JAM3	Junctional adhesion molecule C	Q8N5M9
KARS	Lysine--tRNA ligase	P57105
KCNAB2	Voltage-gated potassium channel subunit beta-2	Q9Y6M4
KDSR	3-ketodihydrospingosine reductase	Q9ULH0
KHSRP	Far upstream element-binding protein 2	P02792
KIAA0020	Pumilio domain-containing protein KIAA0020	Q9BX67
KIAA0391	Mitochondrial ribonuclease P protein 3	P49006
KIDINS220	Kinase D-interacting substrate of 220 kDa	P30085
KIF2A	Kinesin-like protein KIF2A	P46013
KIF2C	Kinesin-like protein KIF2C	O00139
KIF5B	Kinesin-1 heavy chain	Q99661
KPNA3	Importin subunit alpha-4	A1L0T0
KPNB1	Importin subunit beta-1	O00505
KRT1	Keratin, type II cytoskeletal 1	P35908
KRT10	Keratin, type I cytoskeletal 10	Q15397
KRT14	Keratin, type I cytoskeletal 14	P13645
KRT16	Keratin, type I cytoskeletal 16	P02533
KRT17	Keratin, type I cytoskeletal 17	P08779
KRT2	Keratin, type II cytoskeletal 2 epidermal	P35527
KRT5	Keratin, type II cytoskeletal 5	P04264
KRT6C	Keratin, type II cytoskeletal 6C	P13647
KRT84	Keratin, type II cuticular Hb4	P14618
KRT9	Keratin, type I cytoskeletal 9	Q04695
KTN1	Kinectin	P23919
L2HGDH	L-2-hydroxyglutarate dehydrogenase, mitochondrial	Q86UP2
LACTB	Serine beta-lactamase-like protein LACTB, mitochondrial	Q9H9P8

Gene	Protein name	Accession
LAMP1	Lysosome-associated membrane glycoprotein 1	P83111
LAMP2	Lysosome-associated membrane glycoprotein 2	P11279
LAMTOR1	Ragulator complex protein LAMTOR1	Q3MHD2
LAMTOR2	Ragulator complex protein LAMTOR2	Q6IAA8
LAMTOR3	Ragulator complex protein LAMTOR3	Q9Y2Q5
LANCL2	LanC-like protein 2	P13473
LAP3	Cytosol aminopeptidase	P55789
LAPTM5	Lysosomal-associated transmembrane protein 5	Q96RT1
LARP4	La-related protein 4	Q13571
LARS	Leucine--tRNA ligase, cytoplasmic	Q15046
LARS2	Probable leucine--tRNA ligase, mitochondrial	Q9P2J5
LAS1L	Ribosomal biogenesis protein LAS1L	Q71RC2
LAT	Linker for activation of T-cells family member 1	Q01650
LBR	Lamin-B receptor	P05455
LCK	Tyrosine-protein kinase Lck	Q9UIQ6
LCP1	Plastin-2	Q9HBL7
LDHA	L-lactate dehydrogenase A chain	P06239
LDHB	L-lactate dehydrogenase B chain	P00338
LDLR	Low-density lipoprotein receptor	P07195
LEMD2	LEM domain-containing protein 2	O00182
LEPRE1	Prolyl 3-hydroxylase 1	O95747
LETM1	LETM1 and EF-hand domain-containing protein 1, mitochondrial	Q8NC56
LGALS3BP	Galectin-3-binding protein	P16150
LGALS9	Galectin-9	P01130
LIN7C	Protein lin-7 homolog C	Q08380
LMAN1	Protein ERGIC-53	P43034
LMAN2	Vesicular integral-membrane protein VIP36	P49257
LMNB1	Lamin-B1	Q12907
LMNB2	Lamin-B2	P20700
LNPEP	Leucyl-cystinyl aminopeptidase	Q9Y383
LONP1	Lon protease homolog, mitochondrial	Q03252
LPCAT1	Lysophosphatidylcholine acyltransferase 1	Q96AQ6
LRPAP1	Alpha-2-macroglobulin receptor-associated protein	P28838
LRPPRC	Leucine-rich PPR motif-containing protein, mitochondrial	P36776
LRRC59	Leucine-rich repeat-containing protein 59	P42704
LRRC8A	Leucine-rich repeat-containing protein 8A	Q96AG4
LSM12	Protein LSM12 homolog	Q8IWT6
LSS	Lanosterol synthase	Q969X5
LUC7L2	Putative RNA-binding protein Luc7-like 2	Q14739

Gene	Protein name	Accession
LYAR	Cell growth-regulating nucleolar protein	P10253
LYPLAL1	Lysophospholipase-like protein 1	Q9NX58
LYRM4	LYR motif-containing protein 4	Q86UE4
LYRM7	Complex III assembly factor LYRM7	Q9HD34
LYZ	Lysozyme C	Q5U5X0
M6PR	Cation-dependent mannose-6-phosphate receptor	Q10713
MACROD1	O-acetyl-ADP-ribose deacetylase MACROD1	O00754
MAD2L1	Mitotic spindle assembly checkpoint protein MAD2A	Q8NE86
MAFK	Transcription factor MafK	Q9BQ69
MAGOH	Protein mago nashi homolog	Q9BQP7
MAK16	Protein MAK16 homolog	O60675
MALSU1	Mitochondrial assembly of ribosomal large subunit protein 1	Q9NX47
MAN1A2	Mannosyl-oligosaccharide 1,2-alpha-mannosidase IB	Q02978
MAN1B1	Endoplasmic reticulum mannosyl-oligosaccharide 1,2-alpha-mannosidase	O60476
MAN2B1	Lysosomal alpha-mannosidase	Q9UKM7
MANF	Mesencephalic astrocyte-derived neurotrophic factor	Q9BXV0
MAP2K2	Dual specificity mitogen-activated protein kinase kinase 2	P53985
MAPRE1	Microtubule-associated protein RP/EB family member 1	P23368
MARCH5	E3 ubiquitin-protein ligase MARCH5	Q15691
MARCKSL1	MARCKS-related protein	P33527
MARS	Methionine--tRNA ligase, cytoplasmic	Q15031
MARS2	Methionine--tRNA ligase, mitochondrial	P56192
MAT2A	S-adenosylmethionine synthase isoform type-2	Q9H7H0
MAT2B	Methionine adenosyltransferase 2 subunit beta	Q96EH3
MATR3	Matrin-3	Q9NZL9
MAVS	Mitochondrial antiviral-signaling protein	P43243
MBD3	Methyl-CpG-binding domain protein 3	Q9BQG0
MBLAC2	Metallo-beta-lactamase domain-containing protein 2	O95983
MCAT	Malonyl-CoA-acyl carrier protein transacylase, mitochondrial	Q52LJ0
MCCC1	Methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial	O43772
MCCC2	Methylcrotonoyl-CoA carboxylase beta chain, mitochondrial	Q96RQ3
MCEE	Methylmalonyl-CoA epimerase, mitochondrial	Q9HCC0
MCM2	DNA replication licensing factor MCM2	Q96PE7
MCM3	DNA replication licensing factor MCM3	P49736
MCM7	DNA replication licensing factor MCM7	P25205
MCU	Calcium uniporter protein, mitochondrial	Q96AQ8
MCUR1	Mitochondrial calcium uniporter regulator 1	P33993
MDH1	Malate dehydrogenase, cytoplasmic	Q13257
MDH2	Malate dehydrogenase, mitochondrial	P40925

Gene	Protein name	Accession
ME2	NAD-dependent malic enzyme, mitochondrial	P55145
MEAF6	Chromatin modification-related protein MEAF6	Q9HCM4
MECR	Trans-2-enoyl-CoA reductase, mitochondrial	P40926
MED21	Mediator of RNA polymerase II transcription subunit 21	Q9BV79
MED22	Mediator of RNA polymerase II transcription subunit 22	Q13503
MESDC2	LDLR chaperone MESD	Q9BQA1
METTL15	Probable methyltransferase-like protein 15	Q14696
METTL17	Methyltransferase-like protein 17, mitochondrial	A6NJ78
MFF	Mitochondrial fission factor	P31153
MFGE8	Lactadherin	Q9GZY8
MFN1	Mitofusin-1	Q08431
MFN2	Mitofusin-2	Q8IWA4
MGAT1	Alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase	Q9H2D1
MGAT2	Alpha-1,6-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase	P26572
MGME1	Mitochondrial genome maintenance exonuclease 1	Q10469
MGST3	Microsomal glutathione S-transferase 3	P61326
MIA3	Melanoma inhibitory activity protein 3	O14880
MICU1	Calcium uptake protein 1, mitochondrial	Q8N4Q1
MICU2	Calcium uptake protein 2, mitochondrial	Q9BPX6
MINPP1	Multiple inositol polyphosphate phosphatase 1	Q8N183
MIPEP	Mitochondrial intermediate peptidase	Q9Y3D0
MKI67	Antigen KI-67	Q06136
MLEC	Malectin	O14950
MLYCD	Malonyl-CoA decarboxylase, mitochondrial	P27707
MMAA	Methylmalonic aciduria type A protein, mitochondrial	Q14165
MMGT1	Membrane magnesium transporter 1	Q8IVH4
MOB1A	MOB kinase activator 1A	Q02252
MOB1B	MOB kinase activator 1B	Q9H8S9
MOCS1	Molybdenum cofactor biosynthesis protein 1	Q7L9L4
MOGS	Mannosyl-oligosaccharide glucosidase	P26038
MPC2	Mitochondrial pyruvate carrier 2	P36507
MPHOSPH10	U3 small nucleolar ribonucleoprotein protein MPP10	Q00325
MPP1	55 kDa erythrocyte membrane protein	Q15370
MPP6	MAGUK p55 subfamily member 6	O00566
MPST	3-mercaptopyruvate sulfurtransferase	Q86W42
MPV17	Protein Mpv17	P20645
MRM1	rRNA methyltransferase 1, mitochondrial	P39210
MRPL1	39S ribosomal protein L1, mitochondrial	P05387
MRPL11	39S ribosomal protein L11, mitochondrial	Q9BYD2

Gene	Protein name	Accession
MRPL13	39S ribosomal protein L13, mitochondrial	Q9Y3B7
MRPL14	39S ribosomal protein L14, mitochondrial	Q9BYD1
MRPL15	39S ribosomal protein L15, mitochondrial	Q6P1L8
MRPL16	39S ribosomal protein L16, mitochondrial	Q9P015
MRPL17	39S ribosomal protein L17, mitochondrial	Q9NX20
MRPL18	39S ribosomal protein L18, mitochondrial	Q9NRX2
MRPL19	39S ribosomal protein L19, mitochondrial	Q9H0U6
MRPL2	39S ribosomal protein L2, mitochondrial	Q9BYD6
MRPL20	39S ribosomal protein L20, mitochondrial	Q9NWU5
MRPL21	39S ribosomal protein L21, mitochondrial	P49406
MRPL22	39S ribosomal protein L22, mitochondrial	Q7Z2W9
MRPL23	39S ribosomal protein L23, mitochondrial	Q9P0M9
MRPL27	39S ribosomal protein L27, mitochondrial	Q9BYC9
MRPL28	39S ribosomal protein L28, mitochondrial	Q16540
MRPL3	39S ribosomal protein L3, mitochondrial	Q5T653
MRPL30	39S ribosomal protein L30, mitochondrial	Q9BYC8
MRPL32	39S ribosomal protein L32, mitochondrial	Q13084
MRPL35	39S ribosomal protein L35, mitochondrial	Q8TCC3
MRPL37	39S ribosomal protein L37, mitochondrial	Q9NZE8
MRPL38	39S ribosomal protein L38, mitochondrial	Q9NYK5
MRPL39	39S ribosomal protein L39, mitochondrial	Q9BZE1
MRPL4	39S ribosomal protein L4, mitochondrial	P09001
MRPL40	39S ribosomal protein L40, mitochondrial	Q96DV4
MRPL41	39S ribosomal protein L41, mitochondrial	Q9NQ50
MRPL42	39S ribosomal protein L42, mitochondrial	Q8N983
MRPL43	39S ribosomal protein L43, mitochondrial	Q8IXM3
MRPL44	39S ribosomal protein L44, mitochondrial	Q9Y6G3
MRPL46	39S ribosomal protein L46, mitochondrial	Q9H9J2
MRPL47	39S ribosomal protein L47, mitochondrial	Q9H2W6
MRPL48	39S ribosomal protein L48, mitochondrial	Q9HD33
MRPL49	39S ribosomal protein L49, mitochondrial	Q8N5N7
MRPL50	39S ribosomal protein L50, mitochondrial	Q96GC5
MRPL53	39S ribosomal protein L53, mitochondrial	Q13405
MRPL54	39S ribosomal protein L54, mitochondrial	Q96EL3
MRPL55	39S ribosomal protein L55, mitochondrial	Q6P161
MRPL57	Ribosomal protein 63, mitochondrial	Q8WVV3
MRPL9	39S ribosomal protein L9, mitochondrial	Q9BYD3
MRPS10	28S ribosomal protein S10, mitochondrial	P82933
MRPS11	28S ribosomal protein S11, mitochondrial	P82664

Gene	Protein name	Accession
MRPS12	28S ribosomal protein S12, mitochondrial	P82912
MRPS14	28S ribosomal protein S14, mitochondrial	O15235
MRPS15	28S ribosomal protein S15, mitochondrial	O60783
MRPS16	28S ribosomal protein S16, mitochondrial	P82914
MRPS17	28S ribosomal protein S17, mitochondrial	Q9Y3D3
MRPS18A	28S ribosomal protein S18a, mitochondrial	Q9Y2R5
MRPS18B	28S ribosomal protein S18b, mitochondrial	Q9NVS2
MRPS2	28S ribosomal protein S2, mitochondrial	P08865
MRPS21	28S ribosomal protein S21, mitochondrial	Q9Y676
MRPS22	28S ribosomal protein S22, mitochondrial	P82921
MRPS23	28S ribosomal protein S23, mitochondrial	P82650
MRPS24	28S ribosomal protein S24, mitochondrial	Q9Y3D9
MRPS25	28S ribosomal protein S25, mitochondrial	Q96EL2
MRPS26	28S ribosomal protein S26, mitochondrial	P82663
MRPS27	28S ribosomal protein S27, mitochondrial	Q9BYN8
MRPS28	28S ribosomal protein S28, mitochondrial	Q92552
MRPS30	28S ribosomal protein S30, mitochondrial	P51398
MRPS31	28S ribosomal protein S31, mitochondrial	Q9NP92
MRPS33	28S ribosomal protein S33, mitochondrial	Q92665
MRPS34	28S ribosomal protein S34, mitochondrial	Q9Y291
MRPS35	28S ribosomal protein S35, mitochondrial	P82930
MRPS36	28S ribosomal protein S36, mitochondrial	P82673
MRPS5	28S ribosomal protein S5, mitochondrial	Q9Y399
MRPS6	28S ribosomal protein S6, mitochondrial	P82675
MRPS7	28S ribosomal protein S7, mitochondrial	P82932
MRPS9	28S ribosomal protein S9, mitochondrial	Q9Y2R9
MRRF	Ribosome-recycling factor, mitochondrial	Q969S9
MRS2	Magnesium transporter MRS2 homolog, mitochondrial	Q7L0Y3
MSN	Moesin	Q9NZB8
MSRB2	Methionine-R-sulfoxide reductase B2, mitochondrial	Q9HD23
MTA1	Metastasis-associated protein MTA1	Q9Y3D2
MTA2	Metastasis-associated protein MTA2	Q13330
MTCH2	Mitochondrial carrier homolog 2	O94776
MTDH	Protein LYRIC	Q5VWZ2
MTERF	Transcription termination factor, mitochondrial	Q96E29
MTERFD1	mTERF domain-containing protein 1, mitochondrial	Q7Z6M4
MTERFD2	mTERF domain-containing protein 2	P13995
MTFMT	Methionyl-tRNA formyltransferase, mitochondrial	O95466
MTFP1	Mitochondrial fission process protein 1	Q99551

Gene	Protein name	Accession
MTFR1	Mitochondrial fission regulator 1	Q9UDX5
MTFR2	Mitochondrial fission regulator 2	Q15390
MTHFD1	C-1-tetrahydrofolate synthase, cytoplasmic	Q07021
MTHFD1L	Monofunctional C1-tetrahydrofolate synthase, mitochondrial	P11586
MTHFD2	Bifunctional methylenetetrahydrofolate dehydrogenase/cyclohydrolase, mitochondrial	Q9Y6C9
MTIF2	Translation initiation factor IF-2, mitochondrial	P20042
MTIF3	Translation initiation factor IF-3, mitochondrial	P46199
MTO1	Protein MTO1 homolog, mitochondrial	Q6P444
MTPAP	Poly(A) RNA polymerase, mitochondrial	Q13310
MTPN	Myotrophin	Q9Y2Z2
MTRF1	Peptide chain release factor 1, mitochondrial	Q92785
MTX1	Metaxin-1	O75648
MTX2	Metaxin-2	Q13505
MUL1	Mitochondrial ubiquitin ligase activator of NFKB 1	O75431
MUT	Methylmalonyl-CoA mutase, mitochondrial	Q969V5
MYBBP1A	Myb-binding protein 1A	Q7Z434
MYCBP	C-Myc-binding protein	Q92614
MYH9	Myosin-9	Q9HB07
MYL12A	Myosin regulatory light chain 12A	Q9BYG3
MYL12B	Myosin regulatory light chain 12B	P19105
MYO18A	Unconventional myosin-XVIIa	P22033
MYO1B	Unconventional myosin-Ib	P35579
MYO1G	Unconventional myosin-Ig	O43795
MYO7B	Unconventional myosin-VIIb	B011T2
MZB1	Marginal zone B- and B1-cell-specific protein	Q6PIF6
MZT2B	Mitotic-spindle organizing protein 2B	Q8WU39
NAA50	N-alpha-acetyltransferase 50	Q6NZ67
NADK2	NAD kinase 2, mitochondrial	Q9UJ70
NAGK	N-acetyl-D-glucosamine kinase	Q9GZZ1
NAP1L1	Nucleosome assembly protein 1-like 1	O60287
NAPA	Alpha-soluble NSF attachment protein	Q2TAY7
NAPG	Gamma-soluble NSF attachment protein	P54920
NARS	Asparagine--tRNA ligase, cytoplasmic	Q92797
NARS2	Probable asparagine--tRNA ligase, mitochondrial	O43776
NAT10	N-acetyltransferase 10	Q4G0N4
NAT14	N-acetyltransferase 14	Q9H0A0
NBAS	Neuroblastoma-amplified sequence	P00387
NCBP2	Nuclear cap-binding protein subunit 2	A2RRP1

Gene	Protein name	Accession
NCEH1	Neutral cholesterol ester hydrolase 1	P52298
NCL	Nucleolin	P80303
NCLN	Nicalin	Q6PIU2
NDUFA10	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10, mitochondrial	Q86Y39
NDUFA11	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 11	Q9UI09
NDUFA12	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 12	P51970
NDUFA13	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13	O95299
NDUFA2	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 2	O00746
NDUFA4	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 4	O43678
NDUFA5	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 5	O00483
NDUFA6	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 6	Q16718
NDUFA7	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 7	P56556
NDUFA8	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 8	O95182
NDUFAB1	Acyl carrier protein, mitochondrial	Q15067
NDUFAF1	Complex I intermediate-associated protein 30, mitochondrial	Q5T280
NDUFAF2	Mimitin, mitochondrial	Q8IYU8
NDUFAF3	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 3	O95298
NDUFAF4	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 4	Q9BU61
NDUFAF5	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 5	Q9P032
NDUFAF6	NADH dehydrogenase	Q5TEU4
NDUFAF7	NADH dehydrogenase [ubiquinone] complex I, assembly factor 7	Q330K2
NDUFB10	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 10	Q9Y6M9
NDUFB11	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 11, mitochondrial	O96000
NDUFB3	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 3	Q9P0J0
NDUFB4	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 4	O43676
NDUFB5	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 5, mitochondrial	O95168
NDUFB6	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 6	O43674
NDUFB7	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 7	O95139
NDUFB8	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 8, mitochondrial	P17568
NDUFB9	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 9	O95169
NDUFC2	NADH dehydrogenase [ubiquinone] 1 subunit C2	Q9NX14
NDUFS1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	Q7L592
NDUFS2	NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial	P28331
NDUFS3	NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial	O75306
NDUFS4	NADH dehydrogenase [ubiquinone] iron-sulfur protein 4, mitochondrial	O75489

Gene	Protein name	Accession
NDUFS6	NADH dehydrogenase [ubiquinone] iron-sulfur protein 6, mitochondrial	O43181
NDUFS7	NADH dehydrogenase [ubiquinone] iron-sulfur protein 7, mitochondrial	O75380
NDUFV1	NADH dehydrogenase [ubiquinone] flavoprotein 1, mitochondrial	O75251
NDUFV2	NADH dehydrogenase [ubiquinone] flavoprotein 2, mitochondrial	P49821
NEDD1	Protein NEDD1	P19404
NEK2	Serine/threonine-protein kinase Nek2	Q8NHV4
NELFB	Negative elongation factor B	P51955
NENF	Neudesin	Q8WX92
NFU1	NFU1 iron-sulfur cluster scaffold homolog, mitochondrial	Q9BYT8
NFXL1	NF-X1-type zinc finger protein NFXL1	Q9UMS0
NHP2	H/ACA ribonucleoprotein complex subunit 2	P55769
NHP2L1	NHP2-like protein 1	Q6ZNB6
NIFK	MKI67 FHA domain-interacting nucleolar phosphoprotein	Q8IX11
NIP7	60S ribosome subunit biogenesis protein NIP7 homolog	O14745
NIPSNAP1	Protein NipSnap homolog 1	Q9Y221
NIPSNAP3A	Protein NipSnap homolog 3A	P06748
NIT2	Omega-amidase NIT2	O75323
NLN	Neurolysin, mitochondrial	Q8NFW8
NLRX1	NLR family member X1	Q9NQR4
NME4	Nucleoside diphosphate kinase, mitochondrial	O75414
NME6	Nucleoside diphosphate kinase 6	Q969V3
NNT	NAD(P) transhydrogenase, mitochondrial	Q8NCW5
NOA1	Nitric oxide-associated protein 1	Q13423
NOC3L	Nucleolar complex protein 3 homolog	Q9BVI4
NOC4L	Nucleolar complex protein 4 homolog	Q8NC60
NOL11	Nucleolar protein 11	Q9BZE4
NOL6	Nucleolar protein 6	Q9H8H0
NOLC1	Nucleolar and coiled-body phosphoprotein 1	Q9H6R4
NOMO2	Nodal modulator 2	Q14978
NONO	Non-POU domain-containing octamer-binding protein	Q5JPE7
NOP16	Nucleolar protein 16	Q15233
NOP2	Putative ribosomal RNA methyltransferase NOP2	Q9Y3C1
NOP56	Nucleolar protein 56	P46087
NOP58	Nucleolar protein 58	O00567
NPM1	Nucleophosmin	P55209
NPTN	Neuroplastin	Q9UFN0
NR2C2AP	Nuclear receptor 2C2-associated protein	Q9Y639
NRAS	GTPase NRas	Q86YV0
NRM	Nurim	Q86WQ0

Gene	Protein name	Accession
NSDHL	Sterol-4-alpha-carboxylate 3-dehydrogenase, decarboxylating	Q8IXM6
NSF	Vesicle-fusing ATPase	Q9NXX6
NSMCE4A	Non-structural maintenance of chromosomes element 4 homolog A	Q15738
NSUN2	tRNA	Q9NXE4
NSUN4	5-methylcytosine rRNA methyltransferase NSUN4	Q08J23
NT5C3A	Cytosolic 5'-nucleotidase 3A	P08195
NT5DC2	5'-nucleotidase domain-containing protein 2	Q86UY8
NT5DC3	5'-nucleotidase domain-containing protein 3	Q96CB9
NTPCR	Cancer-related nucleoside-triphosphatase	Q9H857
NUBPL	Iron-sulfur protein NUBPL	P35658
NUCB2	Nucleobindin-2	Q8TB37
NUDC	Nuclear migration protein nudC	Q8WVJ2
NUDCD2	NudC domain-containing protein 2	P19338
NUDT1	7,8-dihydro-8-oxoguanine triphosphatase	Q9H0P0
NUDT2	Bis(5'-nucleosyl)-tetraphosphatase [asymmetrical]	P53680
NUDT21	Cleavage and polyadenylation specificity factor subunit 5	Q9P210
NUDT8	Nucleoside diphosphate-linked moiety X motif 8, mitochondrial	Q9Y266
NUFIP2	Nuclear fragile X mental retardation-interacting protein 2	Q8WV74
NUMA1	Nuclear mitotic apparatus protein 1	Q7Z417
NUP107	Nuclear pore complex protein Nup107	Q9BSD7
NUP133	Nuclear pore complex protein Nup133	P57740
NUP153	Nuclear pore complex protein Nup153	Q8WUM0
NUP155	Nuclear pore complex protein Nup155	P49790
NUP160	Nuclear pore complex protein Nup160	O75694
NUP188	Nucleoporin NUP188 homolog	Q12769
NUP205	Nuclear pore complex protein Nup205	Q5SRE5
NUP210	Nuclear pore membrane glycoprotein 210	Q8TCS8
NUP214	Nuclear pore complex protein Nup214	Q92621
NUP35	Nucleoporin NUP53	Q9UKX7
NUP43	Nucleoporin Nup43	Q14980
NUP50	Nuclear pore complex protein Nup50	Q8NFB3
NUP54	Nucleoporin p54	Q8NFB5
NUP62	Nuclear pore glycoprotein p62	Q7Z3B4
NUP85	Nuclear pore complex protein Nup85	P37198
NUP88	Nuclear pore complex protein Nup88	Q8N1F7
NUP93	Nuclear pore complex protein Nup93	Q9BW27
NUP98	Nuclear pore complex protein Nup98-Nup96	Q99567
NUPL1	Nucleoporin p58/p45	P52948
NXF1	Nuclear RNA export factor 1	Q9BVL2

Gene	Protein name	Accession
OARD1	O-acetyl-ADP-ribose deacetylase 1	Q9UBU9
OAT	Ornithine aminotransferase, mitochondrial	Q9Y530
OCLAD1	OCLAD domain-containing protein 1	P04181
OCLAD2	OCLAD domain-containing protein 2	Q9NX40
ODF2	Outer dense fiber protein 2	P12694
OGDH	2-oxoglutarate dehydrogenase, mitochondrial	Q5BJF6
OLA1	Obg-like ATPase 1	Q9H488
ORC4	Origin recognition complex subunit 4	Q9NTK5
ORMDL1	ORM1-like protein 1	O43929
OS9	Protein OS-9	Q9Y3B8
OSBP	Oxysterol-binding protein 1	Q96SU4
OSBPL11	Oxysterol-binding protein-related protein 11	Q13438
OSBPL8	Oxysterol-binding protein-related protein 8	Q9BXB4
OSBPL9	Oxysterol-binding protein-related protein 9	Q9BZF1
OSGEPL1	Probable tRNA N6-adenosine threonylcarbamoyltransferase, mitochondrial	P22059
OXA1L	Mitochondrial inner membrane protein OXA1L	Q9H4B0
OXCT1	Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial	O43819
OXLD1	Oxidoreductase-like domain-containing protein 1	Q15070
OXNAD1	Oxidoreductase NAD-binding domain-containing protein 1	Q5BKU9
OXSM	3-oxoacyl-[acyl-carrier-protein] synthase, mitochondrial	Q96HP4
OXSR1	Serine/threonine-protein kinase OSR1	Q9NWU1
P4HA1	Prolyl 4-hydroxylase subunit alpha-1	Q32P28
P4HB	Protein disulfide-isomerase	Q6L8Q7
PABPC1	Polyadenylate-binding protein 1	P68402
PABPC4	Polyadenylate-binding protein 4	P11940
PAFAH1B1	Platelet-activating factor acetylhydrolase IB subunit alpha	Q9NUP9
PAFAH1B2	Platelet-activating factor acetylhydrolase IB subunit beta	Q86YP4
PAICS	Multifunctional protein ADE2	Q9UHX1
PAM16	Mitochondrial import inner membrane translocase subunit TIM16	Q96DA6
PARK7	Protein DJ-1	Q9NVV4
PARP1	Poly [ADP-ribose] polymerase 1	Q99497
PARP9	Poly [ADP-ribose] polymerase 9	P09874
PARS2	Probable proline--tRNA ligase, mitochondrial	Q16563
PBRM1	Protein polybromo-1	Q8IXQ6
PBXIP1	Pre-B-cell leukemia transcription factor-interacting protein 1	Q86U86
PC	Pyruvate carboxylase, mitochondrial	Q9NRR7
PCBP2	Poly(rC)-binding protein 2	Q8NF37
PCCA	Propionyl-CoA carboxylase alpha chain, mitochondrial	Q15366
PCCB	Propionyl-CoA carboxylase beta chain, mitochondrial	P05165

Gene	Protein name	Accession
PCK2	Phosphoenolpyruvate carboxykinase [GTP], mitochondrial	Q15645
PCM1	Pericentriolar material 1 protein	Q16822
PCMT1	Protein-L-isoaspartate(D-aspartate) O-methyltransferase	Q96S52
PCNA	Proliferating cell nuclear antigen	Q15154
PCNT	Pericentrin	P12004
PCYOX1	Prelycysteine oxidase 1	Q42785
PCYOX1L	Prelycysteine oxidase-like	Q9UHG3
PDCCD11	Protein RRP5 homolog	P56182
PDCCD6	Programmed cell death protein 6	Q8NBM8
PDE12	2',5'-phosphodiesterase 12	O75340
PDF	Peptide deformylase, mitochondrial	Q9H4E7
PDHA1	Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial	P10515
PDHB	Pyruvate dehydrogenase E1 component subunit beta, mitochondrial	P08559
PDHX	Pyruvate dehydrogenase protein X component, mitochondrial	P11177
PDIA3	Protein disulfide-isomerase A3	P07237
PDIA4	Protein disulfide-isomerase A4	P30101
PDIA5	Protein disulfide-isomerase A5	P13667
PDIA6	Protein disulfide-isomerase A6	Q14554
PDK1	[Pyruvate dehydrogenase	Q15120
PDK3	[Pyruvate dehydrogenase	Q9BY77
PDP2	[Pyruvate dehydrogenase [acetyl-transferring]]-phosphatase 2, mitochondrial	Q15118
PDPR	Pyruvate dehydrogenase phosphatase regulatory subunit, mitochondrial	Q9P2J9
PDS5A	Sister chromatid cohesion protein PDS5 homolog A	Q8NCN5
PDS5B	Sister chromatid cohesion protein PDS5 homolog B	Q29RF7
PDSS1	Decaprenyl-diphosphate synthase subunit 1	Q9UHN1
PDSS2	Decaprenyl-diphosphate synthase subunit 2	Q12959
PDZD11	PDZ domain-containing protein 11	Q9NTI5
PEBP1	Phosphatidylethanolamine-binding protein 1	Q5EBL8
PECAM1	Platelet endothelial cell adhesion molecule	P30086
PEO1	Twinkle protein, mitochondrial	P16284
PES1	Pescadillo homolog	Q6Y7W6
PET112	Glutamyl-tRNA(Gln) amidotransferase subunit B, mitochondrial	Q9H0R6
PEX11B	Peroxisomal membrane protein 11B	Q15269
PEX13	Peroxisomal membrane protein PEX13	O00541
PEX14	Peroxisomal membrane protein PEX14	Q92968
PEX16	Peroxisomal membrane protein PEX16	O75381
PEX3	Peroxisomal biogenesis factor 3	Q9Y5Y5
PFDN2	Prefoldin subunit 2	P56589

Gene	Protein name	Accession
PFDN4	Prefoldin subunit 4	Q9UHV9
PFDN5	Prefoldin subunit 5	Q9NQP4
PFKP	6-phosphofructokinase type C	P48668
PFN1	Profilin-1	P78527
PGAM5	Serine/threonine-protein phosphatase PGAM5, mitochondrial	Q99471
PGK1	Phosphoglycerate kinase 1	Q9H7Z7
PGRMC1	Membrane-associated progesterone receptor component 1	Q32NB8
PGRMC2	Membrane-associated progesterone receptor component 2	O00264
PGS1	CDP-diacylglycerol--glycerol-3-phosphate 3-phosphatidyltransferase, mitochondrial	Q8NBL1
PHB	Prohibitin	Q99623
PHB2	Prohibitin-2	O15173
PHGDH	D-3-phosphoglycerate dehydrogenase	Q9UHD8
PHPT1	14 kDa phosphohistidine phosphatase	P35232
PI4K2A	Phosphatidylinositol 4-kinase type 2-alpha	P13674
PIGK	GPI-anchor transamidase	Q8N335
PIGS	GPI transamidase component PIG-S	Q99755
PIN1	Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1	P22061
PIP	Prolactin-inducible protein	P48739
PIP4K2A	Phosphatidylinositol 5-phosphate 4-kinase type-2 alpha	Q9NRX4
PIP5K1A	Phosphatidylinositol 4-phosphate 5-kinase type-1 alpha	P48426
PISD	Phosphatidylserine decarboxylase proenzyme	P12273
PITPNB	Phosphatidylinositol transfer protein beta isoform	Q9H307
PITRM1	Presequence protease, mitochondrial	Q9HCU5
PKM	Pyruvate kinase PKM	O60256
PLEC	Plectin	Q9NUQ2
PLGRKT	Plasminogen receptor	Q8IY17
PLK1	Serine/threonine-protein kinase PLK1	Q15149
PLXNA1	Plexin-A1	P13796
PML	Protein PML	Q9UIW2
PMPCA	Mitochondrial-processing peptidase subunit alpha	Q9NZW5
PMVK	Phosphomevalonate kinase	P29590
PNKD	Probable hydrolase PNKD	Q15126
PNN	Pinin	Q13526
PNPLA6	Neuropathy target esterase	P53350
PNPT1	Polyribonucleotide nucleotidyltransferase 1, mitochondrial	Q8N490
POC1A	POC1 centriolar protein homolog A	Q8TEM1
POFUT1	GDP-fucose protein O-fucosyltransferase 1	O00330
POGLUT1	Protein O-glucosyltransferase 1	P00558

Gene	Protein name	Accession
POLDIP2	Polymerase delta-interacting protein 2	Q15084
POLDIP3	Polymerase delta-interacting protein 3	Q9Y2S7
POLG2	DNA polymerase subunit gamma-2, mitochondrial	O60762
POLR1C	DNA-directed RNA polymerases I and III subunit RPAC1	P52434
POLR2A	DNA-directed RNA polymerase II subunit RPB1	P52435
POLR2B	DNA-directed RNA polymerase II subunit RPB2	P24928
POLR2C	DNA-directed RNA polymerase II subunit RPB3	P30876
POLR2H	DNA-directed RNA polymerases I, II, and III subunit RPABC3	P51991
POLR2J	DNA-directed RNA polymerase II subunit RPB11-a	O15160
POLRMT	DNA-directed RNA polymerase, mitochondrial	P04844
PPA1	Inorganic pyrophosphatase	Q9H2U2
PPA2	Inorganic pyrophosphatase 2, mitochondrial	O00410
PPAN	Suppressor of SW14 1 homolog	P51649
PPIA	Peptidyl-prolyl cis-trans isomerase A	P10619
PIIB	Peptidyl-prolyl cis-trans isomerase B	P62937
PIIF	Peptidyl-prolyl cis-trans isomerase F, mitochondrial	P23284
PIIH	Peptidyl-prolyl cis-trans isomerase H	Q9Y3C6
PPIL1	Peptidyl-prolyl cis-trans isomerase-like 1	P30405
PPIL3	Peptidyl-prolyl cis-trans isomerase-like 3	O43447
PPIL4	Peptidyl-prolyl cis-trans isomerase-like 4	Q9H2H8
PPP1CA	Serine/threonine-protein phosphatase PP1-alpha catalytic subunit	Q8NBT0
PPP2R1A	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform	P30460
PPP2R1B	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A beta isoform	P30153
PPP2R2A	Serine/threonine-protein phosphatase 2A 55 kDa regulatory subunit B alpha isoform	P30154
PRAF2	PRA1 family protein 2	Q9UI14
PRC1	Protein regulator of cytokinesis 1	O60831
PRCP	Lysosomal Pro-X carboxypeptidase	O95613
PRDX1	Peroxisome oxidin-1	O43663
PRDX2	Peroxisome oxidin-2	Q06830
PRDX3	Thioredoxin-dependent peroxide reductase, mitochondrial	P32119
PRDX4	Peroxisome oxidin-4	P30048
PRDX5	Peroxisome oxidin-5, mitochondrial	Q13162
PRDX6	Peroxisome oxidin-6	P30044
PREB	Prolactin regulatory element-binding protein	P30041
PRKACA	cAMP-dependent protein kinase catalytic subunit alpha	P13861
PRKACB	cAMP-dependent protein kinase catalytic subunit beta	P17612

Gene	Protein name	Accession
PRKAG1	5'-AMP-activated protein kinase subunit gamma-1	Q15758
PRKAR2A	cAMP-dependent protein kinase type II-alpha regulatory subunit	Q9UIJ7
PRKCA	Protein kinase C alpha type	P33176
PRKCB	Protein kinase C beta type	P17252
PRKCH	Protein kinase C eta type	P41743
PRKCI	Protein kinase C iota type	P05771
PRKCQ	Protein kinase C theta type	P24723
PRKDC	DNA-dependent protein kinase catalytic subunit	Q5JRX3
PRMT1	Protein arginine N-methyltransferase 1	Q86XL3
PRMT5	Protein arginine N-methyltransferase 5	Q99873
PROSC	Proline synthase co-transcribed bacterial homolog protein	P07737
PRPF19	Pre-mRNA-processing factor 19	O94903
PRPF31	U4/U6 small nuclear ribonucleoprotein Prp31	Q9UMS4
PRPF4	U4/U6 small nuclear ribonucleoprotein Prp4	Q8WWY3
PRPF6	Pre-mRNA-processing factor 6	O43172
PRPF8	Pre-mRNA-processing-splicing factor 8	O94906
PRPSAP2	Phosphoribosyl pyrophosphate synthase-associated protein 2	Q04759
PSAP	Prosaposin	O00422
PSEN1	Presenilin-1	P61289
PSIP1	PC4 and SFRS1-interacting protein	O00232
PSMA1	Proteasome subunit alpha type-1	P62195
PSMA2	Proteasome subunit alpha type-2	P25786
PSMA4	Proteasome subunit alpha type-4	P25787
PSMA6	Proteasome subunit alpha type-6	P25789
PSMA7	Proteasome subunit alpha type-7	P60900
PSMB1	Proteasome subunit beta type-1	O14818
PSMB3	Proteasome subunit beta type-3	P20618
PSMB5	Proteasome subunit beta type-5	P49720
PSMB6	Proteasome subunit beta type-6	P28074
PSMC1	26S protease regulatory subunit 4	P62333
PSMC2	26S protease regulatory subunit 7	P43686
PSMC4	26S protease regulatory subunit 6B	P62191
PSMC5	26S protease regulatory subunit 8	P35998
PSMC6	26S protease regulatory subunit 10B	Q6P2Q9
PSMD1	26S proteasome non-ATPase regulatory subunit 1	O75475
PSMD11	26S proteasome non-ATPase regulatory subunit 11	P28072
PSMD12	26S proteasome non-ATPase regulatory subunit 12	O00231
PSMD2	26S proteasome non-ATPase regulatory subunit 2	Q99460
PSMD5	26S proteasome non-ATPase regulatory subunit 5	Q13200

Gene	Protein name	Accession
PSMD6	26S proteasome non-ATPase regulatory subunit 6	Q06323
PSMD7	26S proteasome non-ATPase regulatory subunit 7	Q16401
PSMD8	26S proteasome non-ATPase regulatory subunit 8	P51665
PSME1	Proteasome activator complex subunit 1	P48556
PSME3	Proteasome activator complex subunit 3	Q15008
PTBP1	Polypyrimidine tract-binding protein 1	P49768
PTCD3	Pentatricopeptide repeat domain-containing protein 3, mitochondrial	Q14761
PTDSS1	Phosphatidylserine synthase 1	Q6GMV3
PTGES2	Prostaglandin E synthase 2	Q96HS1
PTGES3	Prostaglandin E synthase 3	Q9Y2W6
PTK7	Inactive tyrosine-protein kinase 7	Q86Y79
PTPLAD1	Very-long-chain (3R)-3-hydroxyacyl-CoA dehydratase 3	Q9P035
PTPMT1	Phosphatidylglycerophosphatase and protein-tyrosine phosphatase 1	P29350
PTPN1	Tyrosine-protein phosphatase non-receptor type 1	Q06124
PTPN11	Tyrosine-protein phosphatase non-receptor type 11	Q13308
PTPN6	Tyrosine-protein phosphatase non-receptor type 6	P18031
PTPRC	Receptor-type tyrosine-protein phosphatase C	Q8WUK0
PTPRCAP	Protein tyrosine phosphatase receptor type C-associated protein	P26599
PTRH1	Probable peptidyl-tRNA hydrolase	Q96EY7
PTRHD1	Putative peptidyl-tRNA hydrolase PTRHD1	P08575
PUF60	Poly(U)-binding-splicing factor PUF60	P48651
PUS1	tRNA pseudouridine synthase A, mitochondrial	Q96Q11
PWP2	Periodic tryptophan protein 2 homolog	P31939
PXMP2	Peroxisomal membrane protein 2	O96011
PYCR1	Pyrrroline-5-carboxylate reductase 1, mitochondrial	Q9BTU6
PYCR2	Pyrrroline-5-carboxylate reductase 2	P32322
QARS	Glutamine--tRNA ligase	Q7L3T8
QDPR	Dihydropteridine reductase	P00367
QIL1	Protein QIL1	O14949
QPCTL	Glutamyl-peptide cyclotransferase-like protein	Q08257
QRSL1	Glutamyl-tRNA(Gln) amidotransferase subunit A, mitochondrial	Q9NY12
QSOX2	Sulfhydryl oxidase 2	Q9NXS2
QTRT1	Queuine tRNA-ribosyltransferase	O43493
QTRTD1	Queuine tRNA-ribosyltransferase subunit QTRTD1	Q6ZRP7
RAB10	Ras-related protein Rab-10	Q9H974
RAB11B	Ras-related protein Rab-11B	P01111
RAB11FIP1	Rab11 family-interacting protein 1	P35249
RAB14	Ras-related protein Rab-14	P61026
RAB15	Ras-related protein Rab-15	P61106

Gene	Protein name	Accession
RAB18	Ras-related protein Rab-18	P59190
RAB1A	Ras-related protein Rab-1A	Q9NP72
RAB1B	Ras-related protein Rab-1B	P62820
RAB21	Ras-related protein Rab-21	Q9H0U4
RAB22A	Ras-related protein Rab-22A	Q15907
RAB24	Ras-related protein Rab-24	Q9UL25
RAB27A	Ras-related protein Rab-27A	Q9UL26
RAB2A	Ras-related protein Rab-2A	Q969Q5
RAB2B	Ras-related protein Rab-2B	P61019
RAB33B	Ras-related protein Rab-33B	P51159
RAB33B	Putative Rab-43-like protein ENSP00000330714	Q9H082
RAB35	Ras-related protein Rab-35	Q8WUD1
RAB43	Ras-related protein Rab-43	Q15286
RAB4B	Ras-related protein Rab-4B	Q86YS6
RAB5A	Ras-related protein Rab-5A	P61018
RAB5B	Ras-related protein Rab-5B	P20339
RAB5C	Ras-related protein Rab-5C	P61020
RAB6A	Ras-related protein Rab-6A	P51148
RAB7A	Ras-related protein Rab-7a	P20340
RAB7L1	Ras-related protein Rab-7L1	P51149
RAB8A	Ras-related protein Rab-8A	O14966
RAB8B	Ras-related protein Rab-8B	P61006
RABAC1	Prenylated Rab acceptor protein 1	Q8WUA2
RABL3	Rab-like protein 3	Q92930
RAC1	Ras-related C3 botulinum toxin substrate 1	Q5HYI8
RAC2	Ras-related C3 botulinum toxin substrate 2	P63000
RACGAP1	Rac GTPase-activating protein 1	Q14699
RAE1	mRNA export factor	P15153
RALA	Ras-related protein Ral-A	P46060
RALY	RNA-binding protein Raly	P11233
RAN	GTP-binding nuclear protein Ran	P43487
RANBP1	Ran-specific GTPase-activating protein	Q9UKM9
RANBP2	E3 SUMO-protein ligase RanBP2	P38159
RANGAP1	Ran GTPase-activating protein 1	P78406
RAP1B	Ras-related protein Rap-1b	P62826
RAP2B	Ras-related protein Rap-2b	P61224
RARS	Arginine--tRNA ligase, cytoplasmic	P47897
RARS2	Probable arginine--tRNA ligase, mitochondrial	P54136
RASA3	Ras GTPase-activating protein 3	P61225

Gene	Protein name	Accession
RASAL3	RAS protein activator like-3	P01112
RBBP4	Histone-binding protein RBBP4	Q09028
RBM14	RNA-binding protein 14	Q09028
RBM15	Putative RNA-binding protein 15	Q96PK6
RBM25	RNA-binding protein 25	Q96T37
RBM28	RNA-binding protein 28	P49756
RBM34	RNA-binding protein 34	Q9NWX13
RBM4	RNA-binding protein 4	P42696
RBM8A	RNA-binding protein 8A	Q9BWF3
RBMX	RNA-binding motif protein, X chromosome	Q9Y5S9
RCC1	Regulator of chromosome condensation	O00559
RCC2	Protein RCC2	P18754
RCL1	RNA 3'-terminal phosphate cyclase-like protein	Q92600
RCN1	Reticulocalbin-1	Q9Y2P8
RCN2	Reticulocalbin-2	Q15293
RDH11	Retinol dehydrogenase 11	Q14257
RDH13	Retinol dehydrogenase 13	Q9HBB5
RDH14	Retinol dehydrogenase 14	Q8TC12
REEP5	Receptor expression-enhancing protein 5	Q8NBN7
REEP6	Receptor expression-enhancing protein 6	Q00765
REPS1	RalBP1-associated Eps domain-containing protein 1	Q92900
REXO2	Oligoribonuclease, mitochondrial	Q9P0S3
RFC1	Replication factor C subunit 1	P35244
RFC2	Replication factor C subunit 2	P35251
RFC3	Replication factor C subunit 3	P35250
RFC4	Replication factor C subunit 4	P40938
RFK	Riboflavin kinase	P84095
RFTN1	Raftlin	Q6WKZ4
RHEB	GTP-binding protein Rheb	Q9H0H5
RHOA	Transforming protein RhoA	Q53QZ3
RHOF	Rho-related GTP-binding protein RhoF	P61586
RHOG	Rho-related GTP-binding protein RhoG	Q9HBB0
RHOT1	Mitochondrial Rho GTPase 1	Q99797
RHOT2	Mitochondrial Rho GTPase 2	Q8IXI2
RINT1	RAD50-interacting protein 1	Q99496
RMDN1	Regulator of microtubule dynamics protein 1	Q7Z7F7
RMDN3	Regulator of microtubule dynamics protein 3	Q96DB5
RMND1	Required for meiotic nuclear division protein 1 homolog	Q96TC7
RNF130	E3 ubiquitin-protein ligase RNF130	Q14789

Gene	Protein name	Accession
RNF2	E3 ubiquitin-protein ligase RING2	Q969G6
RNF20	E3 ubiquitin-protein ligase BRE1A	O95861
RNF213	E3 ubiquitin-protein ligase RNF213	Q9HC36
RNMTL1	RNA methyltransferase-like protein 1	Q9NWS8
RP2	Protein XRP2	P12956
RPA1	Replication protein A 70 kDa DNA-binding subunit	O75570
RPA3	Replication protein A 14 kDa subunit	P27694
RPF2	Ribosome production factor 2 homolog	P19387
RPL10	60S ribosomal protein L10	P62906
RPL10A	60S ribosomal protein L10a	Q6NUQ1
RPL11	60S ribosomal protein L11	P27635
RPL12	60S ribosomal protein L12	P62913
RPL13	60S ribosomal protein L13	P40429
RPL13A	60S ribosomal protein L13a	P30050
RPL14	60S ribosomal protein L14	P26373
RPL15	60S ribosomal protein L15	P50914
RPL17	60S ribosomal protein L17	P61313
RPL18	60S ribosomal protein L18	Q02543
RPL18A	60S ribosomal protein L18a	P18621
RPL19	60S ribosomal protein L19	Q07020
RPL21	60S ribosomal protein L21	O76021
RPL23	60S ribosomal protein L23	P62750
RPL23A	60S ribosomal protein L23a	P46778
RPL24	60S ribosomal protein L24	P62829
RPL26	60S ribosomal protein L26	P83731
RPL27	60S ribosomal protein L27	P46776
RPL27A	60S ribosomal protein L27a	P61254
RPL28	60S ribosomal protein L28	P61353
RPL29	60S ribosomal protein L29	P46779
RPL3	60S ribosomal protein L3	P63173
RPL30	60S ribosomal protein L30	P47914
RPL31	60S ribosomal protein L31	P62888
RPL32	60S ribosomal protein L32	P62899
RPL34	60S ribosomal protein L34	P62910
RPL35	60S ribosomal protein L35	P18077
RPL35A	60S ribosomal protein L35a	P49207
RPL36	60S ribosomal protein L36	Q969Q0
RPL36A	60S ribosomal protein L36a	P42766
RPL36AL	60S ribosomal protein L36a-like	P83881

Gene	Protein name	Accession
RPL37A	60S ribosomal protein L37a	Q9Y3U8
RPL38	60S ribosomal protein L38	P61513
RPL4	60S ribosomal protein L4	P39023
RPL5	60S ribosomal protein L5	P36578
RPL6	60S ribosomal protein L6	P46777
RPL7	60S ribosomal protein L7	P62424
RPL7A	60S ribosomal protein L7a	Q02878
RPL8	60S ribosomal protein L8	P18124
RPL9	60S ribosomal protein L9	P62917
RPLP0	60S acidic ribosomal protein P0	P32969
RPLP2	60S acidic ribosomal protein P2	P05388
RPN1	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1	Q9H7B2
RPN2	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 2	P04843
RPRD1B	Regulation of nuclear pre-mRNA domain-containing protein 1B	O00411
RPS10	40S ribosomal protein S10	Q15050
RPS11	40S ribosomal protein S11	P46783
RPS12	40S ribosomal protein S12	P62280
RPS13	40S ribosomal protein S13	P25398
RPS14	40S ribosomal protein S14	P62277
RPS15A	40S ribosomal protein S15a	P62263
RPS16	40S ribosomal protein S16	P62244
RPS17	40S ribosomal protein S17	P0CW22
RPS17L	40S ribosomal protein S17-like	P62249
RPS18	40S ribosomal protein S18	P08708
RPS19	40S ribosomal protein S19	P62269
RPS19BP1	Active regulator of SIRT1	Q9UH62
RPS2	40S ribosomal protein S2	P42677
RPS20	40S ribosomal protein S20	P39019
RPS23	40S ribosomal protein S23	P60866
RPS24	40S ribosomal protein S24	P62266
RPS25	40S ribosomal protein S25	P62847
RPS26	40S ribosomal protein S26	P62851
RPS27	40S ribosomal protein S27	P62979
RPS27A	Ubiquitin-40S ribosomal protein S27a	P62854
RPS3	40S ribosomal protein S3	P61247
RPS3A	40S ribosomal protein S3a	P15880
RPS4X	40S ribosomal protein S4, X isoform	P23396
RPS5	40S ribosomal protein S5	P62701
RPS6	40S ribosomal protein S6	P46782

Gene	Protein name	Accession
RPS7	40S ribosomal protein S7	P62753
RPS8	40S ribosomal protein S8	P62081
RPS9	40S ribosomal protein S9	P62241
RPSA	40S ribosomal protein SA	P63162
RPUSD3	RNA pseudouridylate synthase domain-containing protein 3	Q96T51
RQCD1	Cell differentiation protein RCD1 homolog	Q9P258
RRAS2	Ras-related protein R-Ras2	Q9NQG5
RRBP1	Ribosome-binding protein 1	P62070
RRP1	Ribosomal RNA processing protein 1 homolog A	Q14684
RRP12	RRP12-like protein	Q9UI43
RRP1B	Ribosomal RNA processing protein 1 homolog B	Q5JTH9
RRP9	U3 small nucleolar RNA-interacting protein 2	P26368
RRS1	Ribosome biogenesis regulatory protein homolog	Q14690
RSAD1	Radical S-adenosyl methionine domain-containing protein 1, mitochondrial	P46781
RSL1D1	Ribosomal L1 domain-containing protein 1	P84098
RTCB	tRNA-splicing ligase RtcB homolog	Q9BQC6
RTN3	Reticulon-3	Q9Y310
RTN4	Reticulon-4	O95197
RTN4IP1	Reticulon-4-interacting protein 1, mitochondrial	P82909
RUFY1	RUN and FYVE domain-containing protein 1	P08579
RUVBL1	RuvB-like 1	Q6P087
RUVBL2	RuvB-like 2	Q9Y265
S100A9	Protein S100-A9	Q9Y230
SACM1L	Phosphatidylinositide phosphatase SAC1	Q96QD8
SAFB	Scaffold attachment factor B1	Q9NTJ5
SAP18	Histone deacetylase complex subunit SAP18	P23526
SAR1A	GTP-binding protein SAR1a	P07602
SARS2	Serine--tRNA ligase, mitochondrial	Q5T160
SART1	U4/U6.U5 tri-snRNP-associated protein 1	Q13425
SATB1	DNA-binding protein SATB1	Q9NQZ2
SCAMP1	Secretory carrier-associated membrane protein 1	P60468
SCAMP2	Secretory carrier-associated membrane protein 2	O15126
SCAMP3	Secretory carrier-associated membrane protein 3	O15127
SCCPDH	Saccharopine dehydrogenase-like oxidoreductase	P55809
SCD	Acyl-CoA desaturase	Q9NPJ3
SCD5	Stearoyl-CoA desaturase 5	O14828
SCFD1	Sec1 family domain-containing protein 1	Q86SK9
SCFD2	Sec1 family domain-containing protein 2	Q8WVM8
SCML2	Sex comb on midleg-like protein 2	Q6KCM7

Gene	Protein name	Accession
SCO1	Protein SCO1 homolog, mitochondrial	Q9UQR0
SCO2	Protein SCO2 homolog, mitochondrial	O75880
SCP2	Non-specific lipid-transfer protein	Q86UT6
SCRIB	Protein scribble homolog	Q8NBX0
SDCBP	Syntenin-1	Q14160
SDF4	45 kDa calcium-binding protein	Q9H246
SDHA	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	O00560
SDHAF2	Succinate dehydrogenase assembly factor 2, mitochondrial	P31040
SDR39U1	Epimerase family protein SDR39U1	Q8N465
SEC11A	Signal peptidase complex catalytic subunit SEC11A	P43007
SEC11C	Signal peptidase complex catalytic subunit SEC11C	P67812
SEC22B	Vesicle-trafficking protein SEC22b	Q9BY50
SEC23A	Protein transport protein Sec23A	O75396
SEC24C	Protein transport protein Sec24C	Q15436
SEC61B	Protein transport protein Sec61 subunit beta	P53992
SEC62	Translocation protein SEC62	Q12981
SEC63	Translocation protein SEC63 homolog	Q99442
SEH1L	Nucleoporin SEH1	Q9UGP8
SEL1L	Protein sel-1 homolog 1	Q9NX18
SEPT1	Septin-1	O60613
SEPT6	Septin-6	Q8WYJ6
SEPT7	Septin-7	Q14141
SEPT9	Septin-9	Q16181
SERPINC1	Antithrombin-III	Q4KMQ2
SERPINH1	Serpin H1	O43175
SF3A2	Splicing factor 3A subunit 2	P50454
SF3A3	Splicing factor 3A subunit 3	Q15428
SF3B1	Splicing factor 3B subunit 1	Q12874
SF3B6	Splicing factor 3B subunit 6	O75533
SFPQ	Splicing factor, proline- and glutamine-rich	Q9Y3B4
SFT2D2	Vesicle transport protein SFT2B	P23246
SFT2D3	Vesicle transport protein SFT2C	O95562
SFXN1	Sideroflexin-1	Q58719
SFXN2	Sideroflexin-2	Q9H9B4
SFXN3	Sideroflexin-3	Q96NB2
SFXN4	Sideroflexin-4	Q9BWM7
SGPL1	Sphingosine-1-phosphate lyase 1	Q99720
SH2D1A	SH2 domain-containing protein 1A	O95470
SH3BGRL	SH3 domain-binding glutamic acid-rich-like protein	O60880

Gene	Protein name	Accession
SIGMAR1	Sigma non-opioid intracellular receptor 1	Q6P4A7
SIKE1	Suppressor of IKBKE 1	O75368
SIRT3	NAD-dependent protein deacetylase sirtuin-3, mitochondrial	Q9BRV8
SIRT5	NAD-dependent protein deacetylase sirtuin-5, mitochondrial	Q9NTG7
SIT1	Signaling threshold-regulating transmembrane adapter 1	Q9NXA8
SKP1	S-phase kinase-associated protein 1	Q9Y3P8
SLC12A2	Solute carrier family 12 member 2	P06702
SLC16A1	Monocarboxylate transporter 1	Q13724
SLC1A4	Neutral amino acid transporter A	Q01826
SLC1A5	Neutral amino acid transporter B(0)	Q9NRG9
SLC25A1	Tricarboxylate transport protein, mitochondrial	Q8NBS9
SLC25A11	Mitochondrial 2-oxoglutarate/malate carrier protein	P61626
SLC25A12	Calcium-binding mitochondrial carrier protein Aralar1	Q8N0X4
SLC25A13	Calcium-binding mitochondrial carrier protein Aralar2	O75746
SLC25A19	Mitochondrial thiamine pyrophosphate carrier	O14657
SLC25A20	Mitochondrial carnitine/acylcarnitine carrier protein	Q8N8R3
SLC25A22	Mitochondrial glutamate carrier 1	Q92820
SLC25A24	Calcium-binding mitochondrial carrier protein SCaMC-1	Q8WU76
SLC25A25	Calcium-binding mitochondrial carrier protein SCaMC-2	Q6NUK1
SLC25A29	Mitochondrial carnitine/acylcarnitine carrier protein CACL	O43324
SLC25A3	Phosphate carrier protein, mitochondrial	O95563
SLC25A32	Mitochondrial folate transporter/carrier	O95140
SLC25A33	Solute carrier family 25 member 33	P55011
SLC25A38	Solute carrier family 25 member 38	Q9BSK2
SLC25A4	ADP/ATP translocase 1	P22570
SLC25A40	Solute carrier family 25 member 40	Q96DW6
SLC25A46	Solute carrier family 25 member 46	Q8TBP6
SLC25A5	ADP/ATP translocase 2	P12235
SLC25A6	ADP/ATP translocase 3	P05141
SLC29A1	Equilibrative nucleoside transporter 1	Q96AG3
SLC2A1	Solute carrier family 2, facilitated glucose transporter member 1	A4D1E9
SLC38A2	Sodium-coupled neutral amino acid transporter 2	Q99808
SLC3A2	4F2 cell-surface antigen heavy chain	P31937
SLC7A5	Large neutral amino acids transporter small subunit 1	Q9Y4W2
SLC9A3R1	Na(+)/H(+) exchange regulatory cofactor NHE-RF1	Q9NX24
SLIRP	SRA stem-loop-interacting RNA-binding protein, mitochondrial	Q9UIB8
SLMAP	Sarcolemmal membrane-associated protein	Q9GZT3
SLTM	SAFB-like transcription modulator	Q14BN4
SMARCA4	Transcription activator BRG1	Q969G3

Gene	Protein name	Accession
SMARCA5	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A member 5	P51532
SMARCB1	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1	Q7KZF4
SMARCD1	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily D member 1	Q96E16
SMARCE1	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily E member 1	Q96SB8
SMC1A	Structural maintenance of chromosomes protein 1A	Q9NWH9
SMC2	Structural maintenance of chromosomes protein 2	Q14683
SMC3	Structural maintenance of chromosomes protein 3	O95347
SMC4	Structural maintenance of chromosomes protein 4	Q9UQE7
SMC6	Structural maintenance of chromosomes protein 6	Q9NTJ3
SMIM19	Small integral membrane protein 19	P62316
SMPD4	Sphingomyelin phosphodiesterase 4	P46459
SMU1	WD40 repeat-containing protein SMU1	Q96GM5
SNAP23	Synaptosomal-associated protein 23	O43760
SNAP29	Synaptosomal-associated protein 29	O00161
SND1	Staphylococcal nuclease domain-containing protein 1	Q99747
SNRNP200	U5 small nuclear ribonucleoprotein 200 kDa helicase	O43818
SNRNP40	U5 small nuclear ribonucleoprotein 40 kDa protein	O95721
SNRPA1	U2 small nuclear ribonucleoprotein A'	Q9NQC3
SNRPB	Small nuclear ribonucleoprotein-associated proteins B and B'	Q9HA92
SNRPB2	U2 small nuclear ribonucleoprotein B''	P09661
SNRPD1	Small nuclear ribonucleoprotein Sm D1	O60264
SNRPD2	Small nuclear ribonucleoprotein Sm D2	P62314
SNRPN	Small nuclear ribonucleoprotein-associated protein N	P14678
SNTB2	Beta-2-syntrophin	Q96DI7
SNW1	SNW domain-containing protein 1	O43290
SNX3	Sorting nexin-3	Q13573
SOD1	Superoxide dismutase [Cu-Zn]	O60493
SOD2	Superoxide dismutase [Mn], mitochondrial	P00441
SORT1	Sortilin	P04179
SPATA5	Spermatogenesis-associated protein 5	Q9Y5B9
SPC25	Kinetochore protein Spc25	Q8IY81
SPCS2	Signal peptidase complex subunit 2	Q9HBM1
SPCS3	Signal peptidase complex subunit 3	Q15005
SPG7	Paraplegin	O75934
SPN	Leukosialin	O95202

Gene	Protein name	Accession
SPR	Sepiapterin reductase	Q9UQ90
SPRYD4	SPRY domain-containing protein 4	Q5W111
SPRYD7	SPRY domain-containing protein 7	P35270
SPTAN1	Spectrin alpha chain, non-erythrocytic 1	O15269
SPTBN1	Spectrin beta chain, non-erythrocytic 1	Q8WW59
SPTBN2	Spectrin beta chain, non-erythrocytic 2	Q13813
SPTLC1	Serine palmitoyltransferase 1	O15270
SPTLC2	Serine palmitoyltransferase 2	Q01082
SQLE	Squalene monoxygenase	Q6P179
SQRDL	Sulfide:quinone oxidoreductase, mitochondrial	O15020
SRP14	Signal recognition particle 14 kDa protein	Q9Y6N5
SRP19	Signal recognition particle 19 kDa protein	P37108
SRP54	Signal recognition particle 54 kDa protein	P09132
SRP68	Signal recognition particle subunit SRP68	O76094
SRP72	Signal recognition particle subunit SRP72	P61011
SRPK1	SRSF protein kinase 1	Q9UHB9
SRPR	Signal recognition particle receptor subunit alpha	Q9Y5M8
SRPRB	Signal recognition particle receptor subunit beta	Q96SB4
SRRT	Serrate RNA effector molecule homolog	P08240
SRSF1	Serine/arginine-rich splicing factor 1	Q9BXP5
SRSF3	Serine/arginine-rich splicing factor 3	Q07955
SRSF6	Serine/arginine-rich splicing factor 6	P84103
SRSF7	Serine/arginine-rich splicing factor 7	Q13247
SRSF9	Serine/arginine-rich splicing factor 9	Q16629
SSB	Lupus La protein	O43561
SSR1	Translocon-associated protein subunit alpha	Q9NQ55
SSR3	Translocon-associated protein subunit gamma	P43307
SSR4	Translocon-associated protein subunit delta	Q9UNL2
SSRP1	FACT complex subunit SSRP1	P51571
ST13P4	Putative protein FAM10A4	Q08945
STAT3	Signal transducer and activator of transcription 3	Q8IZP2
STAU1	Double-stranded RNA-binding protein Staufen homolog 1	P40763
STAU2	Double-stranded RNA-binding protein Staufen homolog 2	O95793
STIM1	Stromal interaction molecule 1	Q9NUL3
STIP1	Stress-induced-phosphoprotein 1	Q86WV6
STMN1	Stathmin	P31948
STOML2	Stomatin-like protein 2, mitochondrial	P16949
STRAP	Serine-threonine kinase receptor-associated protein	Q9UJZ1
STRN	Striatin	Q9Y3F4

Gene	Protein name	Accession
STT3A	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT3A	O43815
STT3B	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT3B	P46977
STX10	Syntaxin-10	Q8TCJ2
STX12	Syntaxin-12	O60499
STX16	Syntaxin-16	Q86Y82
STX17	Syntaxin-17	O14662
STX18	Syntaxin-18	P56962
STX2	Syntaxin-2	Q9P2W9
STX4	Syntaxin-4	P32856
STX5	Syntaxin-5	Q12846
STX7	Syntaxin-7	Q13190
STX8	Syntaxin-8	O15400
STXBP1	Syntaxin-binding protein 1	Q9UNK0
STXBP2	Syntaxin-binding protein 2	P61764
STXBP3	Syntaxin-binding protein 3	Q15833
SUB1	Activated RNA polymerase II transcriptional coactivator p15	Q13428
SUCLA2	Succinyl-CoA ligase [ADP-forming] subunit beta, mitochondrial	P53597
SUCLG1	Succinyl-CoA ligase [ADP/GDP-forming] subunit alpha, mitochondrial	O00186
SUCLG2	Succinyl-CoA ligase [GDP-forming] subunit beta, mitochondrial	Q9P2R7
SUMF2	Sulfatase-modifying factor 2	Q96199
SUMO2	Small ubiquitin-related modifier 2	Q8NB7
SUPT16H	FACT complex subunit SPT16	Q99523
SUPV3L1	ATP-dependent RNA helicase SUPV3L1, mitochondrial	Q15526
SURF1	Surfeit locus protein 1	P61956
SVIP	Small VCP/p97-interacting protein	Q8IYB8
SYMPK	Symplekin	Q96GW9
SYNGR1	Synaptogyrin-1	Q12824
SYNGR2	Synaptogyrin-2	O43759
SYNJ2BP	Synaptojanin-2-binding protein	Q9NSE4
SYPL1	Synaptophysin-like protein 1	Q96159
TACC1	Transforming acidic coiled-coil-containing protein 1	Q8IUX1
TACO1	Translational activator of cytochrome c oxidase 1	O75410
TAGLN2	Transgelin-2	Q13148
TARDBP	TAR DNA-binding protein 43	Q9BSH4
TARS	Threonine--tRNA ligase, cytoplasmic	Q9NP81
TARS2	Threonine--tRNA ligase, mitochondrial	P26639
TBCA	Tubulin-specific chaperone A	P07437
TBCB	Tubulin-folding cofactor B	O75347

Gene	Protein name	Accession
TBL2	Transducin beta-like protein 2	P23258
TBL3	Transducin beta-like protein 3	Q9Y4P3
TBRG4	Protein TBRG4	Q12788
TCEA1	Transcription elongation factor A protein 1	Q969Z0
TCEB2	Transcription elongation factor B polypeptide 2	Q92556
TCOF1	Treacle protein	P23193
TCP1	T-complex protein 1 subunit alpha	P53999
TDRKH	Tudor and KH domain-containing protein	Q5QJE6
TECR	Very-long-chain enoyl-CoA reductase	Q15185
TEFM	Transcription elongation factor, mitochondrial	Q9NZ01
TESC	Calcineurin B homologous protein 3	Q99653
TEX264	Testis-expressed sequence 264 protein	Q6IBS0
TFAM	Transcription factor A, mitochondrial	Q9Y5Q9
TFB1M	Dimethyladenosine transferase 1, mitochondrial	Q00059
TFB2M	Dimethyladenosine transferase 2, mitochondrial	Q8WVM0
TGFB1	Transforming growth factor beta-1	Q9H5Q4
TGOLN2	Trans-Golgi network integral membrane protein 2	P01137
THEM6	Protein THEM6	Q9BXR0
THNSL1	Threonine synthase-like 1	P10599
THOC1	THO complex subunit 1	Q8IYQ7
THOC2	THO complex subunit 2	Q96FV9
THOC6	THO complex subunit 6 homolog	Q86V81
THRAP3	Thyroid hormone receptor-associated protein 3	Q9UI30
TIMM10B	Mitochondrial import inner membrane translocase subunit Tim10 B	Q9Y2Z4
TIMM13	Mitochondrial import inner membrane translocase subunit Tim13	Q13263
TIMM17A	Mitochondrial import inner membrane translocase subunit Tim17-A	Q16762
TIMM17B	Mitochondrial import inner membrane translocase subunit Tim17-B	Q99595
TIMM21	Mitochondrial import inner membrane translocase subunit Tim21	Q9Y3D7
TIMM23	Mitochondrial import inner membrane translocase subunit Tim23	Q9BVV7
TIMM44	Mitochondrial import inner membrane translocase subunit TIM44	O14925
TIMM50	Mitochondrial import inner membrane translocase subunit TIM50	O43615
TIMM8A	Mitochondrial import inner membrane translocase subunit Tim8 A	Q3ZCQ8
TIMM9	Mitochondrial import inner membrane translocase subunit Tim9	O60220
TIMMDC1	Complex I assembly factor TIMMDC1, mitochondrial	O60830
TLN1	Talin-1	Q9Y5J7
TM9SF2	Transmembrane 9 superfamily member 2	Q96HV5
TM9SF3	Transmembrane 9 superfamily member 3	Q99805
TMCO1	Transmembrane and coiled-coil domain-containing protein 1	Q9HD45
TMED10	Transmembrane emp24 domain-containing protein 10	Q9BVK6

Gene	Protein name	Accession
TMED2	Transmembrane emp24 domain-containing protein 2	Q9UM00
TMED3	Transmembrane emp24 domain-containing protein 3	Q15363
TMED4	Transmembrane emp24 domain-containing protein 4	Q9Y3Q3
TMED5	Transmembrane emp24 domain-containing protein 5	Q7Z7H5
TMED7	Transmembrane emp24 domain-containing protein 7	Q9Y3A6
TMED9	Transmembrane emp24 domain-containing protein 9	Q9Y3B3
TMEM109	Transmembrane protein 109	Q9Y490
TMEM11	Transmembrane protein 11, mitochondrial	Q9NVH6
TMEM126A	Transmembrane protein 126A	Q9Y5J6
TMEM126B	Complex I assembly factor TMEM126B, mitochondrial	Q9H061
TMEM173	Stimulator of interferon genes protein	Q13586
TMEM199	Transmembrane protein 199	Q9BVC6
TMEM206	Transmembrane protein 206	Q8N511
TMEM209	Transmembrane protein 209	Q9H813
TMEM214	Transmembrane protein 214	Q96SK2
TMEM230	Transmembrane protein 230	Q6NUQ4
TMEM261	Transmembrane protein 261	Q96A57
TMEM30A	Cell cycle control protein 50A	Q9P0B6
TMEM33	Transmembrane protein 33	P17152
TMEM41A	Transmembrane protein 41A	Q969M1
TMEM43	Transmembrane protein 43	P57088
TMEM59	Transmembrane protein 59	Q9BTV4
TMEM65	Transmembrane protein 65	Q9BXS4
TMEM70	Transmembrane protein 70, mitochondrial	Q6PI78
TMEM97	Transmembrane protein 97	Q9BUB7
TMF1	TATA element modulatory factor	P49755
TMLHE	Trimethyllysine dioxygenase, mitochondrial	P82094
TMOD3	Tropomodulin-3	Q5BJF2
TMPO	Lamina-associated polypeptide 2, isoform alpha	Q9NS86
TMPO	Lamina-associated polypeptide 2, isoforms beta/gamma	P42166
TMUB1	Transmembrane and ubiquitin-like domain-containing protein 1	Q9NYL9
TMUB2	Transmembrane and ubiquitin-like domain-containing protein 2	Q9BVT8
TMX1	Thioredoxin-related transmembrane protein 1	Q71RG4
TMX2	Thioredoxin-related transmembrane protein 2	Q9H3N1
TMX3	Protein disulfide-isomerase TMX3	Q9Y320
TMX4	Thioredoxin-related transmembrane protein 4	Q96JJ7
TNPO1	Transportin-1	Q9H1E5
TOMM20	Mitochondrial import receptor subunit TOM20 homolog	Q8NFAQ8
TOMM22	Mitochondrial import receptor subunit TOM22 homolog	Q15388

Gene	Protein name	Accession
TOMM40	Mitochondrial import receptor subunit TOM40 homolog	Q9NS69
TOMM40L	Mitochondrial import receptor subunit TOM40B	Q96GE9
TOMM70A	Mitochondrial import receptor subunit TOM70	O96008
TOP1	DNA topoisomerase 1	O94826
TOP2A	DNA topoisomerase 2-alpha	P11387
TOP3A	DNA topoisomerase 3-alpha	P11388
TOR1A	Torsin-1A	Q13472
TOR1AIP2	Torsin-1A-interacting protein 2	P25445
TOR1B	Torsin-1B	O14656
TPI1	Triosephosphate isomerase	Q9HC21
TPM3	Tropomyosin alpha-3 chain	P60174
TPM4	Tropomyosin alpha-4 chain	P06753
TPR	Nucleoprotein TPR	Q8IUR0
TRA2A	Transformer-2 protein homolog alpha	Q9BVS5
TRA2B	Transformer-2 protein homolog beta	Q13595
TRAP1	Heat shock protein 75 kDa, mitochondrial	P62995
TRAPPC3	Trafficking protein particle complex subunit 3	P67936
TRAPPC5	Trafficking protein particle complex subunit 5	O43617
TRBC1	T-cell receptor beta-1 chain C region	A0A5B9
TRBC2	T-cell receptor beta-2 chain C region	Q12931
TRIM27	Zinc finger protein RFP	P01850
TRIM28	Transcription intermediary factor 1-beta	Q9NPL8
TRIM4	Tripartite motif-containing protein 4	P14373
TRIP13	Pachytene checkpoint protein 2 homolog	P05166
TRMT10C	Mitochondrial ribonuclease P protein 1	O15091
TRMT112	tRNA methyltransferase 112 homolog	P12270
TRMT5	tRNA	Q9C037
TRMT61B	tRNA	Q9Y2W1
TRMU	Mitochondrial tRNA-specific 2-thiouridylase 1	P58546
TRNT1	CCA tRNA nucleotidyltransferase 1, mitochondrial	Q32P41
TRUB1	Probable tRNA pseudouridine synthase 1	Q9Y606
TSG101	Tumor susceptibility gene 101 protein	Q8WWH5
TSN	Translin	Q99816
TST	Thiosulfate sulfurtransferase	P25325
TTC13	Tetratricopeptide repeat protein 13	Q15631
TTC19	Tetratricopeptide repeat protein 19, mitochondrial	Q8NBP0
TTL12	Tubulin--tyrosine ligase-like protein 12	Q6DKK2
TUBA1B	Tubulin alpha-1B chain	Q9P031
TUBB	Tubulin beta chain	P68371

Gene	Protein name	Accession
TUBB4B	Tubulin beta-4B chain	P68363
TUBG1	Tubulin gamma-1 chain	Q99426
TUBGCP2	Gamma-tubulin complex component 2	Q92947
TUBGCP3	Gamma-tubulin complex component 3	Q9BSJ2
TUFM	Elongation factor Tu, mitochondrial	Q14156
TUSC3	Tumor suppressor candidate 3	Q14166
TWF2	Twinfilin-2	Q13454
TXN	Thioredoxin	Q99757
TXN2	Thioredoxin, mitochondrial	P42765
TXNDC12	Thioredoxin domain-containing protein 12	Q9Y619
TXNDC15	Thioredoxin domain-containing protein 15	O95881
TXNDC5	Thioredoxin domain-containing protein 5	Q96142
TYMS	Thymidylate synthase	P53007
U2AF1	Splicing factor U2AF 35 kDa subunit	P04818
U2AF2	Splicing factor U2AF 65 kDa subunit	Q01081
UBA1	Ubiquitin-like modifier-activating enzyme 1	P68036
UBE2G2	Ubiquitin-conjugating enzyme E2 G2	Q15029
UBE2I	SUMO-conjugating enzyme UBC9	P22314
UBE2L3	Ubiquitin-conjugating enzyme E2 L3	P60604
UBE2N	Ubiquitin-conjugating enzyme E2 N	P63279
UBE4A	Ubiquitin conjugation factor E4 A	P61088
UBL4A	Ubiquitin-like protein 4A	P17480
UBQLN1	Ubiquilin-1	P45974
UBTF	Nucleolar transcription factor 1	Q14139
UBXN4	UBX domain-containing protein 4	Q9UMX0
UCHL3	Ubiquitin carboxyl-terminal hydrolase isozyme L3	Q92575
UCHL5	Ubiquitin carboxyl-terminal hydrolase isozyme L5	P15374
UFD1L	Ubiquitin fusion degradation protein 1 homolog	P47985
UFL1	E3 UFM1-protein ligase 1	Q92890
UFSP2	Ufm1-specific protease 2	O94874
UGGT1	UDP-glucose:glycoprotein glucosyltransferase 1	Q9NUQ7
UMPS	Uridine 5'-monophosphate synthase	P52758
UPF1	Regulator of nonsense transcripts 1	O75787
UQCC1	Ubiquinol-cytochrome-c reductase complex assembly factor 1	P11172
UQCRB	Cytochrome b-c1 complex subunit 7	P22695
UQCRC1	Cytochrome b-c1 complex subunit 1, mitochondrial	P17812
UQCRC2	Cytochrome b-c1 complex subunit 2, mitochondrial	P31930
UQCRFS1	Cytochrome b-c1 complex subunit Rieske, mitochondrial	Q9Y5K5
UQCRQ	Cytochrome b-c1 complex subunit 8	P14927

Gene	Protein name	Accession
URB1	Nucleolar pre-ribosomal-associated protein 1	Q9Y2X3
URB2	Unhealthy ribosome biogenesis protein 2 homolog	Q9NVA1
USE1	Vesicle transport protein USE1	Q86UX7
USO1	General vesicular transport factor p115	Q9NZ43
USP10	Ubiquitin carboxyl-terminal hydrolase 10	P11441
USP14	Ubiquitin carboxyl-terminal hydrolase 14	Q14694
USP30	Ubiquitin carboxyl-terminal hydrolase 30	P54578
USP5	Ubiquitin carboxyl-terminal hydrolase 5	Q70CQ3
USP9X	Probable ubiquitin carboxyl-terminal hydrolase FAF-X	O60763
UTP11L	Probable U3 small nucleolar RNA-associated protein 11	Q9BVJ6
UTP14A	U3 small nucleolar RNA-associated protein 14 homolog A	Q93008
UTP15	U3 small nucleolar RNA-associated protein 15 homolog	Q9Y3A2
UTP18	U3 small nucleolar RNA-associated protein 18 homolog	Q8TED0
UTP3	Something about silencing protein 10	Q9NR31
UTP6	U3 small nucleolar RNA-associated protein 6 homolog	Q9Y5J1
UTRN	Utrophin	Q9NYH9
UXT	Protein UXT	P46939
VAMP2	Vesicle-associated membrane protein 2	P61421
VAMP3	Vesicle-associated membrane protein 3	P63027
VAMP4	Vesicle-associated membrane protein 4	Q15836
VAMP5	Vesicle-associated membrane protein 5	O75379
VAMP7	Vesicle-associated membrane protein 7	O95183
VANGL1	Vang-like protein 1	P51809
VAPA	Vesicle-associated membrane protein-associated protein A	Q8TAA9
VAPB	Vesicle-associated membrane protein-associated protein B/C	Q9POL0
VAR5	Valine--tRNA ligase	Q9BW92
VAR52	Valine--tRNA ligase, mitochondrial	P26640
VAT1	Synaptic vesicle membrane protein VAT-1 homolog	O95292
VAV1	Proto-oncogene vav	Q9UI12
VCP	Transitional endoplasmic reticulum ATPase	Q96QE5
VDAC1	Voltage-dependent anion-selective channel protein 1	P15498
VDAC2	Voltage-dependent anion-selective channel protein 2	P21796
VDAC3	Voltage-dependent anion-selective channel protein 3	P45880
VIM	Vimentin	Q9Y277
VIMP	15 kDa selenoprotein	Q9BQE4
VIMP	Selenoprotein S	Q96EE3
VMA21	Vacuolar ATPase assembly integral membrane protein VMA21	P08670
VMP1	Vacuole membrane protein 1	Q3ZAAQ7
VPS25	Vacuolar protein-sorting-associated protein 25	Q9Y487

Gene	Protein name	Accession
VPS29	Vacuolar protein sorting-associated protein 29	Q9BRG1
VPS35	Vacuolar protein sorting-associated protein 35	Q9UBQ0
VPS37B	Vacuolar protein sorting-associated protein 37B	Q96GC9
VPS39	Vam6/Vps39-like protein	Q96QK1
VPS45	Vacuolar protein sorting-associated protein 45	Q96JC1
VRK1	Serine/threonine-protein kinase VRK1	Q9NRW7
VRK3	Inactive serine/threonine-protein kinase VRK3	Q99986
VTI1A	Vesicle transport through interaction with t-SNAREs homolog 1A	Q8IV63
VTI1B	Vesicle transport through interaction with t-SNAREs homolog 1B	Q96AJ9
VWA8	von Willebrand factor A domain-containing protein 8	Q9UEU0
WARS2	Tryptophan--tRNA ligase, mitochondrial	Q5ST30
WDR12	Ribosome biogenesis protein WDR12	A3KMH1
WDR18	WD repeat-containing protein 18	Q9GZL7
WDR36	WD repeat-containing protein 36	Q9BV38
WDR43	WD repeat-containing protein 43	Q8NI36
WDR61	WD repeat-containing protein 61	Q15061
WDR74	WD repeat-containing protein 74	Q9GZS3
WDR77	Methylosome protein 50	Q15528
WTAP	Pre-mRNA-splicing regulator WTAP	Q14318
XAB2	Pre-mRNA-splicing factor SYF1	P07814
XPNPEP3	Probable Xaa-Pro aminopeptidase 3	Q9HAV4
XPO1	Exportin-1	Q6RFH5
XPO5	Exportin-5	P55060
XRCC1	DNA repair protein XRCC1	Q9NQH7
XRCC5	X-ray repair cross-complementing protein 5	P18887
XRCC6	X-ray repair cross-complementing protein 6	P13010
YARS	Tyrosine--tRNA ligase, cytoplasmic	Q9UGM6
YARS2	Tyrosine--tRNA ligase, mitochondrial	P54577
YBEY	Putative ribonuclease	O75063
YBX1	Nuclease-sensitive element-binding protein 1	P58557
YBX1	Uncharacterized protein DKFZp762I1415	P67809
YKT6	Synaptobrevin homolog YKT6	O15498
YLPM1	YLP motif-containing protein 1	O15498
YME1L1	ATP-dependent zinc metalloprotease YME1L1	P49750
YRDC	YrdC domain-containing protein, mitochondrial	Q96TA2
YWHAB	14-3-3 protein beta/alpha	P31946
YWHAE	14-3-3 protein epsilon	P31946
YWHAG	14-3-3 protein gamma	Q04917
YWHAH	14-3-3 protein eta	P62258

<b>Gene</b>	<b>Protein name</b>	<b>Accession</b>
YWHAQ	14-3-3 protein theta	P61981
YWHAZ	14-3-3 protein zeta/delta	P27348
ZADH2	Zinc-binding alcohol dehydrogenase domain-containing protein 2	Q86U90
ZAP70	Tyrosine-protein kinase ZAP-70	Q8N4Q0
ZC3H11A	Zinc finger CCCH domain-containing protein 11A	P43403
ZDHHC18	Palmitoyltransferase ZDHHC18	O75152
ZMPSTE24	CAAX prenyl protease 1 homolog	Q01469
ZW10	Centromere/kinetochore protein zw10 homolog	Q9NUE0

### 6.3 Wild-type sample 2 (WT2) proteins

**Table 4: Proteins contained in the wild-type 2 VCV preparation (WT2) measured by mass spectrometry (see 3.5). Listed are gene names, protein names, and UniProt accession numbers.**

Gene	Protein name	Accession
A2M	Alpha-2-macroglobulin	P01023
AARS	Alanine--tRNA ligase, cytoplasmic	P49588
AARS2	Alanine--tRNA ligase, mitochondrial	Q5J7Z9
AASS	Alpha-aminoadipic semialdehyde synthase, mitochondrial	Q9UDR5
ABCB10	ATP-binding cassette sub-family B member 10, mitochondrial	Q9NRK6
ABCB6	ATP-binding cassette sub-family B member 6, mitochondrial	Q9NP58
ABCB7	ATP-binding cassette sub-family B member 7, mitochondrial	O75027
ABCB8	ATP-binding cassette sub-family B member 8, mitochondrial	Q9NUT2
ABCC1	Multidrug resistance-associated protein 1	P33527
ABCC4	Multidrug resistance-associated protein 4	O15439
ABCF1	ATP-binding cassette sub-family F member 1	Q8NE71
ABHD10	Mycophenolic acid acyl-glucuronide esterase, mitochondrial	Q9NUJ1
ABHD11	Alpha/beta hydrolase domain-containing protein 11	Q8NFV4
ABHD17B	Alpha/beta hydrolase domain-containing protein 17B	Q5VST6
ACAA1	3-ketoacyl-CoA thiolase, peroxisomal	P09110
ACAA2	3-ketoacyl-CoA thiolase, mitochondrial	P42765
ACACA	Acetyl-CoA carboxylase 1	Q13085
ACAD8	Isobutyryl-CoA dehydrogenase, mitochondrial	Q9UKU7
ACAD9	Acyl-CoA dehydrogenase family member 9, mitochondrial	Q9H845
ACADS	Short-chain specific acyl-CoA dehydrogenase, mitochondrial	P16219
ACADSB	Short/branched chain specific acyl-CoA dehydrogenase, mitochondrial	P45954
ACADVL	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial	P49748
ACAT1	Acetyl-CoA acetyltransferase, mitochondrial	P24752
ACBD3	Golgi resident protein GCP60	Q9H3P7

Gene	Protein name	Accession
ACIN1	Apoptotic chromatin condensation inducer in the nucleus	Q9UKV3
ACLY	ATP-citrate synthase	P53396
ACO2	Aconitate hydratase, mitochondrial	Q99798
ACOT13	Acyl-coenzyme A thioesterase 13	Q9NPJ3
ACOX1	Peroxisomal acyl-coenzyme A oxidase 1	Q15067
ACSF3	Acyl-CoA synthetase family member 3, mitochondrial	Q4G176
ACSL3	Long-chain-fatty-acid--CoA ligase 3	O95573
ACSS1	Acetyl-coenzyme A synthetase 2-like, mitochondrial	Q9NUB1
ACTB	Actin, cytoplasmic 1	P60709
ACTG1	Actin, cytoplasmic 2	P63261
ACTN1	Alpha-actinin-1	P12814
ACTN4	Alpha-actinin-4	O43707
ACTR1A	Alpha-centractin	P61163
ACTR3	Actin-related protein 3	P61158
ADAM10	Disintegrin and metalloproteinase domain-containing protein 10	O14672
ADCK3	Chaperone activity of bc1 complex-like, mitochondrial	Q8NI60
ADCK4	AarF domain-containing protein kinase 4	Q96D53
ADD1	Alpha-adducin	P35611
ADD3	Gamma-adducin	Q9UEY8
ADPRHL2	Poly(ADP-ribose) glycohydrolase ARH3	Q9NX46
AEBP1	Adipocyte enhancer-binding protein 1	Q8IUX7
AFG3L2	AFG3-like protein 2	Q9Y4W6
AGPAT5	1-acyl-sn-glycerol-3-phosphate acyltransferase epsilon	Q9NUQ2
AGPS	Alkylldihydroxyacetonephosphate synthase, peroxisomal	O00116
AHCY	Adenosylhomocysteinase	P23526
AIFM1	Apoptosis-inducing factor 1, mitochondrial	O95831
AK3	GTP:AMP phosphotransferase AK3, mitochondrial	Q9UIJ7
AKAP1	A-kinase anchor protein 1, mitochondrial	Q92667
AKAP9	A-kinase anchor protein 9	Q99996
AKNA	AT-hook-containing transcription factor	Q7Z591
ALB	Serum albumin	P02768
ALDH18A1	Delta-1-pyrroline-5-carboxylate synthase	P54886
ALDH3A2	Fatty aldehyde dehydrogenase	P51648
ALDH4A1	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial	P30038
ALDH5A1	Succinate-semialdehyde dehydrogenase, mitochondrial	P51649
ALDH6A1	Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial	Q02252
ALDOA	Fructose-bisphosphate aldolase A	P04075
ALG3	Dol-P-Man:Man(5)GlcNAc(2)-PP-Dol alpha-1,3-mannosyltransferase	Q92685
ALG9	Alpha-1,2-mannosyltransferase ALG9	Q9H6U8

Gene	Protein name	Accession
ALOX5AP	Arachidonate 5-lipoxygenase-activating protein	P20292
AMFR	E3 ubiquitin-protein ligase AMFR	Q9UKV5
ANKHD1	Ankyrin repeat and KH domain-containing protein 1	Q8IWZ3
ANO6	Anoctamin-6	Q4KMQ2
ANP32E	Acidic leucine-rich nuclear phosphoprotein 32 family member E	Q9BTT0
ANXA1	Annexin A1	P04083
ANXA11	Annexin A11	P50995
ANXA2	Annexin A2	P07355
ANXA6	Annexin A6	P08133
ANXA7	Annexin A7	P20073
AP1S2	AP-1 complex subunit sigma-2	P56377
AP2A1	AP-2 complex subunit alpha-1	O95782
AP2A2	AP-2 complex subunit alpha-2	O94973
AP2B1	AP-2 complex subunit beta	P63010
APEX1	DNA-(apurinic or apyrimidinic site) lyase	P27695
APMAP	Adipocyte plasma membrane-associated protein	Q9HDC9
APOA1BP	NAD(P)H-hydrate epimerase	Q8NCW5
APOB	Apolipoprotein B-100	P04114
APOL2	Apolipoprotein L2	Q9BQE5
APOO	Apolipoprotein O	Q9BUR5
APOOL	Apolipoprotein O-like	Q6UXV4
APRT	Adenine phosphoribosyltransferase	P07741
ARF4	ADP-ribosylation factor 4	P18085
ARFGAP1	ADP-ribosylation factor GTPase-activating protein 1	Q8N6T3
ARFGEF1	Brefeldin A-inhibited guanine nucleotide-exchange protein 1	Q9Y6D6
ARG1	Arginase-1	P05089
ARG2	Arginase-2, mitochondrial	P78540
ARHGDIB	Rho GDP-dissociation inhibitor 2	P52566
ARL15	ADP-ribosylation factor-like protein 15	Q9NXU5
ARL2	ADP-ribosylation factor-like protein 2	P36404
ARL6IP5	PRA1 family protein 3	O75915
ARMC1	Armadillo repeat-containing protein 1	Q9NVT9
ARMC10	Armadillo repeat-containing protein 10	Q8N2F6
ARMCX3	Armadillo repeat-containing X-linked protein 3	Q9UH62
ARPC1B	Actin-related protein 2/3 complex subunit 1B	O15143
ARPC2	Actin-related protein 2/3 complex subunit 2	O15144
ATAD1	ATPase family AAA domain-containing protein 1	Q8NBU5
ATAD3A	ATPase family AAA domain-containing protein 3A	Q9NVI7
ATF6	Cyclic AMP-dependent transcription factor ATF-6 alpha	P18850

Gene	Protein name	Accession
ATG9A	Autophagy-related protein 9A	Q7Z3C6
ATL3	Atlastin-3	Q6DD88
ATP11B	Probable phospholipid-transporting ATPase IF	Q9Y2G3
ATP11C	Probable phospholipid-transporting ATPase IG	Q8NB49
ATP13A1	Probable cation-transporting ATPase 13A1	Q9HD20
ATP13A3	Probable cation-transporting ATPase 13A3	Q9H7F0
ATP1A1	Sodium/potassium-transporting ATPase subunit alpha-1	P05023
ATP1A3	Sodium/potassium-transporting ATPase subunit alpha-3	P13637
ATP1B3	Sodium/potassium-transporting ATPase subunit beta-3	P54709
ATP2A2	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2	P16615
ATP2A3	Sarcoplasmic/endoplasmic reticulum calcium ATPase 3	Q93084
ATP2B1	Plasma membrane calcium-transporting ATPase 1	P20020
ATP2B4	Plasma membrane calcium-transporting ATPase 4	P23634
ATP5A1	ATP synthase subunit alpha, mitochondrial	P25705
ATP5B	ATP synthase subunit beta, mitochondrial	P06576
ATP5D	ATP synthase subunit delta, mitochondrial	P30049
ATP5F1	ATP synthase F(0) complex subunit B1, mitochondrial	P24539
ATP5H	ATP synthase subunit d, mitochondrial	O75947
ATP5J	ATP synthase-coupling factor 6, mitochondrial	P18859
ATP5O	ATP synthase subunit O, mitochondrial	P48047
ATP6AP1	V-type proton ATPase subunit S1	Q15904
ATP6AP2	Renin receptor	O75787
ATP6V0A2	V-type proton ATPase 116 kDa subunit a isoform 2	Q9Y487
ATP6V0D1	V-type proton ATPase subunit d 1	P61421
ATP6V1A	V-type proton ATPase catalytic subunit A	P38606
ATP6V1B2	V-type proton ATPase subunit B, brain isoform	P21281
ATP6V1C1	V-type proton ATPase subunit C 1	P21283
ATP6V1D	V-type proton ATPase subunit D	Q9Y5K8
ATP6V1E1	V-type proton ATPase subunit E 1	P36543
ATP6V1F	V-type proton ATPase subunit F	Q16864
ATP6V1G1	V-type proton ATPase subunit G 1	O75348
ATP6V1H	V-type proton ATPase subunit H	Q9UII2
ATP7A	Copper-transporting ATPase 1	Q04656
ATP9B	Probable phospholipid-transporting ATPase IIB	O43861
ATPAF1	ATP synthase mitochondrial F1 complex assembly factor 1	Q5TC12
ATPAF2	ATP synthase mitochondrial F1 complex assembly factor 2	Q8N5M1
ATPIF1	ATPase inhibitor, mitochondrial	Q9UII2
ATXN10	Ataxin-10	Q9UBB4
ATXN2L	Ataxin-2-like protein	Q8WWM7

Gene	Protein name	Accession
AUH	Methylglutaconyl-CoA hydratase, mitochondrial	Q13825
AZI1	5-azacytidine-induced protein 1	Q9UPN4
B3GALT6	Beta-1,3-galactosyltransferase 6	Q96L58
B3GAT3	Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3	O94766
BAG2	BAG family molecular chaperone regulator 2	O95816
BAG6	Large proline-rich protein BAG6	P46379
BAK1	Bcl-2 homologous antagonist/killer	Q16611
BAZ1A	Bromodomain adjacent to zinc finger domain protein 1A	Q9NRL2
BAZ1B	Tyrosine-protein kinase BAZ1B	Q9UIG0
BCAP31	B-cell receptor-associated protein 31	P51572
BCAT2	Branched-chain-amino-acid aminotransferase, mitochondrial	O15382
BCKDHA	2-oxoisovalerate dehydrogenase subunit alpha, mitochondrial	P12694
BCL2L1	Bcl-2-like protein 1	Q07817
BCL2L12	Bcl-2-like protein 12	Q9HB09
BCL2L13	Bcl-2-like protein 13	Q9BXX5
BCS1L	Mitochondrial chaperone BCS1	Q9Y276
BDH1	D-beta-hydroxybutyrate dehydrogenase, mitochondrial	Q02338
BET1L	BET1-like protein	Q9NYM9
BICD2	Protein bicaudal D homolog 2	Q8TD16
BID	BH3-interacting domain death agonist	P55957
BLVRA	Biliverdin reductase A	P53004
BNIP1	Vesicle transport protein SEC20	Q12981
BNIP3L	BCL2/adenovirus E1B 19 kDa protein-interacting protein 3-like	O60238
BPHL	Valacyclovir hydrolase	Q86WA6
BRI3BP	BRI3-binding protein	Q8WY22
BSG	Basigin	P35613
BUB3	Mitotic checkpoint protein BUB3	O43684
C10orf35	Uncharacterized protein C10orf35	Q96D05
C14orf166	UPF0568 protein C14orf166	Q9Y224
C16orf54	Transmembrane protein C16orf54	Q6UWD8
C17orf59	Uncharacterized protein C17orf59	Q96GS4
C17orf62	Uncharacterized protein C17orf62	Q9BQA9
C18orf32	UPF0729 protein C18orf32	Q8TCD1
C19orf10	UPF0556 protein C19orf10	Q969H8
C19orf52	Uncharacterized protein C19orf52	Q9BSF4
C1QBP	Complement component 1 Q subcomponent-binding protein, mitochondrial	Q07021
C21orf2	Protein C21orf2	O43822
C21orf33	ES1 protein homolog, mitochondrial	P30042
C2CD2L	C2 domain-containing protein 2-like	O14523

Gene	Protein name	Accession
C2CD3	C2 domain-containing protein 3	Q4AC94
C2orf43	UPF0554 protein C2orf43	Q9H6V9
C2orf47	Uncharacterized protein C2orf47, mitochondrial	Q8WWC4
C4A	Complement C4-A	P0C0L4
C7orf55	UPF0562 protein C7orf55	Q96HJ9
C8orf82	UPF0598 protein C8orf82	Q6P1X6
C9orf89	Bcl10-interacting CARD protein	Q96LW7
CAD	CAD protein	P27708
CALCOCO2	Calcium-binding and coiled-coil domain-containing protein 2	Q13137
CALML3	Calmodulin-like protein 3	P27482
CALML5	Calmodulin-like protein 5	Q9NZT1
CALR	Calreticulin	P27797
CAMLG	Calcium signal-modulating cyclophilin ligand	P49069
CAND1	Cullin-associated NEDD8-dissociated protein 1	Q86VP6
CANX	Calnexin	P27824
CAPRIN1	Caprin-1	Q14444
CAPZA1	F-actin-capping protein subunit alpha-1	P52907
CAPZA2	F-actin-capping protein subunit alpha-2	P47755
CARS2	Probable cysteine--tRNA ligase, mitochondrial	Q9HA77
CAT	Catalase	P04040
CBFB	Core-binding factor subunit beta	Q13951
CBL	E3 ubiquitin-protein ligase CBL	P22681
CBR4	Carbonyl reductase family member 4	Q8N4T8
CBX3	Chromobox protein homolog 3	Q13185
CBX5	Chromobox protein homolog 5	P45973
CCAR2	Cell cycle and apoptosis regulator protein 2	Q8N163
CCBL2	Kynurenine--oxoglutarate transaminase 3	Q6YP21
CCDC109B	Mitochondrial calcium uniporter regulatory subunit MCUb	Q9NWR8
CCDC115	Coiled-coil domain-containing protein 115	Q96NT0
CCDC134	Coiled-coil domain-containing protein 134	Q9H6E4
CCDC167	Coiled-coil domain-containing protein 167	Q9P0B6
CCDC47	Coiled-coil domain-containing protein 47	Q96A33
CCDC51	Coiled-coil domain-containing protein 51	Q96ER9
CCDC88A	Girdin	Q3V6T2
CCDC90B	Coiled-coil domain-containing protein 90B, mitochondrial	Q9GZT6
CCHCR1	Coiled-coil alpha-helical rod protein 1	Q8TD31
CCP110	Centriolar coiled-coil protein of 110 kDa	O43303
CCSMST1	Protein CCSMST1	Q4G0I0
CCT2	T-complex protein 1 subunit beta	P78371

Gene	Protein name	Accession
CCT3	T-complex protein 1 subunit gamma	P49368
CCT4	T-complex protein 1 subunit delta	P50991
CCT5	T-complex protein 1 subunit epsilon	P48643
CCT6A	T-complex protein 1 subunit zeta	P40227
CCT7	T-complex protein 1 subunit eta	Q99832
CCT8	T-complex protein 1 subunit theta	P50990
CD1C	T-cell surface glycoprotein CD1c	P29017
CD2	T-cell surface antigen CD2	P06729
CD247	T-cell surface glycoprotein CD3 zeta chain	P20963
CD3D	T-cell surface glycoprotein CD3 delta chain	P04234
CD3E	T-cell surface glycoprotein CD3 epsilon chain	P07766
CD3G	T-cell surface glycoprotein CD3 gamma chain	P09693
CD47	Leukocyte surface antigen CD47	Q08722
CD82	CD82 antigen	P27701
CDC42	Cell division control protein 42 homolog	P60953
CDK1	Cyclin-dependent kinase 1	P06493
CDK2	Cyclin-dependent kinase 2	P24941
CDK5	Cyclin-dependent kinase 5	Q00535
CDK5RAP2	CDK5 regulatory subunit-associated protein 2	Q96SN8
CDK6	Cyclin-dependent kinase 6	Q00534
CDK9	Cyclin-dependent kinase 9	P50750
CDKAL1	Threonylcarbamoyladenine tRNA methyltransferase	Q5VV42
CDS2	Phosphatidate cytidyltransferase 2	O95674
CECR5	Cat eye syndrome critical region protein 5	Q9BXW7
CENPF	Centromere protein F	P49454
CENPJ	Centromere protein J	Q9HC77
CEP120	Centrosomal protein of 120 kDa	Q8N960
CEP135	Centrosomal protein of 135 kDa	Q66GS9
CEP152	Centrosomal protein of 152 kDa	O94986
CEP250	Centrosome-associated protein CEP250	Q9BV73
CEP290	Centrosomal protein of 290 kDa	O15078
CEP350	Centrosome-associated protein 350	Q5VT06
CEP72	Centrosomal protein of 72 kDa	Q9P209
CEP85L	Centrosomal protein of 85 kDa-like	Q5SZL2
CEP97	Centrosomal protein of 97 kDa	Q8IW35
CFL1	Cofilin-1	P23528
CHCHD1	Coiled-coil-helix-coiled-coil-helix domain-containing protein 1	Q96BP2
CHCHD2	Coiled-coil-helix-coiled-coil-helix domain-containing protein 2, mitochondrial	Q9Y6H1
CHCHD2P9	Putative coiled-coil-helix-coiled-coil-helix domain-containing protein	Q5T1J5

Gene	Protein name	Accession
	CHCHD2P9, mitochondrial	
CHCHD3	Coiled-coil-helix-coiled-coil-helix domain-containing protein 3, mitochondrial	Q9NX63
CHCHD6	Coiled-coil-helix-coiled-coil-helix domain-containing protein 6, mitochondrial	Q9BRQ6
CHD4	Chromodomain-helicase-DNA-binding protein 4	Q14839
CHID1	Chitinase domain-containing protein 1	Q9BWS9
CHP1	Calcineurin B homologous protein 1	Q99653
CHSY1	Chondroitin sulfate synthase 1	Q86X52
CISD1	CDGSH iron-sulfur domain-containing protein 1	Q9NZ45
CISD2	CDGSH iron-sulfur domain-containing protein 2	Q8N5K1
CIT	Citron Rho-interacting kinase	O14578
CKAP4	Cytoskeleton-associated protein 4	Q07065
CKAP5	Cytoskeleton-associated protein 5	Q14008
CLASP1	CLIP-associating protein 1	Q7Z460
CLASP2	CLIP-associating protein 2	O75122
CLCN3	H(+)/Cl(-) exchange transporter 3	P51790
CLCN6	Chloride transport protein 6	P51797
CLCN7	H(+)/Cl(-) exchange transporter 7	P51798
CLEC11A	C-type lectin domain family 11 member A	Q9Y240
CLIC1	Chloride intracellular channel protein 1	O00299
CLPP	ATP-dependent Clp protease proteolytic subunit, mitochondrial	Q16740
CLPTM1	Cleft lip and palate transmembrane protein 1	O96005
CLPX	ATP-dependent Clp protease ATP-binding subunit clpX-like, mitochondrial	O76031
CLTC	Clathrin heavy chain 1	Q00610
CLYBL	Citrate lyase subunit beta-like protein, mitochondrial	Q8N0X4
CMPK1	UMP-CMP kinase	P30085
CNNM3	Metal transporter CNNM3	Q8NE01
CNNM4	Metal transporter CNNM4	Q6P4Q7
CNOT1	CCR4-NOT transcription complex subunit 1	A5YKK6
CNOT10	CCR4-NOT transcription complex subunit 10	Q9H9A5
CNOT3	CCR4-NOT transcription complex subunit 3	O75175
CNP	2',3'-cyclic-nucleotide 3'-phosphodiesterase	P09543
CNPY3	Protein canopy homolog 3	Q9BT09
COA1	Cytochrome c oxidase assembly factor 1 homolog	Q9GZY4
COA3	Cytochrome c oxidase assembly factor 3 homolog, mitochondrial	Q9Y2R0
COG3	Conserved oligomeric Golgi complex subunit 3	Q96JB2
COLGALT1	Procollagen galactosyltransferase 1	Q8NBJ5
COMT	Catechol O-methyltransferase	P21964
COPA	Coatomer subunit alpha	P53621
COPB1	Coatomer subunit beta	P53618

Gene	Protein name	Accession
COPB2	Coatomer subunit beta'	P35606
COPE	Coatomer subunit epsilon	O14579
COPG1	Coatomer subunit gamma-1	Q9Y678
COPZ1	Coatomer subunit zeta-1	P61923
COQ3	Hexaprenyldihydroxybenzoate methyltransferase, mitochondrial	Q9NZJ6
COQ5	2-methoxy-6-polyprenyl-1,4-benzoquinol methylase, mitochondrial	Q5HYK3
COQ6	Ubiquinone biosynthesis monooxygenase COQ6	Q9Y2Z9
CORO1A	Coronin-1A	P31146
COX15	Cytochrome c oxidase assembly protein COX15 homolog	Q7KZN9
COX18	Mitochondrial inner membrane protein COX18	Q8N8Q8
COX4I1	Cytochrome c oxidase subunit 4 isoform 1, mitochondrial	P13073
COX5A	Cytochrome c oxidase subunit 5A, mitochondrial	P20674
COX5B	Cytochrome c oxidase subunit 5B, mitochondrial	P10606
CPD	Carboxypeptidase D	O75976
CPOX	Oxygen-dependent coproporphyrinogen-III oxidase, mitochondrial	P36551
CPT1A	Carnitine O-palmitoyltransferase 1, liver isoform	P50416
CPT2	Carnitine O-palmitoyltransferase 2, mitochondrial	P23786
CPVL	Probable serine carboxypeptidase CPVL	Q9H3G5
CROCC	Rootletin	Q5TZA2
CRYZ	Quinone oxidoreductase	Q08257
CS	Citrate synthase, mitochondrial	O75390
CSDE1	Cold shock domain-containing protein E1	O75534
CSE1L	Exportin-2	P55060
CSPP1	Centrosome and spindle pole-associated protein 1	Q1MSJ5
CTBP1	C-terminal-binding protein 1	Q13363
CTDNEP1	CTD nuclear envelope phosphatase 1	O95476
CTNNA1	Catenin alpha-1	P35221
CTNNB1	Catenin beta-1	P35222
CTPS1	CTP synthase 1	P17812
CTSD	Cathepsin D	P07339
CTSG	Cathepsin G	P08311
CUX1	Protein CASP	Q13948
CXCR4	C-X-C chemokine receptor type 4	P61073
CYB5A	Cytochrome b5	P00167
CYB5B	Cytochrome b5 type B	O43169
CYB5R1	NADH-cytochrome b5 reductase 1	Q9UHQ9
CYB5R3	NADH-cytochrome b5 reductase 3	P00387
CYC1	Cytochrome c1, heme protein, mitochondrial	P08574
CYCS	Cytochrome c	P99999

Gene	Protein name	Accession
CYP20A1	Cytochrome P450 20A1	Q6UW02
DAAM1	Disheveled-associated activator of morphogenesis 1	Q9Y4D1
DAD1	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit DAD1	P61803
DAP3	28S ribosomal protein S29, mitochondrial	P51398
DARS	Aspartate--tRNA ligase, cytoplasmic	P14868
DARS2	Aspartate--tRNA ligase, mitochondrial	Q6PI48
DBT	Lipoamide acyltransferase component of branched-chain alpha-keto acid dehydrogenase complex, mitochondrial	P11182
DCD	Dermcidin	P81605
DCXR	L-xylulose reductase	Q7Z4W1
DDAH2	N(G),N(G)-dimethylarginine dimethylaminohydrolase 2	O95865
DDOST	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 48 kDa subunit	P39656
DDRKG1	DDRKG domain-containing protein 1	Q96HY6
DDX21	Nucleolar RNA helicase 2	Q9NR30
DDX24	ATP-dependent RNA helicase DDX24	Q9GZR7
DDX28	Probable ATP-dependent RNA helicase DDX28	Q9NUL7
DDX39A	ATP-dependent RNA helicase DDX39A	O00148
DDX47	Probable ATP-dependent RNA helicase DDX47	Q9H0S4
DDX5	Probable ATP-dependent RNA helicase DDX5	P17844
DECR1	2,4-dienoyl-CoA reductase, mitochondrial	Q16698
DERL1	Derlin-1	Q9BUN8
DERL2	Derlin-2	Q9GZP9
DGUOK	Deoxyguanosine kinase, mitochondrial	Q16854
DHCR24	Delta(24)-sterol reductase	Q15392
DHCR7	7-dehydrocholesterol reductase	Q9UBM7
DHODH	Dihydroorotate dehydrogenase	Q02127
DHRS4	Dehydrogenase/reductase SDR family member 4	Q9BTZ2
DHRS7	Dehydrogenase/reductase SDR family member 7	Q9Y394
DHTKD1	Probable 2-oxoglutarate dehydrogenase E1 component DHKTD1, mitochondrial	Q96HY7
DHX15	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15	O43143
DHX30	Putative ATP-dependent RNA helicase DHX30	Q7L2E3
DHX9	ATP-dependent RNA helicase A	Q08211
DIABLO	Diablo homolog, mitochondrial	Q9NR28
DIAPH1	Protein diaphanous homolog 1	O60610
DIP2B	Disco-interacting protein 2 homolog B	Q9P265
DIS3	Exosome complex exonuclease RRP44	Q9Y2L1
DLAT	Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex, mitochondrial	P10515

Gene	Protein name	Accession
DLG1	Disks large homolog 1	Q12959
DLST	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex, mitochondrial	P36957
DNAJA1	DnaJ homolog subfamily A member 1	P31689
DNAJA2	DnaJ homolog subfamily A member 2	O60884
DNAJA3	DnaJ homolog subfamily A member 3, mitochondrial	Q96EY1
DNAJB11	DnaJ homolog subfamily B member 11	Q9UBS4
DNAJB12	DnaJ homolog subfamily B member 12	Q9NXW2
DNAJB2	DnaJ homolog subfamily B member 2	P25686
DNAJB6	DnaJ homolog subfamily B member 6	O75190
DNAJC10	DnaJ homolog subfamily C member 10	Q8LXB1
DNAJC13	DnaJ homolog subfamily C member 13	O75165
DNAJC15	DnaJ homolog subfamily C member 15	Q9Y5T4
DNAJC19	Mitochondrial import inner membrane translocase subunit TIM14	Q96DA6
DNAJC3	DnaJ homolog subfamily C member 3	Q13217
DNAJC30	DnaJ homolog subfamily C member 30	Q96LL9
DNAJC5	DnaJ homolog subfamily C member 5	Q9H3Z4
DNLZ	DNL-type zinc finger protein	Q5SXM8
DNTTIP2	Deoxynucleotidyltransferase terminal-interacting protein 2	Q5QJE6
DOCK2	Dedicator of cytokinesis protein 2	Q92608
DOCK7	Dedicator of cytokinesis protein 7	Q96N67
DPM1	Dolichol-phosphate mannosyltransferase subunit 1	O60762
DRG1	Developmentally-regulated GTP-binding protein 1	Q9Y295
DSG1	Desmoglein-1	Q02413
DSG2	Desmoglein-2	Q14126
DSP	Desmoplakin	P15924
DTYMK	Thymidylate kinase	P23919
DUT	Deoxyuridine 5'-triphosphate nucleotidohydrolase, mitochondrial	P33316
DYNC1H1	Cytoplasmic dynein 1 heavy chain 1	Q14204
EARS2	Probable glutamate--tRNA ligase, mitochondrial	Q5JPH6
EBAG9	Receptor-binding cancer antigen expressed on SiSo cells	O00559
ECH1	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	Q13011
ECHDC1	Ethylmalonyl-CoA decarboxylase	Q9NTX5
ECHS1	Enoyl-CoA hydratase, mitochondrial	P30084
ECI2	Enoyl-CoA delta isomerase 2, mitochondrial	O75521
ECSIT	Evolutionarily conserved signaling intermediate in Toll pathway, mitochondrial	Q9BQ95
EDC4	Enhancer of mRNA-decapping protein 4	Q6P2E9
EDEM3	ER degradation-enhancing alpha-mannosidase-like protein 3	Q9BZQ6
EEA1	Early endosome antigen 1	Q15075

Gene	Protein name	Accession
EEF1A1	Elongation factor 1-alpha 1	P68104
EEF1A1P5	Putative elongation factor 1-alpha-like 3	Q5VTE0
EEF1D	Elongation factor 1-delta	P29692
EEF1E1	Eukaryotic translation elongation factor 1 epsilon-1	O43324
EEF1G	Elongation factor 1-gamma	P26641
EEF2	Elongation factor 2	P13639
EFCAB4B	EF-hand calcium-binding domain-containing protein 4B	Q9BSW2
EFHD2	EF-hand domain-containing protein D2	Q96C19
EFTUD2	116 kDa U5 small nuclear ribonucleoprotein component	Q15029
EIF3C	Eukaryotic translation initiation factor 3 subunit C	Q99613
EIF3CL	Eukaryotic translation initiation factor 3 subunit C-like protein	B5ME19
EIF3E	Eukaryotic translation initiation factor 3 subunit E	P60228
EIF3H	Eukaryotic translation initiation factor 3 subunit H	O15372
EIF3I	Eukaryotic translation initiation factor 3 subunit I	Q13347
EIF4A1	Eukaryotic initiation factor 4A-I	P60842
EIF4A3	Eukaryotic initiation factor 4A-III	P38919
EIF4E2	Eukaryotic translation initiation factor 4E type 2	O60573
EIF4G1	Eukaryotic translation initiation factor 4 gamma 1	Q04637
EIF5A	Eukaryotic translation initiation factor 5A-1	P63241
EIF5AL1	Eukaryotic translation initiation factor 5A-1-like	Q6IS14
EIF6	Eukaryotic translation initiation factor 6	P56537
ELAC2	Zinc phosphodiesterase ELAC protein 2	Q9BQ52
ELAVL1	ELAV-like protein 1	Q15717
ELMO1	Engulfment and cell motility protein 1	Q92556
ELMOD2	ELMO domain-containing protein 2	Q8LZ81
EMC1	ER membrane protein complex subunit 1	Q8N766
EMC3	ER membrane protein complex subunit 3	Q9P0I2
EMC4	ER membrane protein complex subunit 4	Q5J8M3
EMC6	ER membrane protein complex subunit 6	Q9BV81
EMC7	ER membrane protein complex subunit 7	Q9NPA0
EMC8	ER membrane protein complex subunit 8	O43402
EMD	Emerin	P50402
ENDOD1	Endonuclease domain-containing 1 protein	O94919
ENO1	Alpha-enolase	P06733
ENPP4	Bis(5'-adenosyl)-triphosphatase ENPP4	Q9Y6X5
EPB41	Protein 4.1	P11171
EPDR1	Mammalian ependymin-related protein 1	Q9UM22
EPHX1	Epoxide hydrolase 1	P07099
EPPK1	Epiplakin	P58107

Gene	Protein name	Accession
EPRS	Bifunctional glutamate/proline--tRNA ligase	P07814
EPS15L1	Epidermal growth factor receptor substrate 15-like 1	Q9UBC2
ERAL1	GTPase Era, mitochondrial	O75616
ERAP1	Endoplasmic reticulum aminopeptidase 1	Q9NZ08
ERAP2	Endoplasmic reticulum aminopeptidase 2	Q6P179
ERBB2IP	Protein LAP2	Q96RT1
ERGIC1	Endoplasmic reticulum-Golgi intermediate compartment protein 1	Q969X5
ERGIC3	Endoplasmic reticulum-Golgi intermediate compartment protein 3	Q9Y282
ERLEC1	Endoplasmic reticulum lectin 1	Q96DZ1
ERLIN2	Erlin-2	O94905
ERO1L	ERO1-like protein alpha	Q96HE7
ERP29	Endoplasmic reticulum resident protein 29	P30040
ERP44	Endoplasmic reticulum resident protein 44	Q9BS26
ESYT1	Extended synaptotagmin-1	Q9BSJ8
ETFA	Electron transfer flavoprotein subunit alpha, mitochondrial	P13804
ETFB	Electron transfer flavoprotein subunit beta	P38117
ETHE1	Persulfide dioxygenase ETHE1, mitochondrial	O95571
EXOC1	Exocyst complex component 1	Q9NV70
EXOG	Nuclease EXOG, mitochondrial	Q9Y2C4
F5	Coagulation factor V	P12259
FABP5	Fatty acid-binding protein, epidermal	Q01469
FADS2	Fatty acid desaturase 2	O95864
FAF2	FAS-associated factor 2	Q96CS3
FAHD1	Acylpyruvase FAHD1, mitochondrial	Q6P587
FAHD2A	Fumarylacetoacetate hydrolase domain-containing protein 2A	Q96GK7
FAM120A	Constitutive coactivator of PPAR-gamma-like protein 1	Q9NZB2
FAM134C	Protein FAM134C	Q86VR2
FAM160B1	Protein FAM160B1	Q5W0V3
FAM162A	Protein FAM162A	Q96A26
FAM20B	Glycosaminoglycan xylosylkinase	O75063
FAM210A	Protein FAM210A	Q96ND0
FAM213A	Redox-regulatory protein FAM213A	Q9BRX8
FAM3C	Protein FAM3C	Q92520
FAM49B	Protein FAM49B	Q9NUQ9
FAM96B	Mitotic spindle-associated MMXD complex subunit MIP18	Q9Y3D0
FANCD2	Fanconi anemia group D2 protein	Q9BXW9
FANCI	Fanconi anemia group I protein	Q9NVI1
FARI	Fatty acyl-CoA reductase 1	Q8WVX9
FARS2	Phenylalanine--tRNA ligase, mitochondrial	O95363

Gene	Protein name	Accession
FAS	Tumor necrosis factor receptor superfamily member 6	P25445
FASN	Fatty acid synthase	P49327
FASTKD1	FAST kinase domain-containing protein 1	Q53R41
FASTKD2	FAST kinase domain-containing protein 2	Q9NYY8
FAT1	Protocadherin Fat 1	Q14517
FDFT1	Squalene synthase	P37268
FDPS	Farnesyl pyrophosphate synthase	P14324
FDX1	Adrenodoxin, mitochondrial	P10109
FDXR	NADPH:adrenodoxin oxidoreductase, mitochondrial	P22570
FECH	Ferrochelatase, mitochondrial	P22830
FEN1	Flap endonuclease 1	P39748
FERMT3	Fermitin family homolog 3	Q86UX7
FGA	Fibrinogen alpha chain	P02671
FGFR1OP	FGFR1 oncogene partner	O95684
FH	Fumarate hydratase, mitochondrial	P07954
FIS1	Mitochondrial fission 1 protein	Q9Y3D6
FKBP11	Peptidyl-prolyl cis-trans isomerase FKBP11	Q9NYL4
FKBP15	FK506-binding protein 15	Q5T1M5
FKBP2	Peptidyl-prolyl cis-trans isomerase FKBP2	P26885
FLG2	Filaggrin-2	Q5D862
FLII	Protein flightless-1 homolog	Q13045
FLNA	Filamin-A	P21333
FLNB	Filamin-B	O75369
FLOT1	Flotillin-1	O75955
FLOT2	Flotillin-2	Q14254
FLVCR1	Feline leukemia virus subgroup C receptor-related protein 1	Q9Y5Y0
FMNL1	Formin-like protein 1	O95466
FN1	Fibronectin	P02751
FNDC3A	Fibronectin type-III domain-containing protein 3A	Q9Y2H6
FOXRED1	FAD-dependent oxidoreductase domain-containing protein 1	Q96CU9
FRG1	Protein FRG1	Q14331
FTH1	Ferritin heavy chain	P02794
FTSJ3	pre-rRNA processing protein FTSJ3	Q8IY81
FUNDC2	FUN14 domain-containing protein 2	Q9BWH2
FUT8	Alpha-(1,6)-fucosyltransferase	Q9BYC5
FXN	Frataxin, mitochondrial	Q16595
FYCO1	FYVE and coiled-coil domain-containing protein 1	Q9BQS8
G6PD	Glucose-6-phosphate 1-dehydrogenase	P11413
GAA	Lysosomal alpha-glucosidase	P10253

Gene	Protein name	Accession
GABARAPL2	Gamma-aminobutyric acid receptor-associated protein-like 2	P60520
GADD45GIP1	Growth arrest and DNA damage-inducible proteins-interacting protein 1	Q8TAE8
GALNT2	Polypeptide N-acetylgalactosaminyltransferase 2	Q10471
GALNT7	N-acetylgalactosaminyltransferase 7	Q86SF2
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase	P04406
GARS	Glycine--tRNA ligase	P41250
GART	Trifunctional purine biosynthetic protein adenosine-3	P22102
GATC	Glutamyl-tRNA(Gln) amidotransferase subunit C, mitochondrial	O43716
GBAS	Protein NipSnap homolog 2	O75323
GBF1	Golgi-specific brefeldin A-resistance guanine nucleotide exchange factor 1	Q92538
GCC2	GRIP and coiled-coil domain-containing protein 2	Q8IWJ2
GCSH	Glycine cleavage system H protein, mitochondrial	P23434
GDAP1	Ganglioside-induced differentiation-associated protein 1	Q8TB36
GDPD1	Glycerophosphodiester phosphodiesterase domain-containing protein 1	Q8N9F7
GFM2	Ribosome-releasing factor 2, mitochondrial	Q969S9
GGH	Gamma-glutamyl hydrolase	Q92820
GHTM	Growth hormone-inducible transmembrane protein	Q9H3K2
GIGYF2	PERQ amino acid-rich with GYF domain-containing protein 2	Q6Y7W6
GIMAP1	GTPase IMAP family member 1	Q8WWP7
GIMAP6	GTPase IMAP family member 6	Q6P9H5
GLG1	Golgi apparatus protein 1	Q92896
GLIPR2	Golgi-associated plant pathogenesis-related protein 1	Q9H4G4
GLRX3	Glutaredoxin-3	O76003
GLRX5	Glutaredoxin-related protein 5, mitochondrial	Q86SX6
GLS	Glutaminase kidney isoform, mitochondrial	O94925
GLUD1	Glutamate dehydrogenase 1, mitochondrial	P00367
GNA13	Guanine nucleotide-binding protein subunit alpha-13	Q14344
GNAI2	Guanine nucleotide-binding protein G(i) subunit alpha-2	P04899
GNAI3	Guanine nucleotide-binding protein G(k) subunit alpha	P08754
GNAQ	Guanine nucleotide-binding protein G(q) subunit alpha	P50148
GNAS	Guanine nucleotide-binding protein G(s) subunit alpha isoforms short	P63092
GNB2	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2	P62879
GNB2L1	Guanine nucleotide-binding protein subunit beta-2-like 1	P63244
GNPTAB	N-acetylglucosamine-1-phosphotransferase subunits alpha/beta	Q3T906
GNS	N-acetylglucosamine-6-sulfatase	P15586
GOLGA2	Golgin subfamily A member 2	Q08379
GOLGA3	Golgin subfamily A member 3	Q08378
GOLGA5	Golgin subfamily A member 5	Q8TBA6
GOLGA7	Golgin subfamily A member 7	Q7Z5G4

Gene	Protein name	Accession
GOLGB1	Golgin subfamily B member 1	Q14789
GOLPH3	Golgi phosphoprotein 3	Q9H4A6
GOPC	Golgi-associated PDZ and coiled-coil motif-containing protein	Q9HD26
GORASP2	Golgi reassembly-stacking protein 2	Q9H8Y8
GOSR1	Golgi SNAP receptor complex member 1	O95249
GOSR2	Golgi SNAP receptor complex member 2	Q35165
GOT2	Aspartate aminotransferase, mitochondrial	P00505
GPR107	Protein GPR107	Q5VW38
GRAP2	GRB2-related adapter protein 2	O75791
GRB2	Growth factor receptor-bound protein 2	P62993
GRHPR	Glyoxylate reductase/hydroxypyruvate reductase	Q9UBQ7
GRPEL1	GrpE protein homolog 1, mitochondrial	Q9HAV7
GRPEL2	GrpE protein homolog 2, mitochondrial	Q8TAA5
GRSF1	G-rich sequence factor 1	Q12849
GSN	Gelsolin	P06396
GSR	Glutathione reductase, mitochondrial	P00390
GSTK1	Glutathione S-transferase kappa 1	Q9Y2Q3
GSTP1	Glutathione S-transferase P	P09211
GTPBP10	GTP-binding protein 10	A4D1E9
GTPBP3	tRNA modification GTPase GTPBP3, mitochondrial	Q969Y2
GTPBP6	Putative GTP-binding protein 6	O43824
GTPBP8	GTP-binding protein 8	Q8N3Z3
GUK1	Guanylate kinase	Q64520
H2AFV	Histone H2A.V	Q71UI9
H2AFX	Histone H2AX	P16104
H2AFY	Core histone macro-H2A.1	O75367
H2AFZ	Histone H2A.Z	P0C0S5
H3F3A	Histone H3.3	P84243
H6PD	GDH/6PGL endoplasmic bifunctional protein	O95479
HADH	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial	Q16836
HADHA	Trifunctional enzyme subunit alpha, mitochondrial	P40939
HADHB	Trifunctional enzyme subunit beta, mitochondrial	P55084
HAGH	Hydroxyacylglutathione hydrolase, mitochondrial	Q16775
HAL	Histidine ammonia-lyase	P42357
HARS2	Probable histidine--tRNA ligase, mitochondrial	P49590
HAUS1	HAUS augmin-like complex subunit 1	Q96CS2
HAUS2	HAUS augmin-like complex subunit 2	Q9NVX0
HAUS4	HAUS augmin-like complex subunit 4	Q9H6D7
HAUS6	HAUS augmin-like complex subunit 6	Q7Z4H7

Gene	Protein name	Accession
HAUS7	HAUS augmin-like complex subunit 7	Q99871
HAUS8	HAUS augmin-like complex subunit 8	Q9BT25
HAX1	HCLS1-associated protein X-1	O00165
HBA1;	Hemoglobin subunit alpha	P69905
HBB	Hemoglobin subunit beta	P68871
HCCS	Cytochrome c-type heme lyase	P53701
HCFC1	Host cell factor 1	P51610
HDHD3	Haloacid dehalogenase-like hydrolase domain-containing protein 3	Q9BSH5
HDLBP	Vigilin	Q00341
HEATR1	HEAT repeat-containing protein 1	Q9H583
HEXB	Beta-hexosaminidase subunit beta	P07686
HIBADH	3-hydroxyisobutyrate dehydrogenase, mitochondrial	P31937
HIBCH	3-hydroxyisobutyryl-CoA hydrolase, mitochondrial	Q6NVY1
HINT1	Histidine triad nucleotide-binding protein 1	P49773
HIST1H1B	Histone H1.5	P16401
HIST1H1C	Histone H1.2	P16403
HIST1H1D	Histone H1.3	P16402
HIST1H2AC	Histone H2A type 1-C	Q93077
HIST1H2BB	Histone H2B type 1-B	P33778
HIST1H2BC	Histone H2B type 1-C/E/F/G/I	P62807
HIST1H2BD	Histone H2B type 1-D	P58876
HIST1H2BH	Histone H2B type 1-H	Q93079
HIST1H2BJ	Histone H2B type 1-J	P06899
HIST1H4A	Histone H4	P62805
HK1	Hexokinase-1	P19367
HK2	Hexokinase-2	P52789
HLA-A	HLA class I histocompatibility antigen, A-3 alpha chain	P04439
HLA-B	HLA class I histocompatibility antigen, B-8 alpha chain	P30460
HLA-E	HLA class I histocompatibility antigen, alpha chain E	P13747
HMI3	Minor histocompatibility antigen H13	Q8TCT9
HMGB1	High mobility group protein B1	P09429
HMGB1P1	Putative high mobility group protein B1-like 1	B2RPK0
HMGB2	High mobility group protein B2	P26583
HMGCL	Hydroxymethylglutaryl-CoA lyase, mitochondrial	P35914
HMGCR	3-hydroxy-3-methylglutaryl-coenzyme A reductase	P04035
HNRNPA0	Heterogeneous nuclear ribonucleoprotein A0	Q13151
HNRNPA1	Heterogeneous nuclear ribonucleoprotein A1	P09651
HNRNPA2B1	Heterogeneous nuclear ribonucleoproteins A2/B1	P22626
HNRNPA3	Heterogeneous nuclear ribonucleoprotein A3	P51991

Gene	Protein name	Accession
HNRNPC	Heterogeneous nuclear ribonucleoproteins C1/C2	P07910
HNRNPD	Heterogeneous nuclear ribonucleoprotein D0	Q14103
HNRNPF	Heterogeneous nuclear ribonucleoprotein F	P52597
HNRNPH1	Heterogeneous nuclear ribonucleoprotein H	P31943
HNRNPH3	Heterogeneous nuclear ribonucleoprotein H3	P31942
HNRNPM	Heterogeneous nuclear ribonucleoprotein M	P52272
HPCAL1	Hippocalcin-like protein 1	P37235
HPRT1	Hypoxanthine-guanine phosphoribosyltransferase	P00492
HRNR	Hornerin	Q86YZ3
HRSP12	Ribonuclease UK114	P52758
HS2ST1	Heparan sulfate 2-O-sulfotransferase 1	Q7LGA3
HSD17B10	3-hydroxyacyl-CoA dehydrogenase type-2	Q99714
HSD17B11	Estradiol 17-beta-dehydrogenase 11	Q8NBQ5
HSD17B12	Estradiol 17-beta-dehydrogenase 12	Q53GQ0
HSD17B4	Peroxisomal multifunctional enzyme type 2	P51659
HSD17B7	3-keto-steroid reductase	P56937
HSD17B8	Estradiol 17-beta-dehydrogenase 8	Q92506
HSDL1	Inactive hydroxysteroid dehydrogenase-like protein 1	Q3SXM5
HSDL2	Hydroxysteroid dehydrogenase-like protein 2	Q6YN16
HSP90AA1	Heat shock protein HSP 90-alpha	P07900
HSP90AB1	Heat shock protein HSP 90-beta	P08238
HSP90B1	Endoplasmic	P14625
HSPA1A	Heat shock 70 kDa protein 1A/1B	P08107
HSPA5	78 kDa glucose-regulated protein	P11021
HSPA8	Heat shock cognate 71 kDa protein	P11142
HSPA9	Stress-70 protein, mitochondrial	P38646
HSPB1	Heat shock protein beta-1	P04792
HSPD1	60 kDa heat shock protein, mitochondrial	P10809
HSPE1	10 kDa heat shock protein, mitochondrial	P61604
HSPH1	Heat shock protein 105 kDa	Q92598
HTRA2	Serine protease HTRA2, mitochondrial	O43464
HVCN1	Voltage-gated hydrogen channel 1	Q96D96
HYOU1	Hypoxia up-regulated protein 1	Q9Y4L1
IARS	Isoleucine--tRNA ligase, cytoplasmic	P41252
IBA57	Putative transferase CAF17, mitochondrial	Q5T440
ICAM2	Intercellular adhesion molecule 2	P13598
ICT1	Peptidyl-tRNA hydrolase ICT1, mitochondrial	Q14197
IDE	Insulin-degrading enzyme	P14735
IDH2	Isocitrate dehydrogenase [NADP], mitochondrial	P48735

Gene	Protein name	Accession
IDH3A	Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial	P50213
IDH3B	Isocitrate dehydrogenase [NAD] subunit beta, mitochondrial	O43837
IDII	Isopentenyl-diphosphate Delta-isomerase 1	Q13907
IFI35	Interferon-induced 35 kDa protein	P80217
IGF2R	Cation-independent mannose-6-phosphate receptor	P11717
IGKC	Ig kappa chain C region	P01834
IGSF8	Immunoglobulin superfamily member 8	Q969P0
IKBKAP	Elongator complex protein 1	O95163
ILF2	Interleukin enhancer-binding factor 2	Q12905
IMMT	Mitochondrial inner membrane protein	Q16891
IMPAD1	Inositol monophosphatase 3	Q9NX62
IMPDH2	Inosine-5'-monophosphate dehydrogenase 2	P12268
INF2	Inverted formin-2	Q27J81
IPO4	Importin-4	Q8TEX9
IPO5	Importin-5	O00410
IPO7	Importin-7	O95373
IPO8	Importin-8	O15397
IQGAP1	Ras GTPase-activating-like protein IQGAP1	P46940
IQGAP2	Ras GTPase-activating-like protein IQGAP2	Q13576
ISCA1	Iron-sulfur cluster assembly 1 homolog, mitochondrial	Q9BUE6
ISCA2	Iron-sulfur cluster assembly 2 homolog, mitochondrial	Q86U28
ISOC1	Isochorismatase domain-containing protein 1	Q96CN7
ISOC2	Isochorismatase domain-containing protein 2, mitochondrial	Q96AB3
ITGA4	Integrin alpha-4	P13612
ITGA5	Integrin alpha-5	P08648
ITGAL	Integrin alpha-L	P20701
ITGB1	Integrin beta-1	P05556
ITM2A	Integral membrane protein 2A	O43736
ITM2B	Integral membrane protein 2B	Q9Y287
ITM2C	Integral membrane protein 2C	Q9NQX7
ITPR1	Inositol 1,4,5-trisphosphate receptor type 1	Q14643
ITPR2	Inositol 1,4,5-trisphosphate receptor type 2	Q14571
ITPR3	Inositol 1,4,5-trisphosphate receptor type 3	Q14573
IVD	Isovaleryl-CoA dehydrogenase, mitochondrial	P26440
JAGN1	Protein jagunal homolog 1	Q8N5M9
JAK1	Tyrosine-protein kinase JAK1	P23458
JAM3	Junctional adhesion molecule C	Q9BX67
JUP	Junction plakoglobin	P14923
KARS	Lysine--tRNA ligase	Q15046

Gene	Protein name	Accession
KDELRL1	ER lumen protein retaining receptor 1	P24390
KHSRP	Far upstream element-binding protein 2	Q92945
KIAA0922	Transmembrane protein 131-like	A2VDJ0
KIAA1731	Centrosomal protein KIAA1731	Q9C0D2
KIDINS220	Kinase D-interacting substrate of 220 kDa	Q9ULH0
KIF11	Kinesin-like protein KIF11	P52732
KIF14	Kinesin-like protein KIF14	Q15058
KIF15	Kinesin-like protein KIF15	Q9NS87
KIF2C	Kinesin-like protein KIF2C	Q99661
KIF4A	Chromosome-associated kinesin KIF4A	O95239
KIF5B	Kinesin-1 heavy chain	P33176
KIFC1	Kinesin-like protein KIFC1	Q9BW19
KPNA2	Importin subunit alpha-1	P52292
KPNB1	Importin subunit beta-1	Q14974
KRT1	Keratin, type II cytoskeletal 1	P04264
KRT10	Keratin, type I cytoskeletal 10	P13645
KRT14	Keratin, type I cytoskeletal 14	P02533
KRT15	Keratin, type I cytoskeletal 15	P19012
KRT16	Keratin, type I cytoskeletal 16	P08779
KRT17	Keratin, type I cytoskeletal 17	Q04695
KRT2	Keratin, type II cytoskeletal 2 epidermal	P35908
KRT5	Keratin, type II cytoskeletal 5	P13647
KRT6A	Keratin, type II cytoskeletal 6A	P02538
KRT6C	Keratin, type II cytoskeletal 6C	P48668
KRT78	Keratin, type II cytoskeletal 78	Q8N1N4
KRT80	Keratin, type II cytoskeletal 80	Q6KB66
KRT9	Keratin, type I cytoskeletal 9	P35527
KTN1	Kinectin	Q86UP2
L2HGDH	L-2-hydroxyglutarate dehydrogenase, mitochondrial	Q9H9P8
LACTB	Serine beta-lactamase-like protein LACTB, mitochondrial	P83111
LAMP1	Lysosome-associated membrane glycoprotein 1	P11279
LAMP2	Lysosome-associated membrane glycoprotein 2	P13473
LAMTOR1	Ragulator complex protein LAMTOR1	Q6IAA8
LAMTOR2	Ragulator complex protein LAMTOR2	Q9Y2Q5
LAMTOR3	Ragulator complex protein LAMTOR3	Q9UHA4
LAP3	Cytosol aminopeptidase	P28838
LAPTM5	Lysosomal-associated transmembrane protein 5	Q13571
LARS	Leucine--tRNA ligase, cytoplasmic	Q9P2J5
LARS2	Probable leucine--tRNA ligase, mitochondrial	Q15031

Gene	Protein name	Accession
LBR	Lamin-B receptor	Q14739
LCLAT1	Lysocardiolipin acyltransferase 1	Q6UWP7
LCP1	Plastin-2	P13796
LDHA	L-lactate dehydrogenase A chain	P00338
LDHB	L-lactate dehydrogenase B chain	P07195
LDLR	Low-density lipoprotein receptor	P01130
LEMD2	LEM domain-containing protein 2	Q8NC56
LEPRE1	Prolyl 3-hydroxylase 1	Q32P28
LETM1	LETM1 and EF-hand domain-containing protein 1, mitochondrial	O95202
LETMD1	LETM1 domain-containing protein 1	Q6P1Q0
LGALS3BP	Galectin-3-binding protein	Q08380
LGALS7	Galectin-7	P47929
LIG3	DNA ligase 3	P49916
LIME1	Lck-interacting transmembrane adapter 1	Q9H400
LMAN1	Protein ERGIC-53	P49257
LMAN2	Vesicular integral-membrane protein VIP36	Q12907
LMAN2L	VIP36-like protein	Q9H0V9
LMNB1	Lamin-B1	P20700
LMNB2	Lamin-B2	Q03252
LMO7	LIM domain only protein 7	Q8WWI1
LNP	Protein lunapark	Q9C0E8
LNPEP	Leucyl-cystinyl aminopeptidase	Q9UIQ6
LONP1	Lon protease homolog, mitochondrial	P36776
LONP2	Lon protease homolog 2, peroxisomal	Q86WA8
LPCAT1	Lysophosphatidylcholine acyltransferase 1	Q8NF37
LPCAT3	Lysophospholipid acyltransferase 5	Q6P1A2
LRPAP1	Alpha-2-macroglobulin receptor-associated protein	P30533
LRRC59	Leucine-rich repeat-containing protein 59	Q96AG4
LRRC8A	Leucine-rich repeat-containing protein 8A	Q8IWT6
LRRC8C	Leucine-rich repeat-containing protein 8C	Q8TDW0
LRRFIP1	Leucine-rich repeat flightless-interacting protein 1	Q32MZ4
LSM12	Protein LSM12 homolog	Q3MHD2
LSS	Lanosterol synthase	P48449
LYPLAL1	Lysophospholipase-like protein 1	Q5VWZ2
LYRM4	LYR motif-containing protein 4	Q9HD34
LYRM7	Complex III assembly factor LYRM7	Q5U5X0
LYZ	Lysozyme C	P61626
MACROD1	O-acetyl-ADP-ribose deacetylase MACROD1	Q9BQ69
MAGED1	Melanoma-associated antigen D1	Q9Y5V3

Gene	Protein name	Accession
MAGOH	Protein mago nashi homolog	P61326
MAGOHB	Protein mago nashi homolog 2	Q96A72
MAGT1	Magnesium transporter protein 1	Q9H0U3
MAN1B1	Endoplasmic reticulum mannosyl-oligosaccharide 1,2-alpha-mannosidase	Q9UKM7
MAN2A1	Alpha-mannosidase 2	Q16706
MAN2A2	Alpha-mannosidase 2x	P49641
MAN2B1	Lysosomal alpha-mannosidase	O00754
MANF	Mesencephalic astrocyte-derived neurotrophic factor	P55145
MAP2K2	Dual specificity mitogen-activated protein kinase kinase 2	P36507
MARCH5	E3 ubiquitin-protein ligase MARCH5	Q9NX47
MARCH6	E3 ubiquitin-protein ligase MARCH6	O60337
MARCKSL1	MARCKS-related protein	P49006
MARS	Methionine--tRNA ligase, cytoplasmic	P56192
MARS2	Methionine--tRNA ligase, mitochondrial	Q96GW9
MAVS	Mitochondrial antiviral-signaling protein	Q7Z434
MBLAC2	Metallo-beta-lactamase domain-containing protein 2	Q68D91
MCAT	Malonyl-CoA-acyl carrier protein transacylase, mitochondrial	Q8IVS2
MCCC1	Methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial	Q96RQ3
MCEE	Methylmalonyl-CoA epimerase, mitochondrial	Q96PE7
MCM2	DNA replication licensing factor MCM2	P49736
MCM3	DNA replication licensing factor MCM3	P25205
MCM4	DNA replication licensing factor MCM4	P33991
MCM5	DNA replication licensing factor MCM5	P33992
MCM6	DNA replication licensing factor MCM6	Q14566
MCM7	DNA replication licensing factor MCM7	P33993
MCU	Calcium uniporter protein, mitochondrial	Q8NE86
MCUR1	Mitochondrial calcium uniporter regulator 1	Q96AQ8
MDC1	Mediator of DNA damage checkpoint protein 1	Q14676
MDH1	Malate dehydrogenase, cytoplasmic	P40925
MDH2	Malate dehydrogenase, mitochondrial	P40926
MDM1	Nuclear protein MDM1	Q8TC05
ME2	NAD-dependent malic enzyme, mitochondrial	P23368
MECR	Trans-2-enoyl-CoA reductase, mitochondrial	Q9BV79
MESDC2	LDLR chaperone MESD	Q14696
METTL15	Probable methyltransferase-like protein 15	A6NJ78
METTL17	Methyltransferase-like protein 17, mitochondrial	Q9H7H0
MFF	Mitochondrial fission factor	Q9GZY8
MFGE8	Lactadherin	Q08431
MFN1	Mitofusin-1	Q8IWA4

Gene	Protein name	Accession
MFN2	Mitofusin-2	O95140
MFSD6	Major facilitator superfamily domain-containing protein 6	Q6ZSS7
MGAT2	Alpha-1,6-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase	Q10469
MGME1	Mitochondrial genome maintenance exonuclease 1	Q9BQP7
MGMT	Methylated-DNA--protein-cysteine methyltransferase	P16455
MGST3	Microsomal glutathione S-transferase 3	O14880
MIA3	Melanoma inhibitory activity protein 3	Q5JRA6
MIB1	E3 ubiquitin-protein ligase MIB1	Q86YT6
MICU2	Calcium uptake protein 2, mitochondrial	Q8IYU8
MKI67	Antigen KI-67	P46013
MLEC	Malectin	Q14165
MLYCD	Malonyl-CoA decarboxylase, mitochondrial	O95822
MMAA	Methylmalonic aciduria type A protein, mitochondrial	Q8IVH4
MMGT1	Membrane magnesium transporter 1	Q8N4V1
MOB1A	MOB kinase activator 1A	Q9H8S9
MOB1B	MOB kinase activator 1B	Q7L9L4
MOCS1	Molybdenum cofactor biosynthesis protein 1	Q9NZB8
MOGS	Mannosyl-oligosaccharide glucosidase	Q13724
MPST	3-mercaptopyruvate sulfurtransferase	P25325
MRM1	rRNA methyltransferase 1, mitochondrial	Q6IN84
MRPL1	39S ribosomal protein L1, mitochondrial	Q9BYD6
MRPL10	39S ribosomal protein L10, mitochondrial	Q7Z7H8
MRPL11	39S ribosomal protein L11, mitochondrial	Q9Y3B7
MRPL13	39S ribosomal protein L13, mitochondrial	Q9BYD1
MRPL14	39S ribosomal protein L14, mitochondrial	Q6P1L8
MRPL15	39S ribosomal protein L15, mitochondrial	Q9P015
MRPL16	39S ribosomal protein L16, mitochondrial	Q9NX20
MRPL17	39S ribosomal protein L17, mitochondrial	Q9NRX2
MRPL19	39S ribosomal protein L19, mitochondrial	P49406
MRPL2	39S ribosomal protein L2, mitochondrial	Q5T653
MRPL20	39S ribosomal protein L20, mitochondrial	Q9BYC9
MRPL21	39S ribosomal protein L21, mitochondrial	Q7Z2W9
MRPL22	39S ribosomal protein L22, mitochondrial	Q9NWU5
MRPL24	39S ribosomal protein L24, mitochondrial	Q96A35
MRPL28	39S ribosomal protein L28, mitochondrial	Q13084
MRPL30	39S ribosomal protein L30, mitochondrial	Q8TCC3
MRPL32	39S ribosomal protein L32, mitochondrial	Q9BYC8
MRPL38	39S ribosomal protein L38, mitochondrial	Q96DV4
MRPL39	39S ribosomal protein L39, mitochondrial	Q9NYK5

Gene	Protein name	Accession
MRPL4	39S ribosomal protein L4, mitochondrial	Q9BYD3
MRPL41	39S ribosomal protein L41, mitochondrial	Q8IXM3
MRPL43	39S ribosomal protein L43, mitochondrial	Q8N983
MRPL44	39S ribosomal protein L44, mitochondrial	Q9H9J2
MRPL45	39S ribosomal protein L45, mitochondrial	Q9BRJ2
MRPL46	39S ribosomal protein L46, mitochondrial	Q9H2W6
MRPL47	39S ribosomal protein L47, mitochondrial	Q9HD33
MRPL48	39S ribosomal protein L48, mitochondrial	Q96GC5
MRPL49	39S ribosomal protein L49, mitochondrial	Q13405
MRPL50	39S ribosomal protein L50, mitochondrial	Q8N5N7
MRPL53	39S ribosomal protein L53, mitochondrial	Q96EL3
MRPL9	39S ribosomal protein L9, mitochondrial	Q9BYD2
MRPS11	28S ribosomal protein S11, mitochondrial	P82912
MRPS12	28S ribosomal protein S12, mitochondrial	O15235
MRPS14	28S ribosomal protein S14, mitochondrial	O60783
MRPS15	28S ribosomal protein S15, mitochondrial	P82914
MRPS16	28S ribosomal protein S16, mitochondrial	Q9Y3D3
MRPS17	28S ribosomal protein S17, mitochondrial	Q9Y2R5
MRPS18B	28S ribosomal protein S18b, mitochondrial	Q9Y676
MRPS2	28S ribosomal protein S2, mitochondrial	Q9Y399
MRPS22	28S ribosomal protein S22, mitochondrial	P82650
MRPS23	28S ribosomal protein S23, mitochondrial	Q9Y3D9
MRPS24	28S ribosomal protein S24, mitochondrial	Q96EL2
MRPS26	28S ribosomal protein S26, mitochondrial	Q9BYN8
MRPS27	28S ribosomal protein S27, mitochondrial	Q92552
MRPS28	28S ribosomal protein S28, mitochondrial	Q9Y2Q9
MRPS30	28S ribosomal protein S30, mitochondrial	Q9NP92
MRPS31	28S ribosomal protein S31, mitochondrial	Q92665
MRPS33	28S ribosomal protein S33, mitochondrial	Q9Y291
MRPS34	28S ribosomal protein S34, mitochondrial	P82930
MRPS35	28S ribosomal protein S35, mitochondrial	P82673
MRPS5	28S ribosomal protein S5, mitochondrial	P82675
MRPS6	28S ribosomal protein S6, mitochondrial	P82932
MRPS7	28S ribosomal protein S7, mitochondrial	Q9Y2R9
MRPS9	28S ribosomal protein S9, mitochondrial	P82933
MRRF	Ribosome-recycling factor, mitochondrial	Q96E11
MRS2	Magnesium transporter MRS2 homolog, mitochondrial	Q9HD23
MSMO1	Methylsterol monooxygenase 1	Q15800
MSN	Moesin	P26038

Gene	Protein name	Accession
MTA2	Metastasis-associated protein MTA2	O94776
MTCH2	Mitochondrial carrier homolog 2	Q9Y6C9
MT-CO2	Cytochrome c oxidase subunit 2	P00403
MT-CYB	Cytochrome b	P00156
MTDH	Protein LYRIC	Q86UE4
MTERFD1	mTERF domain-containing protein 1, mitochondrial	Q96E29
MTERFD2	mTERF domain-containing protein 2	Q7Z6M4
MTFMT	Methionyl-tRNA formyltransferase, mitochondrial	Q96DP5
MTFP1	Mitochondrial fission process protein 1	Q9UDX5
MTFR1	Mitochondrial fission regulator 1	Q15390
MTFR2	Mitochondrial fission regulator 2	Q6P444
MTHFD1	C-1-tetrahydrofolate synthase, cytoplasmic	P11586
MTHFD1L	Monofunctional C1-tetrahydrofolate synthase, mitochondrial	Q6UB35
MTHFD2	Bifunctional methylenetetrahydrofolate dehydrogenase/cyclohydrolase, mitochondrial	P13995
MTIF2	Translation initiation factor IF-2, mitochondrial	P46199
MTIF3	Translation initiation factor IF-3, mitochondrial	Q9H2K0
MTMR3	Myotubularin-related protein 3	Q13615
MT-ND4	NADH-ubiquinone oxidoreductase chain 4	P03905
MT-ND5	NADH-ubiquinone oxidoreductase chain 5	P03915
MTPAP	Poly(A) RNA polymerase, mitochondrial	Q9NVV4
MTPN	Myotrophin	P58546
MTX1	Metaxin-1	Q13505
MTX2	Metaxin-2	O75431
MUL1	Mitochondrial ubiquitin ligase activator of NFKB 1	Q969V5
MUT	Methylmalonyl-CoA mutase, mitochondrial	P22033
MYBBP1A	Myb-binding protein 1A	Q9BQG0
MYH9	Myosin-9	P35579
MYL6	Myosin light polypeptide 6	P60660
MYO18A	Unconventional myosin-XVIIIa	Q92614
MYO1B	Unconventional myosin-Ib	O43795
MZB1	Marginal zone B- and B1-cell-specific protein	Q8WU39
NAA50	N-alpha-acetyltransferase 50	Q9GZZ1
NACA	Nascent polypeptide-associated complex subunit alpha	Q13765
NADK2	NAD kinase 2, mitochondrial	Q4G0N4
NAPA	Alpha-soluble NSF attachment protein	P54920
NAPG	Gamma-soluble NSF attachment protein	Q99747
NARS2	Probable asparagine--tRNA ligase, mitochondrial	Q96159
NAT10	N-acetyltransferase 10	Q9H0A0

Gene	Protein name	Accession
NBAS	Neuroblastoma-amplified sequence	A2RRP1
NCAPG	Condensin complex subunit 3	Q9BPX3
NCKAP1L	Nck-associated protein 1-like	P55160
NCL	Nucleolin	P19338
NCLN	Nicalin	Q969V3
NCSTN	Nicastrin	Q92542
NDFIP1	NEDD4 family-interacting protein 1	Q9BT67
NDUFA11	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 11	Q86Y39
NDUFA12	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 12	Q9UI09
NDUFA13	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13	Q9P0J0
NDUFA6	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 6	P56556
NDUFA7	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 7	O95182
NDUFAF1	Complex I intermediate-associated protein 30, mitochondrial	Q9Y375
NDUFAF2	Mimitin, mitochondrial	Q8N183
NDUFAF3	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 3	Q9BU61
NDUFAF4	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 4	Q9P032
NDUFAF5	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 5	Q5TEU4
NDUFAF6	NADH dehydrogenase	Q330K2
NDUFB10	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 10	O96000
NDUFB3	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 3	O43676
NDUFB4	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 4	O95168
NDUFB9	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 9	Q9Y6M9
NDUFS1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	P28331
NDUFS2	NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial	O75306
NDUFS3	NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial	O75489
NDUFS6	NADH dehydrogenase [ubiquinone] iron-sulfur protein 6, mitochondrial	O75380
NDUFS8	NADH dehydrogenase [ubiquinone] iron-sulfur protein 8, mitochondrial	O00217
NDUFV1	NADH dehydrogenase [ubiquinone] flavoprotein 1, mitochondrial	P49821
NEDD1	Protein NEDD1	Q8NHV4
NENF	Neudesin	Q9UMX5
NFS1	Cysteine desulfurase, mitochondrial	Q9Y697
NFU1	NFU1 iron-sulfur cluster scaffold homolog, mitochondrial	Q9UMS0
NFXL1	NF-X1-type zinc finger protein NFXL1	Q6ZNB6
NIN	Ninein	Q8N4C6
NIPSNAP1	Protein NipSnap homolog 1	Q9BPW8
NIPSNAP3A	Protein NipSnap homolog 3A	Q9UFN0
NISCH	Nischarin	Q9Y2I1
NIT1	Nitrilase homolog 1	Q86X76
NLN	Neurolysin, mitochondrial	Q9BYT8

Gene	Protein name	Accession
NLRX1	NLR family member X1	Q86UT6
NNT	NAD(P) transhydrogenase, mitochondrial	Q13423
NOA1	Nitric oxide-associated protein 1	Q8NC60
NOC2L	Nucleolar complex protein 2 homolog	Q9Y3T9
NOL6	Nucleolar protein 6	Q9H6R4
NOMO2	Nodal modulator 2	Q5JPE7
NONO	Non-POU domain-containing octamer-binding protein	Q15233
NOP2	Putative ribosomal RNA methyltransferase NOP2	P46087
NOP56	Nucleolar protein 56	O00567
NOP58	Nucleolar protein 58	Q9Y2X3
NPC1	Niemann-Pick C1 protein	O15118
NPEPPS	Puromycin-sensitive aminopeptidase	P55786
NPM1	Nucleophosmin	P06748
NPTN	Neuroplastin	Q9Y639
NRAS	GTPase NRas	P01111
NSDHL	Sterol-4-alpha-carboxylate 3-dehydrogenase, decarboxylating	Q15738
NSUN2	tRNA	Q08J23
NSUN4	5-methylcytosine rRNA methyltransferase NSUN4	Q96CB9
NT5DC2	5'-nucleotidase domain-containing protein 2	Q9H857
NUBPL	Iron-sulfur protein NUBPL	Q8TB37
NUCB2	Nucleobindin-2	P80303
NUDC	Nuclear migration protein nudC	Q9Y266
NUDT1	7,8-dihydro-8-oxoguanine triphosphatase	P36639
NUDT21	Cleavage and polyadenylation specificity factor subunit 5	O43809
NUDT5	ADP-sugar pyrophosphatase	Q9UKK9
NUDT8	Nucleoside diphosphate-linked moiety X motif 8, mitochondrial	Q8WV74
NUMA1	Nuclear mitotic apparatus protein 1	Q14980
NUP107	Nuclear pore complex protein Nup107	P57740
NUP133	Nuclear pore complex protein Nup133	Q8WUM0
NUP155	Nuclear pore complex protein Nup155	O75694
NUP160	Nuclear pore complex protein Nup160	Q12769
NUP188	Nucleoporin NUP188 homolog	Q5SRE5
NUP205	Nuclear pore complex protein Nup205	Q92621
NUP210	Nuclear pore membrane glycoprotein 210	Q8TEM1
NUP214	Nuclear pore complex protein Nup214	P35658
NUP35	Nucleoporin NUP53	Q8NFB5
NUP43	Nucleoporin Nup43	Q8NFB3
NUP62	Nuclear pore glycoprotein p62	P37198
NUP88	Nuclear pore complex protein Nup88	Q99567

Gene	Protein name	Accession
NUP93	Nuclear pore complex protein Nup93	Q8N1F7
NUP98	Nuclear pore complex protein Nup98-Nup96	P52948
OAT	Ornithine aminotransferase, mitochondrial	P04181
OCIAD1	OCIA domain-containing protein 1	Q9NX40
OCIAD2	OCIA domain-containing protein 2	Q56VL3
ODF2	Outer dense fiber protein 2	Q5BJF6
OGDH	2-oxoglutarate dehydrogenase, mitochondrial	Q02218
OMA1	Metalloendopeptidase OMA1, mitochondrial	Q96E52
ORMDL1	ORM1-like protein 1	Q9P0S3
ORMDL3	ORM1-like protein 3	Q8N138
OSBP	Oxysterol-binding protein 1	P22059
OSBPL11	Oxysterol-binding protein-related protein 11	Q9BXB4
OSBPL8	Oxysterol-binding protein-related protein 8	Q9BZF1
OSBPL9	Oxysterol-binding protein-related protein 9	Q96SU4
OSGEPL1	Probable tRNA N6-adenosine threonylcarbamoyltransferase, mitochondrial	Q9H4B0
OXCT1	Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial	P55809
OXNAD1	Oxidoreductase NAD-binding domain-containing protein 1	Q96HP4
OXSM	3-oxoacyl-[acyl-carrier-protein] synthase, mitochondrial	Q9NWU1
OXSR1	Serine/threonine-protein kinase OSR1	O95747
P4HB	Protein disulfide-isomerase	P07237
PABPC1	Polyadenylate-binding protein 1	P11940
PAFAH1B1	Platelet-activating factor acetylhydrolase IB subunit alpha	P43034
PAFAH1B3	Platelet-activating factor acetylhydrolase IB subunit gamma	Q15102
PAICS	Multifunctional protein ADE2	P22234
PAM16	Mitochondrial import inner membrane translocase subunit TIM16	Q9Y3D7
PARK7	Protein DJ-1	Q99497
PARL	Presenilins-associated rhomboid-like protein, mitochondrial	Q9H300
PARP1	Poly [ADP-ribose] polymerase 1	P09874
PBXIP1	Pre-B-cell leukemia transcription factor-interacting protein 1	Q96AQ6
PC	Pyruvate carboxylase, mitochondrial	P11498
PCBP2	Poly(rC)-binding protein 2	Q15366
PCCA	Propionyl-CoA carboxylase alpha chain, mitochondrial	P05165
PCCB	Propionyl-CoA carboxylase beta chain, mitochondrial	P05166
PCM1	Pericentriolar material 1 protein	Q15154
PCNT	Pericentrin	O95613
PDCD10	Programmed cell death protein 10	Q9BUL8
PDCD11	Protein RRP5 homolog	Q14690
PDCD6IP	Programmed cell death 6-interacting protein	Q8WUM4
PDE12	2',5'-phosphodiesterase 12	Q6L8Q7

Gene	Protein name	Accession
PDHA1	Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial	P08559
PDHB	Pyruvate dehydrogenase E1 component subunit beta, mitochondrial	P11177
PDHX	Pyruvate dehydrogenase protein X component, mitochondrial	O00330
PDIA3	Protein disulfide-isomerase A3	P30101
PDIA4	Protein disulfide-isomerase A4	P13667
PDIA6	Protein disulfide-isomerase A6	Q15084
PDK1	[Pyruvate dehydrogenase	Q15118
PDK3	[Pyruvate dehydrogenase	Q15120
PDP1	[Pyruvate dehydrogenase [acetyl-transferring]]-phosphatase 1, mitochondrial	Q9P0J1
PDPR	Pyruvate dehydrogenase phosphatase regulatory subunit, mitochondrial	Q8NCN5
PDS5A	Sister chromatid cohesion protein PDS5 homolog A	Q29RF7
PDS5B	Sister chromatid cohesion protein PDS5 homolog B	Q9NTI5
PDSS1	Decaprenyl-diphosphate synthase subunit 1	Q5T2R2
PECAM1	Platelet endothelial cell adhesion molecule	P16284
PECR	Peroxisomal trans-2-enoyl-CoA reductase	Q9BY49
PEX11B	Peroxisomal membrane protein 11B	O96011
PEX14	Peroxisomal membrane protein PEX14	O75381
PEX16	Peroxisomal membrane protein PEX16	Q9Y5Y5
PFN1	Profilin-1	P07737
PGAM1	Phosphoglycerate mutase 1	P18669
PGAM5	Serine/threonine-protein phosphatase PGAM5, mitochondrial	Q96HS1
PGK1	Phosphoglycerate kinase 1	P00558
PGRMC1	Membrane-associated progesterone receptor component 1	O00264
PGRMC2	Membrane-associated progesterone receptor component 2	O15173
PHB	Prohibitin	P35232
PHB2	Prohibitin-2	Q99623
PHGDH	D-3-phosphoglycerate dehydrogenase	O43175
PHIP	PH-interacting protein	Q8WWQ0
PI4K2A	Phosphatidylinositol 4-kinase type 2-alpha	Q9BTU6
PIEZO1	Piezo-type mechanosensitive ion channel component 1	Q92508
PIGO	GPI ethanolamine phosphate transferase 3	Q8TEQ8
PIGR	Polymeric immunoglobulin receptor	P01833
PIGU	Phosphatidylinositol glycan anchor biosynthesis class U protein	Q9H490
PIK3R4	Phosphoinositide 3-kinase regulatory subunit 4	Q99570
PIP4K2A	Phosphatidylinositol 5-phosphate 4-kinase type-2 alpha	P48426
PITRM1	Presequence protease, mitochondrial	Q5JRX3
PKM	Pyruvate kinase PKM	P14618
PKN1	Serine/threonine-protein kinase N1	Q16512

Gene	Protein name	Accession
PKP1	Plakophilin-1	Q13835
PLAA	Phospholipase A-2-activating protein	Q9Y263
PLD6	Mitochondrial cardiolipin hydrolase	Q8N2A8
PLEC	Plectin	Q15149
PLGRKT	Plasminogen receptor	Q9HBL7
PLOD1	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1	Q02809
PML	Protein PML	P29590
PMPCA	Mitochondrial-processing peptidase subunit alpha	Q10713
PMPCB	Mitochondrial-processing peptidase subunit beta	O75439
PMVK	Phosphomevalonate kinase	Q15126
PNO1	RNA-binding protein PNO1	Q9NRX1
PNPLA6	Neuropathy target esterase	Q8IY17
PNPO	Pyridoxine-5'-phosphate oxidase	Q9NVS9
PNPT1	Polyribonucleotide nucleotidyltransferase 1, mitochondrial	Q8TCS8
POC5	Centrosomal protein POC5	Q8NA72
POF1B	Protein POF1B	Q8WVV4
POGLUT1	Protein O-glucosyltransferase 1	Q8NBL1
POLDIP2	Polymerase delta-interacting protein 2	Q9Y2S7
POLDIP3	Polymerase delta-interacting protein 3	Q9BY77
POLG2	DNA polymerase subunit gamma-2, mitochondrial	Q9UHN1
POLR2A	DNA-directed RNA polymerase II subunit RPB1	P24928
POLR2B	DNA-directed RNA polymerase II subunit RPB2	P30876
POLRMT	DNA-directed RNA polymerase, mitochondrial	O00411
POM121	Nuclear envelope pore membrane protein POM 121	Q96HA1
POM121C	Nuclear envelope pore membrane protein POM 121C	A8CG34
POR	NADPH--cytochrome P450 reductase	P16435
PPA2	Inorganic pyrophosphatase 2, mitochondrial	Q9H2U2
PPFIA1	Liprin-alpha-1	Q13136
PPIA	Peptidyl-prolyl cis-trans isomerase A	P62937
PPIB	Peptidyl-prolyl cis-trans isomerase B	P23284
PPIF	Peptidyl-prolyl cis-trans isomerase F, mitochondrial	P30405
PPIH	Peptidyl-prolyl cis-trans isomerase H	O43447
PPOX	Protoporphyrinogen oxidase	P50336
PPP1CA	Serine/threonine-protein phosphatase PP1-alpha catalytic subunit	P62136
PPP2R2A	Serine/threonine-protein phosphatase 2A 55 kDa regulatory subunit B alpha isoform	P63151
PRAF2	PRA1 family protein 2	O60831
PRDX1	Peroxiredoxin-1	Q06830
PRDX2	Peroxiredoxin-2	P32119

Gene	Protein name	Accession
PRDX3	Thioredoxin-dependent peroxide reductase, mitochondrial	P30048
PRDX4	Peroxiredoxin-4	Q13162
PRDX6	Peroxiredoxin-6	P30041
PREB	Prolactin regulatory element-binding protein	Q9HCU5
PRKAG1	5'-AMP-activated protein kinase subunit gamma-1	P54619
PRKARIA	cAMP-dependent protein kinase type I-alpha regulatory subunit	P10644
PRKCH	Protein kinase C eta type	P24723
PRKCQ	Protein kinase C theta type	Q04759
PRKCSH	Glucosidase 2 subunit beta	P14314
PRKDC	DNA-dependent protein kinase catalytic subunit	P78527
PROSC	Proline synthase co-transcribed bacterial homolog protein	O94903
PRPF6	Pre-mRNA-processing factor 6	O94906
PRPF8	Pre-mRNA-processing-splicing factor 8	Q6P2Q9
PSAP	Prosaposin	P07602
PSEN1	Presenilin-1	P49768
PSIP1	PC4 and SFRS1-interacting protein	O75475
PSMA1	Proteasome subunit alpha type-1	P25786
PSMA3	Proteasome subunit alpha type-3	P25788
PSMA5	Proteasome subunit alpha type-5	P28066
PSMA6	Proteasome subunit alpha type-6	P60900
PSMB1	Proteasome subunit beta type-1	P20618
PSMB4	Proteasome subunit beta type-4	P28070
PSMC2	26S protease regulatory subunit 7	P35998
PSMC4	26S protease regulatory subunit 6B	P43686
PSMC5	26S protease regulatory subunit 8	P62195
PSMD11	26S proteasome non-ATPase regulatory subunit 11	O00231
PSMD3	26S proteasome non-ATPase regulatory subunit 3	O43242
PSMD7	26S proteasome non-ATPase regulatory subunit 7	P51665
PSME1	Proteasome activator complex subunit 1	Q06323
PSME2	Proteasome activator complex subunit 2	Q9UL46
PTBP1	Polypyrimidine tract-binding protein 1	P26599
PTCD3	Pentatricopeptide repeat domain-containing protein 3, mitochondrial	Q96EY7
PTDSS1	Phosphatidylserine synthase 1	P48651
PTGES2	Prostaglandin E synthase 2	Q9H7Z7
PTK7	Inactive tyrosine-protein kinase 7	Q13308
PTPLAD1	Very-long-chain (3R)-3-hydroxyacyl-CoA dehydratase 3	Q9P035
PTPLB	Very-long-chain (3R)-3-hydroxyacyl-CoA dehydratase 2	Q6Y1H2
PTPMT1	Phosphatidylglycerophosphatase and protein-tyrosine phosphatase 1	Q8WUK0
PTPN1	Tyrosine-protein phosphatase non-receptor type 1	P18031

Gene	Protein name	Accession
PTPN11	Tyrosine-protein phosphatase non-receptor type 11	Q06124
PTPRC	Receptor-type tyrosine-protein phosphatase C	P08575
PTPRCAP	Protein tyrosine phosphatase receptor type C-associated protein	Q14761
PTPRK	Receptor-type tyrosine-protein phosphatase kappa	Q15262
PTPRS	Receptor-type tyrosine-protein phosphatase S	Q13332
PTRH1	Probable peptidyl-tRNA hydrolase	Q86Y79
PTRH2	Peptidyl-tRNA hydrolase 2, mitochondrial	Q9Y3E5
PTRHD1	Putative peptidyl-tRNA hydrolase PTRHD1	Q6GMV3
PUS1	tRNA pseudouridine synthase A, mitochondrial	Q9Y606
PUSL1	tRNA pseudouridine synthase-like 1	Q8N0Z8
PWP2	Periodic tryptophan protein 2 homolog	Q15269
PXMP2	Peroxisomal membrane protein 2	Q9NR77
PYCR1	Pyrroline-5-carboxylate reductase 1, mitochondrial	P32322
PYCR2	Pyrroline-5-carboxylate reductase 2	Q96C36
QARS	Glutamine--tRNA ligase	P47897
QPCTL	Glutaminyl-peptide cyclotransferase-like protein	Q9NXS2
QSOX2	Sulfhydryl oxidase 2	Q6ZRP7
QTRTD1	Queuine tRNA-ribosyltransferase subunit QTRTD1	Q9H974
RAB10	Ras-related protein Rab-10	P61026
RAB11B	Ras-related protein Rab-11B	Q15907
RAB14	Ras-related protein Rab-14	P61106
RAB18	Ras-related protein Rab-18	Q9NP72
RAB1A	Ras-related protein Rab-1A	P62820
RAB1B	Ras-related protein Rab-1B	Q9H0U4
RAB21	Ras-related protein Rab-21	Q9UL25
RAB22A	Ras-related protein Rab-22A	Q9UL26
RAB24	Ras-related protein Rab-24	Q969Q5
RAB27A	Ras-related protein Rab-27A	P51159
RAB2A	Ras-related protein Rab-2A	P61019
RAB2B	Ras-related protein Rab-2B	Q8WUD1
RAB33B	Ras-related protein Rab-33B	Q9H082
RAB35	Ras-related protein Rab-35	Q15286
RAB37	Ras-related protein Rab-37	Q96AX2
RAB39B	Ras-related protein Rab-39B	Q96DA2
RAB3D	Ras-related protein Rab-3D	O95716
RAB43	Ras-related protein Rab-43	Q86YS6
RAB44	Ras-related protein Rab-44	Q7Z6P3
RAB4B	Ras-related protein Rab-4B	P61018
RAB5A	Ras-related protein Rab-5A	P20339

Gene	Protein name	Accession
RAB5B	Ras-related protein Rab-5B	P61020
RAB5C	Ras-related protein Rab-5C	P51148
RAB6A	Ras-related protein Rab-6A	P20340
RAB7A	Ras-related protein Rab-7a	P51149
RAB7L1	Ras-related protein Rab-7L1	O14966
RAB8A	Ras-related protein Rab-8A	P61006
RAB8B	Ras-related protein Rab-8B	Q92930
RAB9A	Ras-related protein Rab-9A	P51151
RABAC1	Prenylated Rab acceptor protein 1	Q9UI14
RAC2	Ras-related C3 botulinum toxin substrate 2	P15153
RACGAP1	Rac GTPase-activating protein 1	Q9H0H5
RALA	Ras-related protein Ral-A	P11233
RALY	RNA-binding protein Raly	Q9UKM9
RAN	GTP-binding nuclear protein Ran	P62826
RANBP1	Ran-specific GTPase-activating protein	P43487
RANBP2	E3 SUMO-protein ligase RanBP2	P49792
RANGAP1	Ran GTPase-activating protein 1	P46060
RAP1B	Ras-related protein Rap-1b	P61224
RAP2A	Ras-related protein Rap-2a	P10114
RAP2B	Ras-related protein Rap-2b	P61225
RARS	Arginine--tRNA ligase, cytoplasmic	P54136
RARS2	Probable arginine--tRNA ligase, mitochondrial	Q5T160
RASA3	Ras GTPase-activating protein 3	Q14644
RASAL3	RAS protein activator like-3	Q86YV0
RB1	Retinoblastoma-associated protein	P06400
RBBP4	Histone-binding protein RBBP4	Q09028
RBM25	RNA-binding protein 25	P49756
RBM34	RNA-binding protein 34	P42696
RBMX	RNA-binding motif protein, X chromosome	P38159
RCL1	RNA 3'-terminal phosphate cyclase-like protein	Q9Y2P8
RCN1	Reticulocalbin-1	Q15293
RCN2	Reticulocalbin-2	Q14257
RDH11	Retinol dehydrogenase 11	Q8TC12
RDH13	Retinol dehydrogenase 13	Q8NBN7
RDH14	Retinol dehydrogenase 14	Q9HBH5
REEP5	Receptor expression-enhancing protein 5	Q00765
REEP6	Receptor expression-enhancing protein 6	Q96HR9
REPS1	RalBP1-associated Eps domain-containing protein 1	Q96D71
RER1	Protein RER1	O15258

Gene	Protein name	Accession
REXO2	Oligoribonuclease, mitochondrial	Q9Y3B8
RFC2	Replication factor C subunit 2	P35250
RFC3	Replication factor C subunit 3	P40938
RFC4	Replication factor C subunit 4	P35249
RFK	Riboflavin kinase	Q969G6
RFT1	Protein RFT1 homolog	Q96AA3
RHBDD2	Rhomboid domain-containing protein 2	Q6NTF9
RHOA	Transforming protein RhoA	P61586
RHOG	Rho-related GTP-binding protein RhoG	P84095
RHOT2	Mitochondrial Rho GTPase 2	Q8IX11
RMDN1	Regulator of microtubule dynamics protein 1	Q96DB5
RMND1	Required for meiotic nuclear division protein 1 homolog	Q9NWS8
RNF130	E3 ubiquitin-protein ligase RNF130	Q86XS8
RNF213	E3 ubiquitin-protein ligase RNF213	Q63HN8
RNH1	Ribonuclease inhibitor	P13489
RNMTL1	RNA methyltransferase-like protein 1	Q9HC36
RP2	Protein XRP2	O75695
RPA2	Replication protein A 32 kDa subunit	P15927
RPF2	Ribosome production factor 2 homolog	Q9H7B2
RPIA	Ribose-5-phosphate isomerase	P49247
RPL10	60S ribosomal protein L10	P27635
RPL10A	60S ribosomal protein L10a	P62906
RPL11	60S ribosomal protein L11	P62913
RPL12	60S ribosomal protein L12	P30050
RPL13	60S ribosomal protein L13	P26373
RPL13A	60S ribosomal protein L13a	P40429
RPL14	60S ribosomal protein L14	P50914
RPL15	60S ribosomal protein L15	P61313
RPL17	60S ribosomal protein L17	P18621
RPL18	60S ribosomal protein L18	Q07020
RPL19	60S ribosomal protein L19	P84098
RPL23	60S ribosomal protein L23	P62829
RPL23A	60S ribosomal protein L23a	P62750
RPL26	60S ribosomal protein L26	P61254
RPL26L1	60S ribosomal protein L26-like 1	Q9UNX3
RPL28	60S ribosomal protein L28	P46779
RPL31	60S ribosomal protein L31	P62899
RPL34	60S ribosomal protein L34	P49207
RPL35A	60S ribosomal protein L35a	P18077

Gene	Protein name	Accession
RPL4	60S ribosomal protein L4	P36578
RPL6	60S ribosomal protein L6	Q02878
RPL7	60S ribosomal protein L7	P18124
RPL7A	60S ribosomal protein L7a	P62424
RPL8	60S ribosomal protein L8	P62917
RPL9	60S ribosomal protein L9	P32969
RPLP0	60S acidic ribosomal protein P0	P05388
RPLP2	60S acidic ribosomal protein P2	P05387
RPN1	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1	P04843
RPN2	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 2	P04844
RPRD1B	Regulation of nuclear pre-mRNA domain-containing protein 1B	Q9NQG5
RPS11	40S ribosomal protein S11	P62280
RPS13	40S ribosomal protein S13	P62277
RPS14	40S ribosomal protein S14	P62263
RPS15A	40S ribosomal protein S15a	P62244
RPS16	40S ribosomal protein S16	P62249
RPS17	40S ribosomal protein S17	P08708
RPS17L	40S ribosomal protein S17-like	P0CW22
RPS18	40S ribosomal protein S18	P62269
RPS19	40S ribosomal protein S19	P39019
RPS19BP1	Active regulator of SIRT1	Q86WX3
RPS2	40S ribosomal protein S2	P15880
RPS20	40S ribosomal protein S20	P60866
RPS23	40S ribosomal protein S23	P62266
RPS25	40S ribosomal protein S25	P62851
RPS27A	Ubiquitin-40S ribosomal protein S27a	P62979
RPS3	40S ribosomal protein S3	P23396
RPS3A	40S ribosomal protein S3a	P61247
RPS4X	40S ribosomal protein S4, X isoform	P62701
RPS5	40S ribosomal protein S5	P46782
RPS7	40S ribosomal protein S7	P62081
RPS8	40S ribosomal protein S8	P62241
RPS9	40S ribosomal protein S9	P46781
RPSA	40S ribosomal protein SA	P08865
RPUSD3	RNA pseudouridylylase synthase domain-containing protein 3	Q6P087
RQCD1	Cell differentiation protein RCD1 homolog	Q92600
RRAS2	Ras-related protein R-Ras2	P62070
RRP1	Ribosomal RNA processing protein 1 homolog A	P56182
RRP1B	Ribosomal RNA processing protein 1 homolog B	Q14684

Gene	Protein name	Accession
RSAD1	Radical S-adenosyl methionine domain-containing protein 1, mitochondrial	Q9HA92
RTCB	tRNA-splicing ligase RtcB homolog	Q9Y310
RTN3	Reticulon-3	O95197
RTN4	Reticulon-4	Q9NQC3
RTN4IP1	Reticulon-4-interacting protein 1, mitochondrial	Q8WVV3
RUFY1	RUN and FYVE domain-containing protein 1	Q96T51
RUVBL1	RuvB-like 1	Q9Y265
RUVBL2	RuvB-like 2	Q9Y230
S100A11	Protein S100-A11	P31949
SACM1L	Phosphatidylinositide phosphatase SAC1	Q9NTJ5
SAFB	Scaffold attachment factor B1	Q15424
SAR1A	GTP-binding protein SAR1a	Q9NR31
SARS2	Serine--tRNA ligase, mitochondrial	Q9NP81
SART1	U4/U6.U5 tri-snRNP-associated protein 1	O43290
SBF1	Myotubularin-related protein 5	O95248
SCAMP1	Secretory carrier-associated membrane protein 1	O15126
SCAMP2	Secretory carrier-associated membrane protein 2	O15127
SCAMP3	Secretory carrier-associated membrane protein 3	O14828
SCAMP4	Secretory carrier-associated membrane protein 4	Q969E2
SCCPDH	Saccharopine dehydrogenase-like oxidoreductase	Q8NBX0
SCD	Acyl-CoA desaturase	O00767
SCD5	Stearyl-CoA desaturase 5	Q86SK9
SCO1	Protein SCO1 homolog, mitochondrial	O75880
SCO2	Protein SCO2 homolog, mitochondrial	O43819
SCP2	Non-specific lipid-transfer protein	P22307
SCRIB	Protein scribble homolog	Q14160
SDF4	45 kDa calcium-binding protein	Q9BRK5
SDHA	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	P31040
SDHB	Succinate dehydrogenase [ubiquinone] iron-sulfur subunit, mitochondrial	P21912
SDR39U1	Epimerase family protein SDR39U1	Q9NRG7
SEC11A	Signal peptidase complex catalytic subunit SEC11A	P67812
SEC11C	Signal peptidase complex catalytic subunit SEC11C	Q9BY50
SEC22B	Vesicle-trafficking protein SEC22b	O75396
SEC24B	Protein transport protein Sec24B	O95487
SEC24C	Protein transport protein Sec24C	P53992
SEC61A1	Protein transport protein Sec61 subunit alpha isoform 1	P61619
SEC63	Translocation protein SEC63 homolog	Q9UGP8
SEL1L	Protein sel-1 homolog 1	Q9UBV2
SEP15	15 kDa selenoprotein	O60613

Gene	Protein name	Accession
SERBP1	Plasminogen activator inhibitor 1 RNA-binding protein	Q8NC51
SERINC1	Serine incorporator 1	Q9NRX5
SERINC5	Serine incorporator 5	Q86VE9
SERPINB3	Serpin B3	P29508
SERPINB5	Serpin B5	P36952
SF3A2	Splicing factor 3A subunit 2	Q15428
SF3B1	Splicing factor 3B subunit 1	O75533
SF3B3	Splicing factor 3B subunit 3	Q15393
SF3B6	Splicing factor 3B subunit 6	Q9Y3B4
SFN	14-3-3 protein sigma	P31947
SFPQ	Splicing factor, proline- and glutamine-rich	P23246
SFXN1	Sideroflexin-1	Q9H9B4
SFXN3	Sideroflexin-3	Q9BWM7
SFXN4	Sideroflexin-4	Q6P4A7
SGPP1	Sphingosine-1-phosphate phosphatase 1	Q9BX95
SH3KBP1	SH3 domain-containing kinase-binding protein 1	Q96B97
SIGMAR1	Sigma non-opioid intracellular receptor 1	Q99720
SIN3A	Paired amphipathic helix protein Sin3a	Q96ST3
SIPA1L1	Signal-induced proliferation-associated 1-like protein 1	O43166
SIRT3	NAD-dependent protein deacetylase sirtuin-3, mitochondrial	Q9NTG7
SIRT5	NAD-dependent protein deacetylase sirtuin-5, mitochondrial	Q9NXA8
SIT1	Signaling threshold-regulating transmembrane adapter 1	Q9Y3P8
SIX6	Homeobox protein SIX6	O95475
SKIV2L2	Superkiller viralicidic activity 2-like 2	P42285
SLAIN2	SLAIN motif-containing protein 2	Q9P270
SLC12A2	Solute carrier family 12 member 2	P55011
SLC12A7	Solute carrier family 12 member 7	Q9Y666
SLC16A1	Monocarboxylate transporter 1	P53985
SLC16A3	Monocarboxylate transporter 4	O15427
SLC16A7	Monocarboxylate transporter 2	O60669
SLC19A1	Folate transporter 1	P41440
SLC1A4	Neutral amino acid transporter A	P43007
SLC25A1	Tricarboxylate transport protein, mitochondrial	P53007
SLC25A11	Mitochondrial 2-oxoglutarate/malate carrier protein	Q02978
SLC25A12	Calcium-binding mitochondrial carrier protein Aralar1	O75746
SLC25A15	Mitochondrial ornithine transporter 1	Q9Y619
SLC25A19	Mitochondrial thiamine pyrophosphate carrier	Q9HC21
SLC25A20	Mitochondrial carnitine/acylcarnitine carrier protein	O43772
SLC25A22	Mitochondrial glutamate carrier 1	Q9H936

Gene	Protein name	Accession
SLC25A24	Calcium-binding mitochondrial carrier protein SCaMC-1	Q6NUK1
SLC25A29	Mitochondrial carnitine/acylcarnitine carrier protein CACL	Q8N8R3
SLC25A3	Phosphate carrier protein, mitochondrial	Q00325
SLC25A30	Kidney mitochondrial carrier protein 1	Q55VS4
SLC25A33	Solute carrier family 25 member 33	Q9BSK2
SLC25A4	ADP/ATP translocase 1	P12235
SLC25A40	Solute carrier family 25 member 40	Q8TBP6
SLC25A5	ADP/ATP translocase 2	P05141
SLC25A51	Solute carrier family 25 member 51	Q9HIU9
SLC25A6	ADP/ATP translocase 3	P12236
SLC29A1	Equilibrative nucleoside transporter 1	Q99808
SLC2A1	Solute carrier family 2, facilitated glucose transporter member 1	P11166
SLC30A5	Zinc transporter 5	Q8TAD4
SLC30A6	Zinc transporter 6	Q6NXT4
SLC35B1	Solute carrier family 35 member B1	P78383
SLC35B2	Adenosine 3'-phospho 5'-phosphosulfate transporter 1	Q8TB61
SLC35E1	Solute carrier family 35 member E1	Q96K37
SLC35E2B	Solute carrier family 35 member E2B	P0CK96
SLC35F2	Solute carrier family 35 member F2	Q8IXU6
SLC38A10	Putative sodium-coupled neutral amino acid transporter 10	Q9HBR0
SLC38A2	Sodium-coupled neutral amino acid transporter 2	Q96QD8
SLC39A14	Zinc transporter ZIP14	Q15043
SLC3A2	4F2 cell-surface antigen heavy chain	P08195
SLC7A1	High affinity cationic amino acid transporter 1	P30825
SLC7A5	Large neutral amino acids transporter small subunit 1	Q01650
SLC9A3R1	Na(+)/H(+) exchange regulatory cofactor NHE-RF1	O14745
SLIRP	SRA stem-loop-interacting RNA-binding protein, mitochondrial	Q9GZT3
SLIT1	Slit homolog 1 protein	O75093
SLMAP	Sarcolemmal membrane-associated protein	Q14BN4
SLTM	SAFB-like transcription modulator	Q9NWH9
SMARCA4	Transcription activator BRG1	P51532
SMARCA5	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A member 5	O60264
SMARCC1	SWI/SNF complex subunit SMARCC1	Q92922
SMC1A	Structural maintenance of chromosomes protein 1A	Q14683
SMC3	Structural maintenance of chromosomes protein 3	Q9UQE7
SMC4	Structural maintenance of chromosomes protein 4	Q9NTJ3
SNAP23	Synaptosomal-associated protein 23	O00161
SNAP29	Synaptosomal-associated protein 29	O95721

Gene	Protein name	Accession
SND1	Staphylococcal nuclease domain-containing protein 1	Q7KZF4
SNRNP200	U5 small nuclear ribonucleoprotein 200 kDa helicase	O75643
SNRPA1	U2 small nuclear ribonucleoprotein A'	P09661
SNRPD1	Small nuclear ribonucleoprotein Sm D1	P62314
SNRPD2	Small nuclear ribonucleoprotein Sm D2	P62316
SNRPN	Small nuclear ribonucleoprotein-associated protein N	P63162
SOAT1	Sterol O-acyltransferase 1	P35610
SOD1	Superoxide dismutase [Cu-Zn]	P00441
SOD2	Superoxide dismutase [Mn], mitochondrial	P04179
SON	Protein SON	P18583
SORL1	Sortilin-related receptor	Q92673
SPCS2	Signal peptidase complex subunit 2	Q15005
SPICE1	Spindle and centriole-associated protein 1	Q8N0Z3
SPINT2	Kunitz-type protease inhibitor 2	O43291
SPN	Leukosialin	P16150
SPNS1	Protein spinster homolog 1	Q9H2V7
SPPL2B	Signal peptide peptidase-like 2B	Q8TCT7
SPR	Sepiapterin reductase	P35270
SPRYD4	SPRY domain-containing protein 4	Q8WW59
SPTAN1	Spectrin alpha chain, non-erythrocytic 1	Q13813
SPTBN1	Spectrin beta chain, non-erythrocytic 1	Q01082
SPTBN2	Spectrin beta chain, non-erythrocytic 2	O15020
SPTLC1	Serine palmitoyltransferase 1	O15269
SQLE	Squalene monooxygenase	Q14534
SQRDL	Sulfide:quinone oxidoreductase, mitochondrial	Q9Y6N5
SRM	Spermidine synthase	P19623
SRP14	Signal recognition particle 14 kDa protein	P37108
SRP19	Signal recognition particle 19 kDa protein	P09132
SRP68	Signal recognition particle subunit SRP68	Q9UHB9
SRP72	Signal recognition particle subunit SRP72	O76094
SRPK1	SRSF protein kinase 1	Q96SB4
SRPR	Signal recognition particle receptor subunit alpha	P08240
SRPRB	Signal recognition particle receptor subunit beta	Q9Y5M8
SRSF1	Serine/arginine-rich splicing factor 1	Q07955
SRSF3	Serine/arginine-rich splicing factor 3	P84103
SRSF6	Serine/arginine-rich splicing factor 6	Q13247
SSBP1	Single-stranded DNA-binding protein, mitochondrial	Q04837
SSR1	Translocon-associated protein subunit alpha	P43307
SSR4	Translocon-associated protein subunit delta	P51571

Gene	Protein name	Accession
ST13P4	Putative protein FAM10A4	Q8IZP2
STARD3NL	MLN64 N-terminal domain homolog	O95772
STAT3	Signal transducer and activator of transcription 3	P40763
STIM1	Stromal interaction molecule 1	Q13586
STMN1	Stathmin	P16949
STOM	Erythrocyte band 7 integral membrane protein	P27105
STOML2	Stomatin-like protein 2, mitochondrial	Q9UJZ1
STRAP	Serine-threonine kinase receptor-associated protein	Q9Y3F4
STRN	Striatin	O43815
STRN3	Striatin-3	Q13033
STT3A	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT3A	P46977
STT3B	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT3B	Q8TCJ2
STX10	Syntaxin-10	O60499
STX12	Syntaxin-12	Q86Y82
STX16	Syntaxin-16	O14662
STX17	Syntaxin-17	P56962
STX18	Syntaxin-18	Q9P2W9
STX2	Syntaxin-2	P32856
STX3	Syntaxin-3	Q13277
STX4	Syntaxin-4	Q12846
STX5	Syntaxin-5	Q13190
STX6	Syntaxin-6	O43752
STX7	Syntaxin-7	O15400
STX8	Syntaxin-8	Q9UNK0
SUCLG1	Succinyl-CoA ligase [ADP/GDP-forming] subunit alpha, mitochondrial	P53597
SUCLG2	Succinyl-CoA ligase [GDP-forming] subunit beta, mitochondrial	Q96I99
SUGT1	Suppressor of G2 allele of SKP1 homolog	Q9Y2Z0
SUMO2	Small ubiquitin-related modifier 2	P61956
SUPT16H	FACT complex subunit SPT16	Q9Y5B9
SUPV3L1	ATP-dependent RNA helicase SUPV3L1, mitochondrial	Q8IYB8
SURF4	Surfeit locus protein 4	O15260
SV2A	Synaptic vesicle glycoprotein 2A	Q7L0J3
SVIP	Small VCP/p97-interacting protein	Q8NHG7
SYNE2	Nesprin-2	Q8WXH0
SYNGR2	Synaptogyrin-2	O43760
SYNJ2BP	Synaptojanin-2-binding protein	P57105
SYPL1	Synaptophysin-like protein 1	Q16563
TACC1	Transforming acidic coiled-coil-containing protein 1	O75410
TACO1	Translational activator of cytochrome c oxidase 1	Q9BSH4

Gene	Protein name	Accession
TALDO1	Transaldolase	P37837
TAP1	Antigen peptide transporter 1	Q03518
TAPT1	Transmembrane anterior posterior transformation protein 1 homolog	Q6NXT6
TARS	Threonine--tRNA ligase, cytoplasmic	P26639
TARS2	Threonine--tRNA ligase, mitochondrial	Q9BW92
TAX1BP1	Tax1-binding protein 1	Q86VP1
TBC1D15	TBC1 domain family member 15	Q8TC07
TBC1D20	TBC1 domain family member 20	Q96BZ9
TBC1D31	TBC1 domain family member 31	Q96DN5
TBCB	Tubulin-folding cofactor B	Q99426
TBL2	Transducin beta-like protein 2	Q9Y4P3
TBL3	Transducin beta-like protein 3	Q12788
TBRG4	Protein TBRG4	Q969Z0
TCOF1	Treacle protein	Q13428
TCP1	T-complex protein 1 subunit alpha	P17987
TDRKH	Tudor and KH domain-containing protein	Q9Y2W6
TECR	Very-long-chain enoyl-CoA reductase	Q9NZ01
TEFM	Transcription elongation factor, mitochondrial	Q96QE5
TFAM	Transcription factor A, mitochondrial	Q00059
TFB1M	Dimethyladenosine transferase 1, mitochondrial	Q8WVM0
TFB2M	Dimethyladenosine transferase 2, mitochondrial	Q9H5Q4
TFRC	Transferrin receptor protein 1	P02786
TGOLN2	Trans-Golgi network integral membrane protein 2	O43493
THNSL1	Threonine synthase-like 1	Q8IYQ7
THOC1	THO complex subunit 1	Q96FV9
THYN1	Thymocyte nuclear protein 1	Q9P016
TIMM10B	Mitochondrial import inner membrane translocase subunit Tim10 B	Q9Y5J6
TIMM17B	Mitochondrial import inner membrane translocase subunit Tim17-B	O60830
TIMM21	Mitochondrial import inner membrane translocase subunit Tim21	Q9BVV7
TIMM23	Mitochondrial import inner membrane translocase subunit Tim23	O14925
TIMM44	Mitochondrial import inner membrane translocase subunit TIM44	O43615
TIMM50	Mitochondrial import inner membrane translocase subunit TIM50	Q3ZCQ8
TIMMDC1	Complex I assembly factor TIMMDC1, mitochondrial	Q9NPL8
TLN1	Talin-1	Q9Y490
TM7SF3	Transmembrane 7 superfamily member 3	Q9NS93
TM9SF2	Transmembrane 9 superfamily member 2	Q99805
TM9SF3	Transmembrane 9 superfamily member 3	Q9HD45
TM9SF4	Transmembrane 9 superfamily member 4	Q92544
TMCO1	Transmembrane and coiled-coil domain-containing protein 1	Q9UM00

Gene	Protein name	Accession
TMED10	Transmembrane emp24 domain-containing protein 10	P49755
TMED2	Transmembrane emp24 domain-containing protein 2	Q15363
TMED4	Transmembrane emp24 domain-containing protein 4	Q7Z7H5
TMED7	Transmembrane emp24 domain-containing protein 7	Q9Y3B3
TMED9	Transmembrane emp24 domain-containing protein 9	Q9BVK6
TMEM109	Transmembrane protein 109	Q9BVC6
TMEM115	Transmembrane protein 115	Q12893
TMEM126A	Transmembrane protein 126A	Q9H061
TMEM126B	Complex I assembly factor TMEM126B, mitochondrial	Q8IUX1
TMEM160	Transmembrane protein 160	Q9NX00
TMEM165	Transmembrane protein 165	Q9HC07
TMEM173	Stimulator of interferon genes protein	Q86WV6
TMEM199	Transmembrane protein 199	Q8N511
TMEM205	Transmembrane protein 205	Q6UW68
TMEM206	Transmembrane protein 206	Q9H813
TMEM230	Transmembrane protein 230	Q96A57
TMEM245	Transmembrane protein 245	Q9H330
TMEM261	Transmembrane protein 261	Q96GE9
TMEM30A	Cell cycle control protein 50A	Q9NV96
TMEM33	Transmembrane protein 33	P57088
TMEM43	Transmembrane protein 43	Q9BTV4
TMEM59	Transmembrane protein 59	Q9BXS4
TMEM65	Transmembrane protein 65	Q6PI78
TMEM70	Transmembrane protein 70, mitochondrial	Q9BUB7
TMF1	TATA element modulatory factor	P82094
TMLHE	Trimethyllysine dioxygenase, mitochondrial	Q9NVH6
TMPO	Lamina-associated polypeptide 2, isoforms beta/gamma	P42166
TMUB1	Transmembrane and ubiquitin-like domain-containing protein 1	Q9BVT8
TMUB2	Transmembrane and ubiquitin-like domain-containing protein 2	Q71RG4
TMX1	Thioredoxin-related transmembrane protein 1	Q9H3N1
TMX2	Thioredoxin-related transmembrane protein 2	Q9Y320
TMX3	Protein disulfide-isomerase TMX3	Q96JJ7
TMX4	Thioredoxin-related transmembrane protein 4	Q9H1E5
TNPO1	Transportin-1	Q92973
TOMM20	Mitochondrial import receptor subunit TOM20 homolog	Q15388
TOMM22	Mitochondrial import receptor subunit TOM22 homolog	Q9NS69
TOMM40	Mitochondrial import receptor subunit TOM40 homolog	O96008
TOMM40L	Mitochondrial import receptor subunit TOM40B	Q969M1
TOMM70A	Mitochondrial import receptor subunit TOM70	O94826

Gene	Protein name	Accession
TOP2A	DNA topoisomerase 2-alpha	P11388
TOP2B	DNA topoisomerase 2-beta	Q02880
TOR1A	Torsin-1A	O14656
TOR1B	Torsin-1B	O14657
TPD52	Tumor protein D52	P55327
TPGS1	Tubulin polyglutamylase complex subunit 1	Q6ZTW0
TPI1	Triosephosphate isomerase	P60174
TPM3	Tropomyosin alpha-3 chain	P06753
TPM4	Tropomyosin alpha-4 chain	P67936
TPR	Nucleoprotein TPR	P12270
TRAF3IP3	TRAF3-interacting JNK-activating modulator	Q9Y228
TRAPPC1	Trafficking protein particle complex subunit 1	Q9Y5R8
TRAPPC3	Trafficking protein particle complex subunit 3	O43617
TRAPPC5	Trafficking protein particle complex subunit 5	Q8IURO
TREX2	Three prime repair exonuclease 2	Q9BQ50
TRIM23	E3 ubiquitin-protein ligase TRIM23	P36406
TRIM28	Transcription intermediary factor 1-beta	Q13263
TRIP11	Thyroid receptor-interacting protein 11	Q15643
TRIP13	Pachytene checkpoint protein 2 homolog	Q15645
TRMT10C	Mitochondrial ribonuclease P protein 1	Q7L0Y3
TRMT5	tRNA	Q32P41
TRMT61B	tRNA	Q9BVS5
TRMU	Mitochondrial tRNA-specific 2-thiouridylase 1	O75648
TRNT1	CCA tRNA nucleotidyltransferase 1, mitochondrial	Q96Q11
TRPV2	Transient receptor potential cation channel subfamily V member 2	Q9Y5S1
TRUB1	Probable tRNA pseudouridine synthase 1	Q8WWH5
TRUB2	Probable tRNA pseudouridine synthase 2	O95900
TTFM	Elongation factor Ts, mitochondrial	P43897
TSG101	Tumor susceptibility gene 101 protein	Q99816
TSN	Translin	Q15631
TST	Thiosulfate sulfurtransferase	Q16762
TUBA1A	Tubulin alpha-1A chain	Q71U36
TUBA1B	Tubulin alpha-1B chain	P68363
TUBA1C	Tubulin alpha-1C chain	Q9BQE3
TUBB	Tubulin beta chain	P07437
TUBG1	Tubulin gamma-1 chain	P23258
TUBGCP2	Gamma-tubulin complex component 2	Q9BSJ2
TUBGCP3	Gamma-tubulin complex component 3	Q96CW5
TUBGCP6	Gamma-tubulin complex component 6	Q96R17

Gene	Protein name	Accession
TUFM	Elongation factor Tu, mitochondrial	P49411
TUSC3	Tumor suppressor candidate 3	Q13454
TXN	Thioredoxin	P10599
TXN2	Thioredoxin, mitochondrial	Q99757
TXNDC5	Thioredoxin domain-containing protein 5	Q8NBS9
TYMP	Thymidine phosphorylase	P19971
TYMS	Thymidylate synthase	P04818
UBA1	Ubiquitin-like modifier-activating enzyme 1	P22314
UBA6	Ubiquitin-like modifier-activating enzyme 6	A0AVT1
UBAC2	Ubiquitin-associated domain-containing protein 2	Q8NBM4
UBAP2L	Ubiquitin-associated protein 2-like	Q14157
UBB	Polyubiquitin-B	P0CG47
UBC	Polyubiquitin-C	P0CG48
UBE2J1	Ubiquitin-conjugating enzyme E2 J1	Q9Y385
UBE2J2	Ubiquitin-conjugating enzyme E2 J2	Q8N2K1
UBE2K	Ubiquitin-conjugating enzyme E2 K	P61086
UBE2M	NEDD8-conjugating enzyme Ubc12	P61081
UBE2N	Ubiquitin-conjugating enzyme E2 N	P61088
UBE4A	Ubiquitin conjugation factor E4 A	Q14139
UBR4	E3 ubiquitin-protein ligase UBR4	Q5T4S7
UBTF	Nucleolar transcription factor 1	P17480
UBXN4	UBX domain-containing protein 4	Q92575
UCHL5	Ubiquitin carboxyl-terminal hydrolase isozyme L5	Q9Y5K5
UCK2	Uridine-cytidine kinase 2	Q9BZX2
UFL1	E3 UFM1-protein ligase 1	O94874
UFSP2	Ufm1-specific protease 2	Q9NUQ7
UGGT1	UDP-glucose:glycoprotein glucosyltransferase 1	Q9NYU2
UMPS	Uridine 5'-monophosphate synthase	P11172
UNG	Uracil-DNA glycosylase	P13051
UPF1	Regulator of nonsense transcripts 1	Q92900
UQCC1	Ubiquinol-cytochrome-c reductase complex assembly factor 1	Q9NVA1
UQCC2	Ubiquinol-cytochrome-c reductase complex assembly factor 2	Q9BRT2
UQCRB	Cytochrome b-c1 complex subunit 7	P14927
UQCRC1	Cytochrome b-c1 complex subunit 1, mitochondrial	P31930
UQCRC2	Cytochrome b-c1 complex subunit 2, mitochondrial	P22695
UQCRCF1	Cytochrome b-c1 complex subunit Rieske, mitochondrial	P47985
UQCRQ	Cytochrome b-c1 complex subunit 8	O14949
URB1	Nucleolar pre-ribosomal-associated protein 1	O60287
USE1	Vesicle transport protein USE1	Q9NZ43

Gene	Protein name	Accession
USO1	General vesicular transport factor p115	O60763
USP10	Ubiquitin carboxyl-terminal hydrolase 10	Q14694
USP11	Ubiquitin carboxyl-terminal hydrolase 11	P51784
USP9X	Probable ubiquitin carboxyl-terminal hydrolase FAF-X	Q93008
UTP14A	U3 small nucleolar RNA-associated protein 14 homolog A	Q9BVJ6
UTP20	Small subunit processome component 20 homolog	O75691
UTRN	Utrophin	P46939
VAMP3	Vesicle-associated membrane protein 3	Q15836
VAMP4	Vesicle-associated membrane protein 4	O75379
VAMP5	Vesicle-associated membrane protein 5	O95183
VAMP7	Vesicle-associated membrane protein 7	P51809
VAPB	Vesicle-associated membrane protein-associated protein B/C	O95292
VARS	Valine--tRNA ligase	P26640
VARS2	Valine--tRNA ligase, mitochondrial	Q5ST30
VAT1	Synaptic vesicle membrane protein VAT-1 homolog	Q99536
VAV1	Proto-oncogene vav	P15498
VAV3	Guanine nucleotide exchange factor VAV3	Q9UKW4
VCP	Transitional endoplasmic reticulum ATPase	P55072
VDAC1	Voltage-dependent anion-selective channel protein 1	P21796
VDAC2	Voltage-dependent anion-selective channel protein 2	P45880
VDAC3	Voltage-dependent anion-selective channel protein 3	Q9Y277
VIM	Vimentin	P08670
VMA21	Vacuolar ATPase assembly integral membrane protein VMA21	Q3ZAQ7
VPS11	Vacuolar protein sorting-associated protein 11 homolog	Q9H270
VPS13A	Vacuolar protein sorting-associated protein 13A	Q96RL7
VPS13B	Vacuolar protein sorting-associated protein 13B	Q7Z7G8
VPS13C	Vacuolar protein sorting-associated protein 13C	Q709C8
VPS18	Vacuolar protein sorting-associated protein 18 homolog	Q9P253
VPS29	Vacuolar protein sorting-associated protein 29	Q9UBQ0
VPS35	Vacuolar protein sorting-associated protein 35	Q96QK1
VPS39	Vam6/Vps39-like protein	Q96JC1
VTI1A	Vesicle transport through interaction with t-SNAREs homolog 1A	Q96AJ9
VTI1B	Vesicle transport through interaction with t-SNAREs homolog 1B	Q9UEU0
VWA8	von Willebrand factor A domain-containing protein 8	A3KMH1
WARS2	Tryptophan--tRNA ligase, mitochondrial	Q9UGM6
WDR3	WD repeat-containing protein 3	Q9UNX4
WDR36	WD repeat-containing protein 36	Q8NI36
XPO1	Exportin-1	O14980
XRCC5	X-ray repair cross-complementing protein 5	P13010

Gene	Protein name	Accession
XRCC6	X-ray repair cross-complementing protein 6	P12956
XYLT2	Xylosyltransferase 2	Q9H1B5
YARS2	Tyrosine--tRNA ligase, mitochondrial	Q9Y2Z4
YBEY	Putative ribonuclease	P58557
YBX1	Nuclease-sensitive element-binding protein 1	P67809
YIPF3	Protein YIPF3	Q9GZM5
YIPF5	Protein YIPF5	Q969M3
YKT6	Synaptobrevin homolog YKT6	O15498
YME1L1	ATP-dependent zinc metalloprotease YME1L1	Q96TA2
YRDC	YrdC domain-containing protein, mitochondrial	Q86U90
YWHAB	14-3-3 protein beta/alpha	P31946
YWHAE	14-3-3 protein epsilon	P62258
YWHAG	14-3-3 protein gamma	P61981
YWHAH	14-3-3 protein eta	Q04917
YWHAQ	14-3-3 protein theta	P27348
YWHAZ	14-3-3 protein zeta/delta	P63104
ZADH2	Zinc-binding alcohol dehydrogenase domain-containing protein 2	Q8N4Q0
ZAP70	Tyrosine-protein kinase ZAP-70	P43403
ZC3H11A	Zinc finger CCCH domain-containing protein 11A	O75152
ZC3HAV1	Zinc finger CCCH-type antiviral protein 1	Q7Z2W4
ZDHHC13	Palmitoyltransferase ZDHHC13	Q8IUH4
ZMPSTE24	CAAX prenyl protease 1 homolog	O75844
ZW10	Centromere/kinetochore protein zw10 homolog	O43264

## 6.4 Background proteins

**Table 5: Proteins contained in the background sample (BG) measured by mass spectrometry (see 3.5). Listed are gene names, protein names, and UniProt accession numbers.**

Gene	Protein name	Accession
AARS2	Alanine--tRNA ligase, mitochondrial	Q5J TZ9
AASS	Alpha-aminoadipic semialdehyde synthase, mitochondrial	Q9UDR5
ABAT	4-aminobutyrate aminotransferase, mitochondrial	P80404
ABCB10	ATP-binding cassette sub-family B member 10, mitochondrial	Q9NRK6
ABCB7	ATP-binding cassette sub-family B member 7, mitochondrial	O75027
ABCB8	ATP-binding cassette sub-family B member 8, mitochondrial	Q9NUT2
ABCC1	Multidrug resistance-associated protein 1	P33527
ABCC4	Multidrug resistance-associated protein 4	O15439
ABCF1	ATP-binding cassette sub-family F member 1	Q8NE71
ABHD10	Mycophenolic acid acyl-glucuronide esterase, mitochondrial	Q9NUJ1
ABHD11	Alpha/beta hydrolase domain-containing protein 11	Q8N FV4
ABHD17B	Alpha/beta hydrolase domain-containing protein 17B	Q5VST6
ACAA1	3-ketoacyl-CoA thiolase, peroxisomal	P09110
ACAA2	3-ketoacyl-CoA thiolase, mitochondrial	P42765
ACAD8	Isobutyryl-CoA dehydrogenase, mitochondrial	Q9UKU7
ACAD9	Acyl-CoA dehydrogenase family member 9, mitochondrial	Q9H845
ACADM	Medium-chain specific acyl-CoA dehydrogenase, mitochondrial	P11310
ACADS	Short-chain specific acyl-CoA dehydrogenase, mitochondrial	P16219
ACADVL	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial	P49748
ACAP1	Arf-GAP with coiled-coil, ANK repeat and PH domain-containing protein 1	Q15027
ACAT1	Acetyl-CoA acetyltransferase, mitochondrial	P24752
ACBD3	Golgi resident protein GCP60	Q9H3P7
ACIN1	Apoptotic chromatin condensation inducer in the nucleus	Q9UKV3
ACLY	ATP-citrate synthase	P53396

Gene	Protein name	Accession
ACOT13	Acyl-coenzyme A thioesterase 13	Q9NPJ3
ACOT8	Acyl-coenzyme A thioesterase 8	O14734
ACOX1	Peroxisomal acyl-coenzyme A oxidase 1	Q15067
ACP1	Low molecular weight phosphotyrosine protein phosphatase	P24666
ACSF3	Acyl-CoA synthetase family member 3, mitochondrial	Q4G176
ACSS1	Acetyl-coenzyme A synthetase 2-like, mitochondrial	Q9NUB1
ACTG1	Actin, cytoplasmic 2	P63261
ACTL6A	Actin-like protein 6A	O96019
ACTN4	Alpha-actinin-4	O43707
ACTR1A	Alpha-centractin	P61163
ACTR3	Actin-related protein 3	P61158
ADAM10	Disintegrin and metalloproteinase domain-containing protein 10	O14672
ADCK4	AarF domain-containing protein kinase 4	Q96D53
ADD1	Alpha-adducin	P35611
ADD3	Gamma-adducin	Q9UEY8
ADPRHL2	Poly(ADP-ribose) glycohydrolase ARH3	Q9NX46
AEBP1	Adipocyte enhancer-binding protein 1	Q8IUX7
AFG3L2	AFG3-like protein 2	Q9Y4W6
AGK	Acylglycerol kinase, mitochondrial	Q53H12
AGPS	Alkylidihydroxyacetonephosphate synthase, peroxisomal	O00116
AIFM1	Apoptosis-inducing factor 1, mitochondrial	O95831
AIMP1	Aminoacyl tRNA synthase complex-interacting multifunctional protein 1	Q12904
AK3	GTP:AMP phosphotransferase AK3, mitochondrial	Q9UIJ7
AKAP1	A-kinase anchor protein 1, mitochondrial	Q92667
AKAP2	A-kinase anchor protein 2	Q9Y2D5
AKAP9	A-kinase anchor protein 9	Q99996
AKNA	AT-hook-containing transcription factor	Q7Z591
ALB	Serum albumin	P02768
ALDH18A1	Delta-1-pyrroline-5-carboxylate synthase	P54886
ALDH3A2	Fatty aldehyde dehydrogenase	P51648
ALDH4A1	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial	P30038
ALG5	Dolichyl-phosphate beta-glucosyltransferase	Q9Y673
ALKBH1	Alkylated DNA repair protein alkB homolog 1	Q13686
ALKBH7	Alpha-ketoglutarate-dependent dioxygenase alkB homolog 7, mitochondrial	Q9BT30
ALMS1	Alstrom syndrome protein 1	Q8TCU4
AMFR	E3 ubiquitin-protein ligase AMFR	Q9UKV5
ANO6	Anoctamin-6	Q4KMQ2
ANXA1	Annexin A1	P04083
ANXA11	Annexin A11	P50995

Gene	Protein name	Accession
ANXA2	Annexin A2	P07355
ANXA6	Annexin A6	P08133
AP1M1	AP-1 complex subunit mu-1	Q9BXS5
AP1S2	AP-1 complex subunit sigma-2	P56377
AP2A1	AP-2 complex subunit alpha-1	O95782
AP2A2	AP-2 complex subunit alpha-2	O94973
AP2B1	AP-2 complex subunit beta	P63010
AP2M1	AP-2 complex subunit mu	Q96CW1
APEX1	DNA-(apurinic or apyrimidinic site) lyase	P27695
APMAP	Adipocyte plasma membrane-associated protein	Q9HDC9
APOA1BP	NAD(P)H-hydrate epimerase	Q8NCW5
APOB	Apolipoprotein B-100	P04114
APOL2	Apolipoprotein L2	Q9BQE5
APOO	Apolipoprotein O	Q9BUR5
APOOL	Apolipoprotein O-like	Q6UXV4
APRT	Adenine phosphoribosyltransferase	P07741
ARF1	ADP-ribosylation factor 1	P84077
ARF3	ADP-ribosylation factor 3	P61204
ARF4	ADP-ribosylation factor 4	P18085
ARF5	ADP-ribosylation factor 5	P84085
ARF6	ADP-ribosylation factor 6	P62330
ARFGAP1	ADP-ribosylation factor GTPase-activating protein 1	Q8N6T3
ARG2	Arginase-2, mitochondrial	P78540
ARHGAP30	Rho GTPase-activating protein 30	Q7Z6I6
ARHGEF2	Rho guanine nucleotide exchange factor 2	Q92974
ARL1	ADP-ribosylation factor-like protein 1	P40616
ARL15	ADP-ribosylation factor-like protein 15	Q9NXU5
ARL2	ADP-ribosylation factor-like protein 2	P36404
ARL6IP5	PRA1 family protein 3	O75915
ARL8B	ADP-ribosylation factor-like protein 8B	Q9NVJ2
ARMC1	Armadillo repeat-containing protein 1	Q9NVT9
ARMC10	Armadillo repeat-containing protein 10	Q8N2F6
ARMCX3	Armadillo repeat-containing X-linked protein 3	Q9UH62
ARPC1B	Actin-related protein 2/3 complex subunit 1B	O15143
ARPC2	Actin-related protein 2/3 complex subunit 2	O15144
ATAD1	ATPase family AAA domain-containing protein 1	Q8NBU5
ATAD3A	ATPase family AAA domain-containing protein 3A	Q9NVI7
ATF6	Cyclic AMP-dependent transcription factor ATF-6 alpha	P18850
ATL3	Atlastin-3	Q6DD88

Gene	Protein name	Accession
ATP11B	Probable phospholipid-transporting ATPase IF	Q9Y2G3
ATP11C	Phospholipid-transporting ATPase IG	Q8NB49
ATP13A1	Manganese-transporting ATPase 13A1	Q9HD20
ATP13A3	Probable cation-transporting ATPase 13A3	Q9H7F0
ATP1A1	Sodium/potassium-transporting ATPase subunit alpha-1	P05023
ATP1A3	Sodium/potassium-transporting ATPase subunit alpha-3	P13637
ATP2A2	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2	P16615
ATP2A3	Sarcoplasmic/endoplasmic reticulum calcium ATPase 3	Q93084
ATP2B1	Plasma membrane calcium-transporting ATPase 1	P20020
ATP2B4	Plasma membrane calcium-transporting ATPase 4	P23634
ATP5A1	ATP synthase subunit alpha, mitochondrial	P25705
ATP5B	ATP synthase subunit beta, mitochondrial	P06576
ATP5D	ATP synthase subunit delta, mitochondrial	P30049
ATP5F1	ATP synthase F(0) complex subunit B1, mitochondrial	P24539
ATP5H	ATP synthase subunit d, mitochondrial	O75947
ATP5L	ATP synthase subunit g, mitochondrial	O75964
ATP5O	ATP synthase subunit O, mitochondrial	P48047
ATP5S	ATP synthase subunit s, mitochondrial	Q99766
ATP5SL	ATP synthase subunit s-like protein	Q9NW81
ATP6AP1	V-type proton ATPase subunit S1	Q15904
ATP6AP2	Renin receptor	O75787
ATP6V0A1	V-type proton ATPase 116 kDa subunit a isoform 1	Q93050
ATP6V0A2	V-type proton ATPase 116 kDa subunit a isoform 2	Q9Y487
ATP6V0D1	V-type proton ATPase subunit d 1	P61421
ATP6V1A	V-type proton ATPase catalytic subunit A	P38606
ATP6V1B2	V-type proton ATPase subunit B, brain isoform	P21281
ATP6V1D	V-type proton ATPase subunit D	Q9Y5K8
ATP6V1E1	V-type proton ATPase subunit E 1	P36543
ATP6V1F	V-type proton ATPase subunit F	Q16864
ATP6V1G1	V-type proton ATPase subunit G 1	O75348
ATP6V1H	V-type proton ATPase subunit H	Q9UI12
ATP7A	Copper-transporting ATPase 1	Q04656
ATPAF1	ATP synthase mitochondrial F1 complex assembly factor 1	Q5TC12
ATPAF2	ATP synthase mitochondrial F1 complex assembly factor 2	Q8N5M1
ATRX	Transcriptional regulator ATRX	P46100
ATXN10	Ataxin-10	Q9UBB4
AUH	Methylglutaconyl-CoA hydratase, mitochondrial	Q13825
AUP1	Ancient ubiquitous protein 1	Q9Y679
AURKA	Aurora kinase A	O14965

Gene	Protein name	Accession
AURKB	Aurora kinase B	Q96GD4
B3GALT6	Beta-1,3-galactosyltransferase 6	Q96L58
BAG2	BAG family molecular chaperone regulator 2	O95816
BAZ1B	Tyrosine-protein kinase BAZ1B	Q9UIG0
BCAT2	Branched-chain-amino-acid aminotransferase, mitochondrial	O15382
BCKDHA	2-oxoisovalerate dehydrogenase subunit alpha, mitochondrial	P12694
BCL2L1	Bcl-2-like protein 1	Q07817
BCL2L12	Bcl-2-like protein 12	Q9HB09
BCL2L13	Bcl-2-like protein 13	Q9BXK5
BCS1L	Mitochondrial chaperone BCS1	Q9Y276
BET1L	BET1-like protein	Q9NYM9
BICD1	Protein bicaudal D homolog 1	Q96G01
BICD2	Protein bicaudal D homolog 2	Q8TD16
BNIP1	Vesicle transport protein SEC20	Q12981
BNIP3L	BCL2/adenovirus E1B 19 kDa protein-interacting protein 3-like	O60238
BRI3BP	BRI3-binding protein	Q8WY22
BSG	Basigin	P35613
BUB3	Mitotic checkpoint protein BUB3	O43684
C10orf35	Uncharacterized protein C10orf35	Q96D05
C14orf159	UPF0317 protein C14orf159, mitochondrial	Q7Z3D6
C14orf166	UPF0568 protein C14orf166	Q9Y224
C16orf54	Transmembrane protein C16orf54	Q6UWD8
C17orf59	Uncharacterized protein C17orf59	Q96GS4
C18orf32	UPF0729 protein C18orf32	Q8TCD1
C19orf10	UPF0556 protein C19orf10	Q969H8
C19orf52	Uncharacterized protein C19orf52	Q9BSF4
C1QBP	Complement component 1 Q subcomponent-binding protein, mitochondrial	Q07021
C21orf33	ES1 protein homolog, mitochondrial	P30042
C2CD2L	C2 domain-containing protein 2-like	O14523
C2CD3	C2 domain-containing protein 3	Q4AC94
C2orf43	UPF0554 protein C2orf43	Q9H6V9
C2orf47	Uncharacterized protein C2orf47, mitochondrial	Q8WWC4
C3orf33	Protein C3orf33	Q6P1S2
C7orf50	Uncharacterized protein C7orf50	Q9BRJ6
C7orf55	UPF0562 protein C7orf55	Q96HJ9
C8orf82	UPF0598 protein C8orf82	Q6P1X6
C9orf89	Bcl10-interacting CARD protein	Q96LW7
CAD	CAD protein	P27708
CALM1	Calmodulin	P62158

Gene	Protein name	Accession
CALR	Calreticulin	P27797
CAMLG	Calcium signal-modulating cyclophilin ligand	P49069
CAND1	Cullin-associated NEDD8-dissociated protein 1	Q86VP6
CANX	Calnexin	P27824
CAPZA1	F-actin-capping protein subunit alpha-1	P52907
CARS2	Probable cysteine--tRNA ligase, mitochondrial	Q9HA77
CAT	Catalase	P04040
CBFB	Core-binding factor subunit beta	Q13951
CBR4	Carbonyl reductase family member 4	Q8N4T8
CBX3	Chromobox protein homolog 3	Q13185
CCAR2	Cell cycle and apoptosis regulator protein 2	Q8N163
CCBL2	Kynurenine--oxoglutarate transaminase 3	Q6YP21
CCDC109B	Mitochondrial calcium uniporter regulatory subunit MCUb	Q9NWR8
CCDC115	Coiled-coil domain-containing protein 115	Q96NT0
CCDC127	Coiled-coil domain-containing protein 127	Q96BQ5
CCDC134	Coiled-coil domain-containing protein 134	Q9H6E4
CCDC167	Coiled-coil domain-containing protein 167	Q9P0B6
CCDC47	Coiled-coil domain-containing protein 47	Q96A33
CCDC51	Coiled-coil domain-containing protein 51	Q96ER9
CCDC90B	Coiled-coil domain-containing protein 90B, mitochondrial	Q9GZT6
CCP110	Centriolar coiled-coil protein of 110 kDa	O43303
CCSMST1	Protein CCSMST1	Q4G010
CCT2	T-complex protein 1 subunit beta	P78371
CCT3	T-complex protein 1 subunit gamma	P49368
CCT4	T-complex protein 1 subunit delta	P50991
CCT6A	T-complex protein 1 subunit zeta	P40227
CCT7	T-complex protein 1 subunit eta	Q99832
CCT8	T-complex protein 1 subunit theta	P50990
CD1C	T-cell surface glycoprotein CD1c	P29017
CD2	T-cell surface antigen CD2	P06729
CD247	T-cell surface glycoprotein CD3 zeta chain	P20963
CD3D	T-cell surface glycoprotein CD3 delta chain	P04234
CD47	Leukocyte surface antigen CD47	Q08722
CD48	CD48 antigen	P09326
CD81	CD81 antigen	P60033
CD82	CD82 antigen	P27701
CDH2	Cadherin-2	P19022
CDK1	Cyclin-dependent kinase 1	P06493
CDK2	Cyclin-dependent kinase 2	P24941

Gene	Protein name	Accession
CDK5RAP2	CDK5 regulatory subunit-associated protein 2	Q96SN8
CDK5RAP3	CDK5 regulatory subunit-associated protein 3	Q96JB5
CDK6	Cyclin-dependent kinase 6	Q00534
CDK9	Cyclin-dependent kinase 9	P50750
CECR5	Cat eye syndrome critical region protein 5	Q9BXW7
CENPF	Centromere protein F	P49454
CENPJ	Centromere protein J	Q9HC77
CENPM	Centromere protein M	Q9NSP4
CEP120	Centrosomal protein of 120 kDa	Q8N960
CEP131	Centrosomal protein of 131 kDa	Q9UPN4
CEP135	Centrosomal protein of 135 kDa	Q66GS9
CEP152	Centrosomal protein of 152 kDa	O94986
CEP162	Centrosomal protein of 162 kDa	Q5TB80
CEP250	Centrosome-associated protein CEP250	Q9BV73
CEP350	Centrosome-associated protein 350	Q5VT06
CEP41	Centrosomal protein of 41 kDa	Q9BYV8
CEP72	Centrosomal protein of 72 kDa	Q9P209
CEP85L	Centrosomal protein of 85 kDa-like	Q5SZL2
CEP95	Centrosomal protein of 95 kDa	Q96GE4
CEP97	Centrosomal protein of 97 kDa	Q8IW35
CETN3	Centrin-3	O15182
CFL1	Cofilin-1	P23528
CGREF1	Cell growth regulator with EF hand domain protein 1	Q99674
CHCHD1	Coiled-coil-helix-coiled-coil-helix domain-containing protein 1	Q96BP2
CHCHD2P9	Putative coiled-coil-helix-coiled-coil-helix domain-containing protein CHCHD2P9, mitochondrial	Q5T1J5
CHCHD3	Coiled-coil-helix-coiled-coil-helix domain-containing protein 3, mitochondrial	Q9NX63
CHCHD4	Mitochondrial intermembrane space import and assembly protein 40	Q8N4Q1
CHCHD6	Coiled-coil-helix-coiled-coil-helix domain-containing protein 6, mitochondrial	Q9BRQ6
CHD4	Chromodomain-helicase-DNA-binding protein 4	Q14839
CHI3L2	Chitinase-3-like protein 2	Q15782
CHID1	Chitinase domain-containing protein 1	Q9BWS9
CHP1	Calcineurin B homologous protein 1	Q99653
CHST11	Carbohydrate sulfotransferase 11	Q9NPF2
CHST14	Carbohydrate sulfotransferase 14	Q8NCH0
CHSY1	Chondroitin sulfate synthase 1	Q86X52
CISD1	CDGSH iron-sulfur domain-containing protein 1	Q9NZ45
CISD2	CDGSH iron-sulfur domain-containing protein 2	Q8N5K1
CIT	Citron Rho-interacting kinase	O14578

Gene	Protein name	Accession
CKAP2	Cytoskeleton-associated protein 2	Q8WWK9
CKAP4	Cytoskeleton-associated protein 4	Q07065
CKAP5	Cytoskeleton-associated protein 5	Q14008
CKM	Creatine kinase M-type	P06732
CLASP2	CLIP-associating protein 2	O75122
CLEC11A	C-type lectin domain family 11 member A	Q9Y240
CLIC1	Chloride intracellular channel protein 1	O00299
CLN5	Ceroid-lipofuscinosis neuronal protein 5	O75503
CLPB	Caseinolytic peptidase B protein homolog	Q9H078
CLPP	ATP-dependent Clp protease proteolytic subunit, mitochondrial	Q16740
CLPTM1	Cleft lip and palate transmembrane protein 1	O96005
CLPTM1L	Cleft lip and palate transmembrane protein 1-like protein	Q96KA5
CLPX	ATP-dependent Clp protease ATP-binding subunit clpX-like, mitochondrial	O76031
CLTC	Clathrin heavy chain 1	Q00610
CLYBL	Citrate lyase subunit beta-like protein, mitochondrial	Q8N0X4
CMPK2	UMP-CMP kinase 2, mitochondrial	Q5EBM0
CNNM3	Metal transporter CNNM3	Q8NE01
CNOT1	CCR4-NOT transcription complex subunit 1	A5YKK6
CNP	2',3'-cyclic-nucleotide 3'-phosphodiesterase	P09543
CNPY3	Protein canopy homolog 3	Q9BT09
CNTRL	Centriolin	Q7Z7A1
CNTROB	Centrobin	Q8N137
COA1	Cytochrome c oxidase assembly factor 1 homolog	Q9GZY4
COA3	Cytochrome c oxidase assembly factor 3 homolog, mitochondrial	Q9Y2R0
COLGALT1	Procollagen galactosyltransferase 1	Q8NBJ5
COMT	Catechol O-methyltransferase	P21964
COPA	Coatomer subunit alpha	P53621
COPB1	Coatomer subunit beta	P53618
COPB2	Coatomer subunit beta'	P35606
COPE	Coatomer subunit epsilon	O14579
COPG1	Coatomer subunit gamma-1	Q9Y678
COPZ1	Coatomer subunit zeta-1	P61923
COQ10B	Coenzyme Q-binding protein COQ10 homolog B, mitochondrial	Q9H8M1
COQ3	Hexaprenyldihydroxybenzoate methyltransferase, mitochondrial	Q9NZJ6
COQ5	2-methoxy-6-polyprenyl-1,4-benzoquinol methylase, mitochondrial	Q5HYK3
COQ6	Ubiquinone biosynthesis monoxygenase COQ6	Q9Y2Z9
CORO1A	Coronin-1A	P31146
COTL1	Coactosin-like protein	Q14019
COX15	Cytochrome c oxidase assembly protein COX15 homolog	Q7KZN9

Gene	Protein name	Accession
COX18	Mitochondrial inner membrane protein COX18	Q8N8Q8
COX20	Cytochrome c oxidase protein 20 homolog	Q5RI15
COX4I1	Cytochrome c oxidase subunit 4 isoform 1, mitochondrial	P13073
COX5A	Cytochrome c oxidase subunit 5A, mitochondrial	P20674
COX6B1	Cytochrome c oxidase subunit 6B1	P14854
CPD	Carboxypeptidase D	O75976
CPOX	Oxygen-dependent coproporphyrinogen-III oxidase, mitochondrial	P36551
CPT1A	Carnitine O-palmitoyltransferase 1, liver isoform	P50416
CPT2	Carnitine O-palmitoyltransferase 2, mitochondrial	P23786
CPVL	Probable serine carboxypeptidase CPVL	Q9H3G5
CROCC	Rootletin	Q5TZA2
CRYZ	Quinone oxidoreductase	Q08257
CS	Citrate synthase, mitochondrial	O75390
CSE1L	Exportin-2	P55060
CSPP1	Centrosome and spindle pole-associated protein 1	Q1MSJ5
CTPS1	CTP synthase 1	P17812
CTSA	Lysosomal protective protein	P10619
CTSD	Cathepsin D	P07339
CTSG	Cathepsin G	P08311
CUX1	Protein CASP	Q13948
CXCR4	C-X-C chemokine receptor type 4	P61073
CYB5A	Cytochrome b5	P00167
CYB5B	Cytochrome b5 type B	O43169
CYB5R1	NADH-cytochrome b5 reductase 1	Q9UHQ9
CYB5R3	NADH-cytochrome b5 reductase 3	P00387
CYC1	Cytochrome c1, heme protein, mitochondrial	P08574
CYCS	Cytochrome c	P99999
CYP20A1	Cytochrome P450 20A1	Q6UW02
DAAM1	Disheveled-associated activator of morphogenesis 1	Q9Y4D1
DAD1	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit DAD1	P61803
DAP3	28S ribosomal protein S29, mitochondrial	P51398
DARS	Aspartate--tRNA ligase, cytoplasmic	P14868
DARS2	Aspartate--tRNA ligase, mitochondrial	Q6P148
DBN1	Drebrin	Q16643
DBT	Lipoamide acyltransferase component of branched-chain alpha-keto acid dehydrogenase complex, mitochondrial	P11182
DCAKD	Dephospho-CoA kinase domain-containing protein	Q8WVC6
DCD	Dermcidin	P81605
DCPIA	mRNA-decapping enzyme 1A	Q9NP16

Gene	Protein name	Accession
DCTN2	Dynactin subunit 2	Q13561
DCTN3	Dynactin subunit 3	O75935
DCXR	L-xylulose reductase	Q7Z4W1
DDOST	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 48 kDa subunit	P39656
DDRKG1	DDRKG domain-containing protein 1	Q96HY6
DDX1	ATP-dependent RNA helicase DDX1	Q92499
DDX21	Nucleolar RNA helicase 2	Q9NR30
DDX24	ATP-dependent RNA helicase DDX24	Q9GZR7
DDX28	Probable ATP-dependent RNA helicase DDX28	Q9NUL7
DDX39B	Spliceosome RNA helicase DDX39B	Q13838
DDX47	Probable ATP-dependent RNA helicase DDX47	Q9H0S4
DDX51	ATP-dependent RNA helicase DDX51	Q8N8A6
DDX6	Probable ATP-dependent RNA helicase DDX6	P26196
DECR1	2,4-dienoyl-CoA reductase, mitochondrial	Q16698
DECR2	Peroxisomal 2,4-dienoyl-CoA reductase	Q9NUI1
DHCR7	7-dehydrocholesterol reductase	Q9UBM7
DHODH	Dihydroorotate dehydrogenase	Q02127
DHRS4	Dehydrogenase/reductase SDR family member 4	Q9BTZ2
DHRS7	Dehydrogenase/reductase SDR family member 7	Q9Y394
DHRS7B	Dehydrogenase/reductase SDR family member 7B	Q6LAN0
DHX15	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15	O43143
DHX30	Putative ATP-dependent RNA helicase DHX30	Q7L2E3
DHX9	ATP-dependent RNA helicase A	Q08211
DIAPH1	Protein diaphanous homolog 1	O60610
DIP2B	Disco-interacting protein 2 homolog B	Q9P265
DLG1	Disks large homolog 1	Q12959
DLST	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex, mitochondrial	P36957
DNAJA1	DnaJ homolog subfamily A member 1	P31689
DNAJA3	DnaJ homolog subfamily A member 3, mitochondrial	Q96EY1
DNAJB11	DnaJ homolog subfamily B member 11	Q9UBS4
DNAJB12	DnaJ homolog subfamily B member 12	Q9NXW2
DNAJB2	DnaJ homolog subfamily B member 2	P25686
DNAJC10	DnaJ homolog subfamily C member 10	Q8IXB1
DNAJC11	DnaJ homolog subfamily C member 11	Q9NVH1
DNAJC13	DnaJ homolog subfamily C member 13	O75165
DNAJC15	DnaJ homolog subfamily C member 15	Q9Y5T4
DNAJC19	Mitochondrial import inner membrane translocase subunit TIM14	Q96DA6
DNAJC30	DnaJ homolog subfamily C member 30	Q96LL9

Gene	Protein name	Accession
DNAJC5	DnaJ homolog subfamily C member 5	Q9H3Z4
DNAJC9	DnaJ homolog subfamily C member 9	Q8WXX5
DNLZ	DNL-type zinc finger protein	Q5SXM8
DOCK10	Dedicator of cytokinesis protein 10	Q96BY6
DOCK2	Dedicator of cytokinesis protein 2	Q92608
DPM1	Dolichol-phosphate mannosyltransferase subunit 1	O60762
DRG1	Developmentally-regulated GTP-binding protein 1	Q9Y295
DSG1	Desmoglein-1	Q02413
DSP	Desmoplakin	P15924
DTYMK	Thymidylate kinase	P23919
DUT	Deoxyuridine 5'-triphosphate nucleotidohydrolase, mitochondrial	P33316
DYNC1H1	Cytoplasmic dynein 1 heavy chain 1	Q14204
EBP	3-beta-hydroxysteroid-Delta(8),Delta(7)-isomerase	Q15125
ECE1	Endothelin-converting enzyme 1	P42892
ECH1	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	Q13011
ECHDC1	Ethylmalonyl-CoA decarboxylase	Q9NTX5
ECHS1	Enoyl-CoA hydratase, mitochondrial	P30084
ECSIT	Evolutionarily conserved signaling intermediate in Toll pathway, mitochondrial	Q9BQ95
EDC4	Enhancer of mRNA-decapping protein 4	Q6P2E9
EEF1A1	Elongation factor 1-alpha 1	P68104
EEF1A1P5	Putative elongation factor 1-alpha-like 3	Q5VTE0
EEF1E1	Eukaryotic translation elongation factor 1 epsilon-1	O43324
EEF2	Elongation factor 2	P13639
EFCAB4B	EF-hand calcium-binding domain-containing protein 4B	Q9BSW2
EFNB1	Ephrin-B1	P98172
EFTUD2	116 kDa U5 small nuclear ribonucleoprotein component	Q15029
EIF1AY	Eukaryotic translation initiation factor 1A, Y-chromosomal	O14602
EIF2S1	Eukaryotic translation initiation factor 2 subunit 1	P05198
EIF3C	Eukaryotic translation initiation factor 3 subunit C	Q99613
EIF3CL	Eukaryotic translation initiation factor 3 subunit C-like protein	B5ME19
EIF3E	Eukaryotic translation initiation factor 3 subunit E	P60228
EIF3I	Eukaryotic translation initiation factor 3 subunit I	Q13347
EIF4A1	Eukaryotic initiation factor 4A-I	P60842
EIF4A3	Eukaryotic initiation factor 4A-III	P38919
EIF4G1	Eukaryotic translation initiation factor 4 gamma 1	Q04637
EIF5A	Eukaryotic translation initiation factor 5A-1	P63241
EIF5B	Eukaryotic translation initiation factor 5B	O60841
ELAC2	Zinc phosphodiesterase ELAC protein 2	Q9BQ52
ELAVL1	ELAV-like protein 1	Q15717

Gene	Protein name	Accession
ELMOD2	ELMO domain-containing protein 2	Q8IZ81
EMC1	ER membrane protein complex subunit 1	Q8N766
EMC3	ER membrane protein complex subunit 3	Q9P012
EMC6	ER membrane protein complex subunit 6	Q9BV81
EMD	Emerin	P50402
ENDOD1	Endonuclease domain-containing 1 protein	O94919
ENO1	Alpha-enolase	P06733
ENPP4	Bis(5'-adenosyl)-triphosphatase ENPP4	Q9Y6X5
EPRS	Bifunctional glutamate/proline--tRNA ligase	P07814
ERAL1	GTPase Era, mitochondrial	O75616
ERAP1	Endoplasmic reticulum aminopeptidase 1	Q9NZ08
ERAP2	Endoplasmic reticulum aminopeptidase 2	Q6P179
ERBB2IP	Protein LAP2	Q96RT1
ERGIC1	Endoplasmic reticulum-Golgi intermediate compartment protein 1	Q969X5
ERGIC2	Endoplasmic reticulum-Golgi intermediate compartment protein 2	Q96RQ1
ERGIC3	Endoplasmic reticulum-Golgi intermediate compartment protein 3	Q9Y282
ERH	Enhancer of rudimentary homolog	P84090
ERLIN2	Erlin-2	O94905
ERO1L	ERO1-like protein alpha	Q96HE7
ERP29	Endoplasmic reticulum resident protein 29	P30040
ERP44	Endoplasmic reticulum resident protein 44	Q9BS26
ESYT1	Extended synaptotagmin-1	Q9BSJ8
ETFA	Electron transfer flavoprotein subunit alpha, mitochondrial	P13804
ETFB	Electron transfer flavoprotein subunit beta	P38117
ETFDH	Electron transfer flavoprotein-ubiquinone oxidoreductase, mitochondrial	Q16134
ETHE1	Persulfide dioxygenase ETHE1, mitochondrial	O95571
EXD2	Exonuclease 3'-5' domain-containing protein 2	Q9NVH0
EXOC1	Exocyst complex component 1	Q9NV70
EXOC4	Exocyst complex component 4	Q96A65
EXOG	Nuclease EXOG, mitochondrial	Q9Y2C4
EZR	Ezrin	P15311
F5	Coagulation factor V	P12259
FADS2	Fatty acid desaturase 2	O95864
FAF2	FAS-associated factor 2	Q96CS3
FAHD1	Acylpyruvase FAHD1, mitochondrial	Q6P587
FAHD2A	Fumarylacetoacetate hydrolase domain-containing protein 2A	Q96GK7
FAM120A	Constitutive coactivator of PPAR-gamma-like protein 1	Q9NZB2
FAM134B	Protein FAM134B	Q9H6L5
FAM134C	Protein FAM134C	Q86VR2

Gene	Protein name	Accession
FAM162A	Protein FAM162A	Q96A26
FAM20B	Glycosaminoglycan xylosylkinase	O75063
FAM213A	Redox-regulatory protein FAM213A	Q9BRX8
FAM3C	Protein FAM3C	Q92520
FAM49B	Protein FAM49B	Q9NUQ9
FAM96B	Mitotic spindle-associated MMXD complex subunit MIP18	Q9Y3D0
FAR1	Fatty acyl-CoA reductase 1	Q8WVX9
FARS2	Phenylalanine--tRNA ligase, mitochondrial	O95363
FAS	Tumor necrosis factor receptor superfamily member 6	P25445
FASN	Fatty acid synthase	P49327
FASTKD1	FAST kinase domain-containing protein 1	Q53R41
FASTKD2	FAST kinase domain-containing protein 2	Q9NYY8
FASTKD5	FAST kinase domain-containing protein 5	Q7L8L6
FDFT1	Squalene synthase	P37268
FDPS	Farnesyl pyrophosphate synthase	P14324
FDX1	Adrenodoxin, mitochondrial	P10109
FDXR	NADPH:adrenodoxin oxidoreductase, mitochondrial	P22570
FECH	Ferrochelatase, mitochondrial	P22830
FEN1	Flap endonuclease 1	P39748
FERMT3	Fermitin family homolog 3	Q86UX7
FGFR1OP	FGFR1 oncogene partner	O95684
FH	Fumarate hydratase, mitochondrial	P07954
FIS1	Mitochondrial fission 1 protein	Q9Y3D6
FKBP11	Peptidyl-prolyl cis-trans isomerase FKBP11	Q9NYL4
FKBP2	Peptidyl-prolyl cis-trans isomerase FKBP2	P26885
FLNA	Filamin-A	P21333
FLNB	Filamin-B	O75369
FLOT1	Flotillin-1	O75955
FLOT2	Flotillin-2	Q14254
FMNL1	Formin-like protein 1	O95466
FN1	Fibronectin	P02751
FOXRED1	FAD-dependent oxidoreductase domain-containing protein 1	Q96CU9
FRG1	Protein FRG1	Q14331
FRYL	Protein furry homolog-like	O94915
FTL	Ferritin light chain	P02792
FTSJ2	Putative ribosomal RNA methyltransferase 2	Q9U143
FUNDC2	FUN14 domain-containing protein 2	Q9BWH2
FXN	Frataxin, mitochondrial	Q16595
FYN	Tyrosine-protein kinase Fyn	P06241

Gene	Protein name	Accession
G6PD	Glucose-6-phosphate 1-dehydrogenase	P11413
GALNT2	Polypeptide N-acetylgalactosaminyltransferase 2	Q10471
GALNT7	N-acetylgalactosaminyltransferase 7	Q86SF2
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase	P04406
GARS	Glycine--tRNA ligase	P41250
GATC	Glutamyl-tRNA(Gln) amidotransferase subunit C, mitochondrial	O43716
GCAT	2-amino-3-ketobutyrate coenzyme A ligase, mitochondrial	O75600
GCDH	Glutaryl-CoA dehydrogenase, mitochondrial	Q92947
GDAP1	Ganglioside-induced differentiation-associated protein 1	Q8TB36
GDI2	Rab GDP dissociation inhibitor beta	P50395
GFM2	Ribosome-releasing factor 2, mitochondrial	Q969S9
GGH	Gamma-glutamyl hydrolase	Q92820
GIGYF2	PERQ amino acid-rich with GYF domain-containing protein 2	Q6Y7W6
GIMAP1	GTPase IMAP family member 1	Q8WWP7
GIMAP5	GTPase IMAP family member 5	Q96F15
GK	Glycerol kinase	P32189
GLA	Alpha-galactosidase A	P06280
GLG1	Golgi apparatus protein 1	Q92896
GLRX3	Glutaredoxin-3	O76003
GLRX5	Glutaredoxin-related protein 5, mitochondrial	Q86SX6
GLS	Glutaminase kidney isoform, mitochondrial	O94925
GLT8D1	Glycosyltransferase 8 domain-containing protein 1	Q68CQ7
GLUD1	Glutamate dehydrogenase 1, mitochondrial	P00367
GMFG	Glia maturation factor gamma	O60234
GNAI3	Guanine nucleotide-binding protein subunit alpha-13	Q14344
GNAI2	Guanine nucleotide-binding protein G(i) subunit alpha-2	P04899
GNAI3	Guanine nucleotide-binding protein G(k) subunit alpha	P08754
GNAQ	Guanine nucleotide-binding protein G(q) subunit alpha	P50148
GNAS	Guanine nucleotide-binding protein G(s) subunit alpha isoforms short	P63092
GNB1	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-1	P62873
GNB2L1	Guanine nucleotide-binding protein subunit beta-2-like 1	P63244
GNPAT	Dihydroxyacetone phosphate acyltransferase	O15228
GNS	N-acetylglucosamine-6-sulfatase	P15586
GOLGA2	Golgin subfamily A member 2	Q08379
GOLGA3	Golgin subfamily A member 3	Q08378
GOLGA5	Golgin subfamily A member 5	Q8TBA6
GOLGA7	Golgin subfamily A member 7	Q7Z5G4
GOLGB1	Golgin subfamily B member 1	Q14789
GOLM1	Golgi membrane protein 1	Q8NBJ4

Gene	Protein name	Accession
GOPC	Golgi-associated PDZ and coiled-coil motif-containing protein	Q9HD26
GORASP2	Golgi reassembly-stacking protein 2	Q9H8Y8
GOT2	Aspartate aminotransferase, mitochondrial	P00505
GPR89A	Golgi pH regulator A	B7ZAQ6
GPR89C	Putative Golgi pH regulator C	A6NKF9
GRHPR	Glyoxylate reductase/hydroxypyruvate reductase	Q9UBQ7
GRPEL1	GrpE protein homolog 1, mitochondrial	Q9HAV7
GRPEL2	GrpE protein homolog 2, mitochondrial	Q8TAA5
GRSF1	G-rich sequence factor 1	Q12849
GSN	Gelsolin	P06396
GSR	Glutathione reductase, mitochondrial	P00390
GSTK1	Glutathione S-transferase kappa 1	Q9Y2Q3
GSTO1	Glutathione S-transferase omega-1	P78417
GSTP1	Glutathione S-transferase P	P09211
GTPBP10	GTP-binding protein 10	A4D1E9
GTPBP3	tRNA modification GTPase GTPBP3, mitochondrial	Q969Y2
GTPBP8	GTP-binding protein 8	Q8N3Z3
GUK1	Guanylate kinase	Q16774
GYPC	Glycophorin-C	P04921
H2AFV	Histone H2A.V	Q71UI9
H2AFX	Histone H2AX	P16104
H2AFY	Core histone macro-H2A.1	O75367
H2AFZ	Histone H2A.Z	P0C0S5
HADH	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial	Q16836
HADHA	Trifunctional enzyme subunit alpha, mitochondrial	P40939
HADHB	Trifunctional enzyme subunit beta, mitochondrial	P55084
HAGH	Hydroxyacylglutathione hydrolase, mitochondrial	Q16775
HARS2	Probable histidine--tRNA ligase, mitochondrial	P49590
HAUS1	HAUS augmin-like complex subunit 1	Q96CS2
HAUS4	HAUS augmin-like complex subunit 4	Q9H6D7
HAUS6	HAUS augmin-like complex subunit 6	Q7Z4H7
HAUS8	HAUS augmin-like complex subunit 8	Q9BT25
HAX1	HCLS1-associated protein X-1	O00165
HBA1;	Hemoglobin subunit alpha	P69905
HBB	Hemoglobin subunit beta	P68871
HCCS	Cytochrome c-type heme lyase	P53701
HDHD3	Haloacid dehalogenase-like hydrolase domain-containing protein 3	Q9BSH5
HEATR1	HEAT repeat-containing protein 1	Q9H583
HIBADH	3-hydroxyisobutyrate dehydrogenase, mitochondrial	P31937

Gene	Protein name	Accession
HIBCH	3-hydroxyisobutyryl-CoA hydrolase, mitochondrial	Q6NVY1
HINT2	Histidine triad nucleotide-binding protein 2, mitochondrial	Q9BX68
HIST1H1B	Histone H1.5	P16401
HIST1H1C	Histone H1.2	P16403
HIST1H2AG	Histone H2A type 1	P0C0S8
HIST1H2AH	Histone H2A type 1-H	Q96KK5
HIST1H2AJ	Histone H2A type 1-J	Q99878
HIST1H2BB	Histone H2B type 1-B	P33778
HIST1H2BC	Histone H2B type 1-C/E/F/G/I	P62807
HIST1H2BD	Histone H2B type 1-D	P58876
HIST1H2BH	Histone H2B type 1-H	Q93079
HIST1H2BJ	Histone H2B type 1-J	P06899
HIST1H4A	Histone H4	P62805
HK2	Hexokinase-2	P52789
HLA-A	HLA class I histocompatibility antigen, A-3 alpha chain	P04439
HLA-A	HLA class I histocompatibility antigen, A-25 alpha chain	P18462
HLA-A	HLA class I histocompatibility antigen, A-26 alpha chain	P30450
HLA-B	HLA class I histocompatibility antigen, B-8 alpha chain	P30460
HM13	Minor histocompatibility antigen H13	Q8TCT9
HNRNPA0	Heterogeneous nuclear ribonucleoprotein A0	Q13151
HNRNPA1	Heterogeneous nuclear ribonucleoprotein A1	P09651
HNRNPA2B1	Heterogeneous nuclear ribonucleoproteins A2/B1	P22626
HNRNPC	Heterogeneous nuclear ribonucleoproteins C1/C2	P07910
HNRNPD	Heterogeneous nuclear ribonucleoprotein D0	Q14103
HNRNPF	Heterogeneous nuclear ribonucleoprotein F	P52597
HNRNPH1	Heterogeneous nuclear ribonucleoprotein H	P31943
HNRNPH2	Heterogeneous nuclear ribonucleoprotein H2	P55795
HNRNPM	Heterogeneous nuclear ribonucleoprotein M	P52272
HPCAL1	Hippocalcin-like protein 1	P37235
HRSP12	Ribonuclease UK114	P52758
HS2ST1	Heparan sulfate 2-O-sulfotransferase 1	Q7LGA3
HSD17B10	3-hydroxyacyl-CoA dehydrogenase type-2	Q99714
HSD17B11	Estradiol 17-beta-dehydrogenase 11	Q8NBQ5
HSD17B12	Estradiol 17-beta-dehydrogenase 12	Q53GQ0
HSD17B4	Peroxisomal multifunctional enzyme type 2	P51659
HSD17B7	3-keto-steroid reductase	P56937
HSD17B8	Estradiol 17-beta-dehydrogenase 8	Q92506
HSDL1	Inactive hydroxysteroid dehydrogenase-like protein 1	Q3SXM5
HSDL2	Hydroxysteroid dehydrogenase-like protein 2	Q6YN16

Gene	Protein name	Accession
HSP90AA1	Heat shock protein HSP 90-alpha	P07900
HSP90AB1	Heat shock protein HSP 90-beta	P08238
HSP90B1	Endoplasmic	P14625
HSPA5	78 kDa glucose-regulated protein	P11021
HSPA8	Heat shock cognate 71 kDa protein	P11142
HSPD1	60 kDa heat shock protein, mitochondrial	P10809
HSPPE1	10 kDa heat shock protein, mitochondrial	P61604
HSPH1	Heat shock protein 105 kDa	Q92598
HTRA2	Serine protease HTRA2, mitochondrial	O43464
HYOU1	Hypoxia up-regulated protein 1	Q9Y4L1
IARS2	Isoleucine--tRNA ligase, mitochondrial	Q9NSE4
IBA57	Putative transferase CAF17, mitochondrial	Q5T440
ICAM2	Intercellular adhesion molecule 2	P13598
ICT1	Peptidyl-tRNA hydrolase ICT1, mitochondrial	Q14197
IDH2	Isocitrate dehydrogenase [NADP], mitochondrial	P48735
IDH3A	Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial	F50213
IDH3B	Isocitrate dehydrogenase [NAD] subunit beta, mitochondrial	O43837
IDI1	Isopentenyl-diphosphate Delta-isomerase 1	Q13907
IGLL1	Immunoglobulin lambda-like polypeptide 1	P15814
IGSF8	Immunoglobulin superfamily member 8	Q969P0
IKBIP	Inhibitor of nuclear factor kappa-B kinase-interacting protein	Q70UQ0
IMMP2L	Mitochondrial inner membrane protease subunit 2	Q96T52
IMMT	Mitochondrial inner membrane protein	Q16891
IMPAD1	Inositol monophosphatase 3	Q9NXE2
IMPDH2	Inosine-5'-monophosphate dehydrogenase 2	P12268
INA	Alpha-internexin	Q16352
INF2	Inverted formin-2	Q27J81
IPO5	Importin-5	O00410
IQGAP1	Ras GTPase-activating-like protein IQGAP1	P46940
IQGAP2	Ras GTPase-activating-like protein IQGAP2	Q13576
ISCA1	Iron-sulfur cluster assembly 1 homolog, mitochondrial	Q9BU66
ISCA2	Iron-sulfur cluster assembly 2 homolog, mitochondrial	Q86U28
ISOC2	Isochorismatase domain-containing protein 2, mitochondrial	Q96AB3
ITGAL	Integrin alpha-L	P20701
ITGB1	Integrin beta-1	P05556
ITGB2	Integrin beta-2	P05107
ITM2A	Integral membrane protein 2A	O43736
ITM2B	Integral membrane protein 2B	Q9Y287
ITPR2	Inositol 1,4,5-trisphosphate receptor type 2	Q14571

Gene	Protein name	Accession
IVD	Isovaleryl-CoA dehydrogenase, mitochondrial	P26440
JAGN1	Protein jagunal homolog 1	Q8N5M9
JAM3	Junctional adhesion molecule C	Q9BX67
JUP	Junction plakoglobin	P14923
KARS	Lysine--tRNA ligase	Q15046
KDELRL1	ER lumen protein-retaining receptor 1	P24390
KIAA0391	Mitochondrial ribonuclease P protein 3	O15091
KIAA1467	Uncharacterized protein KIAA1467	A2RU67
KIDINS220	Kinase D-interacting substrate of 220 kDa	Q9ULH0
KIF2A	Kinesin-like protein KIF2A	O00139
KIF2C	Kinesin-like protein KIF2C	Q99661
KIF4A	Chromosome-associated kinesin KIF4A	O95239
KIRREL	Kin of IRRE-like protein 1	Q96J84
KPNA2	Importin subunit alpha-1	P52292
KPNB1	Importin subunit beta-1	Q14974
KRT1	Keratin, type II cytoskeletal 1	P04264
KRT10	Keratin, type I cytoskeletal 10	P13645
KRT14	Keratin, type I cytoskeletal 14	P02533
KRT16	Keratin, type I cytoskeletal 16	P08779
KRT17	Keratin, type I cytoskeletal 17	Q04695
KRT2	Keratin, type II cytoskeletal 2 epidermal	P35908
KRT5	Keratin, type II cytoskeletal 5	P13647
KRT6A	Keratin, type II cytoskeletal 6A	P02538
KRT9	Keratin, type I cytoskeletal 9	P35527
KTN1	Kinectin	Q86UP2
LACTB	Serine beta-lactamase-like protein LACTB, mitochondrial	P83111
LAMP1	Lysosome-associated membrane glycoprotein 1	P11279
LAMP2	Lysosome-associated membrane glycoprotein 2	P13473
LAMTOR1	Ragulator complex protein LAMTOR1	Q6IAA8
LAMTOR2	Ragulator complex protein LAMTOR2	Q9Y2Q5
LAMTOR3	Ragulator complex protein LAMTOR3	Q9UHA4
LAP3	Cytosol aminopeptidase	P28838
LARP4	La-related protein 4	Q71RC2
LARS	Leucine--tRNA ligase, cytoplasmic	Q9P2J5
LARS2	Probable leucine--tRNA ligase, mitochondrial	Q15031
LAT	Linker for activation of T-cells family member 1	O43561
LBR	Lamin-B receptor	Q14739
LCK	Tyrosine-protein kinase Lck	P06239
LCP1	Plastin-2	P13796

Gene	Protein name	Accession
LDHA	L-lactate dehydrogenase A chain	P00338
LDHB	L-lactate dehydrogenase B chain	P07195
LEMD2	LEM domain-containing protein 2	Q8NC56
LEPRE1	Prolyl 3-hydroxylase 1	Q32P28
LETM1	LETM1 and EF-hand domain-containing protein 1, mitochondrial	O95202
LETMD1	LETM1 domain-containing protein 1	Q6P1Q0
LGALS3BP	Galectin-3-binding protein	Q08380
LGALS8	Galectin-8	O00214
LGALS9	Galectin-9	O00182
LIAS	Lipoyl synthase, mitochondrial	O43766
LIMD1	LIM domain-containing protein 1	Q9UGP4
LMAN1	Protein ERGIC-53	P49257
LMAN2	Vesicular integral-membrane protein VIP36	Q12907
LMAN2L	VIP36-like protein	Q9H0V9
LMNB1	Lamin-B1	P20700
LMNB2	Lamin-B2	Q03252
LMO7	LIM domain only protein 7	Q8W7W1
LNP	Protein lunapark	Q9C0E8
LNPEP	Leucyl-cystinyl aminopeptidase	Q9UIQ6
LOH12CR1	Loss of heterozygosity 12 chromosomal region 1 protein	Q969J3
LONP1	Lon protease homolog, mitochondrial	P36776
LONP2	Lon protease homolog 2, peroxisomal	Q86WA8
LPCAT1	Lysophosphatidylcholine acyltransferase 1	Q8NF37
LPCAT2	Lysophosphatidylcholine acyltransferase 2	Q7L5N7
LRPPRC	Leucine-rich PPR motif-containing protein, mitochondrial	P42704
LRRC59	Leucine-rich repeat-containing protein 59	Q96AG4
LRRC8D	Volume-regulated anion channel subunit LRRC8D	Q7L1W4
LRRFIP1	Leucine-rich repeat flightless-interacting protein 1	Q32MZ4
LSS	Lanosterol synthase	P48449
LYAR	Cell growth-regulating nucleolar protein	Q9NX58
LYRM4	LYR motif-containing protein 4	Q9HD34
MAGOH	Protein mago nashi homolog	P61326
MAGOHB	Protein mago nashi homolog 2	Q96A72
MAGT1	Magnesium transporter protein 1	Q9H0U3
MALSU1	Mitochondrial assembly of ribosomal large subunit protein 1	Q96EH3
MAN1A2	Mannosyl-oligosaccharide 1,2-alpha-mannosidase IB	O60476
MAN1B1	Endoplasmic reticulum mannosyl-oligosaccharide 1,2-alpha-mannosidase	Q9UKM7
MAN2A1	Alpha-mannosidase 2	Q16706
MANF	Mesencephalic astrocyte-derived neurotrophic factor	P55145

Gene	Protein name	Accession
MAPRE1	Microtubule-associated protein RP/EB family member 1	Q15691
MARCH5	E3 ubiquitin-protein ligase MARCH5	Q9NX47
MARCKSL1	MARCKS-related protein	P49006
MARS	Methionine--tRNA ligase, cytoplasmic	P56192
MARS2	Methionine--tRNA ligase, mitochondrial	Q96GW9
MAVS	Mitochondrial antiviral-signaling protein	Q7Z434
MBLAC2	Metallo-beta-lactamase domain-containing protein 2	Q68D91
MBOAT7	Lysophospholipid acyltransferase 7	Q96N66
MCAT	Malonyl-CoA-acyl carrier protein transacylase, mitochondrial	Q8IVS2
MCCC1	Methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial	Q96RQ3
MCCC2	Methylcrotonoyl-CoA carboxylase beta chain, mitochondrial	Q9HCC0
MCM2	DNA replication licensing factor MCM2	P49736
MCM4	DNA replication licensing factor MCM4	P33991
MCM5	DNA replication licensing factor MCM5	P33992
MCM6	DNA replication licensing factor MCM6	Q14566
MCM7	DNA replication licensing factor MCM7	P33993
MCU	Calcium uniporter protein, mitochondrial	Q8NE86
MCUR1	Mitochondrial calcium uniporter regulator 1	Q96AQ8
MDC1	Mediator of DNA damage checkpoint protein 1	Q14676
MDH1	Malate dehydrogenase, cytoplasmic	P40925
MDH2	Malate dehydrogenase, mitochondrial	P40926
ME2	NAD-dependent malic enzyme, mitochondrial	P23368
MECR	Trans-2-enoyl-CoA reductase, mitochondrial	Q9BV79
METTL15	Probable methyltransferase-like protein 15	A6NJ78
METTL17	Methyltransferase-like protein 17, mitochondrial	Q9H7H0
MFF	Mitochondrial fission factor	Q9GZY8
MFGE8	Lactadherin	Q08431
MFN1	Mitofusin-1	Q8IWA4
MFN2	Mitofusin-2	O95140
MGAT1	Alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase	P26572
MGAT2	Alpha-1,6-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase	Q10469
MGAT4A	Alpha-1,3-mannosyl-glycoprotein 4-beta-N-acetylglucosaminyltransferase A	Q9UM21
MGME1	Mitochondrial genome maintenance exonuclease 1	Q9BQP7
MGST3	Microsomal glutathione S-transferase 3	O14880
MIA3	Melanoma inhibitory activity protein 3	Q5JRA6
MIB1	E3 ubiquitin-protein ligase MIB1	Q86YT6
MICU1	Calcium uptake protein 1, mitochondrial	Q9BPX6
MICU2	Calcium uptake protein 2, mitochondrial	Q8IYU8
MIPEP	Mitochondrial intermediate peptidase	Q99797

Gene	Protein name	Accession
MKI67	Antigen KI-67	P46013
MLEC	Malectin	Q14165
MLYCD	Malonyl-CoA decarboxylase, mitochondrial	O95822
MMAA	Methylmalonic aciduria type A protein, mitochondrial	Q8IVH4
MMGT1	Membrane magnesium transporter 1	Q8N4V1
MOCS1	Molybdenum cofactor biosynthesis protein 1	Q9NZB8
MOGS	Mannosyl-oligosaccharide glucosidase	Q13724
MOV10	Putative helicase MOV-10	Q9HCE1
MPC2	Mitochondrial pyruvate carrier 2	O95563
MPP6	MAGUK p55 subfamily member 6	Q9NZW5
MPST	3-mercaptopyruvate sulfurtransferase	P25325
MRM1	rRNA methyltransferase 1, mitochondrial	Q6IN84
MRPL1	39S ribosomal protein L1, mitochondrial	Q9BYD6
MRPL11	39S ribosomal protein L11, mitochondrial	Q9Y3B7
MRPL13	39S ribosomal protein L13, mitochondrial	Q9BYD1
MRPL14	39S ribosomal protein L14, mitochondrial	Q6P1L8
MRPL15	39S ribosomal protein L15, mitochondrial	Q9P015
MRPL16	39S ribosomal protein L16, mitochondrial	Q9NX20
MRPL17	39S ribosomal protein L17, mitochondrial	Q9NRX2
MRPL18	39S ribosomal protein L18, mitochondrial	Q9H0U6
MRPL19	39S ribosomal protein L19, mitochondrial	P49406
MRPL2	39S ribosomal protein L2, mitochondrial	Q5T653
MRPL20	39S ribosomal protein L20, mitochondrial	Q9BYC9
MRPL21	39S ribosomal protein L21, mitochondrial	Q7Z2W9
MRPL22	39S ribosomal protein L22, mitochondrial	Q9NWU5
MRPL23	39S ribosomal protein L23, mitochondrial	Q16540
MRPL28	39S ribosomal protein L28, mitochondrial	Q13084
MRPL3	39S ribosomal protein L3, mitochondrial	P09001
MRPL30	39S ribosomal protein L30, mitochondrial	Q8TCC3
MRPL32	39S ribosomal protein L32, mitochondrial	Q9BYC8
MRPL37	39S ribosomal protein L37, mitochondrial	Q9BZE1
MRPL38	39S ribosomal protein L38, mitochondrial	Q96DV4
MRPL39	39S ribosomal protein L39, mitochondrial	Q9NYK5
MRPL4	39S ribosomal protein L4, mitochondrial	Q9BYD3
MRPL40	39S ribosomal protein L40, mitochondrial	Q9NQ50
MRPL41	39S ribosomal protein L41, mitochondrial	Q8IXM3
MRPL43	39S ribosomal protein L43, mitochondrial	Q8N983
MRPL44	39S ribosomal protein L44, mitochondrial	Q9H9J2
MRPL45	39S ribosomal protein L45, mitochondrial	Q9BRJ2

Gene	Protein name	Accession
MRPL46	39S ribosomal protein L46, mitochondrial	Q9H2W6
MRPL47	39S ribosomal protein L47, mitochondrial	Q9HD33
MRPL48	39S ribosomal protein L48, mitochondrial	Q96GC5
MRPL49	39S ribosomal protein L49, mitochondrial	Q13405
MRPL50	39S ribosomal protein L50, mitochondrial	Q8N5N7
MRPL55	39S ribosomal protein L55, mitochondrial	Q7Z7F7
MRPL9	39S ribosomal protein L9, mitochondrial	Q9BYD2
MRPS10	28S ribosomal protein S10, mitochondrial	P82664
MRPS11	28S ribosomal protein S11, mitochondrial	P82912
MRPS12	28S ribosomal protein S12, mitochondrial	O15235
MRPS14	28S ribosomal protein S14, mitochondrial	O60783
MRPS15	28S ribosomal protein S15, mitochondrial	P82914
MRPS16	28S ribosomal protein S16, mitochondrial	Q9Y3D3
MRPS17	28S ribosomal protein S17, mitochondrial	Q9Y2R5
MRPS18A	28S ribosomal protein S18a, mitochondrial	Q9NVS2
MRPS18B	28S ribosomal protein S18b, mitochondrial	Q9Y676
MRPS2	28S ribosomal protein S2, mitochondrial	Q9Y399
MRPS22	28S ribosomal protein S22, mitochondrial	P82650
MRPS23	28S ribosomal protein S23, mitochondrial	Q9Y3D9
MRPS24	28S ribosomal protein S24, mitochondrial	Q96EL2
MRPS25	28S ribosomal protein S25, mitochondrial	P82663
MRPS26	28S ribosomal protein S26, mitochondrial	Q9BYN8
MRPS27	28S ribosomal protein S27, mitochondrial	Q92552
MRPS28	28S ribosomal protein S28, mitochondrial	Q9Y2Q9
MRPS31	28S ribosomal protein S31, mitochondrial	Q92665
MRPS34	28S ribosomal protein S34, mitochondrial	P82930
MRPS35	28S ribosomal protein S35, mitochondrial	P82673
MRPS5	28S ribosomal protein S5, mitochondrial	P82675
MRPS6	28S ribosomal protein S6, mitochondrial	P82932
MRPS7	28S ribosomal protein S7, mitochondrial	Q9Y2R9
MRPS9	28S ribosomal protein S9, mitochondrial	P82933
MRRF	Ribosome-recycling factor, mitochondrial	Q96E11
MRS2	Magnesium transporter MRS2 homolog, mitochondrial	Q9HD23
MRT04	mRNA turnover protein 4 homolog	Q9UKD2
MSN	Moesin	P26038
MSRB2	Methionine-R-sulfoxide reductase B2, mitochondrial	Q9Y3D2
MTA2	Metastasis-associated protein MTA2	O94776
MTCH2	Mitochondrial carrier homolog 2	Q9Y6C9
MT-CO2	Cytochrome c oxidase subunit 2	P00403

Gene	Protein name	Accession
MTDH	Protein LYRIC	Q86UE4
MTERF	Transcription termination factor, mitochondrial	Q99551
MTERFD1	mTERF domain-containing protein 1, mitochondrial	Q96E29
MTERFD2	mTERF domain-containing protein 2	Q7Z6M4
MTFMT	Methionyl-tRNA formyltransferase, mitochondrial	Q96DP5
MTFP1	Mitochondrial fission process protein 1	Q9UDX5
MTFR1	Mitochondrial fission regulator 1	Q15390
MTFR2	Mitochondrial fission regulator 2	Q6P444
MTHFD1	C-1-tetrahydrofolate synthase, cytoplasmic	P11586
MTHFD1L	Monofunctional C1-tetrahydrofolate synthase, mitochondrial	Q6UB35
MTHFD2	Bifunctional methylenetetrahydrofolate dehydrogenase/cyclohydrolase, mitochondrial	P13995
MTIF2	Translation initiation factor IF-2, mitochondrial	P46199
MTIF3	Translation initiation factor IF-3, mitochondrial	Q9H2K0
MTPAP	Poly(A) RNA polymerase, mitochondrial	Q9NVV4
MTRF1	Peptide chain release factor 1, mitochondrial	O75570
MTX1	Metaxin-1	Q13505
MTX2	Metaxin-2	O75431
MUL1	Mitochondrial ubiquitin ligase activator of NFKB 1	Q969V5
MUT	Methylmalonyl-CoA mutase, mitochondrial	P22033
MYH9	Myosin-9	P35579
MYL12A	Myosin regulatory light chain 12A	P19105
MYL12B	Myosin regulatory light chain 12B	O14950
MYL6	Myosin light polypeptide 6	P60660
MYO18A	Unconventional myosin-XVIIIa	Q92614
MYO1B	Unconventional myosin-Ib	O43795
MZB1	Marginal zone B- and B1-cell-specific protein	Q8WU39
NADK2	NAD kinase 2, mitochondrial	Q4G0N4
NAPA	Alpha-soluble NSF attachment protein	P54920
NAPG	Gamma-soluble NSF attachment protein	Q99747
NBAS	Neuroblastoma-amplified sequence	A2RRP1
NCLN	Nicalin	Q969V3
NCSTN	Nicastrin	Q92542
NDUFA10	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10, mitochondrial	O95299
NDUFA11	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 11	Q86Y39
NDUFA12	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 12	Q9UI09
NDUFA13	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13	Q9P0J0
NDUFA2	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 2	O43678

Gene	Protein name	Accession
NDUFA5	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 5	Q16718
NDUFA6	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 6	P56556
NDUFA7	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 7	O95182
NDUFA8	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 8	P51970
NDUFAF1	Complex I intermediate-associated protein 30, mitochondrial	Q9Y375
NDUFAF2	Mimitin, mitochondrial	Q8N183
NDUFAF3	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 3	Q9BU61
NDUFAF4	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 4	Q9P032
NDUFAF5	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 5	Q5TEU4
NDUFB10	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 10	O96000
NDUFB11	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 11, mitochondrial	Q9NX14
NDUFB3	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 3	O43676
NDUFB4	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 4	O95168
NDUFB5	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 5, mitochondrial	O43674
NDUFB6	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 6	O95139
NDUFB7	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 7	P17568
NDUFB8	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 8, mitochondrial	O95169
NDUFB9	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 9	Q9Y6M9
NDUFC2	NADH dehydrogenase [ubiquinone] 1 subunit C2	O95298
NDUFS1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	P28331
NDUFS2	NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial	O75306
NDUFS3	NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial	O75489
NDUFS4	NADH dehydrogenase [ubiquinone] iron-sulfur protein 4, mitochondrial	O43181
NDUFS6	NADH dehydrogenase [ubiquinone] iron-sulfur protein 6, mitochondrial	O75380
NDUFS7	NADH dehydrogenase [ubiquinone] iron-sulfur protein 7, mitochondrial	O75251
NDUFV1	NADH dehydrogenase [ubiquinone] flavoprotein 1, mitochondrial	P49821
NDUFV2	NADH dehydrogenase [ubiquinone] flavoprotein 2, mitochondrial	P19404
NEDD1	Protein NEDD1	Q8NHV4
NEK2	Serine/threonine-protein kinase Nek2	P51955
NENF	Neudesin	Q9UMX5
NFS1	Cysteine desulfurase, mitochondrial	Q9Y697
NFU1	NFU1 iron-sulfur cluster scaffold homolog, mitochondrial	Q9UMS0
NFXL1	NF-X1-type zinc finger protein NFXL1	Q6ZNB6
NGRN	Neugrin	Q9NPE2
NHP2	H/ACA ribonucleoprotein complex subunit 2	Q9NX24
NHP2L1	NHP2-like protein 1	P55769

Gene	Protein name	Accession
NIN	Ninein	Q8N4C6
NIPSNAP1	Protein NipSnap homolog 1	Q9BPW8
NISCH	Nischarin	Q9Y2I1
NIT1	Nitrilase homolog 1	Q86X76
NLN	Neurolysin, mitochondrial	Q9BYT8
NME4	Nucleoside diphosphate kinase, mitochondrial	O00746
NOA1	Nitric oxide-associated protein 1	Q8NC60
NOC2L	Nucleolar complex protein 2 homolog	Q9Y3T9
NOLC1	Nucleolar and coiled-body phosphoprotein 1	Q14978
NOMO2	Nodal modulator 2	Q5JPE7
NONO	Non-POU domain-containing octamer-binding protein	Q15233
NOP2	Putative ribosomal RNA methyltransferase NOP2	P46087
NOP58	Nucleolar protein 58	Q9Y2X3
NPC1	Niemann-Pick C1 protein	O15118
NPEPPS	Puromycin-sensitive aminopeptidase	P55786
NPM1	Nucleophosmin	P06748
NSDHL	Sterol-4-alpha-carboxylate 3-dehydrogenase, decarboxylating	Q15738
NSF	Vesicle-fusing ATPase	P46459
NSUN2	tRNA	Q08J23
NT5C3A	Cytosolic 5'-nucleotidase 3A	Q9H0P0
NT5DC2	5'-nucleotidase domain-containing protein 2	Q9H857
NTPCR	Cancer-related nucleoside-triphosphatase	Q9BSD7
NUBPL	Iron-sulfur protein NUBPL	Q8TB37
NUCB2	Nucleobindin-2	P80303
NUDC	Nuclear migration protein nudC	Q9Y266
NUDT1	7,8-dihydro-8-oxoguanine triphosphatase	P36639
NUDT6	Nucleoside diphosphate-linked moiety X motif 6	P53370
NUFIP2	Nuclear fragile X mental retardation-interacting protein 2	Q7Z417
NUMA1	Nuclear mitotic apparatus protein 1	Q14980
NUP107	Nuclear pore complex protein Nup107	P57740
NUP153	Nuclear pore complex protein Nup153	P49790
NUP155	Nuclear pore complex protein Nup155	O75694
NUP205	Nuclear pore complex protein Nup205	Q92621
NUP210	Nuclear pore membrane glycoprotein 210	Q8TEM1
NUP214	Nuclear pore complex protein Nup214	P35658
NUP35	Nucleoporin NUP53	Q8NFFH5
NUP54	Nucleoporin p54	Q7Z3B4
NUP93	Nuclear pore complex protein Nup93	Q8N1F7
NUP98	Nuclear pore complex protein Nup98-Nup96	P52948

Gene	Protein name	Accession
OAT	Ornithine aminotransferase, mitochondrial	P04181
OCIAD1	OCIA domain-containing protein 1	Q9NX40
OCIAD2	OCIA domain-containing protein 2	Q56VL3
ODF2	Outer dense fiber protein 2	Q5BJF6
OGDH	2-oxoglutarate dehydrogenase, mitochondrial	Q02218
OMA1	Metalloendopeptidase OMA1, mitochondrial	Q96E52
OPA1	Dynamin-like 120 kDa protein, mitochondrial	O60313
OPA3	Optic atrophy 3 protein	Q9H6K4
OSBP	Oxysterol-binding protein 1	P22059
OSBPL8	Oxysterol-binding protein-related protein 8	Q9BZF1
OSBPL9	Oxysterol-binding protein-related protein 9	Q96SU4
OSTC	Oligosaccharyltransferase complex subunit OSTC	Q9NRP0
OXA1L	Mitochondrial inner membrane protein OXA1L	Q15070
OXCT1	Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial	P55809
OXSM	3-oxoacyl-[acyl-carrier-protein] synthase, mitochondrial	Q9NWXU1
OXSR1	Serine/threonine-protein kinase OSR1	O95747
P4HB	Protein disulfide-isomerase	P07237
PABPC1	Polyadenylate-binding protein 1	P11940
PAG1	Phosphoprotein associated with glycosphingolipid-enriched microdomains 1	Q9NWXQ8
PAICS	Multifunctional protein ADE2	P22234
PAM16	Mitochondrial import inner membrane translocase subunit TIM16	Q9Y3D7
PARP1	Poly [ADP-ribose] polymerase 1	P09874
PARS2	Probable proline--tRNA ligase, mitochondrial	Q7L3T8
PC	Pyruvate carboxylase, mitochondrial	P11498
PCBP1	Poly(rC)-binding protein 1	Q15365
PCBP2	Poly(rC)-binding protein 2	Q15366
PCCA	Propionyl-CoA carboxylase alpha chain, mitochondrial	P05165
PCCB	Propionyl-CoA carboxylase beta chain, mitochondrial	P05166
PCM1	Pericentriolar material 1 protein	Q15154
PCNA	Proliferating cell nuclear antigen	P12004
PCNT	Pericentrin	O95613
PDCD6IP	Programmed cell death 6-interacting protein	Q8WUM4
PDE12	2',5'-phosphodiesterase 12	Q6L8Q7
PDHA1	Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial	P08559
PDHB	Pyruvate dehydrogenase E1 component subunit beta, mitochondrial	P11177
PDHX	Pyruvate dehydrogenase protein X component, mitochondrial	O00330
PDIA3	Protein disulfide-isomerase A3	P30101
PDIA4	Protein disulfide-isomerase A4	P13667

Gene	Protein name	Accession
PDIA6	Protein disulfide-isomerase A6	Q15084
PDK2	[Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 2, mitochondrial	Q15119
PDK3	[Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 3, mitochondrial	Q15120
PDP2	[Pyruvate dehydrogenase [acetyl-transferring]]-phosphatase 2, mitochondrial	Q9P2J9
PDPFR	Pyruvate dehydrogenase phosphatase regulatory subunit, mitochondrial	Q8NCN5
PDS5A	Sister chromatid cohesion protein PDS5 homolog A	Q29RF7
PDS5B	Sister chromatid cohesion protein PDS5 homolog B	Q9NTI5
PDSS1	Decaprenyl-diphosphate synthase subunit 1	Q5T2R2
PDZD11	PDZ domain-containing protein 11	Q5EBL8
PECAM1	Platelet endothelial cell adhesion molecule	P16284
PECR	Peroxisomal trans-2-enoyl-CoA reductase	Q9BY49
PELO	Protein pelota homolog	Q9BRX2
PEX11B	Peroxisomal membrane protein 11B	O96011
PEX13	Peroxisomal membrane protein PEX13	Q92968
PEX14	Peroxisomal membrane protein PEX14	O75381
PEX16	Peroxisomal membrane protein PEX16	Q9Y5Y5
PEX2	Peroxisome biogenesis factor 2	P28328
PEX3	Peroxisomal biogenesis factor 3	P56589
PFDN2	Prefoldin subunit 2	Q9UHV9
PFKP	ATP-dependent 6-phosphofructokinase, platelet type	Q01813
PFN1	Profilin-1	P07737
PGAM5	Serine/threonine-protein phosphatase PGAM5, mitochondrial	Q96HS1
PGK1	Phosphoglycerate kinase 1	P00558
PGRMC1	Membrane-associated progesterone receptor component 1	O00264
PGRMC2	Membrane-associated progesterone receptor component 2	O15173
PGS1	CDP-diacylglycerol--glycerol-3-phosphate 3-phosphatidyltransferase, mitochondrial	Q32NB8
PHB	Prohibitin	P35232
PHB2	Prohibitin-2	Q99623
PHGDH	D-3-phosphoglycerate dehydrogenase	O43175
PI4K2A	Phosphatidylinositol 4-kinase type 2-alpha	Q9BTU6
PIEZO1	Piezo-type mechanosensitive ion channel component 1	Q92508
PIGG	GPI ethanolamine phosphate transferase 2	Q5H8A4
PIGU	Phosphatidylinositol glycan anchor biosynthesis class U protein	Q9H490
PIP4K2A	Phosphatidylinositol 5-phosphate 4-kinase type-2 alpha	P48426
PIP4K2B	Phosphatidylinositol 5-phosphate 4-kinase type-2 beta	P78356
PIP5K1A	Phosphatidylinositol 4-phosphate 5-kinase type-1 alpha	Q99755

Gene	Protein name	Accession
PITPNB	Phosphatidylinositol transfer protein beta isoform	P48739
PITRM1	Presequence protease, mitochondrial	Q5JRX3
PKM	Pyruvate kinase PKM	P14618
PKP4	Plakophilin-4	Q99569
PLD3	Phospholipase D3	Q8IV08
PLEC	Plectin	Q15149
PLGRKT	Plasminogen receptor	Q9HBL7
PLK1	Serine/threonine-protein kinase PLK1	P53350
PMPCA	Mitochondrial-processing peptidase subunit alpha	Q10713
PMPCB	Mitochondrial-processing peptidase subunit beta	O75439
PMVK	Phosphomevalonate kinase	Q15126
PNO1	RNA-binding protein PNO1	Q9NRX1
PNPLA6	Neuropathy target esterase	Q8IY17
PNPO	Pyridoxine-5'-phosphate oxidase	Q9NVS9
PNPT1	Polyribonucleotide nucleotidyltransferase 1, mitochondrial	Q8TCS8
POC5	Centrosomal protein POC5	Q8NA72
POGLUT1	Protein O-glucosyltransferase 1	Q8NBL1
POLDIP2	Polymerase delta-interacting protein 2	Q9Y2S7
POLDIP3	Polymerase delta-interacting protein 3	Q9BY77
POLG2	DNA polymerase subunit gamma-2, mitochondrial	Q9UHN1
POLR2H	DNA-directed RNA polymerases I, II, and III subunit RPABC3	P52434
POLRMT	DNA-directed RNA polymerase, mitochondrial	O00411
POR	NADPH--cytochrome P450 reductase	P16435
PPA2	Inorganic pyrophosphatase 2, mitochondrial	Q9H2U2
PPIA	Peptidyl-prolyl cis-trans isomerase A	P62937
PPIB	Peptidyl-prolyl cis-trans isomerase B	P23284
PPIF	Peptidyl-prolyl cis-trans isomerase F, mitochondrial	P30405
PPOX	Protoporphyrinogen oxidase	P50336
PPP1CA	Serine/threonine-protein phosphatase PP1-alpha catalytic subunit	P62136
PPP2R1B	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A beta isoform	P30154
PPT1	Palmitoyl-protein thioesterase 1	P50897
PPTC7	Protein phosphatase PTC7 homolog	Q8NI37
PRAF2	PRA1 family protein 2	O60831
PRCP	Lysosomal Pro-X carboxypeptidase	P42785
PRDX1	Peroxioredoxin-1	Q06830
PRDX2	Peroxioredoxin-2	P32119
PRDX3	Thioredoxin-dependent peroxide reductase, mitochondrial	P30048
PRDX4	Peroxioredoxin-4	Q13162

Gene	Protein name	Accession
PRDX5	Peroxisiredoxin-5, mitochondrial	P30044
PREB	Prolactin regulatory element-binding protein	Q9HCU5
PRKAG1	5'-AMP-activated protein kinase subunit gamma-1	P54619
PRKAR1A	cAMP-dependent protein kinase type I-alpha regulatory subunit	P10644
PRKCA	Protein kinase C alpha type	P17252
PRKCSH	Glucosidase 2 subunit beta	P14314
PRKDC	DNA-dependent protein kinase catalytic subunit	P78527
PRMT1	Protein arginine N-methyltransferase 1	Q99873
PROSC	Proline synthase co-transcribed bacterial homolog protein	O94903
PRPF6	Pre-mRNA-processing factor 6	O94906
PRPF8	Pre-mRNA-processing-splicing factor 8	Q6P2Q9
PSAP	Prosaposin	P07602
PSEN1	Presenilin-1	P49768
PSIP1	PC4 and SFRS1-interacting protein	O75475
PSMA6	Proteasome subunit alpha type-6	P60900
PSMC2	26S protease regulatory subunit 7	P35998
PSMC4	26S protease regulatory subunit 6B	P43686
PSMC5	26S protease regulatory subunit 8	P62195
PSMD11	26S proteasome non-ATPase regulatory subunit 11	O00231
PSMD13	26S proteasome non-ATPase regulatory subunit 13	Q9UNM6
PSME1	Proteasome activator complex subunit 1	Q06323
PSME2	Proteasome activator complex subunit 2	Q9UL46
PTBP1	Polypyrimidine tract-binding protein 1	P26599
PTCD2	Pentatricopeptide repeat-containing protein 2, mitochondrial	Q8WV60
PTCD3	Pentatricopeptide repeat domain-containing protein 3, mitochondrial	Q96EY7
PTGES2	Prostaglandin E synthase 2	Q9H7Z7
PTK7	Inactive tyrosine-protein kinase 7	Q13308
PTPMT1	Phosphatidylglycerophosphatase and protein-tyrosine phosphatase 1	Q8WUK0
PTPN1	Tyrosine-protein phosphatase non-receptor type 1	P18031
PTPRC	Receptor-type tyrosine-protein phosphatase C	P08575
PTPRCAP	Protein tyrosine phosphatase receptor type C-associated protein	Q14761
PTRH1	Probable peptidyl-tRNA hydrolase	Q86Y79
PTRH2	Peptidyl-tRNA hydrolase 2, mitochondrial	Q9Y3E5
PTRHD1	Putative peptidyl-tRNA hydrolase PTRHD1	Q6GMV3
PUS1	tRNA pseudouridine synthase A, mitochondrial	Q9Y606
PUSL1	tRNA pseudouridine synthase-like 1	Q8N0Z8
PYCR1	Pyrroline-5-carboxylate reductase 1, mitochondrial	P32322
PYCR2	Pyrroline-5-carboxylate reductase 2	Q96C36
QARS	Glutamine--tRNA ligase	P47897

Gene	Protein name	Accession
QPCTL	Glutaminy-peptide cyclotransferase-like protein	Q9NXS2
QRSL1	Glutamyl-tRNA(Gln) amidotransferase subunit A, mitochondrial	Q9H0R6
QSOX2	Sulfhydryl oxidase 2	Q6ZRP7
QTRTD1	Queuine tRNA-ribosyltransferase subunit QTRTD1	Q9H974
RAB10	Ras-related protein Rab-10	P61026
RAB11B	Ras-related protein Rab-11B	Q15907
RAB11FIP1	Rab11 family-interacting protein 1	Q6WKZ4
RAB14	Ras-related protein Rab-14	P61106
RAB18	Ras-related protein Rab-18	Q9NP72
RAB1A	Ras-related protein Rab-1A	P62820
RAB1B	Ras-related protein Rab-1B	Q9H0U4
RAB21	Ras-related protein Rab-21	Q9UL25
RAB24	Ras-related protein Rab-24	Q969Q5
RAB27A	Ras-related protein Rab-27A	P51159
RAB2A	Ras-related protein Rab-2A	P61019
RAB2B	Ras-related protein Rab-2B	Q8WUD1
RAB35	Ras-related protein Rab-35	Q15286
RAB37	Ras-related protein Rab-37	Q96AX2
RAB43	Ras-related protein Rab-43	Q86YS6
RAB4A	Ras-related protein Rab-4A	P20338
RAB5A	Ras-related protein Rab-5A	P20339
RAB5B	Ras-related protein Rab-5B	P61020
RAB5C	Ras-related protein Rab-5C	P51148
RAB6A	Ras-related protein Rab-6A	P20340
RAB7A	Ras-related protein Rab-7a	P51149
RAB8A	Ras-related protein Rab-8A	P61006
RAB8B	Ras-related protein Rab-8B	Q92930
RAB9A	Ras-related protein Rab-9A	P51151
RABAC1	Prenylated Rab acceptor protein 1	Q9UI14
RAC1	Ras-related C3 botulinum toxin substrate 1	P63000
RACGAP1	Rac GTPase-activating protein 1	Q9H0H5
RALA	Ras-related protein Ral-A	P11233
RALY	RNA-binding protein Raly	Q9UKM9
RANBP2	E3 SUMO-protein ligase RanBP2	P49792
RANGAP1	Ran GTPase-activating protein 1	P46060
RAP1B	Ras-related protein Rap-1b	P61224
RAP2A	Ras-related protein Rap-2a	P10114
RAP2B	Ras-related protein Rap-2b	P61225
RARS2	Probable arginine--tRNA ligase, mitochondrial	Q5T160

Gene	Protein name	Accession
RASA3	Ras GTPase-activating protein 3	Q14644
RASAL3	RAS protein activator like-3	Q86YV0
RBFA	Putative ribosome-binding factor A, mitochondrial	Q8NOV3
RBM14	RNA-binding protein 14	Q96PK6
RBM28	RNA-binding protein 28	Q9NW13
RBM39	RNA-binding protein 39	Q14498
RBM4	RNA-binding protein 4	Q9BWF3
RBMX	RNA-binding motif protein, X chromosome	P38159
RCL1	RNA 3'-terminal phosphate cyclase-like protein	Q9Y2P8
RCN1	Reticulocalbin-1	Q15293
RCN2	Reticulocalbin-2	Q14257
RDH11	Retinol dehydrogenase 11	Q8TC12
RDH13	Retinol dehydrogenase 13	Q8NBN7
RDH14	Retinol dehydrogenase 14	Q9HBH5
REEP4	Receptor expression-enhancing protein 4	Q9H6H4
REEP5	Receptor expression-enhancing protein 5	Q00765
REEP6	Receptor expression-enhancing protein 6	Q96HR9
REXO2	Oligoribonuclease, mitochondrial	Q9Y3B8
RFC2	Replication factor C subunit 2	P35250
RFC3	Replication factor C subunit 3	P40938
RFC4	Replication factor C subunit 4	P35249
RFC5	Replication factor C subunit 5	P40937
RFTN1	Raftlin	Q14699
RHOA	Transforming protein RhoA	P61586
RHOG	Rho-related GTP-binding protein RhoG	P84095
RHOT1	Mitochondrial Rho GTPase 1	Q8IXI2
RHOT2	Mitochondrial Rho GTPase 2	Q8IXI1
RLTPR	Leucine-rich repeat-containing protein 16C	Q6F5E8
RMDN3	Regulator of microtubule dynamics protein 3	Q96TC7
RMND1	Required for meiotic nuclear division protein 1 homolog	Q9NWS8
RNASEH2A	Ribonuclease H2 subunit A	O75792
RNF130	E3 ubiquitin-protein ligase RNF130	Q86XS8
RNF213	E3 ubiquitin-protein ligase RNF213	Q63HN8
RNMTL1	RNA methyltransferase-like protein 1	Q9HC36
RP2	Protein XRP2	O75695
RPA3	Replication protein A 14 kDa subunit	P35244
RPF2	Ribosome production factor 2 homolog	Q9H7B2
RPIA	Ribose-5-phosphate isomerase	P49247
RPL10A	60S ribosomal protein L10a	P62906

Gene	Protein name	Accession
RPL11	60S ribosomal protein L11	P62913
RPL12	60S ribosomal protein L12	P30050
RPL13	60S ribosomal protein L13	P26373
RPL15	60S ribosomal protein L15	P61313
RPL17	60S ribosomal protein L17	P18621
RPL18	60S ribosomal protein L18	Q07020
RPL22	60S ribosomal protein L22	P35268
RPL23A	60S ribosomal protein L23a	P62750
RPL24	60S ribosomal protein L24	P83731
RPL26	60S ribosomal protein L26	P61254
RPL27	60S ribosomal protein L27	P61353
RPL27A	60S ribosomal protein L27a	P46776
RPL28	60S ribosomal protein L28	P46779
RPL3	60S ribosomal protein L3	P39023
RPL31	60S ribosomal protein L31	P62899
RPL34	60S ribosomal protein L34	P49207
RPL35	60S ribosomal protein L35	P42766
RPL35A	60S ribosomal protein L35a	P18077
RPL38	60S ribosomal protein L38	P63173
RPL4	60S ribosomal protein L4	P36578
RPL6	60S ribosomal protein L6	Q02878
RPL7	60S ribosomal protein L7	P18124
RPL7A	60S ribosomal protein L7a	P62424
RPL8	60S ribosomal protein L8	P62917
RPL9	60S ribosomal protein L9	P32969
RPLP0	60S acidic ribosomal protein P0	P05388
RPLP2	60S acidic ribosomal protein P2	P05387
RPN1	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1	P04843
RPN2	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 2	P04844
RPRD1B	Regulation of nuclear pre-mRNA domain-containing protein 1B	Q9NQG5
RPS10	40S ribosomal protein S10	P46783
RPS11	40S ribosomal protein S11	P62280
RPS13	40S ribosomal protein S13	P62277
RPS14	40S ribosomal protein S14	P62263
RPS15A	40S ribosomal protein S15a	P62244
RPS16	40S ribosomal protein S16	P62249
RPS17	40S ribosomal protein S17	P08708
RPS17L	40S ribosomal protein S17-like	P0CW22
RPS18	40S ribosomal protein S18	P62269

Gene	Protein name	Accession
RPS19	40S ribosomal protein S19	P39019
RPS2	40S ribosomal protein S2	P15880
RPS20	40S ribosomal protein S20	P60866
RPS23	40S ribosomal protein S23	P62266
RPS24	40S ribosomal protein S24	P62847
RPS25	40S ribosomal protein S25	P62851
RPS26	40S ribosomal protein S26	P62854
RPS27	40S ribosomal protein S27	P42677
RPS27A	Ubiquitin-40S ribosomal protein S27a	P62979
RPS3	40S ribosomal protein S3	P23396
RPS3A	40S ribosomal protein S3a	P61247
RPS4X	40S ribosomal protein S4, X isoform	P62701
RPS6	40S ribosomal protein S6	P62753
RPS7	40S ribosomal protein S7	P62081
RPS8	40S ribosomal protein S8	P62241
RPS9	40S ribosomal protein S9	P46781
RPSA	40S ribosomal protein SA	P08865
RPUSD3	RNA pseudouridylation synthase domain-containing protein 3	Q6P087
RRAGA	Ras-related GTP-binding protein A	Q7L523
RRP1	Ribosomal RNA processing protein 1 homolog A	P56182
RRP1B	Ribosomal RNA processing protein 1 homolog B	Q14684
RSAD1	Radical S-adenosyl methionine domain-containing protein 1, mitochondrial	Q9HA92
RTN3	Reticulon-3	O95197
RTN4	Reticulon-4	Q9NQC3
RTN4IP1	Reticulon-4-interacting protein 1, mitochondrial	Q8WWV3
RUFY1	RUN and FYVE domain-containing protein 1	Q96T51
RUVBL1	RuvB-like 1	Q9Y265
RUVBL2	RuvB-like 2	Q9Y230
SACM1L	Phosphatidylinositol phosphatase SAC1	Q9NTJ5
SAFB	Scaffold attachment factor B1	Q15424
SAP18	Histone deacetylase complex subunit SAP18	O00422
SARS2	Serine--tRNA ligase, mitochondrial	Q9NP81
SART1	U4/U6.U5 tri-snRNP-associated protein 1	O43290
SBF1	Myotubularin-related protein 5	O95248
SCAMP1	Secretory carrier-associated membrane protein 1	O15126
SCAMP2	Secretory carrier-associated membrane protein 2	O15127
SCAMP3	Secretory carrier-associated membrane protein 3	O14828
SCCPDH	Saccharopine dehydrogenase-like oxidoreductase	Q8NBX0
SCD5	Stearoyl-CoA desaturase 5	Q86SK9

Gene	Protein name	Accession
SCO1	Protein SCO1 homolog, mitochondrial	O75880
SCO2	Protein SCO2 homolog, mitochondrial	O43819
SCP2	Non-specific lipid-transfer protein	P22307
SCPEP1	Retinoid-inducible serine carboxypeptidase	Q9HB40
SCRIB	Protein scribble homolog	Q14160
SDCBP	Syntenin-1	O00560
SDF4	45 kDa calcium-binding protein	Q9BRK5
SDHA	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	P31040
SDHAF2	Succinate dehydrogenase assembly factor 2, mitochondrial	Q9NX18
SDHB	Succinate dehydrogenase [ubiquinone] iron-sulfur subunit, mitochondrial	P21912
SDR39U1	Epimerase family protein SDR39U1	Q9NRG7
SEC11A	Signal peptidase complex catalytic subunit SEC11A	P67812
SEC11C	Signal peptidase complex catalytic subunit SEC11C	Q9BY50
SEC22B	Vesicle-trafficking protein SEC22b	O75396
SEC23B	Protein transport protein Sec23B	Q15437
SEC24B	Protein transport protein Sec24B	O95487
SEC61A1	Protein transport protein Sec61 subunit alpha isoform 1	P61619
SEC62	Translocation protein SEC62	Q99442
SEC63	Translocation protein SEC63 homolog	Q9UGP8
SEL1L	Protein sel-1 homolog 1	Q9UBV2
SELPLG	P-selectin glycoprotein ligand 1	Q14242
SEP15	15 kDa selenoprotein	O60613
SERBP1	Plasminogen activator inhibitor 1 RNA-binding protein	Q8NC51
SERINC1	Serine incorporator 1	Q9NRX5
SERPINH1	Serpin H1	P50454
SF3B1	Splicing factor 3B subunit 1	O75533
SF3B3	Splicing factor 3B subunit 3	Q15393
SF3B6	Splicing factor 3B subunit 6	Q9Y3B4
SFT2D2	Vesicle transport protein SFT2B	O95562
SFT2D3	Vesicle transport protein SFT2C	Q58719
SFXN1	Sideroflexin-1	Q9H9B4
SFXN2	Sideroflexin-2	Q96NB2
SFXN3	Sideroflexin-3	Q9BWM7
SFXN4	Sideroflexin-4	Q6P4A7
SGPL1	Sphingosine-1-phosphate lyase 1	O95470
SIGMAR1	Sigma non-opioid intracellular receptor 1	Q99720
SIRT5	NAD-dependent protein deacetylase sirtuin-5, mitochondrial	Q9NXA8
SIT1	Signaling threshold-regulating transmembrane adapter 1	Q9Y3P8
SLAIN2	SLAIN motif-containing protein 2	Q9P270

Gene	Protein name	Accession
SLC12A2	Solute carrier family 12 member 2	P55011
SLC12A7	Solute carrier family 12 member 7	Q9Y666
SLC16A1	Monocarboxylate transporter 1	P53985
SLC16A7	Monocarboxylate transporter 2	O60669
SLC19A1	Folate transporter 1	P41440
SLC1A4	Neutral amino acid transporter A	P43007
SLC25A1	Tricarboxylate transport protein, mitochondrial	P53007
SLC25A11	Mitochondrial 2-oxoglutarate/malate carrier protein	Q02978
SLC25A12	Calcium-binding mitochondrial carrier protein Aralar1	O75746
SLC25A13	Calcium-binding mitochondrial carrier protein Aralar2	Q9UJS0
SLC25A19	Mitochondrial thiamine pyrophosphate carrier	Q9HC21
SLC25A20	Mitochondrial carnitine/acylcarnitine carrier protein	O43772
SLC25A22	Mitochondrial glutamate carrier 1	Q9H936
SLC25A24	Calcium-binding mitochondrial carrier protein SCaMC-1	Q6NUK1
SLC25A29	Mitochondrial basic amino acids transporter	Q8N8R3
SLC25A3	Phosphate carrier protein, mitochondrial	Q00325
SLC25A32	Mitochondrial folate transporter/carrier	Q9H2D1
SLC25A33	Solute carrier family 25 member 33	Q9BSK2
SLC25A4	ADP/ATP translocase 1	P12235
SLC25A46	Solute carrier family 25 member 46	Q96AG3
SLC25A51	Solute carrier family 25 member 51	Q9H1U9
SLC25A52	Solute carrier family 25 member 52	Q3SY17
SLC25A6	ADP/ATP translocase 3	P12236
SLC27A4	Long-chain fatty acid transport protein 4	Q6P1M0
SLC29A1	Equilibrative nucleoside transporter 1	Q99808
SLC2A1	Solute carrier family 2, facilitated glucose transporter member 1	P11166
SLC2A3	Solute carrier family 2, facilitated glucose transporter member 3	P11169
SLC35B2	Adenosine 3'-phospho 5'-phosphosulfate transporter 1	Q8TB61
SLC35E2B	Solute carrier family 35 member E2B	P0CK96
SLC35F2	Solute carrier family 35 member F2	Q8IXU6
SLC38A1	Sodium-coupled neutral amino acid transporter 1	Q9H2H9
SLC38A10	Putative sodium-coupled neutral amino acid transporter 10	Q9HBR0
SLC38A2	Sodium-coupled neutral amino acid transporter 2	Q96QD8
SLC39A14	Zinc transporter ZIP14	Q15043
SLC3A2	4F2 cell-surface antigen heavy chain	P08195
SLC7A5	Large neutral amino acids transporter small subunit 1	Q01650
SLC9A3R1	Na(+)/H(+) exchange regulatory cofactor NHE-RF1	O14745
SLIRP	SRA stem-loop-interacting RNA-binding protein, mitochondrial	Q9GZT3
SLMAP	Sarcolemmal membrane-associated protein	Q14BN4

Gene	Protein name	Accession
SMARCA5	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A member 5	O60264
SMC2	Structural maintenance of chromosomes protein 2	O95347
SMC4	Structural maintenance of chromosomes protein 4	Q9NTJ3
SMIM12	Small integral membrane protein 12	Q96EX1
SMPD4	Sphingomyelin phosphodiesterase 4	Q9NXE4
SNAP23	Synaptosomal-associated protein 23	O00161
SNAP29	Synaptosomal-associated protein 29	O95721
SNAPIN	SNARE-associated protein Snapin	O95295
SND1	Staphylococcal nuclease domain-containing protein 1	Q7KZF4
SNRNP200	U5 small nuclear ribonucleoprotein 200 kDa helicase	O75643
SNRPD1	Small nuclear ribonucleoprotein Sm D1	P62314
SNRPD2	Small nuclear ribonucleoprotein Sm D2	P62316
SNX3	Sorting nexin-3	O60493
SOAT1	Sterol O-acyltransferase 1	P35610
SPAG5	Sperm-associated antigen 5	Q96R06
SPCS2	Signal peptidase complex subunit 2	Q15005
SPCS3	Signal peptidase complex subunit 3	P61009
SPICE1	Spindle and centriole-associated protein 1	Q8N0Z3
SPN	Leukosialin	P16150
SPR	Sepiapterin reductase	P35270
SPRYD4	SPRY domain-containing protein 4	Q8WW59
SPRYD7	SPRY domain-containing protein 7	Q5W111
SPTAN1	Spectrin alpha chain, non-erythrocytic 1	Q13813
SPTBN1	Spectrin beta chain, non-erythrocytic 1	Q01082
SPTBN2	Spectrin beta chain, non-erythrocytic 2	O15020
SPTLC1	Serine palmitoyltransferase 1	O15269
SPTLC2	Serine palmitoyltransferase 2	O15270
SQRDL	Sulfide:quinone oxidoreductase, mitochondrial	Q9Y6N5
SREBF2	Sterol regulatory element-binding protein 2	Q12772
SRP14	Signal recognition particle 14 kDa protein	P37108
SRP19	Signal recognition particle 19 kDa protein	P09132
SRP54	Signal recognition particle 54 kDa protein	P61011
SRP68	Signal recognition particle subunit SRP68	Q9UHB9
SRP72	Signal recognition particle subunit SRP72	O76094
SRPRB	Signal recognition particle receptor subunit beta	Q9Y5M8
SRSF3	Serine/arginine-rich splicing factor 3	P84103
SSBP1	Single-stranded DNA-binding protein, mitochondrial	Q04837
SSR1	Translocon-associated protein subunit alpha	P43307

Gene	Protein name	Accession
SSR3	Translocon-associated protein subunit gamma	Q9UNL2
SSR4	Translocon-associated protein subunit delta	P51571
SSRP1	FACT complex subunit SSRP1	Q08945
STARD3NL	MLN64 N-terminal domain homolog	O95772
STIM1	Stromal interaction molecule 1	Q13586
STMN1	Stathmin	P16949
STOM	Erythrocyte band 7 integral membrane protein	P27105
STOML2	Stomatin-like protein 2, mitochondrial	Q9UJZ1
STRN	Striatin	O43815
STT3A	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT3A	P46977
STT3B	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT3B	Q8TCJ2
STUB1	E3 ubiquitin-protein ligase CHIP	Q9UNE7
STX10	Syntaxin-10	O60499
STX12	Syntaxin-12	Q86Y82
STX16	Syntaxin-16	O14662
STX18	Syntaxin-18	Q9P2W9
STX2	Syntaxin-2	P32856
STX3	Syntaxin-3	Q13277
STX4	Syntaxin-4	Q12846
STX5	Syntaxin-5	Q13190
STX6	Syntaxin-6	O43752
STX7	Syntaxin-7	O15400
STX8	Syntaxin-8	Q9UNK0
SUCLG1	Succinyl-CoA ligase [ADP/GDP-forming] subunit alpha, mitochondrial	P53597
SUCLG2	Succinyl-CoA ligase [GDP-forming] subunit beta, mitochondrial	Q96199
SUGT1	Suppressor of G2 allele of SKP1 homolog	Q9Y2Z0
SUMF2	Sulfatase-modifying factor 2	Q8NBJ7
SUPT16H	FACT complex subunit SPT16	Q9Y5B9
SUPV3L1	ATP-dependent RNA helicase SUPV3L1, mitochondrial	Q8IYB8
SURF1	Surfeit locus protein 1	Q15526
SVIP	Small VCP/p97-interacting protein	Q8NHG7
SYNGR2	Synaptogyrin-2	O43760
SYNJ2BP	Synaptojanin-2-binding protein	P57105
SYPL1	Synaptophysin-like protein 1	Q16563
TACC1	Transforming acidic coiled-coil-containing protein 1	O75410
TACO1	Translational activator of cytochrome c oxidase 1	Q9BSH4
TAP1	Antigen peptide transporter 1	Q03518
TARDBP	TAR DNA-binding protein 43	Q13148
TARS2	Threonine--tRNA ligase, mitochondrial	Q9BW92

Gene	Protein name	Accession
TAX1BP1	Tax1-binding protein 1	Q86VP1
TBC1D15	TBC1 domain family member 15	Q8TC07
TBC1D31	TBC1 domain family member 31	Q96DN5
TBCB	Tubulin-folding cofactor B	Q99426
TBL2	Transducin beta-like protein 2	Q9Y4P3
TBL3	Transducin beta-like protein 3	Q12788
TBRG4	Protein TBRG4	Q969Z0
TCEB1	Transcription elongation factor B polypeptide 1	Q15369
TCOF1	Treacle protein	Q13428
TCP1	T-complex protein 1 subunit alpha	P17987
TDRKH	Tudor and KH domain-containing protein	Q9Y2W6
TECR	Very-long-chain enoyl-CoA reductase	Q9NZ01
TEFM	Transcription elongation factor, mitochondrial	Q96QE5
TFAM	Transcription factor A, mitochondrial	Q00059
TFB1M	Dimethyladenosine transferase 1, mitochondrial	Q8WVM0
TFB2M	Dimethyladenosine transferase 2, mitochondrial	Q9H5Q4
TFRC	Transferrin receptor protein 1	P02786
TGOLN2	Trans-Golgi network integral membrane protein 2	O43493
THNSL1	Threonine synthase-like 1	Q8IYQ7
TIMM10B	Mitochondrial import inner membrane translocase subunit Tim10 B	Q9Y5J6
TIMM13	Mitochondrial import inner membrane translocase subunit Tim13	Q9Y5L4
TIMM17A	Mitochondrial import inner membrane translocase subunit Tim17-A	Q99595
TIMM17B	Mitochondrial import inner membrane translocase subunit Tim17-B	O60830
TIMM21	Mitochondrial import inner membrane translocase subunit Tim21	Q9BVV7
TIMM23	Mitochondrial import inner membrane translocase subunit Tim23	O14925
TIMM44	Mitochondrial import inner membrane translocase subunit TIM44	O43615
TIMM50	Mitochondrial import inner membrane translocase subunit TIM50	Q3ZCQ8
TIMMDC1	Complex I assembly factor TIMMDC1, mitochondrial	Q9NPL8
TM9SF1	Transmembrane 9 superfamily member 1	O15321
TM9SF2	Transmembrane 9 superfamily member 2	Q99805
TM9SF3	Transmembrane 9 superfamily member 3	Q9HD45
TM9SF4	Transmembrane 9 superfamily member 4	Q92544
TMCO1	Transmembrane and coiled-coil domain-containing protein 1	Q9UM00
TMED1	Transmembrane emp24 domain-containing protein 1	Q13445
TMED10	Transmembrane emp24 domain-containing protein 10	P49755
TMED2	Transmembrane emp24 domain-containing protein 2	Q15363
TMED4	Transmembrane emp24 domain-containing protein 4	Q7Z7H5
TMED7	Transmembrane emp24 domain-containing protein 7	Q9Y3B3
TMED9	Transmembrane emp24 domain-containing protein 9	Q9BVK6

Gene	Protein name	Accession
TMEM109	Transmembrane protein 109	Q9BVC6
TMEM11	Transmembrane protein 11, mitochondrial	P17152
TMEM126A	Transmembrane protein 126A	Q9H061
TMEM160	Transmembrane protein 160	Q9NX00
TMEM165	Transmembrane protein 165	Q9HC07
TMEM192	Transmembrane protein 192	Q8IY95
TMEM199	Transmembrane protein 199	Q8N511
TMEM206	Transmembrane protein 206	Q9H813
TMEM245	Transmembrane protein 245	Q9H330
TMEM261	Transmembrane protein 261	Q96GE9
TMEM30A	Cell cycle control protein 50A	Q9NV96
TMEM33	Transmembrane protein 33	P57088
TMEM43	Transmembrane protein 43	Q9BTV4
TMEM65	Transmembrane protein 65	Q6PI78
TMEM70	Transmembrane protein 70, mitochondrial	Q9BUB7
TMEM97	Transmembrane protein 97	Q5BJF2
TMF1	TATA element modulatory factor	P82094
TMLHE	Trimethyllysine dioxygenase, mitochondrial	Q9NVH6
TMPO	Lamina-associated polypeptide 2, isoform alpha	P42166
TMPO	Lamina-associated polypeptide 2, isoforms beta/gamma	P42167
TMUB1	Transmembrane and ubiquitin-like domain-containing protein 1	Q9BVT8
TMUB2	Transmembrane and ubiquitin-like domain-containing protein 2	Q71RG4
TMX1	Thioredoxin-related transmembrane protein 1	Q9H3N1
TMX2	Thioredoxin-related transmembrane protein 2	Q9Y320
TMX4	Thioredoxin-related transmembrane protein 4	Q9H1E5
TNPO1	Transportin-1	Q92973
TOMM20	Mitochondrial import receptor subunit TOM20 homolog	Q15388
TOMM22	Mitochondrial import receptor subunit TOM22 homolog	Q9NS69
TOMM40	Mitochondrial import receptor subunit TOM40 homolog	O96008
TOMM40L	Mitochondrial import receptor subunit TOM40B	Q969M1
TOP2A	DNA topoisomerase 2-alpha	P11388
TOP2B	DNA topoisomerase 2-beta	Q02880
TOR1A	Torsin-1A	O14656
TOR1AIP2	Torsin-1A-interacting protein 2	Q8NFK8
TOR1B	Torsin-1B	O14657
TP53I11	Tumor protein p53-inducible protein 11	O14683
TPGS1	Tubulin polyglutamylase complex subunit 1	Q6ZTW0
TPM3	Tropomyosin alpha-3 chain	P06753
TPM4	Tropomyosin alpha-4 chain	P67936

Gene	Protein name	Accession
TPR	Nucleoprotein TPR	P12270
TRABD	TraB domain-containing protein	Q9H4I3
TRAF3IP3	TRAF3-interacting JNK-activating modulator	Q9Y228
TRAP1	Heat shock protein 75 kDa, mitochondrial	Q12931
TRAPPC3	Trafficking protein particle complex subunit 3	O43617
TRAPPC5	Trafficking protein particle complex subunit 5	Q8IUR0
TRIM28	Transcription intermediary factor 1-beta	Q13263
TRIP11	Thyroid receptor-interacting protein 11	Q15643
TRIP13	Pachytene checkpoint protein 2 homolog	Q15645
TRMT10C	Mitochondrial ribonuclease P protein 1	Q7L0Y3
TRMT5	tRNA	Q32P41
TRMT61B	tRNA	Q9BVS5
TRMU	Mitochondrial tRNA-specific 2-thiouridylase 1	O75648
TRNT1	CCA tRNA nucleotidyltransferase 1, mitochondrial	Q96Q11
TRPV2	Transient receptor potential cation channel subfamily V member 2	Q9Y5S1
TRUB1	Probable tRNA pseudouridine synthase 1	Q8WVH5
TRUB2	Probable tRNA pseudouridine synthase 2	O95900
TSEFM	Elongation factor Ts, mitochondrial	P43897
TSPAN14	Tetraspanin-14	Q8NG11
TSPAN7	Tetraspanin-7	P41732
TST	Thiosulfate sulfurtransferase	Q16762
TUBA1A	Tubulin alpha-1A chain	Q71U36
TUBA1B	Tubulin alpha-1B chain	P68363
TUBA1C	Tubulin alpha-1C chain	Q9BQE3
TUBB	Tubulin beta chain	P07437
TUBG1	Tubulin gamma-1 chain	P23258
TUBGCP2	Gamma-tubulin complex component 2	Q9BSJ2
TUBGCP3	Gamma-tubulin complex component 3	Q96CW5
TUBGCP6	Gamma-tubulin complex component 6	Q96RT7
TUFM	Elongation factor Tu, mitochondrial	P49411
TUSC3	Tumor suppressor candidate 3	Q13454
TXN	Thioredoxin	P10599
TXN2	Thioredoxin, mitochondrial	Q99757
TXNDC12	Thioredoxin domain-containing protein 12	Q95881
TXNDC5	Thioredoxin domain-containing protein 5	Q8NBS9
TYMS	Thymidylate synthase	P04818
UBA1	Ubiquitin-like modifier-activating enzyme 1	P22314
UBAC2	Ubiquitin-associated domain-containing protein 2	Q8NBM4
UBB	Polyubiquitin-B [Cleaved into: Ubiquitin]	P0CG47

Gene	Protein name	Accession
UBC	Polyubiquitin-C	P0CG48
UBE2G2	Ubiquitin-conjugating enzyme E2 G2	P60604
UBE2J1	Ubiquitin-conjugating enzyme E2 J1	Q9Y385
UBE2N	Ubiquitin-conjugating enzyme E2 N	P61088
UBTF	Nucleolar transcription factor 1	P17480
UBXN4	UBX domain-containing protein 4	Q92575
UCK2	Uridine-cytidine kinase 2	Q9BZX2
UFD1L	Ubiquitin fusion degradation protein 1 homolog	Q92890
UFL1	E3 UFM1-protein ligase 1	O94874
UGGT1	UDP-glucose:glycoprotein glucosyltransferase 1	Q9NYU2
ULBP2	NKG2D ligand 2	Q9BZM5
UMPS	Uridine 5'-monophosphate synthase	P11172
UNG	Uracil-DNA glycosylase	P13051
UQCC1	Ubiquinol-cytochrome-c reductase complex assembly factor 1	Q9NVA1
UQCC2	Ubiquinol-cytochrome-c reductase complex assembly factor 2	Q9BRT2
UQCRB	Cytochrome b-c1 complex subunit 7	P14927
UQCRC1	Cytochrome b-c1 complex subunit 1, mitochondrial	P31930
UQCRC2	Cytochrome b-c1 complex subunit 2, mitochondrial	P22695
UQCRCF1	Cytochrome b-c1 complex subunit Rieske, mitochondrial	P47985
UQCRQ	Cytochrome b-c1 complex subunit 8	O14949
URB1	Nucleolar pre-ribosomal-associated protein 1	O60287
USO1	General vesicular transport factor p115	O60763
USP20	Ubiquitin carboxyl-terminal hydrolase 20	Q9Y2K6
USP30	Ubiquitin carboxyl-terminal hydrolase 30	Q70CQ3
UTP14A	U3 small nucleolar RNA-associated protein 14 homolog A	Q9BVJ6
UTRN	Utrophin	P46939
UXS1	UDP-glucuronic acid decarboxylase 1	Q8NBZ7
VAMP3	Vesicle-associated membrane protein 3	Q15836
VAMP4	Vesicle-associated membrane protein 4	O75379
VAMP5	Vesicle-associated membrane protein 5	O95183
VAMP7	Vesicle-associated membrane protein 7	P51809
VAPA	Vesicle-associated membrane protein-associated protein A	Q9P0L0
VAPB	Vesicle-associated membrane protein-associated protein B/C	O95292
VARS2	Valine--tRNA ligase, mitochondrial	Q5ST30
VAT1	Synaptic vesicle membrane protein VAT-1 homolog	Q99536
VAV1	Proto-oncogene vav	P15498
VCP	Transitional endoplasmic reticulum ATPase	P55072
VDAC1	Voltage-dependent anion-selective channel protein 1	P21796
VDAC2	Voltage-dependent anion-selective channel protein 2	P45880

Gene	Protein name	Accession
VDAC3	Voltage-dependent anion-selective channel protein 3	Q9Y277
VIM	Vimentin	P08670
VIMP	Selenoprotein S	Q9BQE4
VMA21	Vacuolar ATPase assembly integral membrane protein VMA21	Q3ZAQ7
VPS13C	Vacuolar protein sorting-associated protein 13C	Q709C8
VPS29	Vacuolar protein sorting-associated protein 29	Q9UBQ0
VPS35	Vacuolar protein sorting-associated protein 35	Q96QK1
VPS45	Vacuolar protein sorting-associated protein 45	Q9NRW7
VRK1	Serine/threonine-protein kinase VRK1	Q99986
VT11A	Vesicle transport through interaction with t-SNAREs homolog 1A	Q96AJ9
VT11B	Vesicle transport through interaction with t-SNAREs homolog 1B	Q9UEU0
VWA8	von Willebrand factor A domain-containing protein 8	A3KMH1
WARS2	Tryptophan--tRNA ligase, mitochondrial	Q9UGM6
WDFY1	WD repeat and FYVE domain-containing protein 1	Q8IWB7
XPNPEP3	Probable Xaa-Pro aminopeptidase 3	Q9NQH7
XPO1	Exportin-1	O14980
XPR1	Xenotropic and polytropic retrovirus receptor 1	Q9UBH6
XRCC1	DNA repair protein XRCC1	P18887
XRCC5	X-ray repair cross-complementing protein 5	P13010
XRCC6	X-ray repair cross-complementing protein 6	P12956
YARS2	Tyrosine--tRNA ligase, mitochondrial	Q9Y2Z4
YBEY	Putative ribonuclease	P58557
YME1L1	ATP-dependent zinc metalloprotease YME1L1	Q96TA2
YRDC	YrdC domain-containing protein, mitochondrial	Q86U90
YWHAB	14-3-3 protein beta/alpha	P31946
YWHAE	14-3-3 protein epsilon	P62258
YWHAH	14-3-3 protein eta	Q04917
YWHAQ	14-3-3 protein theta	P27348
YWHAZ	14-3-3 protein zeta/delta	P63104
ZADH2	Zinc-binding alcohol dehydrogenase domain-containing protein 2	Q8N4Q0
ZAP70	Tyrosine-protein kinase ZAP-70	P43403
ZC3H11A	Zinc finger CCCH domain-containing protein 11A	O75152
ZC3HAV1	Zinc finger CCCH-type antiviral protein 1	Q7Z2W4
ZDHHC18	Palmitoyltransferase ZDHHC18	Q9NUE0
ZMPSTE24	CAAX prenyl protease 1 homolog	O75844
ZW10	Centromere/kinetochore protein zw10 homolog	O43264





## 7 Literature

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## **8 Danksagung**

Danksagung

## 9 Lebenslauf