

# Scoping review of chronic rhinosinusitis proteomics\*

Stephen Shih-Teng Kao<sup>1</sup>, Ahmed Bassiouni<sup>1</sup>, Mahnaz Ramezanpour<sup>1</sup>, Nusha Chegeni<sup>2</sup>, Alex D. Colella<sup>2</sup>, Timothy K. Chataway<sup>2</sup>, Peter-John Wormald<sup>1</sup>, Sarah Vreugde<sup>1</sup>, Alkis James Psaltis<sup>1</sup>

**Rhinology** 58: 5, 418 - 470, 2020  
<https://doi.org/10.4193/Rhin20.034>

<sup>1</sup> Department of Surgery-Otolaryngology Head and Neck Surgery, The University of Adelaide, Woodville South, Australia

<sup>2</sup> Flinders Proteomic Facility, Department of Human Physiology, Flinders University, Bedford Park, Australia

**\*Received for publication:**

February 2, 2020

**Accepted:** March 29, 2020

## Abstract

**Background:** Progressive advances in proteomic technology has improved our understanding of the chronic rhinosinusitis (CRS) pathogenesis and endotypes. This scoping review aims to present a comprehensive and descriptive analysis of nasal mucosa and mucus proteome of CRS patients.

**Methodology:** Studies investigating the proteome of nasal mucosa and mucus from healthy and CRS patients via mass spectrometry were included. Critical appraisal of methodological quality was conducted with extraction of protein lists. Gene set enrichment analysis (GSEA) was performed on studies including CRS patients.

**Results:** 2962 proteins were identified in the 21 studies included in this review. Eleven studies investigated the nasal mucus proteome and ten studies investigated the nasal mucosa proteome. Studies demonstrated heterogeneity in patients, sampling and mass spectrometry methodology. Samples from CRS patients suggested a trend in enrichment of immune system and programmed cell death pathways. Increased expression of proteins involved in cellular components including the cytoskeleton and adherens junctions was also present in CRS.

**Conclusions:** Alterations in the healthy sinonasal proteome may lead to the increased immunological, metabolic and tissue remodeling processes observed in CRS. However, it is difficult to draw significant conclusions from the GSEA due to the heterogeneity present in the limited literature available. These findings allow us to direct further research to better understand CRS pathogenesis and its endotypes.

**Key words:** chronic rhinosinusitis, mucus, proteomics, scoping review, mass spectrometry

## Introduction

Chronic rhinosinusitis (CRS) is characterised by persisting inflammation of the mucosa in the nasal cavity and paranasal sinuses. The current phenotypic classification of CRS is divided into CRS without nasal polyps (CRSsNP) or CRS with nasal polyps (CRSwNP). These phenotypes, however, do not cover the diverse cellular pathways involved in the complex pathogenesis of CRS. Advances in laboratory techniques has led to investigating CRS endotypes, enabling a better understanding of upstream pathogenic factors that lead to CRS disease manifestation and recalcitrance. Ultimately, CRS endotypes may allow clinicians to predict disease prognosis and develop personalised treatment

regimes.

The mucosal barrier, in concert with an effective mucociliary transport system and a protective mucus layer interact together with the innate and humoral immune system to maintain homeostasis in health. Tight junctions located on the apical aspects of cell membranes inhibit the flow of solutes and water into the paracellular space in addition to forming cell polarity<sup>(1-3)</sup>. Studies have demonstrated down regulation of tight junction transmembrane and associated proteins with reduced transmembrane electrical resistance in patients with CRS<sup>(4-6)</sup>. Furthermore various inflammatory cytokines including IL-17,

IL-33, TLSP have been implicated in the pathogenesis of CRS and nasal polyp formation<sup>(7-10)</sup>. The heterogeneity of immune responses in CRS endotypes certainly plays a significant role in the manifestation of the disease.

Nasal mucus, a vital component of the mucociliary clearance system, is produced by seromucinous glands, goblet cells and the transudation of plasma. It is composed of glycoproteins and polysaccharide chains organised into two layers; the lower periciliary layer and the superficial viscous layer<sup>(11,12)</sup>. The antimicrobial effects of nasal mucus have been well studied<sup>(11,12)</sup>. The overproduction of viscous nasal mucus is commonly reported amongst CRS patients manifested as rhinorrhoea and postnasal drip. This tenacious mucus adversely affects ciliary function, leading to stasis that may result in a nidus for bacterial growth<sup>(13-15)</sup>.

The proteomic analysis of nasal mucus and mucosa is a rapidly evolving field exploring the physiological and pathological mechanisms involved in CRS. In this form of analysis, mucus and tissue samples collected from patients undergo gel electrophoresis or liquid chromatography to separate the proteins<sup>(16)</sup>. Proteins are subjected to mass spectrometry (MS) for identification of peptide sequences, which are compared against known protein databases. Previous studies have provided insight into the proteins involved in various immune responses from mucus and mucosa collected from CRS patients<sup>(16-18)</sup>. The aim of this scoping review was to perform a comprehensive review of the current literature on the CRS proteome and to ascertain differences between CRS and healthy patients. Ultimately, improving the knowledge of CRS endotypes through cellular pathways present will guide prognostication and treatment regimens for CRS patients.

## Methods

The search strategy aimed to capture all English language studies published in Pubmed, CINAHL, Embase and Cochrane CENTRAL databases since their creation. A preliminary initial search of the Pubmed database using the keywords "Chronic rhinosinusitis", "Mucus", and "Proteomics" was initially performed to identify further relevant key words to be included in the final search strategy of all databases (Supplement 1). A second search using all identified keywords and medical subject headings were applied across all databases. This review adhered to the PRISMA guidelines for reporting systematic reviews. The reference lists of all selected studies were searched for additional studies.

Studies conducting proteomic analysis on patients 18 years or older via mass spectrometry on mucus samples or nasal mucosa collected from healthy or CRS patients were included. Studies conducting bottom up proteomics were included, with studies investigating select proteins were excluded. Patients diagnosed

with acute sinusitis or allergic rhinitis or exposure to chemicals or fumes were excluded. Studies utilizing tissue collected from the olfactory bulb, olfactory epithelium, nerve tissue, or tissue grown in vitro were excluded. Proteins mentioned in systemic reviews, meta-analyses, literature reviews and conferences abstracts were excluded to prevent duplication of data.

Papers retrieved that met all inclusion criteria were assessed by two independent reviewers (SSK, AB) for methodological validity prior to inclusion in the review. Differences in assessments between reviewers were resolved through discussion with a third reviewer (TC).

Data extraction focused on proteins identified through mass spectrometry in healthy and CRS patients. Key data extracted included disease status (Healthy or CRS), tissue collection method, tissue specimen examined (Mucus or Mucosa), analytical platform and protein composition. Proteins identified were stratified by mucus or mucosa origin and disease status.

## Statistical analysis

Statistical analysis was conducted with R statistical software (R Core team, Vienna, Austria)<sup>(19)</sup>. All proteins identified from studies were matched manually with their Uniprot accession numbers, protein name and gene. Proteins not in the Uniprot database or not from Homo Sapiens genus were excluded from the analysis. Proteins were stratified into their presence in either CRS, healthy groups or both for mucus and mucosa samples. Mucus and mucosa protein lists were processed separately, due to their differing constituents. Gene set enrichment analysis (GSEA) was conducted, clustering the available differentially expressed genes for analysis. This was performed by uploading protein lists to Enrichr<sup>TM</sup> (Ma'ayan Laboratory, USA), a web-based software<sup>(20,21)</sup>. Reactome 2016 pathway database identified cellular pathways, and the Gene Ontology database identified biological processes, cellular components and molecular functions. Only significant results (Adjusted P-value <0.05 calculated by Enrichr<sup>TM</sup>) were included for further analysis. Mucus and mucosa GSEA results were combined for analysis. No further analysis was possible due to the lack of available numeric quantifiable data from the studies included in the review.

The cellular pathways generated from CRS mucus and mucosa were then combined. This was also performed for the biological processes, cellular components and molecular functions. The same was performed for proteins unique to the healthy group, and proteins present in both healthy and CRS groups.

## Results

The search identified a total of 591 studies in English, with 526 remaining after duplicates were removed. Titles and abstracts

Table 1. Studies investigating proteomics of nasal mucus.

Author	Disease Status	Patients	Collection Method	MS Method	MS Equipment	Proteins Identified
Benson et al. <sup>38</sup>	CRSsNP	6	NLF	Nano-LC-MS/MS	LC (Michrom BioResources Inc; CA, USA) LTQ Linear ion trap MS (ThermoFinnigan; CA, USA)	129
Casado et al. <sup>39</sup>	Healthy	10	NLF	Micro-Capillary LC ESI-Q-TOF MS	CapLC (Waters; Milford, USA) ESI-Q-TOF MS (Micromass; Manchester, UK)	111
Debat et al. <sup>26</sup>	Healthy	16	Suction (Olfactory cleft)	MALDI-TOF-MS	Voyager DE STR+ TOF-MS (Applied Biosystems; CA, USA)	75
Ghafouri et al. <sup>33</sup>	Healthy	5	NLF	MALDI-TOF MS Nanoelectrospray MS/MS	Voyager DE PRO MS (Applied Biosystems; CA, USA) API Q-STAR Pulzer i (Applied biosystems; CA, USA) with nanoelectrospray ion source (MDS-Protana; Odense, Denmark)	20
Lindahl et al. <sup>34</sup>	Healthy	7	NLF	MALDI-TOF-MS	Voyager DE STR MS (PE-Biosystems; CA, USA) or Bruker Reflex (Bruker Daltonics; Bremen, Germany)	12
Mortstedt et al. <sup>35</sup>	Healthy	8	NLF	Micro-LC-MS/MS Nano-LC-Q-TOF MS	LC (UFLCXR, Shimadzu Corporation; Kyoto, Japan) QTRAP 5500 hybrid triple quadrupole/ linear ion trap MS (Applied Biosystems/ MDS Sciex; MA, USA) LC (Agilent 1100 series; CA, USA) QSTAR pulsar hybrid quadrupole TOF MS (Applied Biosystems/MDS Sciex; MA, USA)	331
Schoenebeck et al. <sup>27</sup>	Healthy	N/A	NLF	Nano-LC-MS/MS Micro-LC-MS/MS	LC (Ultimate HPLC system, Dionex; Idstein, Germany) HCT ultra PTM analysis system (Bruker Daltonic; Bremen, Germany) LC (HP Ultimate 300 system, Dionex; Idstein, Germany) LTQ OrbiTrap Velos MS (ThermoFisher Scientific; MA, USA)	34
Tewfik et al. <sup>16</sup>	Healthy CRSwNP	4 4	Suction	Micro-LC-MS/MS	LC (Agilent Technologies; Ontario, Canada) QTRAP 4000 (Sciex-Applied Biosystems; Ontario, Canada)	35
Tomazic et al. <sup>22</sup>	Healthy	29	Suction (Middle meatus)	Nano-LC-MS/MS	Nano-HPLC (Agilent 1200 series; Vienna, Austria) LTQ-FT MS (Thermo Scientific; Vienna, Austria)	247
Tomazic et al. <sup>23</sup>	Healthy	12	Suction (Middle meatus)	Nano-LC-MS/MS	Nano-HPLC (Agilent 1200 series; Vienna, Austria) LTQ-FT MS (Thermo Scientific; Vienna, Austria)	366
Wahlen et al. <sup>37</sup>	Healthy	13	NLF	MALDI-TOF MS	Voyager DE PRO (Applied Biosystems; CA, USA)	48

HPLC: High performance liquid chromatography; LC: Liquid Chromatography; NLF: Nasal lavage fluid; MS: Mass spectrometry; LC-MS/MS: Liquid chromatography-tandem mass spectrometry; ESI-Q-TOF: Electrospray-ionisation quadrupole time-of-flight mass spectrometry; LC-Q-TOF: Liquid chromatography/ quadrupole time-of-flight mass spectrometry; MALDI-TOF MS: Matrix Assisted Laser Desorption/ Ionisation mass spectrometry.

were reviewed against the inclusion criteria yielding a total of 52 studies for full text analysis. 21 studies met the inclusion criteria (Supplement 2).

Studies included were published between 2004 to 2018 originating from Austria<sup>(22,23)</sup>, Canada<sup>(16)</sup>, China<sup>(24)</sup>, Finland<sup>(25)</sup>, France<sup>(26)</sup>, Germany<sup>(18, 27)</sup>, Italy<sup>(28)</sup>, Portugal<sup>(29,30)</sup>, South Korea<sup>(31, 32)</sup>, Sweden<sup>(33-37)</sup> and USA<sup>(17, 38, 39)</sup>.

From the 21 studies, a total of 345 patients were included, consisting of 302 healthy control patients and 43 CRS patients (CRSwNP 34 and CRSsNP 9). Eleven studies involved mucus samples; seven collected by nasal lavage fluid washes and four by suction. Ten studies involved sampling of the nasal mucosa, five

by mucosal brushing and five by intraoperative biopsies.

A total of 2962 proteins were identified after removal of duplicates in the 21 studies. 549 proteins were identified in mucus samples, consisting of 45 unique to CRS samples, 398 unique to healthy and 106 common in both groups. 2829 proteins were identified in mucosa samples, including six unique to CRS samples, 2771 unique to healthy and 52 common in both groups (Supplement 3).

#### Critical analysis of included studies

All 21 studies included in this review focused on the identification and analysis of the nasal mucus and mucosa proteome and all included analysis of control donors and/or CRS patients. Only

Table 2. Studies investigating proteomics of nasal mucosa.

Author	Disease Status	Patients	Collection Method	MS Method	MS Equipment	Proteins Identified
Farajzadeh Deroede et al. <sup>18</sup>	CRSwNP	3	Biopsy (Polyp tissue)	MALDI-TOF-MS	Proteome-Analyser 4700 (Applied Biosystems; CA, USA)	11
Gelardi et al. <sup>28</sup>	Healthy	4	Nasal brushing (Inferior turbinate)	MALDI-TOF-MS	Voyager DE PRO MS (Applied Biosystems; CA, USA)	18
Kim et al. <sup>31</sup>	CRSwNP	13	Biopsy (Polyp tissue)	Nano-LC-MS/MS	Agilent 1100 Series LC/MSD Trap XCT MS (Agilent Technologies; Ontario, Canada)	15
Lee et al. <sup>32</sup>	Healthy	10	Biopsy (Inferior turbinate)	MALDI-TOF MS	Voyager DE STR MS (Applied biosystems; CA, USA)	78
Min-Man et al. <sup>24</sup>	Healthy CRSsNP CRSwNP	7 7 7	Biopsy (Ethmoid sinuses – CRS, Middle turbinate - Healthy)	MALDI-TOF MS ESI-Q-TOF MS	N/A	30
Ndika et al. <sup>36</sup>	Healthy	10	Nasal Brushing (Middle meatus)	Nano-LC-MS/MS	LC (EASY nano LC 1000 (Proxeon, Thermo Fischer Scientific; CA, USA) Electrospray ionization quadrupole-orbitrap MS (Q Exactive, Thermo Fisher Scientific; CA, USA)	Spring 2090 Autumn 2107
Roxo-Rosa et al. <sup>29</sup>	Healthy	8	Nasal Brushing (Middle meatus)	MALDI-TOF MS	Biflex III (Bruker Daltonik; Bremen, Germany) Voyager DE STR MS (Applied Biosystems; Ontario, Canada)	65
Simoës et al. <sup>30</sup>	Healthy	129	Nasal Brushing (Inferior turbinate)	Micro-LC-MS/MS	Thermo LTQ linear ion trap spectrometer (Thermo Scientific, Waltham, MA)	1482
Suojalehto et al. <sup>25</sup>	Healthy	27	Nasal Brushing (Inferior turbinate)	ESI-Q-TOF MS	LC (EASY nano LC 1000 (Proxeon, Thermo Fischer Scientific; CA, USA) Electrospray ionization quadrupole-orbitrap MS (Q Exactive, Thermo Fisher Scientific; CA, USA)	77
Upton DC et al. <sup>17</sup>	Healthy CRSwNP	3 3	Biopsy (Ethmoid, Sphenoid sinuses)	MALDI-TOF MS	Voyager DE Pro mass spectrometer (Protein Core Facility)	15

HPLC: High performance liquid chromatography; LC: Liquid Chromatography; MS: Mass spectrometry; LC-MS/MS: Liquid chromatography-tandem mass spectrometry; ESI-Q-TOF MS: Electrospray-ionisation quadrupole time-of-flight mass spectrometry; LC-Q-TOF MS: Liquid chromatography/quadrupole time-of-flight mass spectrometry; MALDI-TOF MS: Matrix Assisted Laser Desorption/ Ionisation mass spectrometry; Spring: Number of proteins identified in spring; Autumn: Number of proteins identified in autumn.

data from healthy and CRS patients was extracted and included in this review. The focus of the included studies was to identify and ascertain differences in the nasal mucus or tissue proteome between CRS patients and controls, however, there was considerable variability in patient demographics and clinical status. Four studies obtained samples from healthy and allergic rhinitis patients before and after pollen seasons to compare changes in proteome<sup>(23, 25, 33, 36)</sup>. The allergic rhinitis protein content was excluded from this review, and only the healthy proteome was included in the overall protein list. One study did not document the number of patients included<sup>(27)</sup>, and two studies did not include patient age<sup>(33, 35)</sup>. These three studies consisted of only healthy patients, and the proteins identified were included in the catalogue of proteins in this review (Supplement 2). CRS was diagnosed via nasoendoscopic examination in all cases, with the addition of CT imaging in three studies<sup>(17, 24, 31)</sup>. Minimal details were given across the included studies regarding polyp grades

and CT scores with one study grading polyp severity in CRS patients<sup>(18)</sup>. Studies defined healthy patients who demonstrated no clinical or CT evidence of allergic rhinitis or CRS. One study included two smokers<sup>(31)</sup> and two studies utilized oral steroids<sup>(17, 18)</sup>. These details are summarised in Supplement 4.

There was heterogeneity between studies regarding sample collection and preparation prior to analysis with the mass spectrometer. Nasal mucus was collected via nasal lavage fluid (NLF) in seven studies and suction in four studies (Table 1). Nasal tissue samples were collected as nasal brushings in five studies and biopsy of nasal mucosa (inferior turbinate, polyp, ethmoid or sphenoid sinuses) in five studies (Table 2). Heterogeneity in sample collection method and site of tissue extraction is a potential for confounding bias. Seven studies performed additional immunochemistry on cells to identify cellular changes in healthy and CRS patients<sup>(17, 24, 28, 29, 31, 32, 34)</sup>. These studies identified a range

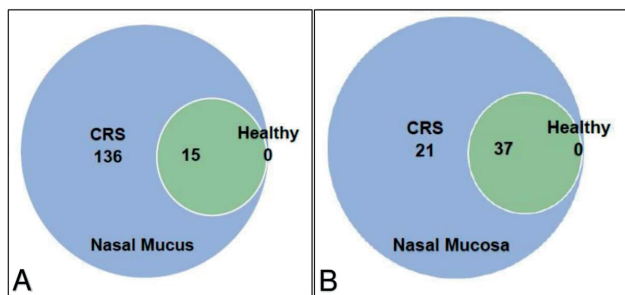


Figure 1. Venn diagram demonstrating total proteins identified in CRS and healthy patients in nasal mucus (A) and nasal mucosa (B).

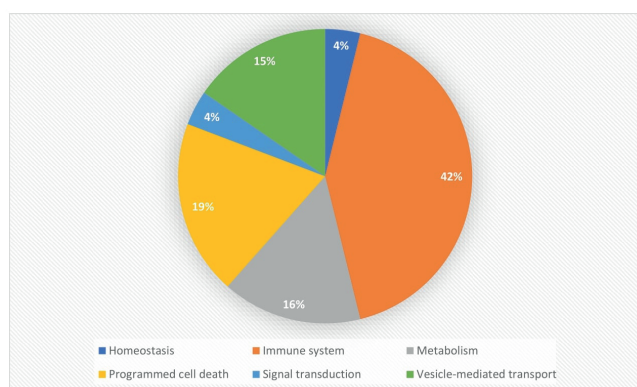


Figure 2. CRS cellular pathways. Twenty-six cellular pathways identified, classified into six common groups. (%) Percentage of all identified cellular pathways in CRS samples.

of nasal mucosal and inflammatory cells, however, there is limited reporting of which specific cell types were tested during the proteomic experiments.

Nasal tissue sample preparation prior to mass spectrometry analysis was variable, however, followed the same principles across all the studies. Nasal mucus samples were run through 2D Gel electrophoresis in seven studies (22, 23, 26, 27, 33, 34, 37). Protein spots of interest were cut and underwent trypsin digestion prior to mass spectrometry analysis. Nasal tissue samples all underwent tissue lysis through combinations of lysis buffers and mechanical disruption via sonification. Protein was collected from these lysed cells and run through 2D gel electrophoresis in eight of the studies (17, 18, 24, 25, 28, 29, 31, 32).

Various techniques of mass spectrometry were employed across the 21 included studies, where some studies used two different techniques. Ion trap LC-MS/MS was used in ten studies, matrix assisted laser desorption/ionisation mass spectrometry (MALDI-TOF) was used in ten studies, electrospray-ionisation quadrupole time-of-flight mass spectrometry (ESI-Q-TOF) was used in three studies and liquid chromatography/quadrupole time-of-flight mass spectrometry (LC-Q-TOF) was used in one

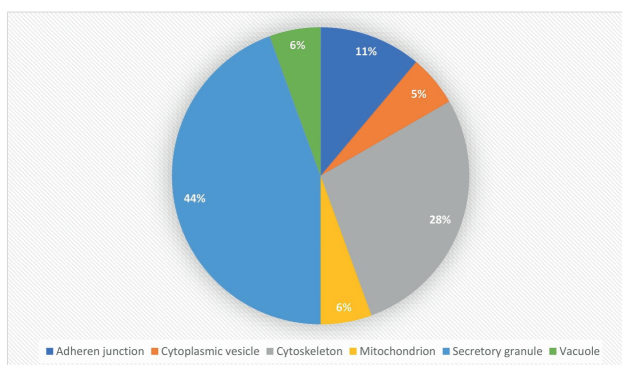


Figure 3. CRS cellular components. Eighteen cellular components classified in six common groups. (%) Percentage of all identified cellular components in CRS samples.

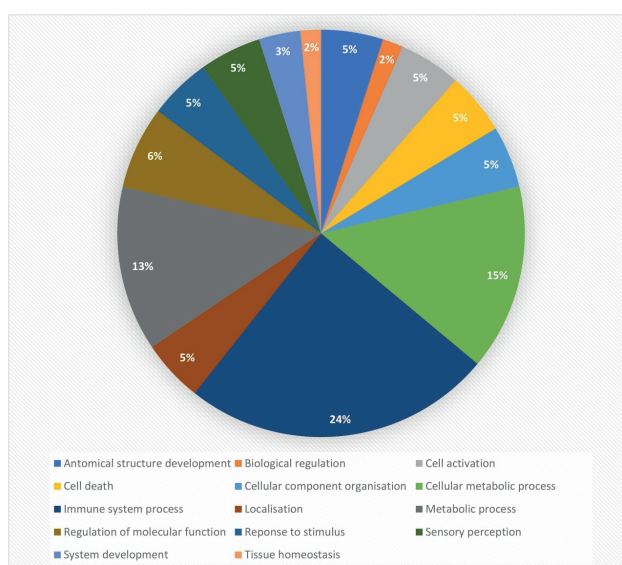


Figure 4. CRS biological processes. Sixty-one biological processes classified into 14 common groups. (%) Percentage of all identified biological processes in CRS samples.

study (Table 1 and Table 2). Notably, the most recent of these studies was published 8 years ago, and since then, there have been considerable advances in MS equipment speed, resolution and sensitivity. Furthermore, various protein identification criteria were employed, including 2-4 peptides present, 10-20% sequence coverage and false discovery rates of less than 5%.

### Nasal mucus and mucosa proteome gene set enrichment analysis

There was substantial skew of studies investigating healthy mucus and mucosa samples compared to CRS samples. Thus, GSEA was only performed on the proteins identified in the six studies that sampled CRS patients. Two of these studies investigated nasal mucus (16, 38) and four studies examined the nasal mucosa (17, 18, 24, 31). Three of these six studies directly compared the proteomes of CRS and healthy patients (16, 17, 24). This was to reduce methodo-



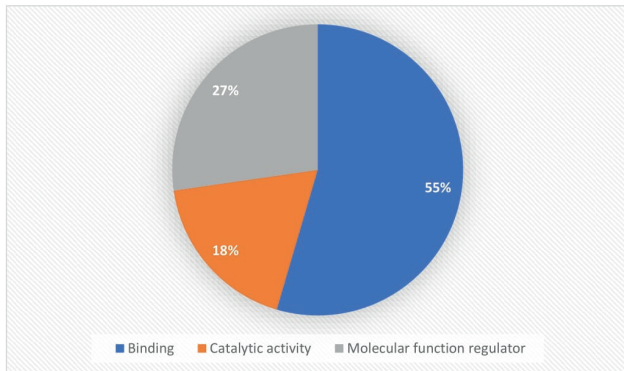


Figure 5. CRS molecular functions. Eleven molecular functions classified into three common groups. (%) Percentage of all identified molecular functions in CRS samples.

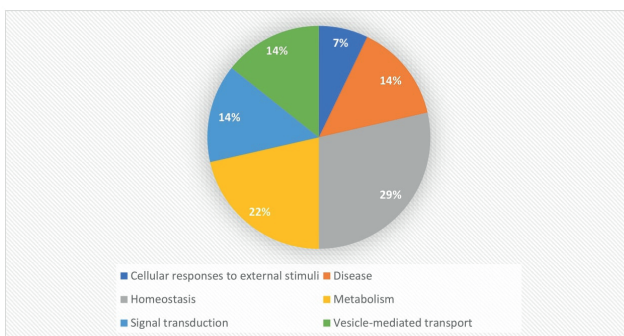


Figure 6. Healthy and CRS cellular pathways. Thirteen cellular pathways identified and stratified into six common pathways. (%) Percentage of all identified cellular pathways in both healthy and CRS samples.

logical bias in the analysis.

151 proteins were identified in the two studies investigating the nasal mucus proteome (Supplement 5 and Figure 1)<sup>(16, 38)</sup>. 136 proteins were uniquely expressed in CRS mucus and 15 were found in both CRS and healthy mucus samples whilst no proteins were found to be unique to the healthy mucus proteome. 58 proteins were identified across four studies investigating the proteomics of nasal mucosa<sup>(17, 18, 24, 31)</sup>. 21 proteins were uniquely expressed in CRS mucosa, 37 proteins were present in both healthy and CRS mucosa and no proteins were unique to the healthy mucosa proteome (Figure 1).

### CRS proteome

Twenty-six cellular pathways were identified in the 136 uniquely expressed CRS mucus proteins and classified into six common groups (Supplement 5). The pathways included immune system (42%), programmed cell death (19%), metabolism (16%), vesicle mediated transport (15%), homeostasis (4%) and signal transduction (4%) (Figure 2). No significant cellular pathways were identified in CRS mucosa samples.

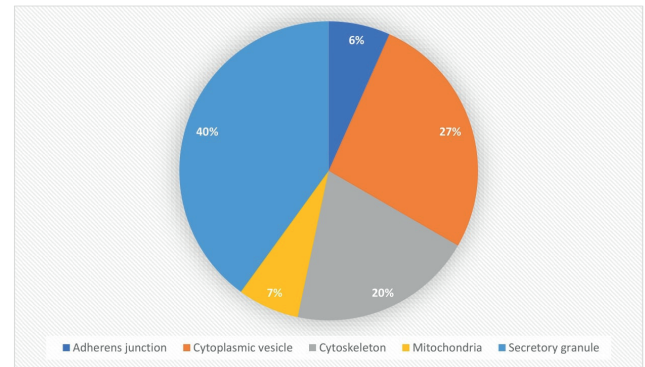


Figure 7. Healthy and CRS cellular components. Fifteen cellular components identified and classified in five common groups. (%) Percentage of all identified cellular components in both healthy and CRS samples.

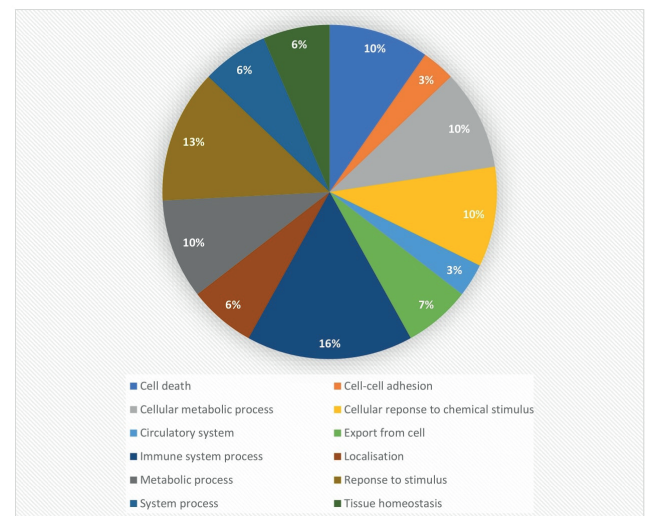


Figure 8. Healthy and CRS biological processes. Thirty-one biological processes classified in twelve common biological processes. (%) Percentage of all identified biological processes.

Eighteen cellular components were uniquely identified in CRS mucus and mucosa samples, classified into six common groups consisting of secretory granules (44%), cytoskeleton (28%), adherens junction (11%), vacuoles (6%), mitochondrion (6%) and cytoplasmic vesicles (5%) (Supplement 5 and Figure 3).

Sixty-one biological processes were identified in CRS mucus and mucosa samples, stratified into 14 common groups (Supplement 5). These processes included mainly immune system process (24%), cellular metabolic process (15%), metabolic process (13%), regulation of molecular function (6%) as well as anatomical structure development, biological regulation, cell activation, cellular component organisation, localisation, function, response to stimulus, sensory perception, system development and tissue homeostasis (all  $\leq 5\%$ ) (Figure 4).

Eleven molecular functions were significantly present in CRS mucus, classified into three common functions consisting of binding (55%), molecular function regulation (27%) and catalytic activity (18%) (Supplement 5 and Figure 5). No molecular functions were identified in CRS mucosa samples.

### Common proteome in CRS and healthy

All proteins identified in healthy mucus<sup>(15)</sup> and mucosa<sup>(37)</sup> samples were also present in CRS mucus and mucosa samples, respectively.

Thirteen cellular pathways were identified in both healthy and CRS mucus and mucosa samples were classified into six common pathways: homeostasis (29%), metabolism (22%), vesicle-mediated transport (14%), signal transduction (14%), disease (14%) and cellular responses to external stimuli (7%) (Supplement 5 and Figure 6).

Fifteen cellular components were found to be present in both healthy and CRS mucus and mucosa samples. These were grouped into five common groups consisting of secretory granules (40%), cytoplasmic vesicles (27%), cytoskeleton (20%), mitochondrion (7%) and adherens junctions (6%) (Supplement 5 and Figure 7).

Thirty-one biological processes were present in both healthy and CRS mucus and mucosa samples (Supplement 5). These were grouped into twelve common biological processes consisting mainly of immune processes (16%), response to stimulus (13%), metabolic process (10%), cellular metabolic process (10%), cellular response to chemical stimulus (10%), cell death (10%), cellular metabolic process (10%), export from cell (7%), as well as localisation, system processes, tissue homeostasis and tissue homeostasis, cell-cell adhesion and circulatory system (all ≤6%) (Figure 8).

Signal recognition particle binding (GO:0005047) was the only significant molecular function present in both CRS and healthy mucus samples (Supplement 5). No other molecular functions were identified in either the healthy or CRS mucosa samples.

## Discussion

Chronic rhinosinusitis is a multifactorial disease believed to be secondary to a complex interplay between pathogens, the immune system and environmental factors<sup>(40)</sup>. This results in chronic mucosal inflammation and recurrent infections. The currently used phenotypic classification which is based on the presence or absence of polyps has been shown to be inadequate in defining the numerous inflammatory subtypes within CRS. To better define the heterogeneous disease process in CRS, there have been numerous studies investigating the pathophysiology

and classification of CRS endotypes<sup>(7,40)</sup>. This scoping review has identified 21 studies investigating the nasal mucus and mucosa proteome of healthy and CRS patients that may give insights into the protein composition and down-stream alterations that occur in sinus disease. The various methodologies of all included studies were summarised and critically appraised. There was significant heterogeneity in methodology and patients across the current available literature. Gene set enrichment analysis (GSEA) was conducted on six proteomic studies that had data comparing the proteome of CRS and healthy cohorts<sup>(16-18, 24, 31, 38)</sup>. These results suggest an increased proportion of both innate and adaptive immunologic pathways including complement, phagocytosis and B cell functions, with increases to tissue remodelling pathways, apoptosis and metabolic processes in CRS patients compared to the common proteome group. These differences as well as their associated imbalances in cellular pathways may account for the disease manifestation observed in CRS, however, further studies are required to confirm these findings.

Dysregulation of the innate and adaptive immune system response has been proposed as a contributing factor to the underlying chronic inflammatory state observed in CRS<sup>(41-43)</sup>. Using GSEA this review demonstrated an increased presence of complement activation processes (GO:0006958) and phagocyte activity (GO:0006909) in the CRS group. Both these factors are part of the innate immune system which is vital against inhaled pathogens in the airway. Studies have identified upregulation of complement components and deposition along the basement membrane in CRS nasal polyp tissue<sup>(44, 45)</sup>. This deposition is associated with epithelial-to-mesenchymal transition, a form of tissue remodelling observed in CRS mucosa<sup>(46, 47)</sup>. Additionally, C5a has been found to induce production of Oncostatin M, a potent cytokine, known to disrupt epithelial barrier integrity in CRSwNP<sup>(48)</sup>. Macrophages and neutrophils are prominent phagocytic cells in CRS, with their dysregulation potentially accounting for the epithelial injury and increased paracellular permeability observed in CRS<sup>(41, 49, 50)</sup>. The increased expression of these innate immune system pathways in CRS patients may account for the barrier dysfunction associated with the sinonasal inflammatory response. In turn, differences in pathway expression can be used to endotype CRS and aid in prognostication and treatment.

Secretory granules are important constituents in phagocyte function in the innate immune response, with similar compositions found between the CRS and common proteome groups following GSEA. Elevated levels of neutrophils observed in CRS patients may lead to over production of neutrophil granules and serine proteases, which may lead to barrier disruption as collateral damage<sup>(50)</sup>. This review identified differences in endopeptidase (GO:0052548) and peptidase (GO:0052547) activity in CRS mucus which was not present in the common group. Neutrophil

elastase, an endopeptidase, is vital in the fight against pathogens has been associated with epithelial barrier disruption<sup>(50)</sup>. The imbalance between proteases and protease inhibitors at the epithelial barrier is hypothesised to be an initiating and perpetuating factor in inflammatory airway disease<sup>(51,52)</sup>. Further targeted studies are required to determine if differences in protein expression of these inflammatory mediators reflect the increased infiltration of inflammatory cells with consequent barrier disruption.

The adaptive immune response is also implicated in the pathogenesis of CRS. Our GSEA confirms this with increased proportion of B cell activation (GO:0050871) and function (GO:0050853) pathways in CRS mucus samples. These findings correlate with previous studies identifying elevated levels of B cells and plasma infiltrates in CRS<sup>(53-55)</sup>. B cells are fundamental in the adaptive immune response, by evolving into plasma cells or memory B cells upon activation. From research by our department, we have also recently demonstrated immune cell infiltrates clustering into germinal centres called tertiary lymphoid organs (TLO). We proposed that the presence of TLO in nasal polyp samples in recalcitrant CRS patients may be secondary to chronic antigen presentation<sup>(56)</sup>. Studies have speculated the role of TLO in the activation of autoreactive B and T cell clones in chronic inflammation and autoimmunity<sup>(42,57,58)</sup>. Further research is required to understand the contribution of the innate and adaptive immune response in CRS endotypes, and its role of tissue remodelling and the development of polyps.

GSEA also demonstrated an impairment in immune response against pathogen invasion including the defence response biological processes against bacterium (GO:0042742) and fungus (GO:0050832), that were only found to be present in the CRS group. These pathways need to be explored to determine if the proteins involved are downregulated or upregulated in CRS patients. Furthermore, three sensory perception processes identified in CRS mucus were involved with bitter taste. The bitter taste receptor gene family, particularly T2R38, has been associated with activation of the local innate immune response through increased mucociliary clearance and bactericidal activity<sup>(59,60)</sup>. It has been proposed that polymorphisms in bitter taste receptors play a role in sinonasal immunity in CRS<sup>(61)</sup>. The impairment in immunological pathways present may account for the impaired innate and adaptive immune response with secondary bacterial dysbiosis observed in CRS<sup>(62,63)</sup>.

Tissue remodelling with associated barrier dysfunction secondary to inflammation is a hallmark feature of CRS<sup>(64)</sup>. Epithelial-to-mesenchymal transition (EMT) is a remodelling process where epithelial cells lose their normal morphology, polarity and junctional attachments to neighbouring cells becoming

spindle shaped mesenchymal cells in response to chronic inflammation<sup>(65)</sup>. These cellular changes with loss of tight and adherens junctions from CRS mucosa are well documented<sup>(66,67)</sup>. This review identified increased proportion of cytoskeletal and adherens junction components in the CRS group compared to the common proteome group. Furthermore, proteins involved in cell-cell binding played the largest role in molecular functions of the CRS group. These differences may reflect the cellular morphological changes observed in CRS described in the barrier disruption hypothesis of CRS pathogenesis. Lastly, the increased proportion of actin-filaments (GO:0005884) and intermediate filament cytoskeleton (GO:0045111) present in the CRS group may account for increased activity during tissue remodelling. Further research is required to identify differences in expression of barrier and cytoskeletal structure proteins that reflect the changes observed in CRS.

Interestingly, our review also showed an increased expression of programmed cell death pathways and biological processes to be present in CRS patients. Apoptosis has a fundamental role in regulating tissue homeostasis via the elimination of unwanted cells. The apoptotic cleavage pathway of cell adhesion proteins leads to rearrangements of tight junctions, adherens junctions and desmosomes. Immune-mediated apoptosis of intestinal epithelial cells demonstrated increased permeability with associated restructuring of epithelial cells<sup>(68)</sup>. Caspases released during apoptosis causes cleavage of desmosomal proteins leading to disruption of cell-cell contacts. This is followed by remodelling of the intermediate filament cytoskeleton, as a homeostatic mechanism observed in colonic epithelial cells to maintain barrier function<sup>(69)</sup>. These findings correlate with cytokine-mediated changes in tight junctions with increased paracellular permeability present in inflammatory bowel disease<sup>(70-72)</sup>. This pathway may account for the increased paracellular permeability without epithelial cell cytotoxicity observed in human nasal epithelial cells exposed to CRS mucus<sup>(6)</sup>. Further research is required to determine differences in the upstream regulation of apoptotic pathways present in CRS, followed by clarifying if apoptosis-induced morphological changes in nasal epithelial is associated with barrier dysfunction and paracellular permeability.

The dysregulation of the coagulation cascade has been hypothesised to play a role in the pathogenesis of many inflammatory conditions including asthma, rheumatoid arthritis and Crohn's disease<sup>(73)</sup>. This review identified the platelet degranulation pathways with similar distributions in both groups. Elevated expression of platelet-derived growth factor (PDGF) has been identified in nasal polyps suggesting involvement in epithelial proliferation observed in CRS<sup>(74)</sup>. PDGF is chemotactic and mitogenic for fibroblasts, and involved in the pathogenesis of



fibrosis<sup>(75)</sup>. Additionally, factor XIII-A in the coagulation cascade, present in platelets and macrophages, is also elevated in nasal polyp tissues of CRSwNP patients<sup>(76)</sup>. It was hypothesised that overproduction of factor XIII-A may lead to an accelerated coagulation cascade with subsequent excessive fibrin deposition, leading to tissue remodelling and oedema of the submucosa within nasal polyp tissue<sup>(73)</sup>. Further research is required to ascertain the differences in protein regulation upstream in platelet pathways which may be responsible for the increased fibrin deposition in tissue remodelling.

The maintenance of cellular metabolism is vital in healthy tissue homeostasis. This review identified increased expression of metabolic processes, particularly with carbohydrate metabolism, was present in the CRS-only group. Persistent exposure of nasal epithelial cells to external pathogens and irritants leads to injury with chronic healing and remodelling. Reactive oxygen species released in response to pathogens further add to the oxidative stress in chronic disease<sup>(77)</sup>. This process is counterbalanced by a range of antioxidant pathways identified in both healthy and CRS mucus. Previous studies have demonstrated reduced levels of antioxidant enzymes in CRS patients compared to healthy individuals<sup>(78, 79)</sup>. Consequently, the increased energy demand from their epithelial cells require a constant glucose reservoir for the maintenance of cell function and tissue integrity<sup>(30)</sup>. Elevated breath glucose has been identified in patients with cystic fibrosis without diabetes with inflammatory lung changes. It was hypothesised the elevated glucose in airway fluid was due to increased paracellular permeability and glucose leakage into respiratory fluid or impaired glucose removal<sup>(80)</sup>. Further studies are required to investigate imbalances between oxidant and antioxidant processes likely contributing to the inflammation of the epithelium observed in CRS patients<sup>(81)</sup>. Additionally, further research is required to determine if elevated levels of glucose are present in the nasal secretions of CRS patients, and its association with disease severity and barrier dysfunction.

### Limitations

The proteomic analysis of nasal mucosa and mucus samples is a powerful technique in understanding CRS pathogenesis and its endotypes. Heterogeneity in methods of sample collection and location of tissue collected are potential areas of bias. Studies are required to determine if the proteome collected from nasal brushings are as representative as mucosal biopsy specimens. Furthermore, future research is required to determine differences between the nasal mucosa and mucus proteome samples from the same patients. Cellular lysates obtained from nasal mucosa are more challenging to process due to the magnitude of proteins present compared to mucus. Additionally, the protein composition between healthy and CRS cells are likely similar as all cells require similar organelle to survive. The lack of cellular

pathways identified from the GSEA of CRS mucosa is likely due to the decreased number of unique proteins (21 vs 136) identified and inputted into the analysis. Therefore secretions, such as mucus, may be more representative of the disease process.

Researchers should aim for a standardised mucus and mucosal collection method to reduce sample variability. Targeted methods of sample collection from specific subsites of the nasal cavity, such as with an absorbable sponge or suctioning, will provide more detailed information. Further studies should determine if samples collected from different subsites contain similar quantities of inflammatory cytokines and cells. Furthermore, differing sample processing methods, in conjunction with differing mass spectrometry methods adds confounding bias. Advances in mass spectrometry resolution and sensitivity will allow for the detection of lower abundance proteins present in mucus and mucosa samples to improve our understanding of CRS. GSEA was unable to be performed on all 21 studies due to the skew of studies containing only healthy patients. This factor in conjunction with the heterogeneity in sample preparation and analysis across the studies was a potential for cumulative methodological bias. Therefore, this is a potential explanation for the lack of unique healthy proteins identified. The included studies reporting protein qualification was limited and thus this review was only able to comment on the presence of certain proteins and not the quantity. Due to this lack of standardized reporting of up-regulated and/or down-regulated proteins across the studies, we could not collate the data and express it in a meaningful and semi-quantitative way. This is a potential avenue for future research. Thus, GSEA conducted was only capable of presenting pathways present, and not which pathways were up- or down-regulated. Ultimately, more studies with direct comparisons between healthy and CRS proteomes are required. This includes quantitative studies to determine differences in protein and cellular pathway expressions. Lastly, future studies require standardised reporting and methodology to allow improved comparisons in future reviews. Despite these limitations this review has been able to collate a comprehensive list of the nasal proteome, with a descriptive analysis of different cellular processes between healthy and CRS patients.

### Conclusion

Proteomic analysis of nasal mucus and mucosa is a vital step in better understanding the pathophysiology of CRS and its endotypes. This descriptive scoping review has identified 2962 proteins from healthy and CRS patients in the current literature. Preliminary GSEA from the current limited and heterogenous literature suggests a trend of increased presence of immunological, metabolic, tissue remodelling and apoptotic pathways in CRS. Furthermore, the lack of standardisation in methodology across the current literature has been identified. We hope this

review provides a reference resource of the current literature to improve standardisation of methodology and direct further research to improve the knowledge of CRS pathogenesis and endotypes.

## Acknowledgements

The project was supported by the Adelaide University Research Training Program Scholarship, Bertha Sudholz Scholarship and Garnett Passe Rodney Williams Memorial Foundation Scholarship.

## Authorship contribution

SSK: Study inception, study selection, data collection and analysis, manuscript writing; AB: study selection, data collection and analysis; MR: study selection, data analysis, manuscript writing; NC: data collection and analysis, manuscript writing; ADC: data analysis, manuscript writing; TKC: study selection, data analysis, manuscript writing; PJW: study inception, manuscript writing; SV: study inception, manuscript writing; AJP: study inception, manuscript writing.

## Conflict of interest

The authors declare no conflicts of interest.

## References

- van Meer G, Simons K. The function of tight junctions in maintaining differences in lipid composition between the apical and the basolateral cell surface domains of MDCK cells. *EMBO journal*. 1986;5(7):1455-64.
- Cereijido M, Valdes J, Shoshani L, Contreras RG. Role of tight junctions in establishing and maintaining cell polarity. *Annu Rev Physiol*. 1998;60:161-77.
- Kojima T, Go M, Takano K, Kurose M, Ohkuni T, Koizumi J, et al. Regulation of tight junctions in upper airway epithelium. *Biomed Res Int*. 2013;2013:947072.
- Soyka MB, Wawrzyniak P, Eiwegger T, Holzmann D, Treis A, Wanke K, et al. Defective epithelial barrier in chronic rhinosinusitis: the regulation of tight junctions by IFN-gamma and IL-4. *J Allergy Clin Immunol*. 2012;130(5):1087-96.e10.
- Tieu DD, Kern RC, Schleimer RP. Alterations in epithelial barrier function and host defense responses in chronic rhinosinusitis. *J Allergy Clin Immunol*. 2009;124(1):37-42.
- Kao SS, Ramezanzpour M, Bassiouni A, Finnie J, Wormald PJ, Vreugde S, et al. Barrier disruptive effects of mucus isolated from chronic rhinosinusitis patients. *Allergy*. 2019.
- Yip J, Monteiro E, Chan Y. Endotypes of chronic rhinosinusitis. *Current opinion in otolaryngology & head and neck surgery*. 2019;27(1):14-9.
- Ramezanzpour M, Moraitis S, Smith JLP, Wormald PJ, Vreugde S. Th17 Cytokines Disrupt the Airway Mucosal Barrier in Chronic Rhinosinusitis. *Mediators Inflamm*. 2016;2016:9798206.
- Kim DK, Jin HR, Eun KM, Mo JH, Cho SH, Oh S, et al. The role of interleukin-33 in chronic rhinosinusitis. *Thorax*. 2017;72(7):635-45.
- Song W, Wang C, Zhou J, Pan S, Lin S. IL-33 Expression in Chronic Rhinosinusitis with Nasal Polyps and Its Relationship with Clinical Severity. *ORL; journal for oto-rhino-laryngology and its related specialties*. 2017;79(6):323-30.
- Beule AG. Physiology and pathophysiology of respiratory mucosa of the nose and the paranasal sinuses. *GMS Current Topics in Otorhinolaryngology, Head and Neck Surgery*. 2010;9:Doc07.
- Fahy JV, Dickey BF. Airway mucus function and dysfunction. *N Engl J Med*. 2010;363(23):2233-47.
- Mahdavinia M, Keshavarzian A, Tobin MC, Landay AL, Schleimer RP. A comprehensive review of the nasal microbiome in chronic rhinosinusitis (CRS). *Clinical and experimental allergy*. 2016;46(1):21-41.
- Stressmann FA, Rogers GB, Chan SW, Howarth PH, Harries PG, Bruce KD, et al. Characterization of bacterial community diversity in chronic rhinosinusitis infections using novel culture-independent techniques. *Am J Rhinol Allergy*. 2011;25(4):e133-40.
- Bucher S, Schmid-Grendelmeier P, Soyka MB. Altered Viscosity of Nasal Secretions in Postnasal Drip. *Chest*. 2019;156(4):659-66.
- Tewfik MA, Latterich M, DiFalco MR, Samaha M. Proteomics of nasal mucus in chronic rhinosinusitis. *Am J Rhinol*. 2007;21(6):680-5.
- Upton DC, Welham NV, Kuo JS, Walker JW, Pasic TR. Chronic Rhinosinusitis With Nasal Polyps: A Proteomic Analysis. *Annals of Otolaryngology & Laryngology*. 2011;120(12):780-6.
- Farajzadeh Deroe A, Oweinah J, Naraghi M, Hosemann W, Athari B, Volker U, et al. Regression of polypoid nasal mucosa after systemic corticosteroid therapy: a proteomics study. *American journal of rhinology & allergy*. 2009;23(5):480-5.
- R. Development Core Team. R: A Language and Environment for Statistical Computing [Internet]. Vienna AAHW R-po.
- Kuleshov MV, Jones MR, Rouillard AD, Fernandez NF, Duan Q, Wang Z, et al. Enrichr: a comprehensive gene set enrichment analysis web server 2016 update. *Nucleic acids research*. 2016;44(W1):W90-7.
- Chen EY, Tan CM, Kou Y, Duan Q, Wang Z, Meirelles GV, et al. Enrichr: interactive and collaborative HTML5 gene list enrichment analysis tool. *BMC bioinformatics*. 2013;14:128.
- Tomazic PV, Birner-Gruenberger R, Leitner A, Obrist B, Spoerk S, Lang-Loidolt D. Nasal mucus proteomic changes reflect altered immune responses and epithelial permeability in patients with allergic rhinitis. *Journal of Allergy and Clinical Immunology*. 2014;133(3):741-50.
- Tomazic PV, Birner-Gruenberger R, Leitner A, Spoerk S, Lang-Loidolt D. Seasonal proteome changes of nasal mucus reflect perennial inflammatory response and reduced defence mechanisms and plasticity in allergic rhinitis. *Journal of proteomics*. 2016;133:153-60.
- Min-Man W, Hong S, Zhi-Qiang X, Xue-Ping F, Chang-Qi L, Dan L. Differential proteomic analysis of nasal polyps, chronic sinusitis, and normal nasal mucosa tissues. *Otolaryngology-Head & Neck Surgery*. 2009;141(3):364-8.
- Suojalehto H, Lindström I, Wolff H, Puustinen A. Nasal protein profiles in work-related asthma caused by different exposures. *Allergy: European Journal of Allergy and Clinical Immunology*. 2018;73(3):653-63.
- Debat H, Eloit C, Blon F, Sarazin B, Henry C, Huet JC, et al. Identification of human olfactory cleft mucus proteins using proteomic analysis. *Journal of proteome research*. 2007;6(5):1985-96.
- Schoenebeck B, May C, Guldner C, Respondek G, Mollenhauer B, Hoeglinger G, et al. Improved preparation of nasal lavage fluid (NLF) as a noninvasive sample for proteomic biomarker discovery. *Biochimica et biophysica acta*. 2015;1854(7):741-5.
- Gelardi M, Siciliano RA, Papa F, Mazzeo MF, De Nitto E, Quaranta N, et al. Proteomic analysis of human nasal mucosa: different expression profile in rhino-pathologic states. *European annals of allergy and clinical immunology*. 2014;46(5):164-71.
- Roxo-Rosa M, da Costa G, Luider TM, Scholte BJ, Coelho AV, Amaral MD, et al. Proteomic analysis of nasal cells from cystic fibrosis patients and non-cystic fibrosis control individuals: search for novel biomarkers of cystic fibrosis lung disease. *Proteomics*. 2006;6(7):2314-25.
- Simões T, Charro N, Blonder J, Faria D, Couto FM, Chan KC, et al. Molecular profiling of the human nasal epithelium: A proteomics approach. *Journal of proteomics*.

- 2011;75(1):56-69.
31. Kim T, Lee S, Park J, Park S, Jang A, Lee J, et al. Fatty acid binding protein 1 is related with development of aspirin-exacerbated respiratory disease. *Allergy: European Journal of Allergy and Clinical Immunology*. 2011;66:466-7.
  32. Lee JY, Byun JY, Lee SH. Proteomic analysis of normal human nasal mucosa: Establishment of a two-dimensional electrophoresis reference map. *Clinical biochemistry*. 2009;42(7-8):692-700.
  33. Ghafouri B, Irander K, Lindbom J, Tagesson C, Lindahl M. Comparative proteomics of nasal fluid in seasonal allergic rhinitis. *Journal of proteome research*. 2006;5(2):330-8.
  34. Lindahl M, Irander K, Tagesson C, Stahlbom B. Nasal lavage fluid and proteomics as means to identify the effects of the irritating epoxy chemical dimethylbenzylamine. *Biomarkers* 2004;9(1):56-70.
  35. Mortstedt H, Karedal MH, Jonsson BA, Lindh CH. Screening method using selected reaction monitoring for targeted proteomics studies of nasal lavage fluid. *Journal of proteome research*. 2013;12(1):234-47.
  36. Ndika J, Airaksinen L, Suojalehto H, Karisola P, Fyhrquist N, Puustinen A, et al. Epithelial proteome profiling suggests the essential role of interferon-inducible proteins in patients with allergic rhinitis. *Journal of Allergy and Clinical Immunology*. 2017;140(5):1288-98.
  37. Wahlen K, Fornander L, Olausson P, Ydreborg K, Flodin U, Graff P, et al. Protein profiles of nasal lavage fluid from individuals with work-related upper airway symptoms associated with moldy and damp buildings. *Indoor air*. 2016;26(5):743-54.
  38. Benson LM, Mason CJ, Friedman O, Kita H, Bergen HR, 3rd, Plager DA. Extensive fractionation and identification of proteins within nasal lavage fluids from allergic rhinitis and asthmatic chronic rhinosinusitis patients. *J Sep Sci*. 2009;32(1):44-56.
  39. Casado B, Pannell LK, Iadarola P, Baraniuk JN. Identification of human nasal mucous proteins using proteomics. *Proteomics*. 2005;5(11):2949-59.
  40. Fokkens WJ. EPOS2020: a major step forward. *Rhinology*. 2020;58(1):1.
  41. Lane AP. The role of innate immunity in the pathogenesis of chronic rhinosinusitis. *Current allergy and asthma reports*. 2009;9(3):205-12.
  42. Tan BK, Peters AT, Schleimer RP, Hulse KE. Pathogenic and protective roles of B cells and antibodies in patients with chronic rhinosinusitis. *The Journal of allergy and clinical immunology*. 2018;141(5):1553-60.
  43. Schleimer RP. Immunopathogenesis of Chronic Rhinosinusitis and Nasal Polyposis. *Annual review of pathology*. 2017;12:331-57.
  44. Van Roey GA, Vanison CC, Wu J, Huang JH, Suh LA, Carter RG, et al. Classical complement pathway activation in the nasal tissue of patients with chronic rhinosinusitis. *The Journal of allergy and clinical immunology*. 2017;140(1):89-100.e2.
  45. Schlosser RJ, Mulligan RM, Casey SE, Varela JC, Harvey RJ, Atkinson C. Alterations in gene expression of complement components in chronic rhinosinusitis. *American journal of rhinology & allergy*. 2010;24(1):21-5.
  46. Tang Z, Lu B, Hatch E, Sacks SH, Sheerin NS. C3a mediates epithelial-to-mesenchymal transition in proteinuric nephropathy. *Journal of the American Society of Nephrology : JASN*. 2009;20(3):593-603.
  47. Shin HW, Cho K, Kim DW, Han DH, Khalmuratova R, Kim SW, et al. Hypoxia-inducible factor 1 mediates nasal polypogenesis by inducing epithelial-to-mesenchymal transition. *Am J Respir Crit Care Med*. 2012;185(9):944-54.
  48. Pothoven KL, Norton JE, Hulse KE, Suh LA, Carter RG, Rocci E, et al. Oncostatin M promotes mucosal epithelial barrier dysfunction, and its expression is increased in patients with eosinophilic mucosal disease. *The Journal of allergy and clinical immunology*. 2015;136(3):737-46.e4.
  49. Van Drunen CM, Mjösberg JM, Segboer CL, Cornet ME, Fokkens WJ. Role of innate immunity in the pathogenesis of chronic rhinosinusitis: Progress and new avenues. *Current allergy and asthma reports*. 2012;12(2):120-6.
  50. Kao SS, Ramezanzpour M, Bassiouni A, Wormald PJ, Psaltis AJ, Vreugde S. The effect of neutrophil serine proteases on human nasal epithelial cell barrier function. *International forum of allergy & rhinology*. 2019.
  51. Kouzaki H, Matsumoto K, Kikuoka H, Kato T, Tojima I, Shimizu S, et al. Endogenous Protease Inhibitors in Airway Epithelial Cells Contribute to Eosinophilic Chronic Rhinosinusitis. *Am J Respir Crit Care Med*. 2017;195(6):737-47.
  52. Pfeiffer PE, Corrigan CJ. An Imbalance between Proteases and Endogenous Protease Inhibitors in Eosinophilic Airway Disease. *Am J Respir Crit Care Med*. 2017;195(6):707-8.
  53. Stoop AE, van der Heijden HA, Biewenga J, van der Baan S. Lymphocytes and non-lymphoid cells in human nasal polyps. *The Journal of allergy and clinical immunology*. 1991;87(2):470-5.
  54. Psaltis AJ, Schlosser RJ, Yawn JR, Henriquez O, Mulligan JK. Characterization of B-cell subpopulations in patients with chronic rhinosinusitis. *International forum of allergy & rhinology*. 2013;3(8):621-9.
  55. Miljkovic D, Psaltis A, Wormald P-J, Vreugde S. Naive and effector B-cell subtypes are increased in chronic rhinosinusitis with polyps. *American journal of rhinology & allergy*. 2018;32(1):3-6.
  56. Paramasivan S, Lester S, Lau A, Ou J, Psaltis AJ, Wormald P-J, et al. Tertiary lymphoid organs: A novel target in patients with chronic rhinosinusitis. *Journal of Allergy and Clinical Immunology*. 2018;142(5):1673-6.
  57. Carragher DM, Rangel-Moreno J, Randall TD. Ectopic lymphoid tissues and local immunity. *Semin Immunol*. 2008;20(1):26-42.
  58. Aloisi F, Pujol-Borrell R. Lymphoid neogenesis in chronic inflammatory diseases. *Nat Rev Immunol*. 2006;6(3):205-17.
  59. Cohen NA. The genetics of the bitter taste receptor T2R38 in upper airway innate immunity and implications for chronic rhinosinusitis. *The Laryngoscope*. 2017;127(1):44-51.
  60. Lee RJ, Cohen NA. Sinonasal solitary chemosensory cells "taste" the upper respiratory environment to regulate innate immunity. *American journal of rhinology & allergy*. 2014;28(5):366-73.
  61. Maina IW, Workman AD, Cohen NA. The role of bitter and sweet taste receptors in upper airway innate immunity: Recent advances and future directions. *World Journal of Otorhinolaryngology - Head and Neck Surgery*. 2018;4(3):200-8.
  62. Vickery TW, Ramakrishnan VR. Bacterial Pathogens and the Microbiome. *Otolaryngol Clin North Am*. 2017;50(1):29-47.
  63. Sivasubramaniam R, Douglas R. The microbiome and chronic rhinosinusitis. *World journal of otorhinolaryngology - head and neck surgery*. 2018;4(3):216-21.
  64. Van Bruaene N, Bachert C. Tissue remodeling in chronic rhinosinusitis. *Current opinion in allergy and clinical immunology*. 2011;11(1):8-11.
  65. Zhang N, Van Crombruggen K, Gevaert E, Bachert C. Barrier function of the nasal mucosa in health and type-2 biased airway diseases. *Allergy*. 2016;71(3):295-307.
  66. Hupin C, Gohy S, Bouzin C, Lecocq M, Polette M, Pilette C. Features of mesenchymal transition in the airway epithelium from chronic rhinosinusitis. *Allergy*. 2014;69(11):1540-9.
  67. Rogers GA, Den Beste K, Parkos CA, Nusrat A, Delgado JM, Wise SK. Epithelial tight junction alterations in nasal polyposis. *International forum of allergy & rhinology*. 2011;1(1):50-4.
  68. Abreu MT, Palladino AA, Arnold ET, Kwon RS, McRoberts JA. Modulation of barrier function during Fas-mediated apoptosis in human intestinal epithelial cells. *Gastroenterology*. 2000;119(6):1524-36.
  69. Weiske J, Schoneberg T, Schroder W, Hatzfeld M, Tauber R, Huber O. The fate of desmosomal proteins in apoptotic cells. *The Journal of biological chemistry*. 2001;276(44):41175-81.
  70. Colgan SP, Resnick MB, Parkos CA, Delp- Archer C, McGuirk D, Bacarra AE, et al. IL-4 directly modulates function of a model human intestinal epithelium. *Journal of immunology*. 1994;153(5):2122-9.
  71. Schmitz H, Fromm M, Bentzel CJ, Scholz P, Detjen K, Mankertz J, et al. Tumor necrosis factor-alpha (TNFalpha) regulates the epithelial barrier in the human intestinal cell line HT-29/B6. *Journal of cell science*. 1999;112 ( Pt 1):137-46.

72. Youakim A, Ahdieh M. Interferon-gamma decreases barrier function in T84 cells by reducing ZO-1 levels and disrupting apical actin. *The American journal of physiology*. 1999;276(5):G1279-88.
73. Kim DY, Cho SH, Takabayashi T, Schleimer RP. Chronic Rhinosinusitis and the Coagulation System. *Allergy Asthma Immunol Res*. 2015;7(5):421-30.
74. Coste A, Wang Q-P, Roudot-Thoraval F, Chapelin C, Bedbeder P, Poron F, et al. Epithelial Cell Proliferation in Nasal Polyps Could Be Up-Regulated by Platelet-Derived Growth Factor. *The Laryngoscope*. 1996;106(5):578-83.
75. Antoniadis HN, Bravo MA, Avila RE, Galanopoulos T, Neville-Golden J, Maxwell M, et al. Platelet-derived growth factor in idiopathic pulmonary fibrosis. *The Journal of clinical investigation*. 1990;86(4):1055-64.
76. Muszbek L, Bereczky Z, Bagoly Z, Komaromi I, Katona E. Factor XIII: a coagulation factor with multiple plasmatic and cellular functions. *Physiological reviews*. 2011;91(3):931-72.
77. Kirkham P, Rahman I. Oxidative stress in asthma and COPD: antioxidants as a therapeutic strategy. *Pharmacology & therapeutics*. 2006;111(2):476-94.
78. Westerveld GJ, Dekker I, Voss HP, Bast A, Scheeren RA. Antioxidant levels in the nasal mucosa of patients with chronic sinusitis and healthy controls. *Archives of otolaryngology--head & neck surgery*. 1997;123(2):201-4.
79. Kassim SK, Elbeigermly M, Nasr GF, Khalil R, Nassar M. The role of interleukin-12, and tissue antioxidants in chronic sinusitis. *Clinical biochemistry*. 2002;35(5):369-75.
80. Baker EH, Clark N, Brennan AL, Fisher DA, Gyi KM, Hodson ME, et al. Hyperglycemia and cystic fibrosis alter respiratory fluid glucose concentrations estimated by breath condensate analysis. *Journal of Applied Physiology*. 2007;102(5):1969-75.
81. Fordham MT, Mulligan JK, Casey SE, Mulligan RM, Wang EW, Sansoni ER, et al. Reactive oxygen species in chronic rhinosinusitis and secondhand smoke exposure. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*. 2013;149(4):633.

**Alkis Psaltis, MBBS PhD FRACS**  
**Head of Department Otolaryngology**  
**Head and Neck Surgery**  
**The Queen Elizabeth Hospital**  
**28 Woodville Road**  
**Woodville South**  
**South Australia 5011**  
**Australia**

**E-mail: [alkis.psaltis@adelaide.edu.au](mailto:alkis.psaltis@adelaide.edu.au)**



## SUPPLEMENTARY INFORMATION

### Supplement 1: Database search.

#### Pubmed 26/03/2019

Sinusitis[mh] OR Sinus\*[tw] OR Sinusitides[tw] OR Chronic rhinosinusitis[tw] OR CRS[tw] OR CRSwNP[tw] OR CRSsNP[tw] OR Nasal polyps[mh] OR Papillom\*[tw] Polyps[mh] OR Polyp\*[tw] OR Nose[mh] OR Nose[tw] OR Nasal\*[tw]

AND

Mucus [mh] OR Mucus [tw] OR Bodily secretions [mh] OR Secret\* [tw] OR Fluids and Secretions [mh] OR Fluid\* [tw] OR Mucus membrane [mh] OR Mucus membrane [tw] OR Respiratory mucosa [mh] OR Respiratory mucosa [tw] OR Nasal mucosa [mh] OR Nasal mucosa [tw] OR Mucosa\* [tw] OR Epitheli\*[tw] OR Tissue\* [tw]

AND

Proteomics [mh] OR Proteom\* [tw] OR Proteogenomic [mh] OR Proteogenomic [tw] OR Secretome[tw]

#### Embase 26/03/2019

Sinusitis/syn OR Sinusitis/exp OR Sinus\*:ti,ab OR "Chronic rhinosinusitis":ti,ab OR CRS:ti,ab OR CRSsNP:ti,ab OR "Nose polyp"/syn OR "Nose polyp"/exp OR "Nose polyp\*":ti,ab OR "Nasal polyp\*":ti,ab OR Papillom\*:ti,ab Polyp/syn OR Polyp/exp OR Polyp\*:ti,ab OR Nose/syn OR Nose/exp OR Nos\*:ti,ab

AND

Mucus/syn OR Mucus/exp OR Mucus:ti,ab OR Mucosa\*:ti,ab OR "Nose mucus"/syn OR "Nose mucus"/exp OR "Nose fluid":ti,ab OR "Nasal fluid":ti,ab OR Bodily secretions/syn OR Bodily secretions/exp OR Bodily secretion\*:ti,ab OR Secret\*:ti,ab OR Bodily fluid/syn OR Bodily fluid/exp OR Fluid\*:ti,ab OR Mucosa/syn OR Mucosa/exp OR Nose mucosa/syn OR Nose mucosa/exp OR Paranasal sinus mucosa/syn OR Paranasal sinus mucosa/exp OR Nasal tissue/syn OR Nasal tissue/exp OR Tissue\*:ti,ab OR Nose epithelium/syn OR Nose epithelium/exp OR Epitheli\*:ti,ab

AND

Proteomics/syn OR Proteomics/exp OR Proteom\*:ti,ab OR Proteogenomics/syn OR Proteogenomics/exp OR Proteogenomic\*:ti,ab OR Secretome:ti,ab

#### CINAHL 26/03/2019

MH Sinusitis OR TI Sinus\* OR AB Sinus\* OR TA Chronic rhinosinusitis OR AB Chronic rhinosinusitis OR TI CRS OR AB CRS OR TI CRSsNP OR AB CRSsNP OR MH Nasal polyps OR TI Nasal polyp\* OR AB Nasal polyp\* OR TI Nose polyp\* OR AB Nose polyp\* OR TI Papillom\* OR AB Papillom\* OR MH Polyps OR TI Polyp\* OR AB Polyp\*

AND

MH Mucus OR TI Muc\* OR AB Muc\* OR TI Nasal muc\* OR AB Nasal muc\* OR TI Nasal fluid\* OR AB Nasal fluid\* OR MH Secretions OR MH Fluids and secretions OR TI Secret\* OR AB Secret\* OR TI Fluid\* OR AB Fluid OR MH Mucus membrane OR MH Nasal mucosa OR MH Paranasal sinuses OR MH Tissue OR TI Tissue\* OR AB Tissue\* OR MH Epithelium OR TI Epitheli\*

OR AB Epitheli\*

AND

MH Proteomics OR TI Proteomic\* OR AB Proteomic\* OR TI Proteogenomic\* OR AB Proteogenomic\* OR TI Secretome OR AB Secretome

#### Cochrane 26/03/2019

Sinus\* OR Chronic rhinosinusitis OR CRS OR CRSsNP OR Nose polyp\* OR Nasal polyp\* OR Papillom\* OR Polyp\*

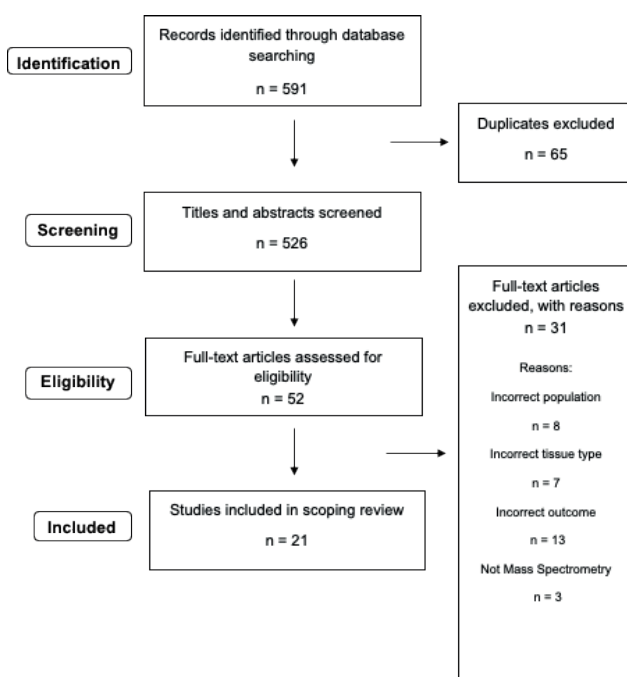
AND

Mucus\* OR Muc\* OR Secret\* OR Fluid\* OR Epitheli\* OR Tissue\*

AND

Proteom\* OR Proteogenomic OR Secretome

### Supplement 2. PRISMA Flow Diagram. Illustration of the systematic review process of study inclusion and exclusion.



## Supplement 3: Comprehensive protein list.

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
1	A1BG	M0R009	l,s,r	45	ACOT9	Q9Y305	l
2	A2M	P01023	i,b,s,r,l,p,o	46	ACOX3	O15254	l
3	AAAS	Q9NRG9	o	47	ACP1	P24666	l
4	AAMDC	E9PJP1	l	48	ACP2	P11117	o,l
5	AARS	P49588	s,l	49	ACP6	Q9NPH0	l
6	ABCA13	Q86UQ4	o	50	ACSF2	Q96CM8	l
7	ABCA7	Q8IZY2	o	51	ACSL1	P33121	o
8	ABCB10	Q9NRK6	o	52	ACSL3	O95573	o,l
9	ABCB6	Q9NPF58	o	53	ACSL5	Q9ULC5	o
10	ABCB7	O75027	o	54	ACSS1	Q9NUB1	l
11	ABCB8	Q9NUT2	o	55	ACTA2	P62736	o,l
12	ABCC1	P33527	o	56	ACTB	P60709	n,s,k,c,b,o,t,p,m,a,t,g
13	ABCC3	O15438	o	57	ACTBL2	Q562R1	s
14	ABCC4	O15439	o	58	ACTC1	P68032	s
15	ABCD1	P33897	o	59	ACTG1	P63261	n,r,c,t,l,t
16	ABCD3	P28288	l,o	60	ACTN1	P12814	s,o,l
17	ABCE1	P61221	l	61	ACTN4	O43707	s,r,o,l,p
18	ABHD10	Q9NUJ1	l	62	ACTR1A	P61163	l
19	ABHD11	Q8NFV4	l	63	ACTR1B	P42025	l
20	ABHD12	Q8N2K0	o	64	ACTR2	P61160	r,o,l
21	ABHD12B	Q7Z5M8	s	65	ACTR3	P61158	s,r,o,l,d
22	ABHD14B	Q96IU4	l	66	ACY1	F8WC59	l
23	ABHD16A	O95870	o	67	ACYP1	P07311	l
24	ABHD6	Q9BV23	o	68	ADAM10	O14672	o
25	ABI1	Q8IZP0	l	69	ADAR	P55265	o,l
26	ABRACL	Q9P1F3	l	70	ADCYAP1	P18509	jj
27	ACAA1	P09110	l	71	ADD1	P35611	l
28	ACAD8	Q9UKU7	l	72	ADH1A	P07327	o
29	ACAD9	Q9H845	o	73	ADH1B	P00325	l
30	ACADM	P11310	m,o,l	74	ADH1C	P00326	s,r,l,o
31	ACADS	P16219	o,l	75	ADH5	P11766	l
32	ACADSB	P45954	l	76	ADH7	P40394	r,s,l
33	ACADVL	P49748	o,l	77	ADI1	Q9BV57	l
34	ACAT1	P24752	o,l	78	ADIRF	Q15847	l,o
35	ACAT2	Q9BWD1	l	79	ADK	P55263	l
36	ACBD3	Q9H3P7	o,l	80	ADPRHL2	Q9NX46	l
37	ACBD7	Q8N6N7	l	81	ADRM1	Q16186	l
38	ACIN1	Q9UKV3	o,l	82	ADSL	P30566	l
39	ACLY	P53396	l	83	ADSS	P30520	l
40	ACO1	P21399	o,l	84	ADSSL1	Q8N142	l
41	ACO2	Q99798	o,l	85	AFDN	P55196	l
42	ACOT13	Q9NPJ3	l	86	AFG3L2	Q9Y4W6	o
43	ACOT2	P49753	l	87	AFM	P43652	l
44	ACOT7	O00154	l	88	AGK	Q53H12	l,o

	Gene	UniProt Accession Number	Studies
89	AGL	P35573	l
90	AGPAT3	Q9NRZ7	o
91	AGPAT5	Q9NUQ2	o
92	AGPS	O00116	l
93	AGR2	O95994	s,r,o,l
94	AGR3	Q8TD06	l,o
95	AGT	P01019	s,l
96	AHCY	P23526	l,o
97	AHNAK	Q09666	o,l
98	AHSA1	O95433	s,l
99	AHSG	P02765	s,r,u,l,a
100	AIF1	P55008	l
101	AIFM1	O95831	l,o
102	AIFM2	Q9BRQ8	b
103	AIMP1	Q12904	l
104	AIMP2	Q13155	l
105	AIP	O00170	l
106	AK1	P00568	s,o,l
107	AK2	P54819	o,l
108	AK3	Q9UIJ7	o,l
109	AK7	Q96M32	l
110	AK8	Q96MA6	l
111	AKAP4	Q5JQC9	s,o
112	AKR1A1	P14550	s,r,c,m,p,l,o
113	AKR1B10	O60218	o,l
114	AKR1C1	Q04828	r,s,o,l
115	AKR1C2	P52895	s,l,o,m
116	AKR1C3	P42330	l
117	AKR7A2	O43488	l,o
118	AKT1S1	Q96B36	l
119	ALAD	P13716	l
120	ALB	H0YA55	u,u,s,r,k,b,c,i,f,u,q,p,m,o,e,q,a
121	ALCAM	Q13740	o,l
122	ALDH16A1	Q8IZ83	l
123	ALDH18A1	P54886	l,o
124	ALDH1A1	P00352	c,s,r,o,m,t,e,l,p,t,d
125	ALDH1A3	P47895	l
126	ALDH1B1	P30837	l
127	ALDH1L1	O75891	l
128	ALDH2	P05091	b,o,l,e
129	ALDH3A1	P30838	r,s,c,p,e,o,l
130	ALDH3A2	P51648	o,l
131	ALDH3B1	P43353	o,l
132	ALDH4A1	P30038	g
133	ALDH5A1	P51649	o,l
134	ALDH7A1	P49419	o,l

	Gene	UniProt Accession Number	Studies
135	ALDH8A1	Q9H2A2	m
136	ALDH9A1	P49189	l,o
137	ALDOA	P04075	s,r,o,p,l,a
138	ALDOC	P09972	s,o,l
139	ALG1	Q9BT22	o,l
140	ALG14	Q96F25	o
141	ALG2	Q9H553	o
142	ALG5	Q9Y673	o
143	ALG9	Q9H6U8	o
144	ALOX15	P16050	s,r,o,l
145	ALOX5AP	P20292	o
146	ALPL	P05186	o
147	ALYREF	Q86V81	l
148	AMBN	Q9NP70	s
149	AMBP	P02760	l
150	AMDHD2	Q9Y303	l
151	AMY1A	P04745	k,l
152	AMY1B	P04745	k,l
153	AMY1C	P04745	k,l
154	AMY2B	P19961	a
155	ANG	P03950	l
156	ANK1	P16157	o
157	ANK3	Q12955	o,l
158	ANKEF1	Q9NU02	s
159	ANKS1A	Q92625	l
160	ANP32A	P39687	l
161	ANP32B	Q92688	l
162	ANP32E	Q9BTT0	l
163	ANPEP	P15144	o,l
164	ANXA1	P04083	n,s,r,k,c,l,p,m,t,o,a,t
165	ANXA11	P50995	o,l
166	ANXA2	P07355	n,s,r,b,c,p,m,l,o,a
167	ANXA3	P12429	n,s,r,c,p,l,o
168	ANXA4	P09525	l,o
169	ANXA5	P08758	s,r,p,m,l,o
170	ANXA6	P08133	l,o
171	ANXA7	P20073	c,o,l
172	ANXA8	P13928	l
173	AP1B1	H7C034	l
174	AP1G1	B4DGE1	l,o
175	AP1M1	Q9BXS5	l
176	AP1M2	Q9Y6Q5	l
177	AP2A1	O95782	l,o
178	AP2B1	P63010	l
179	AP2M1	Q96CW1	l
180	AP2S1	P53680	l
181	AP3B1	O00203	l,o

	Gene	UniProt Accession Number	Studies
182	AP3D1	O14617	l
183	APCS	P02743	p,l
184	APEH	P13798	l
185	APEX1	P27695	o,l
186	API5	Q9BZZ5	l
187	APMAP	Q9HDC9	o,l
188	APOA1	P02647	r,f,s,k,u,b,c,o,t,l,t
189	APOA2	P02652	r,s,l
190	APOA4	P06727	c,l
191	APOB	P04114	l
192	APOC3	P02656	h
193	APOD	P05090	b
194	APOH	P02749	r,l
195	APOL2	Q9BQE5	o
196	APOOL	Q6UXV4	o
197	APPL2	Q8NEU8	l
198	APRT	P07741	p,o,l
199	AQP5	P55064	o
200	ARCN1	P48444	o,l
201	ARF1	P84077	r,o
202	ARF3	P61204	s,l
203	ARF4	P18085	l
204	ARF6	P62330	l
205	ARFGAP3	Q9NP61	l
206	ARFGEF1	Q9Y6D6	l
207	ARFGEF3	Q5TH69	o
208	ARFIP1	P53367	l
209	ARFIP2	P53365	l
210	ARHGAP1	Q07960	l,o
211	ARHGAP18	Q8N392	l
212	ARHGDI A	P52565	r,s,o,j,l,m,j
213	ARHGDI B	P52566	n,r,s,o,t,l,j,t,j
214	ARHGEF16	Q5VV41	l
215	ARID3B	Q8IVW6	s
216	ARL1	P40616	l
217	ARL3	P36405	l
218	ARL6IP5	O75915	o,l
219	ARMCX3	Q9UH62	o
220	ARMT1	Q9H993	l
221	ARPC1A	Q92747	l
222	ARPC1B	O15143	l
223	ARPC2	O15144	o,l
224	ARPC3	O15145	o,l
225	ARPC4	P59998	r,o,l
226	ARPC5	O15511	s,l
227	ARPC5L	Q9BPX5	l
228	ARPP19	P56211	l

	Gene	UniProt Accession Number	Studies
229	ARRB1	P49407	l
230	ARSD	P51689	o
231	ASAH1	Q13510	s,o,l
232	ASL	P04424	l
233	ASMT	P46597	l,l
234	ASNA1	O43681	l
235	ASPH	Q12797	o
236	ASPRV1	Q53RT3	a
237	ASRGL1	Q7L266	l
238	ASS1	P00966	l,p,o
239	ATAD3A	Q9NVI7	l,o
240	ATG3	Q9NT62	l
241	ATG7	O95352	l
242	ATIC	P31939	o,l
243	ATL3	F5H617	l
244	ATOX1	O00244	l
245	ATP12A	P54707	o
246	ATP13A1	Q9HD20	o
247	ATP1A1	P05023	o,l
248	ATP1B1	P05026	o,l
249	ATP1B3	P54709	o,l
250	ATP2A1	O14983	o
251	ATP2A2	P16615	o,l
252	ATP2A3	Q93084	o,l
253	ATP2B1	P20020	o
254	ATP2B4	P23634	o,l
255	ATP2C1	P98194	o
256	ATP5F1A	P25705	s,l,o
257	ATP5F1B	P06576	r,c,s,m,l,o
258	ATP5F1C	P36542	l,o
259	ATP5MD	Q96IX5	l
260	ATP5ME	P56385	l,o
261	ATP5MF	P56134	l,o
262	ATP5MG	O75964	l,o
263	ATP5PB	P24539	l,o
264	ATP5PD	O75947	m,o,l,j
265	ATP5PF	P18859	l
266	ATP5PO	P48047	l,o
267	ATP6AP1	Q15904	o
268	ATP6V0A1	Q93050	o
269	ATP6V0A2	Q9Y487	o
270	ATP6V0A4	Q9HBG4	o
271	ATP6V0C	P27449	o
272	ATP6V0D1	P61421	h
273	ATP6V1A	P38606	o,l,h
274	ATP6V1B2	P21281	l
275	ATP6V1C1	P21283	l



	Gene	UniProt Accession Number	Studies
276	ATP6V1D	Q9Y5K8	l
277	ATP6V1E1	P36543	o
278	ATP6V1F	Q16864	l
279	ATP6V1H	Q9UI12	l
280	ATP7B	P35670	o
281	ATP8B1	O43520	o
282	ATP9A	O75110	o
283	AZGP1	P25311	b,u,r,k,s,l,p,a
284	AZU1	P20160	s
285	B2M	P61769	f,b,s,r,k,l,a
286	B3GAT3	O94766	o
287	B3GNT3	Q9Y2A9	o
288	B4GALT4	O60513	o
289	BAG1	Q99933	l
290	BAG3	O95817	l
291	BAG5	G3V274	l
292	BAG6	P46379	l
293	BAIAP2	Q9UQB8	l
294	BANF1	O75531	l
295	BAP18	Q8IXM2	l
296	BASP1	P80723	r,k,o,l
297	BBS1	Q8NFJ9	l
298	BCAM	P50895	o
299	BCAP29	Q9UHQ4	o
300	BCAP31	P51572	l,o
301	BCAS1	O75363	l,o
302	BCAT2	O15382	l
303	BCCIP	Q9P287	l
304	BDH1	Q02338	o,l
305	BDH2	Q9BUT1	l
306	BFSP1	Q12934	h
307	BHMT	E5RJH0	g
308	BID	P55957	l
309	BLMH	Q13867	l
310	BLVRA	P53004	l
311	BLVRB	P30043	o,l
312	BOLA2	Q9H3K6	l
313	BOLA2B	Q9H3K6	l
314	BPGM	P07738	s
315	BPHL	Q86WA6	l
316	BPI	P17213	b,r,s,o
317	BPIFA1	Q9NP55	s,r,b,f,l,p,m,e,o,j,a,j
318	BPIFB1	Q8TDL5	s,k,r,b,l,o
319	BPIFB2	Q8N4F0	s,r,k,q,l,q
320	BPIFB3	P59826	s
321	BPIFB4	P59827	s,r,k,l,o
322	BPNT1	O95861	l,m

	Gene	UniProt Accession Number	Studies
323	BRCC3	P46736	l
324	BRI3BP	Q8WY22	o
325	BROX	Q5VW32	l
326	BSG	P35613	o
327	BTF3	P20290	l
328	BUB3	O43684	l
329	BUD31	P41223	l
330	BZW2	Q9Y6E2	l
331	C11orf54	Q9H0W9	l
332	C12orf10	Q9HB07	l
333	C1QB	P02746	l
334	C1QBP	Q07021	l,o
335	C1QC	P02747	l,p
336	C1R	P00736	l
337	C1orf87	Q8N0U7	l
338	C21orf59-TCP10L	H7BZW1	l
339	C2CD2L	O14523	o
340	C3	P01024	s,r,k,b,p,l,o
341	C4A	P0C0L4	b,l,o
342	C4B	P0C0L5	s,r,l
343	C4BPA	P04003	l,o
344	C4BPB	P20851	h
345	C4B_2	P0C0L5	s,r,l
346	C5	P01031	s,l
347	C6	P13671	l
348	C7	P10643	l
349	C8B	P07358	l
350	C8G	P07360	l
351	C9	P02748	l
352	C9orf64	Q5T6V5	l
353	CA1	P00915	c,t,l,o,t
354	CA13	Q8N1Q1	l
355	CA2	P00918	b,l,o
356	CAB39	Q9Y376	l
357	CACYBP	Q9HB71	l
358	CAD	P27708	l,o
359	CALM1	P0DP23	s,r,l,a
360	CALM2	P0DP24	o
361	CALML3	P27482	o,l
362	CALML5	Q9NZT1	r,k,l,a
363	CALR	P27797	c,m,o,l
364	CALU	O43852	o,l
365	CAMK2D	Q13557	l
366	CAMP	P49913	s,o
367	CAND1	Q86VP6	l,o
368	CANX	P27824	o,l

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
369	CAP1	Q01518	r,s,o,l	416	CCT5	P48643	c,l,o
370	CAPG	P40121	s,o,l	417	CCT6A	P40227	l
371	CAPN1	P07384	o,l	418	CCT7	Q99832	l
372	CAPN13	Q6MZZ7	l	419	CCT8	P50990	o,l,d
373	CAPN2	P17655	o,l	420	CD14	P08571	o,l
374	CAPN5	O15484	o	421	CD2AP	Q9Y5K6	l
375	CAPNS1	P04632	s,l,o	422	CD38	P28907	o
376	CAPRIN1	Q14444	l	423	CD44	P16070	o,l
377	CAPS	Q13938	s,r,c,l,p,o,m	424	CD47	Q08722	o
378	CAPZA1	P52907	s,o,l	425	CD59	P13987	o,l
379	CAPZA2	P47755	l	426	CD5L	O43866	l
380	CAPZB	P47756	s,o,l	427	CD63	P08962	o
381	CARHSP1	Q9Y2V2	l	428	CD74	P04233	o,l
382	CARMIL1	Q5VZK9	l	429	CD81	P60033	o
383	CARS	P49589	l	430	CD82	P27701	o
384	CASK	O14936	l	431	CD9	P21926	o,l
385	CASP1	P29466	l	432	CD97	P48960	o
386	CASP12	Q6UXS9	s	433	CDA	P32320	s,r
387	CASP14	P31944	r,k,a	434	CDC37	Q16543	o,l
388	CASP3	P42574	l	435	CDC42	P60953	l
389	CASP7	P55210	l	436	CDC5L	Q99459	l
390	CAST	P20810	o,l	437	CDCP1	Q9H5V8	o
391	CAT	P04040	s,r,p,o,l,t,t	438	CDH1	P12830	o,l
392	CBR1	P16152	s,r,o,l	439	CDIPT	O14735	o
393	CBR3	O75828	l	440	CDK5	Q00535	l
394	CBS	P35520	h	441	CDK5RAP3	Q96JB5	l
395	CBX3	Q13185	o,l	442	CDKL1	Q00532	s
396	CBX5	P45973	l	443	CDS1	Q92903	o,l
397	CC2D1A	Q6P1N0	l	444	CDS2	O95674	o
398	CCAR2	Q8N163	o,l	445	CDV3	Q9UKY7	l
399	CCDC102B	Q68D86	s	446	CEACAM5	P06731	o,l
400	CCDC124	Q96CT7	l	447	CENPF	P49454	m
401	CCDC151	A5D8V7	l	448	CEP128	Q6ZU80	o
402	CCDC17	Q96LX7	l	449	CEP131	Q9UPN4	o
403	CCDC170	Q8IYT3	o	450	CEP135	Q66GS9	l,o
404	CCDC171	Q6TFL3	s	451	CERS2	Q96G23	o
405	CCDC22	O60826	l	452	CES1	P23141	s,o,l
406	CCDC39	Q9UFE4	l,l	453	CES2	O00748	o,l
407	CCDC47	Q96A33	o	454	CETN2	P41208	l
408	CCDC6	Q16204	l	455	CFAP20	Q9Y6A4	l
409	CCDC78	A2IDD5	l	456	CFAP52	Q8N1V2	l
410	CCDC81	Q6ZN84	m	457	CFAP57	Q96MR6	l
411	CCND1	P24385	h	458	CFAP70	Q5T0N1	l
412	CCS	O14618	l	459	CFB	P00751	r,u,s,p,l
413	CCT2	P78371	c,o,l	460	CFH	P08603	l
414	CCT3	P49368	o,l	461	CFI	P05156	l
415	CCT4	P50991	o,l	462	CFL1	P23528	s,r,o,l,p

	Gene	UniProt Accession Number	Studies
463	CGN	Q9P2M7	l
464	CGNL1	Q0VF96	s
465	CHCHD10	Q8WYQ3	l
466	CHCHD3	Q9NX63	o
467	CHD4	Q14839	o
468	CHDH	Q8NE62	o
469	CHI3L2	Q15782	s
470	CHL1	O00533	l
471	CHMP4B	Q9H444	l
472	CHMP5	Q9NZZ3	l
473	CHORDC1	Q9UHD1	l
474	CHP1	Q99653	o
475	CHTOP	Q9Y3Y2	o
476	CIAO1	O76071	l
477	CIB1	Q99828	l,h
478	CIRBP	Q14011	l
479	CISD1	Q9NZ45	o,l
480	CKAP4	Q07065	o,l
481	CKAP5	Q14008	s
482	CKB	P12277	s,r,c,l,p,o
483	CKMT1A	P12532	l,o
484	CKMT1B	P12532	l,o
485	CLC	Q05315	l,t,p,t
486	CLDN1	O95832	o,l
487	CLDN3	O15551	o,l
488	CLDN4	O14493	l
489	CLDN6	P56747	l
490	CLDN7	O95471	l
491	CLDN9	O95484	l
492	CLEC3B	P05452	l
493	CLEC4F	Q8N1N0	k
494	CLIC1	O00299	c,r,s,o,p,l
495	CLIC6	Q96NY7	o,l
496	CLINT1	H0YCL3	l,o
497	CLIP1	P30622	l
498	CLMN	Q96JQ2	l
499	CLTA	P09496	l,o
500	CLTC	Q00610	r,s,l,o
501	CLU	P10909	b,s,r,k,o,l
502	CLUH	O75153	l
503	CMAS	Q8NFW8	l
504	CMBL	Q96DG6	l
505	CMPK1	P30085	j,o,l,m,j
506	CMPK2	Q5EBM0	l
507	CNBP	P62633	l
508	CNDP2	Q96KP4	s,r,l,o
509	CNN1	P51911	o

	Gene	UniProt Accession Number	Studies
510	CNN2	Q99439	s,l
511	CNP	P09543	o
512	CNTN2	Q02246	s
513	COASY	Q13057	l,o
514	COG5	Q9UP83	o
515	COG7	P83436	l
516	COG8	Q96MW5	l
517	COL1A1	P02452	a
518	COL1A2	P08123	o,a
519	COL28A1	Q2UY09	s
520	COL4A3BP	Q9Y5P4	l
521	COL5A3	P25940	s
522	COL7A1	Q02388	o
523	COMMD3	Q9UBI1	l
524	COMMD9	Q9P000	l
525	COMT	P21964	l
526	COPA	P53621	o,l
527	COPB1	P53618	o,l
528	COPB2	P35606	o
529	COPE	O14579	l
530	COPG1	H0Y8X7	l
531	COPG2	Q9UBF2	l
532	COPS2	P61201	l
533	COPS4	Q9BT78	h,l
534	COPS5	Q92905	l
535	COPS6	Q7L5N1	l
536	COPS7A	Q9UBW8	l
537	COPS8	Q99627	l
538	COPZ1	F8VXR1	l
539	COQ6	Q9Y2Z9	s
540	CORO1A	P31146	s,r,o,l
541	CORO1B	Q9BR76	l
542	CORO1C	Q9ULV4	l
543	CORO7	P57737	l
544	COTL1	Q14019	l
545	COX4I1	P13073	l,o
546	COX5A	P20674	l,o
547	COX5B	P10606	l,o
548	COX6A1	P12074	l
549	COX6B1	P14854	l
550	COX6C	P09669	o
551	COX7A2	P14406	l,o
552	COX7B	P24311	o
553	COX7C	P15954	o
554	CP	P00450	s,r,i,o,l
555	CPB2	Q96IY4	l
556	CPD	O75976	o

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
557	CPNE1	Q99829	l	604	CTSC	P53634	l
558	CPNE3	O75131	l	605	CTSD	P07339	s,r,o,m,l
559	CPPED1	Q9BRF8	l	606	CTSG	P08311	s,r,o,l
560	CPS1	P31327	g	607	CTSH	P09668	l
561	CPSF3	Q9UKF6	l	608	CTSS	P25774	l
562	CPSF6	Q16630	l	609	CTSZ	Q9UBR2	l
563	CPSF7	Q8N684	l	610	CTTN	Q14247	o,l
564	CPT1A	P50416	o	611	CUL1	Q13616	s,l
565	CPT2	P23786	l,o	612	CUL2	Q13617	l
566	CRABP2	P29373	l	613	CUL3	Q13618	l
567	CRIP1	P50238	l	614	CUL5	Q93034	l
568	CRIP2	P52943	l	615	CUTA	O60888	l
569	CRISP3	P54108	r,s,l	616	CXCL1	P09341	l
570	CRK	P46108	l	617	CXCL17	Q6UXB2	r
571	CRKL	P46109	l	618	CYB561	P49447	o
572	CRNN	Q9UBG3	l	619	CYB5A	P00167	l
573	CROCC	Q5TZA2	o,l	620	CYB5B	J3QR91	l,o
574	CROCCP3	Q8IVE0	l	621	CYB5R1	Q9UHQ9	l
575	CROT	Q9UKG9	l	622	CYB5R2	Q6BCY4	l
576	CRYL1	Q9Y2S2	l	623	CYB5R3	P00387	o,l
577	CRYM	Q14894	o,l	624	CYBA	P13498	o
578	CRYZ	Q08257	o,l	625	CYBB	P04839	o
579	CRYZL1	O95825	l	626	CYBC1	Q9BQA9	o
580	CS	O75390	o,l	627	CYC1	P08574	o,l
581	CSDE1	O75534	l	628	CYCS	P99999	l,o
582	CSE1L	P55060	s,l	629	CYFIP1	Q7L576	o,l
583	CSF1	P09603	h	630	CYP1B1	Q16678	o
584	CSK	P41240	l	631	CYP2A6	P11509	o
585	CSNK1A1	P48729	l	632	CYP2J2	P51589	o
586	CSNK2A1	P68400	l	633	CYP2S1	Q96SQ9	o,l
587	CSRP1	P21291	l	634	CYP3A43	Q9HB55	a
588	CSRP2	Q16527	l	635	CYP4B1	P13584	o
589	CST1	P01037	f,c,s,k,l	636	CYP4F11	Q9HBI6	o
590	CST3	P01034	f,s,r,k,l	637	CYP4F12	Q9HCS2	o
591	CST4	P01036	s,r,k,l,a	638	CYP4F2	P78329	o
592	CSTA	P01040	f,l,a	639	CZIB	Q9NWW4	l
593	CSTB	P04080	s,r,k,o,l,a	640	DAD1	P61803	o
594	CTBP1	Q13363	l	641	DAG1	Q14118	l
595	CTBP2	P56545	l	642	DARS	P14868	l,o
596	CTNNA1	E5RJP7	l,o	643	DAW1	Q8N136	l
597	CTNNA2	P26232	l	644	DAZAP1	Q96EP5	l
598	CTNNB1	P35222	o,l	645	DBI	P07108	r,s,l
599	CTNBL1	Q8WYA6	l	646	DBNL	Q9UJU6	l,o
600	CTNND1	C9JZR2	l,o	647	DCD	P81605	s,r,o,a
601	CTPS1	P17812	l	648	DCPS	Q96C86	l
602	CTPS2	Q9NRF8	l	649	DCTD	P32321	l
603	CTSB	P07858	r,o,m,h,l	650	DCTN1	Q14203	l



	Gene	UniProt Accession Number	Studies
651	DCTN2	Q13561	l
652	DCTN4	Q9UJW0	l
653	DCUN1D1	Q96GG9	l
654	DCXR	Q7Z4W1	l
655	DDAH1	O94760	l
656	DDAH2	O95865	l
657	DDB1	Q16531	l,o
658	DDI2	Q5TDH0	l
659	DDOST	P39656	l,o
660	DDRGK1	Q96HY6	o,l
661	DDTL	A6NHG4	l
662	DDX1	Q92499	l
663	DDX17	Q92841	o,l
664	DDX18	Q9NVP1	o
665	DDX19B	Q9UMR2	l
666	DDX21	Q9NR30	o
667	DDX39A	O00148	o
668	DDX39B	Q13838	l
669	DDX3X	O00571	l,o
670	DDX42	Q86XP3	l
671	DDX46	Q7L014	l
672	DDX5	P17844	o,l
673	DDX51	Q8N8A6	o
674	DDX58	O95786	l
675	DDX6	P26196	o,l
676	DECR1	Q16698	o,l
677	DEFA1	P59665	s,o,a
678	DEFA1B	P59665	s,o,a
679	DEFA3	P59666	r,k
680	DERL1	Q9BUN8	o
681	DES	P17661	m,o
682	DFFA	O00273	l
683	DGAT1	O75907	o
684	DGKA	P23743	l
685	DGLUCY	Q7Z3D6	l
686	DHCR7	Q9UBM7	o
687	DHODH	Q02127	o
688	DHRS1	Q96LJ7	l
689	DHRS3	O75911	o
690	DHRS7	Q9Y394	o,l
691	DHRS7B	Q6IAN0	l
692	DHRS9	Q9BPW9	l,o
693	DHX15	O43143	o,l
694	DHX30	Q7L2E3	o
695	DHX9	Q08211	o,l
696	DIABLO	Q9NR28	l,l
697	DIAPH1	O60610	l

	Gene	UniProt Accession Number	Studies
698	DIDO1	Q9BTC0	o
699	DIS3	Q9Y2L1	l
700	DLAT	P10515	o,l
701	DLD	P09622	l,o
702	DLST	P36957	o,l
703	DMBT1	Q9UGM3	r,s,k,l,o
704	DMTF1	Q9Y222	h
705	DNAH5	Q8TE73	l,o
706	DNAH8	Q96JB1	o
707	DNAH9	Q9NYC9	l,o
708	DNAI1	Q9UI46	l
709	DNAI2	Q9GZS0	l
710	DNAJA1	P31689	l
711	DNAJA2	O60884	l
712	DNAJA3	Q96EY1	o
713	DNAJA4	Q8WW22	l
714	DNAJB1	P25685	l
715	DNAJB12	Q9NXW2	o
716	DNAJB13	P59910	l
717	DNAJB6	O75190	l
718	DNAJC11	Q9NVH1	l,o
719	DNAJC13	O75165	o
720	DNAJC2	Q99543	l
721	DNAJC8	O75937	l
722	DNAL1	Q4LDG9	l
723	DNALI1	O14645	l
724	DNM1L	O00429	l
725	DNM2	P50570	l
726	DNPEP	Q9ULA0	l
727	DNPH1	O43598	l
728	DOHH	Q9BU89	l
729	DPCD	Q9BVM2	l
730	DPP3	Q9NY33	l
731	DPP7	Q9UHL4	l
732	DPY30	Q9C005	l
733	DPYS	Q14117	l
734	DPYSL2	Q16555	l
735	DRG1	Q9Y295	l
736	DRG2	P55039	l
737	DSG1	Q02413	a
738	DSG2	Q14126	o,l
739	DSG3	P32926	o,l
740	DSP	P15924	l,o,a
741	DSTN	P60981	s,l
742	DTX3L	Q8TDB6	l
743	DUOX1	Q9NRD9	o
744	DUOX2	Q9NRD8	o

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
745	DUSP23	Q9BVJ7	l	792	EIF2S3	P41091	l
746	DYNC1H1	Q14204	l,o	793	EIF3A	Q14152	l,o
747	DYNC1I2	Q13409	l,o	794	EIF3B	P55884	l
748	DYNC1LI1	Q9Y6G9	l	795	EIF3C	Q99613	o,l
749	DYNC1LI2	O43237	l	796	EIF3D	O15371	l
750	DYNC2H1	Q8NCM8	l	797	EIF3E	P60228	l
751	DYNLL1	P63167	l	798	EIF3F	O00303	l
752	DYNLRB1	Q9NP97	l	799	EIF3G	O75821	l
753	DYNLRB2	Q8TF09	l	800	EIF3H	O15372	l
754	DYNLT1	P63172	l	801	EIF3I	Q13347	l,h
755	DYSF	O75923	o	802	EIF3K	Q9UBQ5	l
756	EBP	Q15125	l	803	EIF3L	Q9Y262	l
757	ECE1	P42892	o	804	EIF3M	Q7L2H7	l
758	ECH1	Q13011	l,o	805	EIF4A1	P60842	s,o,l
759	ECHDC1	Q9NTX5	l	806	EIF4A2	Q14240	l
760	ECHS1	P30084	o,j,m,l,j	807	EIF4A3	P38919	o,l
761	ECI1	P42126	o,l	808	EIF4B	P23588	o,l
762	ECPAS	Q5VYK3	l	809	EIF4E	P06730	l
763	EDC4	Q6P2E9	l	810	EIF4G1	Q04637	l,o
764	EDF1	O60869	l	811	EIF4G2	P78344	o
765	EEA1	Q15075	l	812	EIF4H	Q15056	l
766	EEF1A1	P68104	s,o,a	813	EIF5	P55010	l
767	EEF1A1P5	Q5VTE0	r,l	814	EIF5A	P63241	r,l
768	EEF1B2	P24534	l,o	815	EIF5B	O60841	l
769	EEF1D	P29692	l,o	816	EIF6	P56537	l
770	EEF1E1	O43324	l	817	ELANE	P08246	s,r,k,o,l
771	EEF1G	P26641	l	818	ELAVL1	Q15717	l,o
772	EEF2	P13639	s,r,l,o	819	ELMOD2	Q8IZ81	o
773	EFCAB1	Q9HAE3	l	820	ELOB	Q15370	l
774	EFHC1	Q5JVL4	l	821	EMC1	Q8N766	o
775	EFHC2	Q5JST6	l	822	EMC3	Q9P0I2	o
776	EFHD2	Q96C19	l	823	EMC6	Q9BV81	o
777	EFTUD2	Q15029	l	824	EMC7	Q9NPA0	o
778	EGFR	P00533	o	825	EMD	P50402	o,l
779	EHD2	Q9NZN4	h	826	EML1	O00423	l
780	EHD3	Q9NZN3	l	827	EML2	O95834	l
781	EHD4	Q9H223	o,l	828	EML4	Q9HC35	l
782	EHHADH	Q08426	o	829	EMP2	P54851	c
783	EIF1	P41567	l	830	ENDOG	Q14249	l
784	EIF1AY	O14602	l	831	ENO1	P06733	c,s,r,n,m,l,o,a
785	EIF2A	Q9BY44	l	832	ENO2	P09104	h,l
786	EIF2AK2	P19525	l	833	ENOPH1	Q9UHY7	l
787	EIF2B1	Q14232	l	834	ENSA	O43768	l
788	EIF2B2	P49770	l	835	ENTPD3	O75355	o
789	EIF2B3	Q9NR50	l	836	EPB41L1	Q9H4G0	o,l
790	EIF2S1	P05198	l,d	837	EPB42	P16452	o
791	EIF2S2	P20042	l	838	EPCAM	P16422	l,o

	Gene	UniProt Accession Number	Studies
839	EPHA2	P29317	o
840	EPHX1	P07099	o,l
841	EPHX2	P34913	l
842	EPM2AIP1	Q7L775	l
843	EPPK1	P58107	s,l,o
844	EPRS	P07814	l,o
845	EPS8	Q12929	l
846	EPS8L2	Q9H6S3	l
847	EPX	P11678	o
848	ERAP1	Q9NZ08	o,l
849	ERBB2	P04626	o
850	ERGIC1	Q969X5	l,o
851	ERH	P84090	o
852	ERICH3	Q5RHP9	l
853	ERICH5	Q6P6B1	o
854	ERLIN1	O75477	o
855	ERLIN2	O94905	l,o
856	ERMP1	Q7Z2K6	o
857	ERN2	Q76MJ5	o
858	ERO1A	Q96HE7	o,l
859	ERP29	P30040	m,o,l
860	ERP44	Q9BS26	o,l
861	ESD	P10768	l,p
862	ESYT1	Q9BSJ8	l,o
863	ESYT2	A0FGR8	o
864	ETF1	P62495	l
865	ETFA	P13804	l,o
866	ETFB	P38117	l
867	ETFDH	Q16134	o,l
868	ETHE1	O95571	o,l
869	EVPL	Q92817	o,l
870	EWSR1	Q01844	o,l
871	EXD2	Q9NVH0	o
872	EXOC1	Q9NV70	l
873	EXOC2	Q96KP1	l
874	EZR	P15311	s,r,o,l
875	F11R	Q9Y624	o
876	F12	P00748	l
877	F13B	P05160	l
878	F2	P00734	r,l
879	F3	P13726	o,l
880	FABP1	P07148	g
881	FABP4	P15090	c
882	FABP5	Q01469	r,s,n,u,k,o,l,p,a
883	FAF2	Q96CS3	o
884	FAH	P16930	l
885	FAHD1	Q6P587	l

	Gene	UniProt Accession Number	Studies
886	FAM107B	Q9H098	l
887	FAM114A1	Q8IWE2	l
888	FAM120A	Q9NZB2	o,l
889	FAM162A	Q96A26	o
890	FAM169A	Q9Y6X4	s
891	FAM174A	Q8TBP5	o
892	FAM3C	Q92520	o
893	FAM3D	Q96BQ1	l,o
894	FAM49B	Q9NUQ9	l
895	FAM81B	Q96LP2	l,o
896	FAM98C	Q17RN3	l
897	FANCD2	Q9BXW9	l
898	FARSA	Q9Y285	l
899	FARSB	Q9NSD9	l
900	FASN	P49327	o,l
901	FAT3	Q8TDW7	l
902	FAU	P62861	l
903	FBL	P22087	o,l
904	FBLN1	P23142	l
905	FBP1	P09467	s,o,l
906	FBXL4	Q9UKA2	l
907	FBXO2	Q9UK22	l
908	FBXO22	Q8NEZ5	l
909	FBXW9	Q5XUX1	l
910	FCGBP	Q9Y6R7	s,r,k,o,l
911	FCGR3B	O75015	l
912	FCSK	Q8N0W3	l
913	FDFT1	P37268	o
914	FDPS	P14324	l
915	FDXR	P22570	o,l
916	FECH	P22830	o
917	FEN1	P39748	l
918	FER1L6	Q2WGJ9	l
919	FERMT3	Q86UX7	l
920	FGA	P02671	s,r,l,o
921	FGB	P02675	b,s,r,k,l,o
922	FGG	P02679	s,r,l,j,o,j
923	FH	P07954	o,l
924	FHAD1	B1AJZ9	l
925	FHIT	P49789	l
926	FIS1	Q9Y3D6	l
927	FKBP11	Q9NYL4	o
928	FKBP1A	P62942	s,l
929	FKBP2	P26885	l
930	FKBP3	Q00688	l
931	FKBP4	Q02790	l
932	FKBP5	Q13451	l

	Gene	UniProt Accession Number	Studies
933	FKBP8	Q14318	o
934	FLAD1	Q8NFF5	l
935	FLG	P20930	r,a
936	FLII	Q13045	l
937	FLNA	P21333	o,l
938	FLNB	O75369	o,l
939	FLOT1	O75955	l,o
940	FLOT2	Q14254	o
941	FMC1	Q96HJ9	l
942	FMO3	P31513	l,o
943	FN1	P02751	o,l
944	FNTA	P49354	l
945	FOXO3	O43524	l
946	FSCN1	Q16658	l
947	FTH1	P02794	l
948	FTL	P02792	l
949	FTO	Q9C0B1	l
950	FUBP1	Q96AE4	o,l
951	FUCA1	P04066	l
952	FUS	P35637	o,l
953	FUT2	Q10981	o
954	FUT3	P21217	o,l
955	FUT6	P51993	o,l
956	FUT8	Q9BYC5	o
957	G3BP1	Q13283	l,o
958	G6PD	P11413	r,l
959	GAA	P10253	o,l
960	GALE	Q14376	l
961	GALK1	P51570	l
962	GALM	Q96C23	l
963	GALNT1	Q10472	o
964	GALNT12	Q8IXK2	o
965	GALNT4	Q8N4A0	o
966	GALNT5	Q7Z7M9	o
967	GALNT6	Q8NCL4	l
968	GALNT7	Q865F2	o
969	GANAB	Q14697	o,l
970	GAPDH	P04406	s,r,c,o,l,p,t,a,t
971	GAPVD1	Q14C86	l
972	GAR1	Q9NY12	o
973	GARS	P41250	l,o
974	GART	P22102	l
975	GATD3A	P0DPI2	o,l
976	GBE1	Q04446	l
977	GBP1	P32455	l
978	GBP2	P32456	l
979	GBP4	Q96PP9	l

	Gene	UniProt Accession Number	Studies
980	GBP5	Q96PP8	l
981	GBP6	Q6ZN66	l
982	GC	P02774	r,s,u,k,c,l
983	GCA	P28676	l
984	GCHFR	P30047	l
985	GCLC	P48506	o,l
986	GCLM	P48507	l
987	GCN1	Q92616	o,l
988	GDAP1	Q8TB36	o
989	GDI1	P31150	l
990	GDI2	P50395	r,s,o,l,p
991	GDPD3	Q7L5L3	o
992	GDPGP1	Q6ZNW5	l
993	GFAP	P14136	b
994	GFPT1	Q06210	o,l
995	GGCT	O75223	l
996	GGPS1	O95749	l
997	GH1	P01241	s
998	GHITM	Q9H3K2	o
999	GIPC1	O14908	l
1000	GK3P	Q14409	l
1001	GLA	P06280	l,h
1002	GLB1	P16278	o,l
1003	GLCE	O94923	o
1004	GLG1	Q92896	o,l
1005	GLIPR2	Q9H4G4	o
1006	GLO1	Q04760	l,j
1007	GLOD4	Q9HC38	l
1008	GLRX	P35754	l
1009	GLRX3	O76003	l
1010	GLTP	Q9NZD2	l
1011	GLUD1	P00367	c,o,l
1012	GLUD2	P49448	m
1013	GLUL	P15104	o,l
1014	GM2A	P17900	l
1015	GMDS	O60547	l
1016	GMFB	P60983	l
1017	GMFG	O60234	l
1018	GMPPA	Q96IJ6	l
1019	GMPPB	Q9Y5P6	l
1020	GMPR	P36959	l
1021	GMPR2	Q9P2T1	l
1022	GMPS	P49915	l
1023	GNA11	P29992	o,l
1024	GNAI1	P63096	o
1025	GNAI2	P04899	o,l
1026	GNAI3	P08754	o

	Gene	UniProt Accession Number	Studies
1027	GNAS	Q5JWF2	o
1028	GNB1	P62873	o,l
1029	GNB2	P62879	l
1030	GENE	Q9Y223	l
1031	GNG12	Q9UBI6	o
1032	GNG13	Q9P2W3	h
1033	GNG5	P63218	o
1034	GNL1	P36915	l
1035	GNPDA1	P46926	l
1036	GNPDA2	Q8TDQ7	l
1037	GNPNAT1	Q96EK6	l
1038	GNS	P15586	l
1039	GOLGB1	Q14789	o,l
1040	GOLM1	Q8NBJ4	o,l
1041	GOLPH3L	Q9H4A5	l
1042	GOLT1B	Q9Y3E0	o
1043	GORASP2	Q9H8Y8	l
1044	GOSR1	O95249	o
1045	GOT1	P17174	l
1046	GOT2	P00505	l,o
1047	GPAA1	O43292	o
1048	GPD1L	Q8N335	l
1049	GPD2	P43304	o,l
1050	GPI	P06744	s,r,l,p,o
1051	GPNMB	Q14956	l
1052	GPR107	Q5VW38	o
1053	GPR89A	B7ZAQ6	o
1054	GPS1	Q13098	l
1055	GPX1	P07203	o,l
1056	GPX2	P18283	l
1057	GPX4	P36969	l
1058	GRB2	P62993	l
1059	GRHPR	Q9UBQ7	l
1060	GRN	P28799	s,r,l
1061	GSDMB	Q8TAX9	l
1062	GSDMD	P57764	l
1063	GSN	P06396	s,r,o,l
1064	GSPT1	P15170	l
1065	GSR	P00390	o,l
1066	GSS	P48637	l,p
1067	GSTA1	P08263	s,c,l,o
1068	GSTA2	P09210	r,l,e
1069	GSTA3	Q16772	l
1070	GSTA5	Q7RTV2	l
1071	GSTK1	Q9Y2Q3	o,l
1072	GSTM1	P09488	l
1073	GSTM2	P28161	l

	Gene	UniProt Accession Number	Studies
1074	GSTM3	P21266	l,h
1075	GSTM4	Q03013	l
1076	GSTO1	P78417	o,l
1077	GSTP1	P09211	c,s,r,e,m,o,l,p,a,j
1078	GSTT1	P30711	l
1079	GSTZ1	O43708	l
1080	GTF2I	P78347	l
1081	GTPBP1	O00178	l
1082	GUSB	P08236	l
1083	GYG1	P46976	l
1084	GYS1	P13807	l
1085	H1FO	P07305	o,l
1086	H1FX	Q92522	l
1087	H2AFV	Q71UI9	l
1088	H2AFY	O75367	l,o
1089	H2AFY2	Q9P0M6	l
1090	H2AFZ	P0C055	s
1091	H3F3A	P84243	s
1092	H3F3B	P84243	s
1093	H6PD	O95479	l
1094	HACD3	Q9P035	l
1095	HADH	Q16836	l,o
1096	HADHA	P40939	o,l
1097	HADHB	P55084	o,l
1098	HAGH	Q16775	l
1099	HAL	P42357	p
1100	HARS	P12081	l,p
1101	HBA1	P69905	s,r,b,c,k,o,l,a
1102	HBA2	P69905	s,r,b,c,k,o,l,a
1103	HBB	P68871	s,r,b,c,q,p,m,o,e,l,q,a
1104	HBD	P02042	s,o,l
1105	HBG1	P69891	o
1106	HCLS1	P14317	l
1107	HDAC1	Q13547	l
1108	HDCC2	Q7Z4H3	l
1109	HDCC3	Q8N4P3	l
1110	HDGF	P51858	o,l
1111	HDGFL3	Q9Y3E1	l
1112	HDHD2	Q9H0R4	l
1113	HDHD3	Q9BSH5	l
1114	HDLBP	Q00341	o,l
1115	HEATR1	Q9H583	l
1116	HEBP1	Q9NRV9	l
1117	HEBP2	Q9Y5Z4	o,l
1118	HERC4	Q5GLZ8	l
1119	HEXA	P06865	l
1120	HEXB	P07686	l,o

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
1121	HIBADH	P31937	o,l	1168	HIST1H4L	P62805	b,s,r,l,o,a
1122	HIBCH	Q6NVY1	l	1169	HIST2H2AA3	Q6FI13	l
1123	HID1	Q8IV36	o	1170	HIST2H2AA4	Q6FI13	l
1124	HINT1	P49773	l	1171	HIST2H2AB	Q8IUE6	k
1125	HINT2	Q9BX68	o,l	1172	HIST2H2AC	Q16777	s
1126	HIST1H1A	Q02539	o,l	1173	HIST2H3A	Q71DI3	s,r
1127	HIST1H1B	P16401	o,l	1174	HIST2H3C	Q71DI3	s,r
1128	HIST1H1C	P16403	o	1175	HIST2H3D	Q71DI3	s,r
1129	HIST1H1D	P16402	r	1176	HIST2H4A	P62805	b,s,r,l,o,a
1130	HIST1H1E	P10412	s,l	1177	HIST2H4B	P62805	b,s,r,l,o,a
1131	HIST1H2AA	Q96QV6	o	1178	HIST3H2BB	Q8N257	l
1132	HIST1H2AB	P04908	o	1179	HIST3H3	Q16695	o
1133	HIST1H2AC	Q93077	k	1180	HIST4H4	P62805	b,s,r,l,o,a
1134	HIST1H2AD	P20671	r,o	1181	HK1	P19367	o,l
1135	HIST1H2AE	P04908	o	1182	HK3	P52790	l
1136	HIST1H2AH	Q96KK5	s	1183	HLA-A	P01892	l,l,h,l
1137	HIST1H2BA	Q96A08	b,o	1184	HLA-B	P01889	o,l,o,h
1138	HIST1H2BB	P33778	o	1185	HLA-C	P30510	l
1139	HIST1H2BC	P62807	o	1186	HLA-DPA1	P20036	l
1140	HIST1H2BE	P62807	o	1187	HLA-DQB1	P01920	o
1141	HIST1H2BF	P62807	o	1188	HLA-DRA	P01903	l,o
1142	HIST1H2BG	P62807	o	1189	HLA-DRB1	P13760	l
1143	HIST1H2BI	P62807	o	1190	HM13	Q8TCT9	o
1144	HIST1H2BJ	P06899	s	1191	HMGA1	P17096	l
1145	HIST1H2BK	O60814	s	1192	HMGB1	P09429	s,l
1146	HIST1H2BL	Q99880	l	1193	HMGB2	P26583	s,l
1147	HIST1H2BM	Q99879	r	1194	HMGB3	O15347	l
1148	HIST1H3A	P68431	s,o	1195	HMGCL	P35914	o,l
1149	HIST1H3B	P68431	s,o	1196	HMGCS2	P54868	o,l
1150	HIST1H3C	P68431	s,o	1197	HMGNI	P05114	o
1151	HIST1H3D	P68431	s,o	1198	HMGNI2	P05204	o
1152	HIST1H3E	P68431	s,o	1199	HMGNI5	P82970	l
1153	HIST1H3F	P68431	s,o	1200	HMOX2	P30519	o
1154	HIST1H3G	P68431	s,o	1201	HNMT	P50135	l
1155	HIST1H3H	P68431	s,o	1202	HNRNPA0	Q13151	l
1156	HIST1H3I	P68431	s,o	1203	HNRNPA1	P09651	l,o
1157	HIST1H3J	P68431	s,o	1204	HNRNPA1L2	Q32P51	s
1158	HIST1H4A	P62805	b,s,r,l,o,a	1205	HNRNPA2B1	P22626	r,s,o,l
1159	HIST1H4B	P62805	b,s,r,l,o,a	1206	HNRNPA3	P51991	s,o,l
1160	HIST1H4C	P62805	b,s,r,l,o,a	1207	HNRNPAB	Q99729	l
1161	HIST1H4D	P62805	b,s,r,l,o,a	1208	HNRNPC	P07910	r,s,o,l
1162	HIST1H4E	P62805	b,s,r,l,o,a	1209	HNRNPCL1	O60812	o
1163	HIST1H4F	P62805	b,s,r,l,o,a	1210	HNRNPD	Q14103	r,s,o,l
1164	HIST1H4H	P62805	b,s,r,l,o,a	1211	HNRNPDL	O14979	l
1165	HIST1H4I	P62805	b,s,r,l,o,a	1212	HNRNPF	P52597	l,o
1166	HIST1H4J	P62805	b,s,r,l,o,a	1213	HNRNPH1	P31943	o,l
1167	HIST1H4K	P62805	b,s,r,l,o,a	1214	HNRNPH2	P55795	l



	Gene	UniProt Accession Number	Studies
1215	HNRNPH3	P31942	o,l
1216	HNRNPK	P61978	c,r,s,o,l
1217	HNRNPL	P14866	l
1218	HNRNPM	P52272	r,o,l
1219	HNRNPR	O43390	o,l
1220	HNRNPU	Q00839	o,l
1221	HNRNPUL1	Q9BUJ2	l
1222	HNRNPUL2	Q1KMD3	o,l
1223	HOXA4	Q00056	o
1224	HOXB4	P17483	o
1225	HP	P00738	b,s,r,f,k,o,p,l,a
1226	HP1BP3	Q555J5	l
1227	HPR	P00739	a
1228	HPRT1	P00492	l
1229	HPX	P02790	u,s,r,k,c,l
1230	HRG	P04196	r,l
1231	HRNR	Q86YZ3	a
1232	HSBP1	O75506	l
1233	HSD11B2	P80365	o
1234	HSD17B10	Q99714	l,o
1235	HSD17B11	Q8NBQ5	o
1236	HSD17B12	Q53GQ0	o,l
1237	HSD17B13	Q7Z5P4	l,o
1238	HSD17B4	P51659	o,l
1239	HSD17B8	Q92506	o
1240	HSDL2	Q6YN16	l
1241	HSP90AA1	P07900	s,r,o,l
1242	HSP90AB1	P08238	s,o,l
1243	HSP90AB2P	Q58FF8	l
1244	HSP90B1	P14625	t,o,d,t,l
1245	HSPA14	Q0VDF9	l,l
1246	HSPA1A	P0DMV8	s,r,c,l,o,m
1247	HSPA1L	P34931	o
1248	HSPA2	P54652	o,l
1249	HSPA4	P34932	o
1250	HSPA4L	O95757	l
1251	HSPA5	P11021	c,l,o,m,d
1252	HSPA8	P11142	s,c,o,l,p,m
1253	HSPA9	P38646	c,m,o,l,g
1254	HSPB1	P04792	s,r,k,c,o,l,p,m,a
1255	HSPB11	Q9Y547	l
1256	HSPBP1	Q9NZL4	l
1257	HSPD1	P10809	c,l,o,m,g
1258	HSPE1	P61604	l,o
1259	HSPG2	P98160	s
1260	HSPH1	Q92598	l
1261	HTATIP2	Q9BUP3	o

	Gene	UniProt Accession Number	Studies
1262	HTRA1	Q92743	l
1263	HTRA2	O43464	l
1264	HTT	P42858	o
1265	HUWE1	Q7Z6Z7	l
1266	HYOU1	Q9Y4L1	l,o
1267	IAH1	Q2TAA2	l
1268	IARS	P41252	l
1269	IARS2	Q9NSE4	l
1270	ICAM3	P32942	o
1271	IDE	P14735	l
1272	IDH1	O75874	r,s,c,p,o,l
1273	IDH2	P48735	o,l
1274	IDH3A	P50213	o,l
1275	IDH3G	P51553	l
1276	IDI1	Q13907	l
1277	IDO1	P14902	l
1278	IFI16	Q16666	l,o
1279	IFI35	P80217	l
1280	IFIT1	P09914	l
1281	IFIT3	O14879	l
1282	IFIT5	Q13325	l
1283	IFITM1	P13164	o
1284	IFT122	Q9HBG6	l
1285	IFT140	Q96RY7	l
1286	IFT172	Q9UG01	l
1287	IFT20	Q8IY31	l
1288	IFT27	H0Y6C7	l
1289	IFT46	Q9NQC8	l
1290	IFT57	Q9NWB7	l
1291	IFT74	Q96LB3	l,h
1292	IFT80	Q9P2H3	l
1293	IGF1R	P08069	o
1294	IGFALS	P35858	l
1295	IGHA1	P01876	q,s,k,u,r,b,l,p,q,a
1296	IGHA2	P01877	i,s,k,b,l,o,a
1297	IGHD	P01880	l
1298	IGHG1	P01857	b,u,s,k,r,l,o,a
1299	IGHG2	P01859	s,k,b,l,a
1300	IGHG3	P01860	s,b,l,a
1301	IGHG4	P01861	s,l,a
1302	IGHM	A0A1B0GUU9	b,r,s,k,b,l,p,o,a
1303	IGHV1-2	P23083	l
1304	IGHV1-46	P01743	k
1305	IGHV3-13	P01766	r,s,l
1306	IGHV3-23	P01764	r,k,s,l,a
1307	IGHV3-30	P01768	s,h
1308	IGHV3-33	P01772	k,h

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
1309	IGHV3-48	P01763	l	1356	ISOC1	Q96CN7	l
1310	IGHV3-53	P01767	s,l	1357	ISOC2	Q96AB3	l
1311	IGHV3-7	P01780	r,s,l	1358	IST1	P53990	l
1312	IGHV4-34	P06331	s,l	1359	ISYNA1	Q9NPH2	l
1313	IGKC	P01834	u,s,k,r,l,o,a,d	1360	ITGA2	P17301	o,l
1314	IGKV1-16	P04430	l	1361	ITGA3	P26006	o
1315	IGKV1-17	P01599	l	1362	ITGA6	P23229	o
1316	IGKV1-39	P01597	s	1363	ITGAM	P11215	o
1317	IGKV1-5	P01602	q,s,l,q	1364	ITGAV	P06756	o
1318	IGKV1D-12	P01611	s	1365	ITGB1	P05556	o,l
1319	IGKV1D-33	P01593	s,r,b,l	1366	ITGB2	P05107	o
1320	IGKV2D-28	P01615	s,l	1367	ITGB4	P16144	o
1321	IGKV3-11	P04433	s,l	1368	ITIH1	P19827	l
1322	IGKV3-20	P01619	s,k,r,b,l	1369	ITIH2	P19823	l
1323	IGKV4-1	P06312	s,b,l	1370	ITIH4	Q14624	l
1324	IGLC1	P0CG04	k,a	1371	ITLN1	Q8WWA0	l
1325	IGLC2	P0DOY2	b,s,r,l,o	1372	ITPA	Q9BY32	l
1326	IGLC3	P0DOY3	s,h	1373	ITPR1	Q14643	o
1327	IGLC7	A0M8Q6	s	1374	ITPR2	Q14571	s
1328	IGLL1	P15814	l	1375	ITPR3	Q14573	o
1329	IGLL5	B9A064	s,l	1376	IVD	P26440	l
1330	IGLV1-47	P01700	s,k	1377	IVL	P07476	o,a
1331	IGLV1-51	P01701	l	1378	JCHAIN	P01591	n,f,r,b,c,s,k,q,l,a,q
1332	IGLV2-11	P01706	b	1379	JMJD7	P0C870	l
1333	IGLV3-19	P01714	s,r,l	1380	JPT1	Q9UK76	l
1334	IGLV3-21	P80748	s,k,r,l	1381	JPT2	Q9H910	l
1335	IGLV3-25	P01717	s,l	1382	JUP	P14923	o,l,a
1336	IL1RN	P18510	l	1383	KARS	Q15046	l
1337	ILF2	Q12905	o,l	1384	KCNIP3	Q9Y2W7	h
1338	ILF3	Q12906	o,l	1385	KCNJ5	P48544	h
1339	ILVBL	A1L0T0	l	1386	KCTD12	Q96CX2	l
1340	IMMT	Q16891	o	1387	KDM5A	P29375	s
1341	IMPA1	P29218	l	1388	KHDRBS1	Q07666	l
1342	IMPDH2	P12268	l	1389	KHSRP	Q92945	l,o
1343	INPP1	P49441	l	1390	KIAA1217	Q5T5P2	o
1344	INPP4B	O15327	l	1391	KIAA1328	Q86T90	s
1345	IPO4	Q8TEX9	l	1392	KIF13B	Q9NQT8	l
1346	IPO5	O00410	l	1393	KIF21A	Q7Z4S6	l
1347	IPO7	O95373	l	1394	KIF2A	O00139	l
1348	IQGAP1	P46940	o,l,d	1395	KIF5B	P33176	o,l
1349	IQGAP2	Q13576	l	1396	KLC4	Q9NSK0	l
1350	IRF2BP2	Q7Z5L9	l	1397	KLHL34	Q8N239	s
1351	IRF6	O14896	l	1398	KLK11	Q9UBX7	l
1352	IRGQ	Q8WZA9	l	1399	KLK7	P49862	p
1353	IRX4	P78413	s	1400	KLRF1	Q9NZS2	s
1354	ISG15	P05161	l	1401	KMT2B	Q9UMN6	o
1355	ISG20	Q96AZ6	l	1402	KNG1	P01042	r,l

	Gene	UniProt Accession Number	Studies
1403	KPNA3	O00505	l
1404	KPNA4	O00629	l
1405	KPNB1	Q14974	l,o
1406	KPRP	Q5T749	a
1407	KRT1	P04264	b,s,r,o
1408	KRT10	P13645	b,s,r,o,a
1409	KRT12	Q99456	b
1410	KRT13	P13646	s,o
1411	KRT14	P02533	b,s,o,a
1412	KRT15	P19012	o
1413	KRT16	P08779	b,s,o,a
1414	KRT17	Q04695	o,a
1415	KRT18	P05783	s,r,c,o,l
1416	KRT19	P08727	b,s,c,o,m,l
1417	KRT2	P35908	s,b,o,a
1418	KRT20	P35900	a
1419	KRT23	Q9C075	o
1420	KRT28	Q7Z3Y7	b
1421	KRT3	P12035	b,o,a
1422	KRT31	Q15323	a
1423	KRT32	Q14532	a
1424	KRT33A	O76009	a
1425	KRT33B	Q14525	a
1426	KRT34	O76011	a
1427	KRT35	Q92764	a
1428	KRT36	O76013	r,a
1429	KRT37	O76014	a
1430	KRT38	O76015	a
1431	KRT4	P19013	b,s,o,a
1432	KRT5	P13647	b,s,o,m,a
1433	KRT6A	P02538	b,s,c,o,a
1434	KRT6B	P04259	b,s,a
1435	KRT6C	P48668	b,k
1436	KRT7	P08729	s,b,c,o,a
1437	KRT76	Q01546	a
1438	KRT77	Q7Z794	a
1439	KRT79	Q5XKE5	b,a
1440	KRT8	P05787	b,s,c,j,o,t,m,j,t
1441	KRT81	Q14533	a
1442	KRT82	Q9NSB4	a
1443	KRT83	P78385	a
1444	KRT84	Q9NSB2	a
1445	KRT85	P78386	a
1446	KRT86	O43790	a
1447	KRT9	P35527	b,s,r,o,a
1448	KRTAP10-3	P60369	a
1449	KRTAP13-2	Q52LG2	a

	Gene	UniProt Accession Number	Studies
1450	KRTAP2-4	Q9BYR9	a
1451	KRTAP4-9	Q9BYQ8	a
1452	KRTAP9-8	Q9BYQ0	a
1453	KTN1	Q86UP2	o,l
1454	KYAT3	Q6YP21	l
1455	KYNU	Q16719	l
1456	LACRT	Q9GZZ8	k,s,r,l,a
1457	LACTB2	Q53H82	l
1458	LAMB4	A4D0S4	l
1459	LAMP1	P11279	o,l
1460	LAMTOR1	Q6IAA8	o
1461	LANCL1	O43813	l
1462	LANCL2	Q9NS86	l
1463	LAP3	P28838	c,r,l,o
1464	LARS	Q9P2J5	l
1465	LAS1L	Q9Y4W2	o
1466	LASP1	Q14847	l,o
1467	LBR	Q14739	o
1468	LCMT1	Q9UIC8	h
1469	LCN1	P31025	n,b,u,s,r,k,f,l,a
1470	LCN15	Q6UWW0	s,r,k,n,l
1471	LCN2	P80188	u,r,s,b,k,o,l
1472	LCP1	P13796	s,r,o,l
1473	LCP2	Q13094	l
1474	LDHA	P00338	s,l,o,a
1475	LDHB	P07195	s,r,l,o
1476	LEG1	Q6P5S2	q,s,r,k,l,q
1477	LEMD3	Q9Y2U8	o
1478	LETM1	O95202	o
1479	LGALS1	P09382	l
1480	LGALS3	P17931	s,o,l
1481	LGALS3BP	Q08380	r,s,k,l,o
1482	LGALS7	P47929	l,a
1483	LGALS7B	P47929	l,a
1484	LGMN	Q99538	l
1485	LHPP	Q9H008	l
1486	LIMA1	Q9UHB6	o,l
1487	LIMK2	P53671	l
1488	LLGL2	Q6P1M3	o,l
1489	LMAN1	P49257	o,l
1490	LMAN2	Q12907	o,l
1491	LMNA	P02545	r,o,l,a
1492	LMNB1	P20700	l,o
1493	LMNB2	Q03252	l,o
1494	LMO7	Q8WWI1	o,l
1495	LNPB	Q9C0E8	o
1496	LONP1	P36776	l

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
1497	LPCAT2	Q7L5N7	o	1544	MAPK3	P27361	l
1498	LPCAT3	Q6P1A2	o	1545	MAPRE1	Q15691	l
1499	LPCAT4	Q643R3	o	1546	MAPRE3	Q9UPY8	l
1500	LPGAT1	Q92604	o	1547	Mar-05	Q9NX47	o
1501	LPO	P22079	s,r,l	1548	MARCKS	P29966	o,l
1502	LPP	Q93052	l	1549	MARCKSL1	P49006	o
1503	LRBA	P50851	o,l	1550	MARS	P56192	l,o
1504	LRG1	P02750	k,l	1551	MAT2A	P31153	l
1505	LRIG1	Q96JA1	o	1552	MAT2B	Q9NZL9	l
1506	LRP1B	Q9NZR2	s	1553	MATK	P42679	s
1507	LRPPRC	P42704	o,l	1554	MATR3	P43243	l,l,o,o
1508	LRRC46	Q96FV0	l	1555	MAX	Q6V3B1	m
1509	LRRC47	Q8N1G4	l,o	1556	MB	P02144	l,a
1510	LRRC59	Q96AG4	o,l	1557	MBOAT2	Q6ZWT7	o
1511	LRRC71	Q8N4P6	l	1558	MCCC1	Q96RQ3	l,o
1512	LRRFIP1	Q32MZ4	o,l	1559	MCCC2	Q9HCC0	l
1513	LSM2	Q9Y333	l	1560	MCEMP1	Q8IX19	o
1514	LSM3	P62310	l	1561	MCM2	P49736	l
1515	LSM5	Q9Y4Y9	l	1562	MCTS1	Q9ULC4	l
1516	LSP1	P33241	s,l	1563	MCU	Q8NE86	l
1517	LSR	Q86X29	o	1564	MDH1	P40925	r,s,o,l
1518	LSS	P48449	o	1565	MDH2	P40926	r,s,o
1519	LTA4H	P09960	r,l,o	1566	ME1	P48163	l
1520	LTF	P02788	f,b,c,u,s,r,k,q,o,p,l,a,q	1567	ME2	P23368	o,l
1521	LUM	P51884	l	1568	METAP1	P53582	l
1522	LXN	Q9BS40	l	1569	METAP2	P50579	l
1523	LY6D	Q14210	o	1570	METTL7A	Q9H8H3	o,l
1524	LYN	P07948	o,l	1571	MFN2	O95140	o
1525	LYPLA1	O75608	l	1572	MGA	Q8IWI9	s
1526	LYPLAL1	Q5VWZ2	l	1573	MGAT1	P26572	o
1527	LYST	Q99698	o	1574	MGAT2	Q10469	o
1528	LYZ	P61626	f,c,b,u,s,r,k,q,o,l,a,q	1575	MGMT	P16455	l
1529	LZIC	Q8WZA0	l	1576	MGST1	P10620	o,l
1530	LZTFL1	Q9NQ48	l	1577	MGST2	Q99735	o
1531	M6PR	P20645	o	1578	MGST3	O14880	o,l
1532	MAGED2	Q9UNF1	l	1579	MICU2	Q8IYU8	o
1533	MAGI1	Q96QZ7	l	1580	MIEN1	Q9BRT3	l
1534	MAGOHB	Q96A72	l	1581	MIER1	Q8N108	h
1535	MAN2A1	Q16706	o	1582	MIF	P14174	s,l
1536	MANF	P55145	l	1583	MLEC	Q14165	l,o
1537	MAOA	P21397	l,o	1584	MLF1	P58340	l
1538	MAOB	P27338	l,o	1585	MMP10	P09238	l
1539	MAP1A	P78559	l	1586	MMP8	P22894	s,r,l
1540	MAP4	P27816	o,l	1587	MMP9	P14780	s,r,o,l
1541	MAPK1	P28482	l	1588	MMS19	Q96T76	l
1542	MAPK11	Q15759	h	1589	MMUT	P22033	l
1543	MAPK14	Q16539	l	1590	MNAT1	P51948	h

	Gene	UniProt Accession Number	Studies
1591	MNDA	P41218	s,r,o,l
1592	MOB1B	Q7L9L4	l
1593	MOGS	Q13724	o,l
1594	MOS	P00540	s
1595	MPC2	O95563	o
1596	MPI	P34949	l
1597	MPO	P05164	s,r,k,o,l
1598	MPST	P25325	l
1599	MRI1	Q9BV20	l
1600	MRPL12	P52815	l
1601	MRPL15	Q9P015	o
1602	MRPS31	Q92665	l
1603	MSH2	P43246	l
1604	MSI2	Q96DH6	l
1605	MSLN	Q13421	s,k,l
1606	MSMB	P08118	s,r,k,l
1607	MSN	P26038	s,o,l
1608	MSRA	Q9UJ68	l
1609	MST1R	Q04912	o
1610	MT-CO2	P00403	o,l
1611	MT-ND1	P03886	o
1612	MT-ND4	P03905	o
1613	MT-ND5	P03915	o,l
1614	MTAP	Q13126	l
1615	MTCH1	Q9NZJ7	o,l
1616	MTCH2	Q9Y6C9	o,l
1617	MTDH	Q86UE4	o
1618	MTFP1	Q9UDX5	o
1619	MTHFD1	P11586	l
1620	MTPN	P58546	l
1621	MTREX	P42285	l
1622	MTX1	Q13505	o
1623	MUC1	P15941	o,l
1624	MUC13	Q9H3R2	o
1625	MUC16	Q8WXI7	l
1626	MUC2	Q02817	o,l
1627	MUC4	Q99102	o,l
1628	MUC5AC	P98088	b,s,k,l
1629	MUC5B	Q9HC84	b,q,s,r,k,l,q
1630	MUC7	Q8TAX7	s,r,k
1631	MVK	Q03426	l
1632	MVP	Q14764	o,l
1633	MX1	P20591	l,o
1634	MXRA7	P84157	o
1635	MYADM	Q96S97	o
1636	MYBBP1A	Q9BQG0	o
1637	MYCBP	Q99417	l

	Gene	UniProt Accession Number	Studies
1638	MYDGF	Q969H8	o,l
1639	MYF5	P13349	h
1640	MYH10	P35580	o
1641	MYH11	P35749	o
1642	MYH13	Q9UKX3	a
1643	MYH14	Q7Z406	o,l
1644	MYH9	P35579	s,r,o,l,a
1645	MYL12A	P19105	l
1646	MYL4	P12829	jj
1647	MYL6	P60660	s,o,l
1648	MYO1B	O43795	o,l
1649	MYO1C	O00159	o
1650	MYO1D	O94832	l,o
1651	MYO1E	Q12965	l
1652	MYO1G	B0I1T2	m
1653	MYO5B	Q9ULV0	l,o
1654	MYO5C	Q9NQX4	o
1655	MYO6	Q9UM54	o,l
1656	MYOF	Q9NZM1	o,l
1657	MYOZ2	Q9NPC6	s
1658	NAA15	Q9BXJ9	l
1659	NAA38	Q9BRA0	l
1660	NAA50	Q9GZZ1	l
1661	NACA	Q13765	o,l
1662	NAE1	Q13564	l
1663	NAGK	Q9UJ70	l,o
1664	NAGLU	P54802	l
1665	NAMPT	P43490	r,l,o
1666	NANS	Q9NR45	o,l
1667	NAP1L1	P55209	l
1668	NAP1L4	Q99733	o,l
1669	NAPA	P54920	l
1670	NAPG	Q99747	l
1671	NAPRT	Q6XQN6	l
1672	NARS	O43776	l
1673	NASP	P49321	o,l
1674	NAT1	P18440	l
1675	NAT10	Q9H0A0	o
1676	NAXD	Q8IW45	l
1677	NAXE	Q8NCW5	l
1678	NCBP1	Q09161	l
1679	NCEH1	Q6PIU2	o
1680	NCF1C	A8MVU1	l
1681	NCF4	Q15080	h
1682	NCKAP1	Q9Y2A7	o,l
1683	NCL	P19338	o,l
1684	NCLN	Q969V3	o

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
1685	NCS1	P62166	h	1732	NME4	O00746	jj
1686	NCSTN	Q92542	o	1733	NME5	P56597	l
1687	NDC1	Q9BTX1	o	1734	NMES1	Q9C002	l
1688	NDE1	Q9NXR1	h	1735	NMI	Q13287	l
1689	NDRG2	Q9UN36	l	1736	NMRAL1	Q9HBL8	l
1690	NDUFA10	O95299	l	1737	NMT1	P30419	l
1691	NDUFA11	Q86Y39	l	1738	NNT	Q13423	l,o
1692	NDUFA12	Q9UI09	o	1739	NOL3	O60936	l
1693	NDUFA13	Q9P0J0	o,l	1740	NOLC1	Q14978	l,o
1694	NDUFA4	O00483	o	1741	NONO	Q15233	o,l
1695	NDUFA4L2	Q9NRX3	l	1742	NOP56	O00567	o
1696	NDUFA5	Q16718	l	1743	NOP58	Q9Y2X3	l,o
1697	NDUFA9	Q16795	l,o	1744	NOS2	P35228	o
1698	NDUFB10	O96000	o	1745	NPC1	O15118	o
1699	NDUFB4	O95168	o,l	1746	NPC2	P61916	s,r,l
1700	NDUFB6	O95139	o	1747	NPEPL1	Q8NDH3	l
1701	NDUFB7	P17568	o	1748	NPEPPS	P55786	o,l
1702	NDUFB8	O95169	o	1749	NPLOC4	Q8TAT6	l
1703	NDUFC2	O95298	o	1750	NPM1	P06748	l,o
1704	NDUFS1	P28331	o,l	1751	NPR3	P17342	h
1705	NDUFS2	O75306	l,o	1752	NPTN	Q9Y639	l,o
1706	NDUFS3	O75489	l,m,o	1753	NQO1	P15559	s,r,l,o
1707	NDUFS5	O43920	l	1754	NQO2	P16083	l
1708	NDUFS7	O75251	o	1755	NRBP1	Q9UHY1	l
1709	NDUFS8	O00217	o,jj	1756	NRDC	O43847	l
1710	NDUFV1	P49821	l	1757	NSDHL	Q15738	o
1711	NDUFV2	P19404	l	1758	NSF	P46459	o,l
1712	NEB	P20929	o	1759	NSFL1C	Q9UNZ2	l
1713	NECAP2	Q9NVZ3	l	1760	NSUN2	Q08J23	l
1714	NEDD8	Q15843	l	1761	NT5C	Q8TCD5	l
1715	NEFL	P07196	h	1762	NT5C2	P49902	l
1716	NEO1	Q92859	s	1763	NT5C3A	Q9H0P0	l
1717	NFKB1	P19838	l	1764	NT5DC1	Q5TFE4	l
1718	NHLRC2	Q8NBF2	l	1765	NUCB1	Q02818	o,l
1719	NIBAN1	Q9BZQ8	o,l	1766	NUCB2	P80303	s,r,k,o,l
1720	NIBAN2	Q96TA1	o,l	1767	NUCKS1	Q9H1E3	l
1721	NIF3L1	Q9GZT8	l	1768	NUDC	Q9Y266	o,l
1722	NIPSNAP1	Q9BPW8	o	1769	NUDCD2	Q8WVJ2	l
1723	NIPSNAP2	O75323	o,l	1770	NUDT12	Q9BQG2	l
1724	NIPSNAP3A	Q9UFN0	l	1771	NUDT14	O95848	l
1725	NIT1	Q86X76	l	1772	NUDT15	Q9NV35	l
1726	NIT2	Q9NQR4	l	1773	NUDT16	Q96DE0	l
1727	NLN	Q9BYT8	o	1774	NUDT16L1	Q9BRJ7	l
1728	NME1	P15531	p	1775	NUDT2	P50583	l
1729	NME2	P22392	r,p	1776	NUDT21	O43809	l
1730	NME2P1	O60361	l	1777	NUDT5	Q9UKK9	l
1731	NME3	Q13232	o	1778	NUDT9	Q9BW91	l



	Gene	UniProt Accession Number	Studies
1779	NUMA1	Q14980	o,l
1780	NUP155	O75694	o
1781	NUP160	Q12769	o
1782	NUP205	Q92621	l,o
1783	NUP210	Q8TEM1	o
1784	NUP62	P37198	l
1785	NUP93	Q8N1F7	l,o
1786	NUTF2	P61970	l
1787	NXN	Q6DKJ4	l
1788	OAS2	P29728	l,o
1789	OAS3	Q9Y6K5	l,o
1790	OAT	P04181	o,l
1791	OBP2A	Q9NY56	c
1792	OBSCN	Q5VST9	o
1793	OCIAD2	Q56VL3	l
1794	ODF3B	A8MYP8	l
1795	OGDH	Q02218	o,l
1796	OGFR	Q9NZT2	l
1797	OLA1	Q9NTK5	o,l
1798	OPA1	O60313	o,l
1799	OPLAH	O14841	l
1800	OPRPN	Q99935	s,r,k,l
1801	OR1L6	Q8NGR2	s
1802	ORM1	P02763	s,r,u,q,l,a,q
1803	ORM2	P19652	s,l
1804	OSBP	P22059	l
1805	OSBPL5	Q9H0X9	o
1806	OSBPL8	Q9BZF1	o
1807	OSCP1	Q8WVF1	l
1808	OSTF1	Q92882	l
1809	OTOR	Q9NRC9	h
1810	OTUB1	Q96FW1	o,l
1811	OXA1L	Q15070	l,o
1812	OXCT1	P55809	o,l
1813	OXR1	Q8N573	l
1814	OXSRI	O95747	l
1815	P3H1	Q32P28	h
1816	P4HB	P07237	r,m,o,l,p,d
1817	PA2G4	Q9UQ80	l
1818	PABPC1	P11940	o,l
1819	PABPC4	Q13310	l
1820	PABPN1	Q86U42	l
1821	PACRG	Q96M98	l
1822	PACSIN2	Q9UNF0	l
1823	PAFAH1B1	P43034	o,l
1824	PAFAH1B2	P68402	l
1825	PAFAH1B3	Q15102	l

	Gene	UniProt Accession Number	Studies
1826	PAICS	P22234	l
1827	PAIP1	Q9H074	l
1828	PAK1	Q13153	l
1829	PAK2	Q13177	l
1830	PALLD	Q8WX93	l
1831	PAPSS1	O43252	l
1832	PAPSS2	O95340	l
1833	PARK7	Q99497	s,r,j,m,o,l,j,d
1834	PARP1	P09874	l
1835	PARP10	Q53GL7	l
1836	PARP4	Q9UUK3	s,l
1837	PARP9	Q8IXQ6	l
1838	PATJ	Q8NI35	s
1839	PBDC1	Q9BVG4	l
1840	PBLD	P30039	l
1841	PCBD1	P61457	l
1842	PCBD2	Q9H0N5	l
1843	PCBP1	Q15365	o,l
1844	PCBP2	Q15366	o,l
1845	PCK2	Q16822	l
1846	PCM1	Q15154	o,l
1847	PCMT1	P22061	l
1848	PCNA	P12004	l
1849	PCNT	O95613	l,o
1850	PCYOX1	Q9UHG3	o
1851	PCYT1B	Q9Y5K3	l
1852	PDAP1	Q13442	l
1853	PDCD10	Q9BUL8	l
1854	PDCD11	Q14690	o
1855	PDCD4	Q53EL6	l
1856	PDCD5	O14737	l
1857	PDCD6	O75340	l
1858	PDCD6IP	Q8WUM4	l
1859	PDCL	Q13371	h
1860	PDE12	F6T1Q0	l
1861	PDE1A	P54750	h
1862	PDE9A	O76083	h
1863	PDHA1	P08559	l,o
1864	PDHB	P11177	j,l,j
1865	PDIA3	P30101	r,c,m,o,l
1866	PDIA4	P13667	o,l
1867	PDIA6	Q15084	o,l
1868	PDLIM1	O00151	o,l
1869	PDLIM4	P50479	l
1870	PDLIM5	Q96HC4	l
1871	PDS5A	Q29RF7	r
1872	PDXDC1	Q6P996	l

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
1873	PDXK	O00764	o,l	1920	PITRM1	Q5JRX3	l
1874	PEA15	Q15121	l	1921	PKM	P14618	s,r,c,o,l,p,a
1875	PEBP1	P30086	r,s,p,t,l,o,t	1922	PKP1	Q13835	o,a
1876	PEBP4	Q96596	l	1923	PKP2	Q99959	l,o
1877	PELP1	Q8IZL8	o	1924	PKP3	Q9Y446	o
1878	PEPD	P12955	l	1925	PLA2G2A	P14555	s,r,k
1879	PEX11B	O96011	o	1926	PLAA	Q9Y263	l
1880	PFAS	O15067	l	1927	PLBD1	Q6P4A8	l
1881	PFDN2	Q9UHV9	l	1928	PLCL2	Q9UPR0	b
1882	PFDN4	Q9NQP4	l	1929	PLD2	O14939	o
1883	PFDN5	Q99471	l	1930	PLEC	Q15149	l,o
1884	PFDN6	O15212	l	1931	PLEK	P08567	l
1885	PFKL	P17858	l,o	1932	PLEKHJ1	Q9NW61	l
1886	PFKM	P08237	l	1933	PLG	P00747	b,l
1887	PFKP	Q01813	l,o	1934	PLGRKT	Q9HBL7	o
1888	PFN1	P07737	s,r,k,o,l	1935	PLIN3	O60664	l
1889	PFN2	P35080	l	1936	PLLP	Q9Y342	o
1890	PGAM1	P18669	c,s,r,o,l	1937	PLPBP	O94903	l
1891	PGD	P52209	s,r,p,h,l,o	1938	PLPP3	O14495	o
1892	PGK1	P00558	s,r,o,l	1939	PLS1	Q14651	o,l
1893	PGLS	O95336	o,l	1940	PLS3	P13797	l
1894	PGLYRP1	O75594	s,l	1941	PLTP	P55058	r,l
1895	PGLYRP2	Q96PD5	l	1942	PML	P29590	o,l
1896	PGM1	P36871	o,l	1943	PMM2	O15305	l
1897	PGM2	Q96G03	l	1944	PMPCA	Q10713	l
1898	PGM2L1	Q6PCE3	l	1945	PMPCB	O75439	l
1899	PGM3	O95394	l	1946	PMVK	Q15126	l
1900	PGP	A6NDG6	l	1947	PNN	Q9H307	o
1901	PGRMC1	O00264	l,o	1948	PNP	P00491	l
1902	PGRMC2	O15173	o	1949	PNPO	Q9NVS9	l
1903	PHB	P35232	c,o,l,m	1950	POC5	Q8NA72	o
1904	PHB2	Q99623	o,l	1951	PODXL	O00592	o
1905	PHF6	Q8IWS0	s	1952	POF1B	Q8WVV4	o,l
1906	PHGDH	O43175	l	1953	POLE2	P56282	s
1907	PHPT1	Q9NRX4	l,h	1954	POLR1C	O15160	l
1908	PHYHD1	Q5SRE7	l	1955	POLR2B	P30876	l
1909	PI3	P19957	r,k,l	1956	POLR2H	P52434	l
1910	PIGG	Q5H8A4	o	1957	PON1	P27169	r,l
1911	PIGO	Q8TEQ8	o	1958	POR	P16435	o,l
1912	PIGR	P01833	r,s,u,k,b,c,o,p,l,a	1959	POTEE	Q6S8J3	o
1913	PIN1	Q13526	l	1960	POTEJ	P0CG39	l
1914	PIP	P12273	n,f,b,s,r,k,u,l,p,a	1961	PPA1	Q15181	j,l,j
1915	PIP4K2C	Q8TBX8	l	1962	PPA2	Q9H2U2	o,l
1916	PIR	O00625	l	1963	PPCS	Q9HAB8	l
1917	PITHD1	Q9GZP4	l	1964	PPIA	P62937	s,r,o,p,l
1918	PITPNA	Q00169	l	1965	PPIB	P23284	o,l
1919	PITPNB	P48739	l	1966	PPIC	P45877	l

	Gene	UniProt Accession Number	Studies
1967	PPID	Q08752	l
1968	PPIL1	Q9Y3C6	l
1969	PPIL3	Q9H2H8	l
1970	PPL	O60437	o,l
1971	PPM1B	O75688	l
1972	PPM1F	P49593	l
1973	PPM1G	O15355	l
1974	PPME1	Q9Y570	l
1975	PPOX	P50336	o,l
1976	PPP1CA	P62136	o,l
1977	PPP1CB	P62140	l
1978	PPP1CC	P36873	l
1979	PPP1R1A	Q13522	l
1980	PPP1R7	Q15435	l
1981	PPP1R8	Q12972	l
1982	PPP2CA	P67775	h,l
1983	PPP2CB	P62714	l
1984	PPP2R1A	P30153	o,l
1985	PPP2R2A	P63151	l
1986	PPP3CA	Q08209	l
1987	PPP4C	P60510	l
1988	PPP4R3B	Q5MIZ7	l
1989	PPP5C	P53041	l
1990	PPP6C	O00743	l
1991	PPT1	P50897	l
1992	PRAF2	O60831	o
1993	PRAM1	Q96QH2	s
1994	PRB1	P04280	k
1995	PRB2	P02812	c,s,r,k,a
1996	PRB3	Q04118	o,a
1997	PRB4	P10163	k,c
1998	PRDM1	O75626	l
1999	PRDX1	Q06830	c,s,r,o,m,l,p
2000	PRDX2	P32119	c,s,b,j,o,m,l,p,a,j
2001	PRDX3	P30048	o,l
2002	PRDX4	Q13162	o,l
2003	PRDX5	P30044	c,s,r,e,o,p,l
2004	PRDX6	P30041	c,s,r,o,m,l
2005	PREB	Q9HCU5	o
2006	PREP	P48147	l
2007	PRG4	Q92954	o
2008	PRH1	P02810	s,a
2009	PRH2	P02810	s,a
2010	PRKAA1	Q13131	l
2011	PRKACA	P17612	l
2012	PRKAG1	P54619	l
2013	PRKAR1A	P10644	l

	Gene	UniProt Accession Number	Studies
2014	PRKAR2A	P13861	l,o,h
2015	PRKCD	Q05655	l
2016	PRKCSH	P14314	l,o
2017	PRKDC	P78527	o,l
2018	PRKRA	O75569	l
2019	PRMT1	Q99873	l
2020	PRMT5	O14744	l
2021	PRODH	O43272	o,h
2022	PROM1	O43490	o,l
2023	PROS1	P07225	l
2024	PRPF19	Q9UMS4	o,l
2025	PRPF6	O94906	o,l
2026	PRPF8	Q6P2Q9	o,l
2027	PRPS1	P60891	l
2028	PRPS2	P11908	l
2029	PRPSAP1	Q14558	l
2030	PRPSAP2	O60256	l
2031	PRR15	Q8IV56	l
2032	PRR4	Q16378	b,s,r,k,l
2033	PRRC1	Q96M27	l
2034	PRRC2A	P48634	o
2035	PRSS8	Q16651	o
2036	PRTN3	P24158	s,r,l,o
2037	PRUNE2	Q8WUY3	l
2038	PRXL2A	Q9BRX8	o,l
2039	PSAP	P07602	s,r,l,o
2040	PSEN1	P49768	o
2041	PSIP1	O75475	l
2042	PSMA1	P25786	l,o
2043	PSMA2	P25787	l
2044	PSMA3	P25788	l,o
2045	PSMA4	P25789	l
2046	PSMA5	P28066	s,l,p
2047	PSMA6	P60900	l
2048	PSMA7	O14818	l
2049	PSMB1	P20618	r,l
2050	PSMB10	P40306	l
2051	PSMB2	P49721	l,o
2052	PSMB3	P49720	l
2053	PSMB4	P28070	l
2054	PSMB6	P28072	l
2055	PSMB7	Q99436	l
2056	PSMB8	P28062	l
2057	PSMB9	P28065	l
2058	PSMC1	P62191	l
2059	PSMC2	P35998	l,o
2060	PSMC3	P17980	l,o

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
2061	PSMC4	P43686	l	2108	PYCARD	Q9ULZ3	l
2062	PSMC5	P62195	l	2109	PYCR3	Q53H96	l
2063	PSMC6	P62333	l	2110	PYGB	P11216	r,l,o
2064	PSMD1	Q99460	l	2111	PYGL	P06737	l
2065	PSMD10	O75832	l	2112	PYM1	Q9BRP8	l
2066	PSMD11	O00231	p,l	2113	QARS	P47897	l,o
2067	PSMD12	O00232	l	2114	QDPR	P09417	l
2068	PSMD13	Q9UNM6	l	2115	QSOX1	O00391	s,r,o,l
2069	PSMD14	O00487	l,h	2116	RAB10	P61026	l,o
2070	PSMD2	Q13200	l,o	2117	RAB11A	P62491	o
2071	PSMD3	O43242	l	2118	RAB11B	Q15907	l
2072	PSMD4	P55036	l	2119	RAB13	P51153	o,l
2073	PSMD5	Q16401	l	2120	RAB14	P61106	l,o
2074	PSMD6	Q15008	l	2121	RAB18	Q9NP72	l
2075	PSMD7	P51665	l	2122	RAB1A	P62820	o
2076	PSMD8	P48556	l	2123	RAB1B	Q9H0U4	l,o
2077	PSMD9	O00233	l	2124	RAB21	Q9UL25	l,o
2078	PSME1	Q06323	r,o,j,l,h,j	2125	RAB22A	Q9UL26	o
2079	PSME2	Q9UL46	r,o,l	2126	RAB2A	P61019	o,l
2080	PSME3	P61289	l	2127	RAB35	Q15286	o
2081	PSME4	Q14997	l	2128	RAB37	Q96AX2	o
2082	PSMF1	Q92530	l	2129	RAB3C	Q96E17	h
2083	PSMG2	Q969U7	l	2130	RAB3D	O95716	l,o
2084	PSPC1	Q8WXF1	l	2131	RAB5A	P20339	o
2085	PTBP1	P26599	s,o,l	2132	RAB5B	P61020	l,o
2086	PTBP3	O95758	l	2133	RAB5C	P51148	o,l
2087	PTDSS2	Q9BVG9	o	2134	RAB6A	P20340	o,l
2088	PTER	Q96BW5	l	2135	RAB7A	P51149	l,o
2089	PTGES	O14684	o	2136	RAB8A	P61006	l
2090	PTGES3	Q15185	l	2137	RABGGTA	Q92696	l,h
2091	PTGFRN	Q9P2B2	o	2138	RABL2A	Q9UBK7	l
2092	PTGR1	Q14914	l	2139	RABL6	Q3YEC7	o,l
2093	PTGR2	Q8N8N7	l	2140	RAC1	P63000	o,l
2094	PTMA	P06454	o	2141	RAC2	P15153	s,l
2095	PTMS	P20962	o	2142	RACK1	P63244	l,o
2096	PTPA	Q15257	l	2143	RAD23B	P54727	o,l
2097	PTPN1	P18031	o	2144	RAD50	Q92878	l
2098	PTPN11	Q06124	l	2145	RAI1	Q7Z5J4	o
2099	PTPN13	Q12923	c	2146	RALA	P11233	o
2100	PTPN6	P29350	l	2147	RALGAPA1	Q6GYQ0	l
2101	PTPRC	P08575	o,l	2148	RALY	Q9UKM9	l
2102	PTPRJ	Q12913	o	2149	RAN	P62826	l
2103	PTRHD1	Q6GMV3	l	2150	RANBP1	P43487	l
2104	PUDP	Q08623	l	2151	RANBP2	P49792	o
2105	PUF60	Q9UHX1	l	2152	RANBP3	Q9H6Z4	h,l
2106	PURA	Q00577	l	2153	RANGAP1	P46060	l
2107	PURB	Q96QR8	l	2154	RAP1A	P62834	o

	Gene	UniProt Accession Number	Studies
2155	RAP1B	P61224	l
2156	RARRES1	P49788	l
2157	RARS	P54136	l,o
2158	RBBP4	Q09028	l,o
2159	RBBP7	Q16576	l
2160	RBBP8	Q99708	b
2161	RBBP9	O75884	l
2162	RBKS	Q9H477	l
2163	RBM12	Q9NTZ6	l
2164	RBM14	Q96PK6	o
2165	RBM25	P49756	l
2166	RBM3	P98179	s,l
2167	RBM39	Q14498	l
2168	RBM47	A0AV96	l
2169	RBMX	P38159	o,l
2170	RBP1	P09455	l
2171	RBP4	P02753	j,l,j
2172	RCC1	P18754	l
2173	RCC2	Q9P258	l
2174	RCN1	Q15293	l,o
2175	RCN2	Q14257	l
2176	RDH10	Q8IZV5	l
2177	RDH11	Q8TC12	o
2178	RDH14	Q9HBH5	o
2179	RDX	P35241	l
2180	RECQL	F5H2L2	l
2181	REEP5	Q00765	o
2182	RELA	Q04206	l
2183	RELCH	Q9P260	l
2184	RER1	O15258	o
2185	RETN	Q9HD89	r,l
2186	RETREG3	Q86VR2	o
2187	RETSAT	Q6NUM9	o
2188	RHBDD2	Q6NTF9	l
2189	RHOA	P61586	l
2190	RHOC	P08134	l
2191	RHOG	P84095	o
2192	RHOT2	Q8IX11	o,l
2193	RIDA	P52758	l,g
2194	RMDN3	Q96TC7	o,l
2195	RMND1	Q9NWS8	o
2196	RNASE1	P07998	s,r,k,l
2197	RNASE2	P10153	l
2198	RNASE3	P12724	s,r,l,o
2199	RNASE4	P34096	l
2200	RNASSET2	O00584	l
2201	RNF170	Q96K19	o

	Gene	UniProt Accession Number	Studies
2202	RNF213	Q63HN8	o,l
2203	RNF40	O75150	l
2204	RNH1	P13489	o,l
2205	RNMT	O43148	l
2206	RNPEP	Q9H4A4	l
2207	RO60	P10155	l
2208	ROCK2	O75116	l
2209	ROPN1L	Q96C74	l
2210	RPA1	P27694	l
2211	RPA3	P35244	l
2212	RPE	Q96AT9	l
2213	RPIA	P49247	l
2214	RPL10	P27635	o
2215	RPL10A	P62906	l,o
2216	RPL10L	Q96L21	o
2217	RPL11	P62913	l,o
2218	RPL12	P30050	l,o
2219	RPL13	P26373	l,o
2220	RPL13A	P40429	l
2221	RPL14	P50914	l,o
2222	RPL15	P61313	l
2223	RPL17	P18621	l,o
2224	RPL18	Q07020	l,o
2225	RPL18A	Q02543	l,o
2226	RPL19	P84098	l,o
2227	RPL21	P46778	o
2228	RPL22	P35268	l
2229	RPL23	P62829	l,o
2230	RPL23A	P62750	l,o
2231	RPL24	P83731	l,o
2232	RPL26	P61254	l
2233	RPL26L1	Q9UNX3	o
2234	RPL27	P61353	l
2235	RPL27A	P46776	l,o
2236	RPL28	P46779	o
2237	RPL29	P47914	o
2238	RPL3	P39023	l,o
2239	RPL30	P62888	l
2240	RPL31	P62899	l
2241	RPL32	P62910	o
2242	RPL34	P49207	o
2243	RPL35	P42766	o
2244	RPL35A	P18077	o
2245	RPL37A	G5E9R3	l
2246	RPL38	P63173	l
2247	RPL4	P36578	l,o
2248	RPL5	P46777	l,o

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
2249	RPL6	Q02878	l,o	2296	RRAS2	P62070	o,h
2250	RPL7	P18124	l,o	2297	RRBP1	Q9P2E9	o,l
2251	RPL7A	P62424	l,o	2298	RSF1	Q96T23	k
2252	RPL8	P62917	o	2299	RSL1D1	O76021	o
2253	RPL9	P32969	l	2300	RSPH1	Q8WYR4	l
2254	RPL9P7	P32969	l	2301	RSPH3	Q86UC2	l
2255	RPL9P8	P32969	l	2302	RSPH4A	Q5TD94	l
2256	RPL9P9	P32969	l	2303	RSPH9	Q9H1X1	l
2257	RPLP0	P05388	o	2304	RSU1	Q15404	l
2258	RPLP0P6	Q8NHW5	l	2305	RTCA	O00442	l
2259	RPLP1	P05386	s,l	2306	RTCB	Q9Y310	l
2260	RPLP2	P05387	s,r,l,o	2307	RTN3	O95197	o,l
2261	RPN1	P04843	l,o	2308	RTN4	Q9NQC3	o,l
2262	RPN2	P04844	l,o	2309	RTRAF	Q9Y224	l
2263	RPRD1B	Q9NQG5	l	2310	RUNX2	Q13950	s
2264	RPS10P5	Q9NQ39	l	2311	RUVBL1	Q9Y265	s,r,o,l
2265	RPS11	P62280	l	2312	RUVBL2	Q9Y230	o,l
2266	RPS12	P25398	l	2313	S100A10	P60903	o,l
2267	RPS13	P62277	l,o	2314	S100A11	P31949	s,r,o,e,l,a
2268	RPS14	P62263	l,o	2315	S100A12	P80511	s,r,l
2269	RPS15A	P62244	l,o	2316	S100A13	Q99584	l
2270	RPS16	P62249	l,o	2317	S100A14	Q9HCY8	l,o
2271	RPS17	P08708	l,o	2318	S100A16	Q96FQ6	o
2272	RPS18	P62269	l,o	2319	S100A2	P29034	l
2273	RPS19	P39019	l,o	2320	S100A4	P26447	r,l,o
2274	RPS2	P15880	l,o	2321	S100A6	P06703	s,r,o,l
2275	RPS20	P60866	l,o	2322	S100A7	P31151	s,r,l,a
2276	RPS21	P63220	l,o	2323	S100A8	P05109	c,f,u,s,r,n,p,t,l,o,a,t
2277	RPS23	P62266	o	2324	S100A9	P06702	c,i,f,q,s,u,r,n,l,p,o,q,a
2278	RPS24	P62847	l,o	2325	S100P	P25815	s,r,l,o
2279	RPS25	P62851	l,o	2326	SAA1	P0DJ18	l
2280	RPS26P11	Q5JNZ5	l	2327	SAE1	Q9UBE0	l
2281	RPS27	P42677	l,o	2328	SAFB	Q15424	o
2282	RPS27L	Q71UM5	o	2329	SAFB2	Q14151	l
2283	RPS28	P62857	l,o	2330	SAG	P10523	h
2284	RPS3	P23396	l,o	2331	SAMD9	Q5K651	l
2285	RPS3A	P61247	l,o	2332	SAMHD1	Q9Y3Z3	r,s,l,o
2286	RPS4X	P62701	l,o	2333	SAMM50	Q9Y512	o,l
2287	RPS5	P46782	l	2334	SAR1A	Q9NR31	l
2288	RPS6	P62753	l,o	2335	SAR1B	Q9Y6B6	l
2289	RPS6KA1	Q15418	l	2336	SARG	Q9BW04	l
2290	RPS6KA3	P51812	l	2337	SARS	P49591	l
2291	RPS7	P62081	l,o	2338	SART3	Q15020	l
2292	RPS8	P62241	l,o	2339	SAXO2	Q658L1	l
2293	RPS9	P46781	l,o	2340	SBDS	Q9Y3A5	l
2294	RPSA	P08865	l,o	2341	SCAMP1	O15126	o
2295	RRAD	P55042	l	2342	SCAMP2	O15127	o,l



	Gene	UniProt Accession Number	Studies
2343	SCAMP3	O14828	o
2344	SCARB2	Q14108	l,o
2345	SCCPDH	Q8NBX0	o,l
2346	SEEL	O95171	o
2347	SCFD1	Q8WVM8	l
2348	SCGB1A1	P11684	q,s,r,k,q
2349	SCGB1D1	O95968	k,s,r
2350	SCGB1D2	O95969	k,s,r,l
2351	SCGB2A1	O75556	f,s,r,k,l
2352	SCGB2A2	Q13296	k,b
2353	SCGN	O76038	h
2354	SCIN	Q9Y6U3	l
2355	SCLY	Q96115	l
2356	SCP2	P22307	l,o
2357	SCPEP1	Q9HB40	l
2358	SCRIB	Q14160	o
2359	SCRN1	Q12765	l
2360	SCRN2	Q96FV2	l
2361	SDC1	P18827	o,l
2362	SDC4	P31431	o,l
2363	SDF4	G3V1E2	l
2364	SDHA	P31040	o,l
2365	SDHB	P21912	l
2366	SDR39U1	Q9NRG7	l
2367	SEC11A	P67812	o
2368	SEC11C	Q9BY50	o
2369	SEC13	P55735	l
2370	SEC14L2	O76054	l
2371	SEC14L3	Q9UDX4	l
2372	SEC16A	O15027	l,o
2373	SEC22B	O75396	o,l
2374	SEC23A	Q15436	l
2375	SEC23B	Q15437	l
2376	SEC23IP	Q9Y6Y8	o,l
2377	SEC24A	O95486	l
2378	SEC24C	P53992	o,l
2379	SEC24D	O94855	l
2380	SEC31A	O94979	l
2381	SEC61A1	P61619	o
2382	SEC62	Q99442	o
2383	SEC63	Q9UGP8	o
2384	SEL1L3	Q68CR1	s
2385	SELENBP1	Q13228	c,r,s,o,l,p,e
2386	SELENOS	Q9BQE4	o
2387	SEMG1	P04279	a
2388	SEMG2	Q02383	a
2389	SEPHS1	P49903	l

	Gene	UniProt Accession Number	Studies
2390	SEPHS2	Q99611	l
2391	SEPTIN10	Q9P0V9	l
2392	SEPTIN11	Q9NVA2	l
2393	SEPTIN2	Q15019	o,h,l
2394	SEPTIN6	Q14141	l
2395	SEPTIN7	Q16181	l
2396	SEPTIN8	Q92599	l
2397	SEPTIN9	Q9UHD8	o,l
2398	SERBP1	Q8NC51	l
2399	SERINC1	Q9NRX5	o
2400	SERPINA1	P01009	f,b,c,s,r,k,n,j,p,l,o,a,j
2401	SERPINA3	P01011	s,r,k,l,a
2402	SERPINA4	P29622	l
2403	SERPINA6	P08185	l
2404	SERPINB1	P30740	s,r,n,p,l,o
2405	SERPINB10	P48595	l
2406	SERPINB12	Q96P63	a
2407	SERPINB13	Q9UIV8	l
2408	SERPINB2	P05120	p,l,h
2409	SERPINB3	P29508	s,r,b,c,m,p,l,e,o,a
2410	SERPINB4	P48594	s,l,o,a,d
2411	SERPINB5	P36952	o,l
2412	SERPINB6	P35237	l
2413	SERPINB9	P50453	l
2414	SERPINC1	P01008	r,l
2415	SERPIND1	P05546	l
2416	SERPINF1	P36955	l
2417	SERPINF2	P08697	l
2418	SERPING1	P05155	l
2419	SET	Q01105	s,l,o
2420	SF3A1	Q15459	l
2421	SF3A3	Q12874	l,o
2422	SF3B1	O75533	o,l
2423	SF3B2	Q13435	l
2424	SF3B3	Q15393	l,o
2425	SFN	P31947	s,n,l,o,p,a
2426	SFPQ	P23246	o,l
2427	SFXN1	Q9H9B4	o
2428	SFXN2	Q96NB2	o
2429	SFXN3	Q9BWM7	l,o
2430	SFXN4	Q6P4A7	o
2431	SGPL1	O95470	o
2432	SGTA	O43765	l
2433	SH2D4A	Q9H788	l
2434	SH3BGRL	O75368	l,o
2435	SH3BGRL2	Q9UJC5	l
2436	SH3BGRL3	Q9H299	s,l

	Gene	UniProt Accession Number	Studies
2437	SH3GLB1	Q9Y371	l
2438	SH3GLB2	Q9NR46	l
2439	SHMT1	P34896	l
2440	SHMT2	P34897	o
2441	SHPK	Q9UHV6	l
2442	SHTN1	A0MZ66	l
2443	SIGIRR	Q6IA17	o
2444	SKIV2L	Q15477	l
2445	SKP1	P63208	l
2446	SLC12A2	P55011	l,o
2447	SLC12A6	H0YMQ9	h,o
2448	SLC12A7	Q9Y666	o
2449	SLC16A1	P53985	o
2450	SLC16A3	O15427	o
2451	SLC16A6	O15403	s
2452	SLC1A4	P43007	o
2453	SLC1A5	Q15758	o
2454	SLC22A18	Q96BI1	o
2455	SLC22A4	Q9H015	o
2456	SLC25A1	P53007	o,l
2457	SLC25A10	Q9UBX3	o
2458	SLC25A11	Q02978	l,o
2459	SLC25A12	O75746	o,l
2460	SLC25A13	Q9UJS0	l,o
2461	SLC25A17	O43808	o
2462	SLC25A20	O43772	o
2463	SLC25A22	Q9H936	o
2464	SLC25A24	Q6NUK1	l
2465	SLC25A3	Q00325	l,o
2466	SLC25A4	P12235	l,o
2467	SLC25A5	P05141	l,o
2468	SLC25A6	P12236	l,l,o,o
2469	SLC27A1	Q6PCB7	o
2470	SLC27A2	O14975	o,l
2471	SLC27A3	Q5K4L6	o
2472	SLC27A4	Q6P1M0	o
2473	SLC2A1	P11166	o
2474	SLC2A14	Q8TDB8	o
2475	SLC33A1	O00400	o
2476	SLC35A1	P78382	o
2477	SLC35A3	Q9Y2D2	o
2478	SLC35B2	Q8TB61	o
2479	SLC35F6	Q8N357	o
2480	SLC37A4	O43826	o
2481	SLC3A2	P08195	o
2482	SLC44A1	Q8WWI5	o
2483	SLC44A2	Q8IWA5	o

	Gene	UniProt Accession Number	Studies
2484	SLC44A4	Q53GD3	o
2485	SLC4A1	P02730	l,o
2486	SLC4A4	Q9Y6R1	o
2487	SLC5A1	P13866	o
2488	SLC6A14	Q9UN76	o
2489	SLC9A1	P19634	o
2490	SLC9A3R1	O14745	l,o
2491	SLK	Q9H2G2	l
2492	SLPI	P03973	s,r,k,q,c,l,q
2493	SMAD9	O15198	l
2494	SMAP2	Q8WU79	l
2495	SMARCA2	P51531	o
2496	SMARCA5	O60264	o
2497	SMARCC1	Q92922	s
2498	SMC1A	Q14683	o,l
2499	SMC3	Q9UQE7	o,l
2500	SMPD2	O60906	o,l
2501	SMPD3	Q9NY59	o
2502	SMPD4	Q9NXE4	o
2503	SMR3B	P02814	k
2504	SMS	P52788	l
2505	SMU1	Q2TAY7	l
2506	SMYD5	Q6GMV2	l
2507	SNAP23	O00161	o
2508	SNAP91	O60641	l
2509	SNCA	P37840	l
2510	SNCG	O76070	l
2511	SND1	Q7KZF4	o,l
2512	SNRNP200	O75643	o,l
2513	SNRNP40	Q96DI7	l
2514	SNRNP70	P08621	o,l
2515	SNRPA	P09012	l
2516	SNRPA1	P09661	l
2517	SNRPB	P14678	l
2518	SNRPD1	P62314	s,l
2519	SNRPD2	P62316	l
2520	SNRPD3	P62318	l,o
2521	SNRPE	P62304	l
2522	SNRPF	P62306	l,o
2523	SNU13	P55769	l
2524	SNX11	Q9Y5W9	h
2525	SNX16	P57768	h
2526	SNX2	O60749	l
2527	SNX3	O60493	l
2528	SNX5	Q9Y5X3	l
2529	SNX6	Q9UNH7	l
2530	SOAT1	P35610	o

	Gene	UniProt Accession Number	Studies
2531	SOD1	P00441	c,s,r,o,j,p,l,j
2532	SOD2	P04179	m,m,o,o,l,l
2533	SOD3	P08294	h,l
2534	SORD	Q00796	r,o,l
2535	SORL1	Q92673	o
2536	SP100	P23497	l
2537	SPA17	Q15506	l
2538	SPACA9	Q96E40	l
2539	SPAG6	O75602	o,l
2540	SPAG9	O60271	l
2541	SPATA18	Q8TC71	o,l
2542	SPATA6	Q9NWH7	l
2543	SPCS1	Q9Y6A9	o
2544	SPCS2	Q15005	o
2545	SPCS3	P61009	o
2546	SPEN	Q96T58	o
2547	SPNS1	Q9H2V7	b
2548	SPR	P35270	l
2549	SPRR1A	P35321	r,l,a
2550	SPRR1B	P22528	s,r,l,a
2551	SPRR2B	P35325	r,a
2552	SPRR3	Q9UBC9	r,l
2553	SPTAN1	Q13813	l,o
2554	SPTBN1	Q01082	o,l
2555	SPTBN2	O15020	l,o
2556	SQOR	Q9Y6N5	o,l
2557	SRI	P30626	l,m
2558	SRP14	P37108	l
2559	SRP68	Q9UHB9	o,l
2560	SRP72	O76094	l
2561	SRPRA	P08240	o
2562	SRPRB	Q9Y5M8	o
2563	SRRM1	Q8IYB3	l
2564	SRRM2	Q9UQ35	o
2565	SRRT	Q9BXP5	l
2566	SRSF1	Q07955	l,o
2567	SRSF10	O75494	l
2568	SRSF11	Q05519	l
2569	SRSF2	Q01130	l,o
2570	SRSF3	P84103	o,l
2571	SRSF5	Q13243	l
2572	SRSF7	Q16629	l,o
2573	SSB	P05455	o,l
2574	SSBP1	Q04837	l
2575	SSH3	Q8TE77	l
2576	SSR1	P43307	o,l
2577	SSR3	Q9UNL2	o

	Gene	UniProt Accession Number	Studies
2578	SSR4	P51571	o,l
2579	SSRP1	Q08945	l
2580	ST13	P50502	o,l
2581	ST14	Q9Y5Y6	o
2582	ST3GAL4	Q11206	o
2583	STARD10	Q9Y365	l
2584	STAT1	P42224	l
2585	STAT2	P52630	l
2586	STAT3	P40763	o,l
2587	STAT6	P42226	l
2588	STATH	P02808	s,r,f,i,l
2589	STAU1	O95793	l
2590	STIM1	Q13586	o
2591	STIM2	Q9P246	o
2592	STIP1	P31948	c,o,l
2593	STK24	Q9Y6E0	l
2594	STK33	Q9BYT3	l
2595	STK38	Q15208	l
2596	STK39	Q9UEW8	l
2597	STK4	Q13043	h
2598	STMN1	P16949	l
2599	STOM	P27105	o
2600	STOML2	Q9UJZ1	o,l
2601	STOML3	Q8TAV4	o
2602	STRAP	Q9Y3F4	l
2603	STS	P08842	o
2604	STT3A	P46977	l,o
2605	STT3B	Q8TCJ2	o
2606	STX11	O75558	h
2607	STX12	Q86Y82	o
2608	STX18	Q9P2W9	o
2609	STX4	Q12846	o
2610	STX5	Q13190	o
2611	STX7	O15400	o
2612	STX8	Q9UNK0	o
2613	STXBP3	O00186	o
2614	SUB1	P53999	l
2615	SUCLA2	Q9P2R7	o,l
2616	SUCLG1	P53597	o,l
2617	SUCLG2	Q96199	o,l
2618	SUGT1	Q9Y2Z0	l
2619	SULT1A2	P50226	l
2620	SULT1A3	P0DMM9	l
2621	SULT2A1	Q06520	h
2622	SUMF2	Q8NBJ7	l
2623	SUN1	O94901	o
2624	SUN2	Q9UH99	o

	Gene	UniProt Accession Number	Studies
2625	SURF1	Q15526	o
2626	SURF4	O15260	l,o
2627	SVIL	O95425	s
2628	SWAP70	Q9UH65	l
2629	SYNCRIP	O60506	l,o
2630	SYNE1	Q8NF91	b,l,o
2631	SYNE2	Q8WXH0	o,l
2632	SYNGR1	O43759	o
2633	SYNGR2	O43760	o
2634	SYNJ2BP	P57105	o
2635	SYPL1	Q16563	l
2636	SYTL1	Q8IYJ3	l
2637	SYVN1	Q86TM6	o
2638	TACC2	O95359	l
2639	TACSTD2	P09758	o,l
2640	TAF15	Q92804	l
2641	TAGLN2	P37802	s,r,o,l
2642	TALDO1	P37837	s,r,l,o
2643	TAOK1	Q7L7X3	g
2644	TAP1	Q03518	o
2645	TAP2	Q03519	l,o
2646	TAPBP	O15533	o,l
2647	TAPBPL	Q9BX59	o
2648	TARDBP	Q13148	l
2649	TARS	P26639	l
2650	TAX1BP3	O14907	l
2651	TBC1D1	Q86T10	l,o
2652	TBC1D15	Q8TC07	l
2653	TBCA	O75347	l
2654	TBCB	Q99426	l
2655	TBCD	Q98TW9	l
2656	TBL2	Q9Y4P3	o
2657	TCERG1	O14776	l
2658	TCF3	P15923	i,f
2659	TCIRG1	Q13488	o
2660	TCN1	P20061	b,s,r,k,l
2661	TCOF1	Q13428	o
2662	TCP1	P17987	o,l
2663	TECR	Q9NZ01	o,l
2664	TEKT1	Q969V4	l
2665	TEKT2	Q9UIF3	l
2666	TERT	O14746	h
2667	TES	Q9UGI8	l
2668	TEX10	Q9NXF1	o
2669	TF	P02787	s,r,k,q,i,b,c,p,l,o,a,q
2670	TFAM	Q00059	l
2671	TFF3	Q07654	s,r,l

	Gene	UniProt Accession Number	Studies
2672	TFG	Q92734	l
2673	TFRC	P02786	o
2674	TGM2	P21980	l,o
2675	TGM3	Q08188	p,a
2676	TGOLN2	O43493	o
2677	THOP1	P52888	l
2678	THRAP3	Q9Y2W1	o,l
2679	THUMPD1	Q9NXG2	l
2680	THYN1	Q9P016	l
2681	TIGAR	Q9NQ88	l
2682	TIMM17B	O60830	o
2683	TIMM50	Q3ZCQ8	l,o
2684	TIMMDC1	Q9NPL8	o
2685	TIMP1	P01033	s,r,k,l
2686	TIPRL	O75663	l
2687	TJP2	Q9UDY2	o,l
2688	TJP3	O95049	o,l
2689	TKFC	Q3LXA3	l
2690	TKT	P29401	s,r,k,o,l,g
2691	TLN1	Q9Y490	l,o
2692	TLR3	O15455	o
2693	TM7SF2	O76062	o
2694	TM9SF1	O15321	o
2695	TM9SF2	Q99805	o,l
2696	TM9SF3	Q9HD45	o,l
2697	TM9SF4	Q92544	o
2698	TMBIM6	P55061	o
2699	TMCO1	Q9UM00	o
2700	TMED1	Q13445	o
2701	TMED10	P49755	l,o
2702	TMED2	Q15363	o
2703	TMED4	Q7Z7H5	o
2704	TMED7	Q9Y3B3	l,o
2705	TMED9	Q9BVK6	o,l
2706	TMEM109	Q9BVC6	o
2707	TMEM126A	Q9H061	o
2708	TMEM128	Q5BJH2	o
2709	TMEM14C	Q9P0S9	o
2710	TMEM165	Q9HC07	o
2711	TMEM173	Q86WV6	l,o
2712	TMEM200C	A6NKL6	s
2713	TMEM205	Q6UW68	l
2714	TMEM231	Q9H6L2	l
2715	TMEM245	Q9H330	o
2716	TMEM259	Q4ZIN3	o
2717	TMEM30A	Q9NV96	o
2718	TMEM30B	Q3MIR4	o

	Gene	UniProt Accession Number	Studies
2719	TMEM33	P57088	o
2720	TMEM63A	O94886	o
2721	TMEM63B	Q5T3F8	o
2722	TMEM65	Q6PI78	o
2723	TMEM67	Q5HYA8	o
2724	TMOD3	Q9NYL9	l
2725	TMPO	P42166	o,l
2726	TMPRSS11D	O60235	o
2727	TMPRSS4	Q9NRS4	o
2728	TMSB4X	P62328	s,r,l,o
2729	TMTC3	Q6ZXV5	o
2730	TMUB1	Q9BVT8	o
2731	TMX1	Q9H3N1	o,l
2732	TMX3	Q96JJ7	o
2733	TMX4	Q9H1E5	o
2734	TNC	P24821	l
2735	TNFAIP8	O95379	l
2736	TNIK	Q9UKE5	l
2737	TNPO1	Q92973	l
2738	TNXB	P22105	s
2739	TOM1	O60784	l
2740	TOMM22	Q9NS69	o
2741	TOMM34	Q15785	l
2742	TOMM40	O96008	o
2743	TOMM70	O94826	l,o
2744	TOP2B	Q02880	o
2745	TOR1AIP1	Q5JTV8	o,l
2746	TP53I3	Q53FA7	l
2747	TP53RK	Q96S44	l
2748	TPBG	Q13641	o
2749	TPD52	P55327	l
2750	TPD52L2	O43399	l
2751	TPI1	P60174	n,c,s,r,l,o,a
2752	TPM1	P09493	o,j,p,j
2753	TPM3	P06753	c,r,s,o,m,l
2754	TPM4	P67936	o,p,l
2755	TPMT	P51580	l
2756	TPP1	O14773	o,l
2757	TPP2	P29144	l
2758	TPPP	O94811	l
2759	TPPP3	Q9BW30	r,s,o,l
2760	TPR	P12270	l
2761	TPRKB	Q9Y3C4	l
2762	TPT1	P13693	j,p,l,o,j
2763	TRA2A	Q13595	l
2764	TRA2B	P62995	l
2765	TRADD	Q15628	l

	Gene	UniProt Accession Number	Studies
2766	TRAM1	Q15629	o
2767	TRANK1	O15050	l
2768	TRAPPC3	O43617	l
2769	TRBC1	P01850	h
2770	TRBV16	A0A087WV62	h
2771	TRIM2	Q9C040	l
2772	TRIM25	Q14258	l
2773	TRIM28	Q13263	l,o
2774	TRIM29	Q14134	o,l
2775	TRIM56	Q9BRZ2	o
2776	TRIP11	Q15643	o
2777	TRIP12	Q14669	o
2778	TRIP6	Q15654	l
2779	TRMT112	Q9UI30	l
2780	TRMT12	Q53H54	m
2781	TRMT61A	Q96FX7	l
2782	TRPM4	Q8TD43	o
2783	TSC22D1	Q15714	l
2784	TSG101	Q99816	l
2785	TSGA10	Q9BZW7	l
2786	TSN	Q15631	l
2787	TSNAX	Q99598	l
2788	TSPAN1	O60635	s,l
2789	TSPAN3	O60637	o
2790	TST	Q16762	o,l
2791	TSTA3	Q13630	l,p
2792	TSTD1	Q8NFU3	l
2793	TTBK1	Q5TCY1	b
2794	TTC21A	Q8NDW8	l
2795	TTC25	Q96NG3	l
2796	TTC26	A0AVF1	l
2797	TTLL12	Q14166	l
2798	TTN	Q8WZ42	s,r,o,l
2799	TTR	P02766	r,s,i,l,j,j
2800	TUBA1A	Q71U36	s,l,o,a
2801	TUBA1B	P68363	s,r,c,m,l
2802	TUBA1C	Q9BQE3	c,m
2803	TUBA4A	P68366	c,l
2804	TUBA8	Q9NY65	c
2805	TUBB	P07437	s,c,m,l,o
2806	TUBB1	Q9H4B7	o
2807	TUBB2B	Q9BVA1	l
2808	TUBB3	Q13509	l
2809	TUBB4A	P04350	s,l
2810	TUBB4B	P68371	r,s,o
2811	TUBB6	Q9BUF5	l
2812	TUBB8	Q3ZCM7	l

	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
2813	TUFM	P49411	c,m,l,o	2860	UGDH	O60701	s,o,l
2814	TUSC3	Q13454	o	2861	UGGT1	Q9NYU2	o,l
2815	TWF1	Q12792	l	2862	UGP2	Q16851	l
2816	TWF2	Q6IB50	l	2863	UGT1A6	P19224	o
2817	TXN	P10599	s,r,o,l,p,e	2864	UGT2A1	Q9Y4X1	o,l
2818	TXN2	Q99757	l	2865	UMPS	P11172	l
2819	TXNDC12	O95881	l	2866	UNC93B1	Q9H1C4	o
2820	TXNDC17	Q9BRA2	l	2867	UPF1	Q92900	l
2821	TXNDC5	Q8NBS9	j,l,j	2868	UQCR10	Q9UDW1	l
2822	TXNL1	O43396	l	2869	UQCRB	P14927	l,o
2823	TXNRD1	Q16881	r,s,l	2870	UQCRC1	P31930	c,l,o,j,j
2824	TXNRD2	Q9NNW7	l	2871	UQCRC2	P22695	l,o
2825	TYMP	P19971	s,r,o,l	2872	UQCRFS1	P47985	o
2826	U2AF1	Q01081	o	2873	UQCRFS1P1	P0C7P4	l
2827	U2AF1L4	Q8WU68	l	2874	UQCRH	P07919	l
2828	U2AF2	P26368	l	2875	UQCRQ	O14949	o
2829	UAP1	Q16222	l	2876	URB2	Q14146	b
2830	UBA1	P22314	s,r,o,l	2877	UROD	P06132	l
2831	UBA2	Q9UBT2	l	2878	USO1	O60763	l
2832	UBA3	Q8TBC4	l	2879	USP14	P54578	l
2833	UBA5	Q9GZZ9	l	2880	USP5	P45974	l,t,o,t
2834	UBA52	P62987	l	2881	USP7	Q93009	l
2835	UBA6	A0AVT1	l	2882	USP9X	Q93008	l,o
2836	UBC	P0CG48	s,o,a	2883	UTRN	P46939	o,l
2837	UBE2A	P49459	l	2884	VAMP2	P63027	o
2838	UBE2D3	P61077	l	2885	VAMP8	Q9BV40	o,l
2839	UBE2I	P63279	l	2886	VANGL1	Q8TAA9	o
2840	UBE2K	P61086	l	2887	VAPA	Q9P0L0	o,l
2841	UBE2L3	P68036	l	2888	VAPB	O95292	l
2842	UBE2L6	O14933	l	2889	VARS	P26640	l,o
2843	UBE2M	P61081	l	2890	VASP	P50552	o,l
2844	UBE2N	P61088	o,l	2891	VAT1	Q99536	l,o
2845	UBE2O	Q9C0C9	l	2892	VBP1	P61758	l
2846	UBE2V1	Q13404	l	2893	VCL	P18206	o,l
2847	UBLCP1	Q8WVY7	l	2894	VCP	P55072	r,c,s,l,o
2848	UBQLN1	Q9UMX0	l	2895	VDAC1	P21796	o,l
2849	UBR4	Q5T457	l	2896	VDAC2	P45880	o,l
2850	UBXN1	Q04323	l	2897	VDAC3	Q9Y277	o,l
2851	UBXN11	Q5T124	l	2898	VILL	O15195	l
2852	UBXN4	Q92575	o	2899	VIM	P08670	s,r,o,l,a
2853	UBXN6	Q9BZV1	l	2900	VMO1	Q7Z5L0	l
2854	UCHL3	P15374	l	2901	VPS13C	Q709C8	l,o
2855	UCHL5	Q9Y5K5	l	2902	VPS26A	O75436	l
2856	UFC1	Q9Y3C8	l	2903	VPS29	Q9UBQ0	l
2857	UFD1	Q92890	l	2904	VPS35	Q96QK1	l
2858	UFL1	O94874	l,o	2905	VPS36	Q86VN1	l
2859	UFM1	P61960	l	2906	VPS4A	Q9UN37	l



	Gene	UniProt Accession Number	Studies		Gene	UniProt Accession Number	Studies
2907	VPS4B	O75351	l	2935	YARS2	Q9Y2Z4	o
2908	VPS9D1	Q9Y2B5	o	2936	YBX1	P67809	o
2909	VTA1	Q9NP79	l	2937	YBX3	P16989	o,l
2910	VTI1B	Q9UEU0	o	2938	YIF1A	O95070	o
2911	VTN	P04004	l	2939	YIPF3	Q9GZM5	o
2912	VWA5A	O00534	l	2940	YIPF6	Q96EC8	o
2913	WARS	P23381	r,l,p,o	2941	YME1L1	Q96TA2	o
2914	WASF2	Q9Y6W5	l	2942	YWHAB	P31946	s,o
2915	WASHC2A	Q641Q2	l	2943	YWHAE	P62258	s,o,l,p
2916	WASHC4	Q2M389	l	2944	YWHAG	P61981	s,o,l
2917	WDR1	O75083	o,l	2945	YWHAH	Q04917	o,l
2918	WDR13	Q9H1Z4	l	2946	YWHAQ	P27348	s,l,o
2919	WDR54	Q9H977	l	2947	YWHAZ	P63104	s,r,o,l,p,a
2920	WDR61	Q9GZS3	l	2948	ZC3H15	Q8WU90	l
2921	WDR77	Q9BQA1	l	2949	ZDHHC13	Q8IUH4	o
2922	WDR92	Q96MX6	l	2950	ZFAND1	Q8TCF1	l
2923	WFDC2	Q14508	s,r,k,l	2951	ZFP2	Q6ZN57	m
2924	WFS1	O76024	o	2952	ZG16B	Q96DA0	k,b,s,r,l
2925	WHAMM	Q8TF30	l	2953	ZMPSTE24	O75844	l,o
2926	WRB	O00258	o	2954	ZMYND10	O75800	l
2927	XDH	P47989	l	2955	ZNF106	Q9H2Y7	s
2928	XPNPEP1	Q9NQW7	l	2956	ZNF165	P49910	s
2929	XPO1	O14980	l	2957	ZNF185	O15231	o,l
2930	XPO7	Q9UIA9	l	2958	ZNF207	O43670	l
2931	XRCC5	P13010	o,l	2959	ZNF263	O14978	s
2932	XRCC6	P12956	o,l	2960	ZNF609	O15014	g
2933	XRN2	Q9H0D6	l	2961	ZSCAN31	Q96LW9	h
2934	YARS	P54577	l	2962	ZW10	O43264	l

## Studies.

	Author	Title
a	Benson et al.	Extensive fractionation and identification of Proteins within nasal lavage fluids from allergic rhinitis and asthmatic chronic rhinosinusitis patients
b	Casado et al.	Identification of human nasal mucous proteins using proteomics
c	Debat et al.	Identification of human olfactory cleft mucus proteins using proteomic analysis
d	Farajzadeh Deroee et al.	Regression of polypoid nasal mucosa after systemic corticosteroid therapy: a proteomics study
e	Gelardi et al.	Proteomic analysis of human nasal mucosa: different expression profile in rhino-pathologic states
f	Ghafouri et al.	Comparative proteomics of nasal fluid in seasonal allergic rhinitis
g	Kim et al.	Fatty acid binding protein 1 is related with development of aspirin-exacerbated respiratory disease
h	Lee et al.	Proteomic analysis of normal human nasal mucosa: Establishment of a two-dimensional electrophoresis reference map
i	Lindahl et al.	Nasal lavage fluid and proteomics as means to identify the effects of the irritating epoxy chemical dimethylbenzylamine
j	Min-Man et al.	Differential proteomic analysis of nasal polyps, chronic sinusitis, and normal nasal mucosa tissues
k	Mortstedt et al.	Screening method using selected reaction monitoring for targeted proteomics studies of nasal lavage fluid

	Author	Title
l	Ndika et al.	Epithelial proteome profiling suggests the essential role of interferon-inducible proteins in patients with allergic rhinitis
m	Roxo-Rosa et al.	Proteomic analysis of nasal cells from cystic fibrosis patients and non-cystic fibrosis control individuals: search for novel biomarkers of cystic fibrosis lung disease
n	Schoenebeck et al.	Improved preparation of nasal lavage fluid (NLF) as a noninvasive sample for proteomic biomarker discovery
o	Simoes et al.	Molecular profiling of the human nasal epithelium: A proteomics approach
p	Suojalehto et al.	Nasal protein profiles in work-related asthma caused by different exposures
q	Tewfik et al.	Proteomics of nasal mucus in chronic rhinosinusitis
r	Tomazic et al.	Nasal mucus proteomic changes reflect altered immune responses and epithelial permeability in patients with allergic rhinitis
s	Tomazic et al.	Seasonal proteome changes of nasal mucus reflect perennial inflammatory response and reduced defence mechanisms and plasticity in allergic rhinitis
t	Upton et al.	Chronic Rhinosinusitis With Nasal Polyps: A Proteomic Analysis
u	Wahlen et al.	Protein profiles of nasal lavage fluid from individuals with work-related upper airway symptoms associated with moldy and damp buildings

**Supplement IV: Study demographics.**

Author	Patient selection	Diagnostic criteria	Co-morbidities	Smoking	Oral steroid
Benson et al.	NR	NR	Asthma	0	0
Casado et al.	Outpatient Clinic	Clinical symptoms (Facial pain, tenderness, mucopurulent discharge)	0	NR	0
Debat et al.	Hospital Clinic	Nasoendoscopy	0	0	0
Ghafouri et al.	NR	Nasal symptoms scores Nasoendoscopy	0	0	0
Lindahl et al.	NR	Nasoendoscopy	DMBA exposure	0	NR
Mortstedt et al.	NR	NR	NR	NR	NR
Schoenebeck et al.	NR	NR	0	NR	NR
Tewfik et al.	Outpatient Clinic	Nasoendoscopy CT Sinuses (Sinus Health Allergy Partnership criteria)	0	0	0
Tomazic et al.	NR	Nasoendoscopy (EPOS Criteria)	0	NR	0
Tomazic et al.	NR	Nasoendoscopy (EPOS Criteria)	0	0	0
Wahlen et al.	NR	NR	0	0	NR
Farajzadeh Deroee et al.	Hospital Clinic	Nasoendoscopy	0	0	3
Gelardi et al.	Hospital Clinic	Clinical symptoms Nasoendoscopy	0	NR	NR
Kim et al.	NR	Clinical symptoms Nasoendoscopy CT Sinuses	Asthma ATA 8 AERD 5	ATA 2	0
Lee et al.	NR	Clinical symptoms Nasoendoscopy	0	NR	0
Min-Man et al.	Hospital Clinic	Nasoendoscopy CT Sinuses	0	NR	0
Ndika J et al.	Hospital Clinic	Seasonal allergy symptoms questionnaire	0	0	NR
Roxo-Rosa et al.	NR	Clinical symptoms	0	0	0
Simoes et al.	NR	NR	NR	NR	NR
Suojalehto et al.	Hospital Clinic	NR	0	0	NR
Upton DC et al.	Outpatient Clinic	Nasoendoscopy CT Sinuses (AAO-HNS CRS TF criteria)	NR	0	3

AAO-HNS: American Academy of Otolaryngology-Head and Neck Surgery Chronic Rhinosinusitis Task Force; ATA: Aspirin-tolerant asthma; AERD: Aspirin-exacerbated respiratory disease; DMBA: Dimethylbenzylamine; EPOS: European Position Paper on Chronic Rhinosinusitis and Nasal Polyps; NR: Not reported.

**Supplement V: Cellular pathways/ cellular components/ biological processes/ molecular functions / cellular pathways.**

Pathway	Classification	Source	Adjusted P-value	Genes
Antigen activates B Cell Receptor (BCR) leading to generation of second messengers_Homo sapiens_R-HSA-983695	Immune system	Mucus CRS	0.00148	IGHM;IGKC;IGHV3-23;IGLC1;CALM1
Apoptosis_Homo sapiens_R-HSA-109581	Programmed cell death	Mucus CRS	0.00152	DSP;UBC;LMNA;PKP1;DSG1;SFN;VIM;YWHAZ
Apoptotic cleavage of cell adhesion proteins_Homo sapiens_R-HSA-351906	Programmed cell death	Mucus CRS	0.00373	DSP;DSG1;PKP1
Apoptotic cleavage of cellular proteins_Homo sapiens_R-HSA-111465	Programmed cell death	Mucus CRS	0.00054	DSP;LMNA;DSG1;PKP1;VIM
Apoptotic execution phase_Homo sapiens_R-HSA-75153	Programmed cell death	Mucus CRS	0.00199	DSP;LMNA;DSG1;PKP1;VIM
Binding and Uptake of Ligands by Scavenger Receptors_Homo sapiens_R-HSA-2173782	Vesicle-mediated transport	Mucus CRS	0.00000	COL1A1;COL1A2;IGKC;IGHV3-23;HP;IGLC1;HBA1;HPR;IGHA2
Binding and Uptake of Ligands by Scavenger Receptors_Homo sapiens_R-HSA-2173782	Vesicle-mediated transport	Mucus Healthy + CRS	0.00017	IGKV1-5;ALB;HBB;IGHA1
CD22 mediated BCR regulation_Homo sapiens_R-HSA-5690714	Immune system	Mucus CRS	0.00059	IGHM;IGKC;IGHV3-23;IGLC1
Classical antibody-mediated complement activation_Homo sapiens_R-HSA-173623	Immune system	Mucus CRS	0.00001	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
Complement cascade_Homo sapiens_R-HSA-166658	Immune system	Mucus CRS	0.00017	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
Creation of C4 and C2 activators_Homo sapiens_R-HSA-166786	Immune system	Mucus CRS	0.00001	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
Detoxification of Reactive Oxygen Species_Homo sapiens_R-HSA-3299685	Cellular responses to external stimuli	Mucosa Healthy + CRS	0.02341	PRDX2;CAT;SOD1
Diseases associated with visual transduction_Homo sapiens_R-HSA-2474795	Disease	Mucosa Healthy + CRS	0.02021	RBP4;TTR
FCERI mediated Ca+2 mobilization_Homo sapiens_R-HSA-2871809	Immune system	Mucus CRS	0.04948	IGKC;IGHV3-23;IGLC1;CALM1
Fcgamma receptor (FCGR) dependent phagocytosis_Homo sapiens_R-HSA-2029480	Immune system	Mucus CRS	0.00003	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;MYH9;IGLC1;ACTB
FCGR activation_Homo sapiens_R-HSA-2029481	Immune system	Mucus CRS	0.00001	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
Gluconeogenesis_Homo sapiens_R-HSA-70263	Metabolism	Mucus CRS	0.00462	TPI1;ENO1;ALDOA;GAPDH
Glucose metabolism_Homo sapiens_R-HSA-70326	Metabolism	Mucus CRS	0.00017	TPI1;PKM;UBC;ENO1;ALDOA;CALM1;GAPDH
Glycolysis_Homo sapiens_R-HSA-70171	Metabolism	Mucus CRS	0.00028	TPI1;PKM;ENO1;ALDOA;GAPDH
Initial triggering of complement_Homo sapiens_R-HSA-166663	Immune system	Mucus CRS	0.00003	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
Metabolism of carbohydrates_Homo sapiens_R-HSA-71387	Metabolism	Mucus CRS	0.04885	TPI1;PKM;AMY2B;UBC;ENO1;CALM1;ALDOA;GAPDH
Metabolism of fat-soluble vitamins_Homo sapiens_R-HSA-6806667	Metabolism	Mucosa Healthy + CRS	0.02495	RBP4;TTR;APOA1
Metabolism_Homo sapiens_R-HSA-1430728	Metabolism	Mucosa Healthy + CRS	0.00556	ECHS1;APOA1;NME4;PDHB;CA1;RBP4;TTR;NDUF58;ALDH1A1;CAT;CMPK1;UQCRC1;PSME1;GAPDH
Platelet degranulation_Homo sapiens_R-HSA-114608	Homeostasis	Mucosa Healthy + CRS	0.02114	SERPINA1;FGG;APOA1;SOD1
Platelet degranulation_Homo sapiens_R-HSA-114608	Homeostasis	Mucus CRS	0.04631	SERPINA3;SERPINA1;AHSG;CALM1;ALDOA

Pathway	Classification	Source	Adjusted P-value	Genes
Platelet degranulation_Homo sapiens_R-HSA-114608	Homeostasis	Mucus Healthy + CRS	0.03116	ORM1;TF;ALB
Programmed Cell Death_Homo sapiens_R-HSA-5357801	Programmed cell death	Mucus CRS	0.00155	DSP;UBC;LMNA;PKP1;DSG1;SFN;VIM;YWHAZ
Regulation of actin dynamics for phagocytic cup formation_Homo sapiens_R-HSA-2029482	Immune system	Mucus CRS	0.00001	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;MYH9;IGLC1;ACTB
Response to elevated platelet cytosolic Ca2+_Homo sapiens_R-HSA-76005	Homeostasis	Mucosa Healthy + CRS	0.01902	SERPINA1;FGG;APOA1;SOD1
Response to elevated platelet cytosolic Ca2+_Homo sapiens_R-HSA-76005	Homeostasis	Mucus Healthy + CRS	0.02685	ORM1;TF;ALB
Retinoid cycle disease events_Homo sapiens_R-HSA-2453864	Disease	Mucosa Healthy + CRS	0.02274	RBP4;TTR
Retinoid metabolism and transport_Homo sapiens_R-HSA-975634	Metabolism, Signal transduction	Mucosa Healthy + CRS	0.01948	RBP4;TTR;APOA1
RHO GTPases activate PKNs_Homo sapiens_R-HSA-5625740	Signal transduction	Mucus CRS	0.04735	HIST1H4A;MYH9;SFN;YWHAZ
Role of phospholipids in phagocytosis_Homo sapiens_R-HSA-2029485	Immune system	Mucus CRS	0.00003	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
Scavenging of heme from plasma_Homo sapiens_R-HSA-2168880	Vesicle-mediated transport	Mucus CRS	0.00001	IGKC;IGHV3-23;HP;IGLC1;HPR;HBA1;IGHA2
Scavenging of heme from plasma_Homo sapiens_R-HSA-2168880	Vesicle-mediated transport	Mucus Healthy + CRS	0.00005	IGKV1-5;ALB;HBB;IGHA1
Signal Transduction_Homo sapiens_R-HSA-162582	Signal transduction	Mucosa Healthy + CRS	0.01752	ANXA1;FGG;PEBP1;APOA1;PDHB;ACTB;ACTG1;ADCYAP1;RBP4;TTR;ARHGDI1A;ARHGDI1B;ALDH1A1;PSME1
Translocation of GLUT4 to the plasma membrane_Homo sapiens_R-HSA-1445148	Vesicle-mediated transport	Mucus CRS	0.04940	MYH13;SFN;CALM1;YWHAZ
Vesicle-mediated transport_Homo sapiens_R-HSA-5653656	Vesicle-mediated transport	Mucus CRS	0.00017	SERPINA1;IGHV3-23;HP;HPR;HBA1;YWHAZ;COL1A1;COL1A2;IGKC;UBC;MYH13;SFN;IGLC1;CALM1;IGHA2

### Cellular components.

Cellular Component	Classification	Source	Adjusted P-value	Genes
actin filament (GO:0005884)	Cytoskeleton	Mucosa Healthy + CRS	0.01684	ANXA1;TPM1;ACTG1
azurophil granule (GO:0042582)	Secretory granule	Mucus CRS	0.00049	SERPINB3;SERPINA3;PIGR;ANXA2;FABP5;DEFA1;S100A7;HRNR
azurophil granule lumen (GO:0035578)	Secretory granule	Mucus CRS	0.00014	SERPINB3;SERPINA3;ANXA2;FABP5;DEFA1;S100A7;HRNR
cytoplasmic vesicle lumen (GO:0060205)	Cytoplasmic vesicle	Mucus CRS	0.00000	EEF1A1;SERPINA3;CSTB;PKM;AHSG;GSTP1;HBA1;ALDOA;S100A8;S100A11
cytoplasmic vesicle lumen (GO:0060205)	Cytoplasmic vesicle	Mucus Healthy + CRS	0.00735	TF;HBB;S100A9
cytoplasmic vesicle lumen (GO:0060205)	Cytoplasmic vesicle	Mucosa Healthy + CRS	0.01417	CAT;APOA1;S100A8;HSP90B1
cytoskeleton (GO:0005856)	Cytoskeleton	Mucus CRS	0.00232	KRT4;JUP;HSPB1;KRT77;ACTB;TUBA1A;KRT17;KRT16;MYH9;VIM;ALDOA;GAPDH;S100A8
cytoskeleton (GO:0005856)	Cytoskeleton	Mucosa Healthy + CRS	0.00089	ARHGDI1A;ARHGDI1B;TPM1;KRT8;GAPDH;ACTB;S100A8;ACTG1
endocytic vesicle lumen (GO:0071682)	Cytoplasmic vesicle	Mucus Healthy + CRS	0.00593	HBB;LTF

Cellular Component	Classification	Source	Adjusted P-value	Genes
endocytic vesicle lumen (GO:0071682)	Cytoplasmic vesicle	Mucosa Healthy + CRS	0.03186	APOA1;HSP90B1
ficolin-1-rich granule (GO:0101002)	Secretory granule	Mucus CRS	0.00000	EEF1A1;DSP;CSTB;SERPINB12;SERPINA1;PKM;CALML5;JUP;GSTP1;PKP1;DSG1;ALDOA
ficolin-1-rich granule lumen (GO:1904813)	Secretory granule	Mucus CRS	0.00012	EEF1A1;CSTB;SERPINA1;PKM;CALML5;JUP;GSTP1;ALDOA
ficolin-1-rich granule membrane (GO:0101003)	Secretory granule	Mucus CRS	0.02500	DSP;SERPINB12;DSG1;PKP1
focal adhesion (GO:0005925)	Adheren junction	Mucus CRS	0.02430	ANXA1;JUP;HSPB1;MYH9;VIM;B2M;YWHAZ;ACTB;S100A7
focal adhesion (GO:0005925)	Adheren junction	Mucosa CRS	0.00632	HSPA9;ACTR3;HSPA5;IQGAP1;P4HB
focal adhesion (GO:0005925)	Adheren junction	Mucosa Healthy + CRS	0.03570	ANXA1;CAT;ACTB;HSP90B1;ACTG1
intermediate filament (GO:0005882)	Cytoskeleton	Mucus CRS	0.00000	KRT82;FLG;DSP;KRT4;KRT3;KRT2;KRT7;KRT5;KRT10;KRT76;KRT20;KRT84;KRT16;KRT14;PKP1;VIM;KRT6A
intermediate filament cytoskeleton (GO:0045111)	Cytoskeleton	Mucus CRS	0.00000	DSP;FLG;KRT4;KRT3;KRT2;KRT7;KRT5;KRT76;KRT10;KRT20;KRT17;KRT16;KRT14;PKP1;VIM;S100A8;KRT6A
keratin filament (GO:0045095)	Cytoskeleton	Mucus CRS	0.00000	KRT82;KRT4;KRT3;KRT14;KRT5;KRT84
mitochondrial matrix (GO:0005759)	Mitochondria	Mucosa CRS	0.00631	HSPA9;ALDH4A1;RIDA;CPS1;HSPD1
mitochondrion (GO:0005739)	Mitochondria	Mucosa Healthy + CRS	0.04277	ECHS1;NDUFS8;CAT;UQCRC1;NME4;PDHB;PARK7;SOD1
platelet alpha granule lumen (GO:0031093)	Secretory granule	Mucus CRS	0.03316	SERPINA3;SERPINA1;AHSG;ALDOA
polymeric cytoskeletal fiber (GO:0099513)	Cytoskeleton	Mucus CRS	0.00000	FLG;DSP;ANXA1;KRT4;KRT3;KRT2;KRT7;KRT5;KRT76;KRT10;KRT20;TUBA1A;KRT16;KRT14;PKP1;VIM;KRT6A
polymeric cytoskeletal fiber (GO:0099513)	Cytoskeleton	Mucosa Healthy + CRS	0.04082	ANXA1;TPM1;KRT8;ACTG1
secretory granule lumen (GO:0034774)	Secretory granule	Mucus CRS	0.00000	SERPINB3;SERPINA3;CSTB;SERPINA1;JUP;ANXA2;AHSG;GSTP1;DEFA1;HRNR;EEF1A1;PKM;FABP5;ALDOA;B2M;S100A8;S100A11;S100A7
secretory granule lumen (GO:0034774)	Secretory granule	Mucus Healthy + CRS	0.00000	ORM1;TF;SLPI;ALB;LYZ;S100A9;LTF
secretory granule lumen (GO:0034774)	Secretory granule	Mucosa Healthy + CRS	0.00073	SERPINA1;TTR;FGG;CAT;APOA1;S100A8;TXNDC5
specific granule (GO:0042581)	Secretory granule	Mucus Healthy + CRS	0.00057	ORM1;SLPI;LYZ;LTF
specific granule lumen (GO:0035580)	Secretory granule	Mucus Healthy + CRS	0.00002	ORM1;SLPI;LYZ;LTF
tertiary granule (GO:0070820)	Secretory granule	Mucus CRS	0.00470	DSP;CSTB;SERPINB12;PKP1;DSG1;ALDOA;B2M
tertiary granule (GO:0070820)	Secretory granule	Mucus Healthy + CRS	0.00051	ORM1;HBB;LYZ;LTF
tertiary granule lumen (GO:1904724)	Secretory granule	Mucus Healthy + CRS	0.00002	ORM1;HBB;LYZ;LTF
vacuolar lumen (GO:0005775)	Vacuole	Mucus CRS	0.00454	SERPINB3;SERPINA3;ANXA2;FABP5;DEFA1;S100A7;HRNR

### Biological pathways

Biological Process	Classification	Source	Adjusted P-value	Genes
4-hydroxyproline metabolic process (GO:0019471)	Cellular metabolic process	Mucosa CRS	0.02989	ALDH4A1;P4HB
antibacterial humoral response (GO:0019731)	Immune system process	Mucus CRS	0.00004	IGHM;BPIFA1;SEMG2;SEMG1;DEFA1;IGHA2
antibacterial humoral response (GO:0019731)	Immune system process	Mucus Healthy + CRS	0.00003	SLPI;IGHA1;JCHAIN;LTF

Biological Process	Classification	Source	Adjusted P-value	Genes
antigen receptor-mediated signaling pathway (GO:0050851)	Immune system process	Mucus CRS	0.00144	IGHG3;IGHG4;IGHM;IGHG1;IGHG2;IGKC;IGHV3-23;UBC;IGLC1;IGHA2
antimicrobial humoral immune response mediated by antimicrobial peptide (GO:0061844)	Immune system process	Mucus CRS	0.00020	BPIFA1;SEMG1;DEFA1;GAPDH;KRT6A;S100A7
ATP generation from ADP (GO:0006757)	Cellular metabolic process	Mucus CRS	0.00269	LDHA;TPI1;PKM;ALDOA
B cell receptor signaling pathway (GO:0050853)	Immune system process	Mucus CRS	0.00001	IGHG3;IGHG4;IGHM;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;IGHA2
canonical glycolysis (GO:0061621)	Metabolic process	Mucus CRS	0.00016	TPI1;PKM;ENO1;ALDOA;GAPDH
carbohydrate catabolic process (GO:0016052)	Metabolic process	Mucus CRS	0.01105	LDHA;TPI1;PKM;ALDOA
cellular protein metabolic process (GO:0044267)	Cellular metabolic process	Mucus Healthy + CRS	0.01029	TF;BPIFB2;ALB;LYZ;LTF
cellular response to oxidative stress (GO:0034599)	Cellular response to chemical stimulus	Mucosa Healthy + CRS	0.00231	PRDX2;TPM1;CAT;PARK7;SOD1
cellular response to superoxide (GO:0071451)	Cellular response to chemical stimulus	Mucosa Healthy + CRS	0.04045	PRDX2;SOD1
complement activation, classical pathway (GO:0006958)	Immune system process	Mucus CRS	0.00004	IGHG3;IGHG4;IGHM;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;IGHA2
defense response to bacterium (GO:0042742)	Response to stimulus	Mucus CRS	0.00000	IGHM;IGHV3-23;DEFA1;IGHG3;IGHG4;IGHG1;BPIFA1;IGHG2;IGKC;SEMG2;PRB3;SEMG1;IGLC1;IGHA2;LACRT;S100A8;KRT6A;S100A7
defense response to bacterium (GO:0042742)	Response to stimulus	Mucus Healthy + CRS	0.00002	SLPI;LYZ;IGHA1;S100A9;JCHAIN;LTF
defense response to fungus (GO:0050832)	Response to stimulus	Mucus Healthy + CRS	0.02586	S100A9;LTF
detection of chemical stimulus involved in sensory perception of bitter taste (GO:0001580)	Sensory perception	Mucus CRS	0.01812	PIGR;AZGP1;PIP;CST4
detection of chemical stimulus involved in sensory perception of taste (GO:0050912)	Sensory perception	Mucus CRS	0.02456	PIGR;AZGP1;PIP;CST4
endocytosis (GO:0006897)	Localisation	Mucus CRS	0.04151	ANXA1;IGKC;AHSG;IGHV3-23;IGLC1;HPR;HBA1;IGHA2
endocytosis (GO:0006897)	Localisation	Mucus Healthy + CRS	0.00066	IGKV1-5;ALB;HBB;IGHA1;JCHAIN
epidermal cell differentiation (GO:0009913)	Antomical structure development	Mucus CRS	0.00000	DSP;FLG;CSTA;ANXA1;KRT16;KRT10;SPRR2B;SPRR1A;TGM3;IVL;SPRR1B;S100A7
epidermis development (GO:0008544)	Antomical structure development	Mucus CRS	0.00000	DSP;FLG;CALML5;KRT2;KRT34;KRT5;KRT32;KRT31;KRT85;KRT9;KRT83;HRNR;CASP14;KRT17;FABP5;KRT16;KRT14;SPRR2B;SPRR1A;SPRR1B;S100A7
establishment of skin barrier (GO:0061436)	Antomical structure development	Mucus CRS	0.00059	FLG;KRT16;SFN;HRNR
Fc receptor mediated stimulatory signaling pathway (GO:0002431)	Immune system process	Mucus CRS	0.00063	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;ACTB
Fc-gamma receptor signaling pathway (GO:0038094)	Immune system process	Mucus CRS	0.00062	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;ACTB
Fc-gamma receptor signaling pathway involved in phagocytosis (GO:0038096)	Immune system process	Mucus CRS	0.00060	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;ACTB
glomerular filtration (GO:0003094)	System process	Mucus Healthy + CRS	0.01092	IGHA1;JCHAIN
gluconeogenesis (GO:0006094)	Metabolic process	Mucus CRS	0.01912	TPI1;ENO1;ALDOA;GAPDH
glucose catabolic process to pyruvate (GO:0061718)	Metabolic process	Mucus CRS	0.00015	TPI1;PKM;ENO1;ALDOA;GAPDH
glycolytic process (GO:0006096)	Cellular metabolic process	Mucus CRS	0.00199	LDHA;TPI1;PKM;ALDOA

Biological Process	Classification	Source	Adjusted P-value	Genes
glycolytic process through glucose-6-phosphate (GO:0061620)	Cellular metabolic process	Mucus CRS	0.00016	TPI1;PKM;ENO1;ALDOA;GAPDH
heart contraction (GO:0060047)	Circulatory system	Mucosa Healthy + CRS	0.04000	MYL4;TPM1;SOD1
hexose biosynthetic process (GO:0019319)	Metabolic process	Mucus CRS	0.02409	TPI1;ENO1;ALDOA;GAPDH
homotypic cell-cell adhesion (GO:0034109)	Cell-cell adhesion	Mucosa Healthy + CRS	0.03709	FGG;ACTB;ACTG1
humoral immune response mediated by circulating immunoglobulin (GO:0002455)	Immune system process	Mucus CRS	0.00004	IGHG3;IGHG4;IGHM;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;IGHA2
hydrogen peroxide metabolic process (GO:0042743)	Cellular metabolic process	Mucosa Healthy + CRS	0.00024	PRDX2;CAT;PARK7;SOD1
intermediate filament organization (GO:0045109)	Cellular component organisation	Mucus CRS	0.00001	DSP;KRT14;PKP1;KRT20;KRT9
keratinocyte differentiation (GO:0030216)	System development	Mucus CRS	0.00000	DSP;FLG;CSTA;ANXA1;KRT16;KRT10;SPRR2B;SPRR1A;TGM3;IVL;SPRR1B;S100A7
negative regulation of apoptotic process (GO:0043066)	Cell death	Mucosa CRS	0.02026	HSPA9;FABP1;HSPA5;GSTP1;GLO1;HSPD1
negative regulation of apoptotic process (GO:0043066)	Cell death	Mucosa Healthy + CRS	0.00048	PRDX2;ANXA1;ARHGDI1;CAT;PARK7;TPT1;HSP90B1;TXNDC5;SOD1
negative regulation of cellular protein metabolic process (GO:0032269)	Cellular metabolic process	Mucus CRS	0.03466	SERPINB3;CSTB;CSTA;GAPDH;CST4
negative regulation of endopeptidase activity (GO:0010951)	Regulation of molecular function	Mucus CRS	0.00003	SERPINB3;SERPINA3;SERPINB4;SERPINB12;SERPINA1;AHSG;GAPDH;CST4
negative regulation of peptidase activity (GO:0010466)	Regulation of molecular function	Mucus CRS	0.00000	SERPINB3;SERPINA3;SERPINB4;CSTB;SERPINB12;CSTA;SERPINA1;AHSG;GAPDH
negative regulation of programmed cell death (GO:0043069)	Cell death	Mucosa CRS	0.01505	HSPA9;FABP1;HSPA5;GSTP1;GLO1;HSPD1
negative regulation of programmed cell death (GO:0043069)	Cell death	Mucosa Healthy + CRS	0.00112	PRDX2;ANXA1;ARHGDI1;CAT;PARK7;TPT1;HSP90B1;TXNDC5
negative regulation of proteolysis (GO:0045861)	Cellular metabolic process	Mucus CRS	0.00133	SERPINB3;CSTB;SERPINB4;CSTA;CST4
neutrophil activation involved in immune response (GO:0002283)	Immune system process	Mucus CRS	0.00000	DSP;SERPINB3;SERPINA3;PIGR;CSTB;SERPINB12;SERPINA1;CALML5;JUP;ANXA2;AHSG;GSTP1;DEFA1;HRNR;EEF1A1;PKM;FABP5;PKP1;DSG1;ALDOA;B2M;S100A8;S100A11;S100A7
neutrophil activation involved in immune response (GO:0002283)	Immune system process	Mucus Healthy + CRS	0.00069	ORM1;SLPI;HBB;LYZ;S100A9;LTF
neutrophil degranulation (GO:0043312)	Immune system process	Mucus CRS	0.00000	DSP;SERPINB3;SERPINA3;PIGR;CSTB;SERPINB12;SERPINA1;CALML5;JUP;ANXA2;AHSG;GSTP1;DEFA1;HRNR;EEF1A1;PKM;FABP5;PKP1;DSG1;ALDOA;B2M;S100A8;S100A11;S100A7
neutrophil degranulation (GO:0043312)	Immune system process	Mucus Healthy + CRS	0.00079	ORM1;SLPI;HBB;LYZ;S100A9;LTF
neutrophil mediated immunity (GO:0002446)	Immune system process	Mucus CRS	0.00000	DSP;SERPINB3;SERPINA3;PIGR;CSTB;SERPINB12;SERPINA1;CALML5;JUP;ANXA2;AHSG;GSTP1;DEFA1;HRNR;EEF1A1;PKM;FABP5;PKP1;DSG1;ALDOA;B2M;S100A8;S100A11;S100A7
neutrophil mediated immunity (GO:0002446)	Immune system process	Mucus Healthy + CRS	0.00062	ORM1;SLPI;HBB;LYZ;S100A9;LTF
nicotinamide nucleotide metabolic process (GO:0046496)	Cellular metabolic process	Mucus CRS	0.02575	LDHA;TPI1;PKM;ALDOA
pattern recognition receptor signaling pathway (GO:0002221)	Immune system process	Mucosa Healthy + CRS	0.03975	FGG;S100A8;HSP90B1



Biological Process	Classification	Source	Adjusted P-value	Genes
peptide cross-linking (GO:0018149)	Cellular metabolic process	Mucus CRS	0.00000	FLG;DSP;CSTA;ANXA1;KRT2;KRT10;SPRR2B;SPRR1A;TGM3;SPRR1B;IVL
peptidyl-cysteine modification (GO:0018198)	Cellular metabolic process	Mucosa Healthy + CRS	0.03937	PARK7;S100A8
phagocytosis (GO:0006909)	Localisation	Mucus CRS	0.00000	IGHG3;IGHG4;IGHM;IGHG1;IGHG2;ANXA1;IGKC;IGHV3-23;MYH9;IGLC1;IGHA2
phagocytosis, engulfment (GO:0006911)	Localisation	Mucus CRS	0.00000	IGHG3;IGHG4;IGHM;IGHG1;IGHG2;IGKC;IGHV3-23;MYH9;IGLC1;IGHA2
plasma membrane invagination (GO:0099024)	Cellular component organisation	Mucus CRS	0.00000	IGHG3;IGHG4;IGHM;IGHG1;IGHG2;IGKC;IGHV3-23;MYH9;IGLC1;IGHA2
platelet aggregation (GO:0070527)	Response to stimulus	Mucosa Healthy + CRS	0.02851	FGG;ACTB;ACTG1
platelet degranulation (GO:0002576)	Export from cell	Mucus Healthy + CRS	0.03274	ORM1;TF;ALB
platelet degranulation (GO:0002576)	Export from cell	Mucosa Healthy + CRS	0.03797	SERPINA1;FGG;APOA1;SOD1
positive regulation of B cell activation (GO:0050871)	Cell activation	Mucus CRS	0.00003	IGHG3;IGHG4;IGHM;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;IGHA2
positive regulation of lymphocyte activation (GO:0051251)	Cell activation	Mucus CRS	0.00001	IGHG3;IGHG4;IGHM;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;IGHA2
positive regulation of metabolic process (GO:0009893)	Metabolic process	Mucus Healthy + CRS	0.02714	IGHA1;JCHAIN
positive regulation of respiratory burst (GO:0060267)	Metabolic process	Mucus Healthy + CRS	0.00831	IGHA1;JCHAIN
protein heterooligomerization (GO:0051291)	Cellular component organisation or biogenesis	Mucus CRS	0.00266	HIST1H4A;ANXA2;SEM2;SEM1;HBA1
pyruvate metabolic process (GO:0006090)	Cellular metabolic process	Mucus CRS	0.02748	LDHA;TPI1;PKM;ALDOA
receptor-mediated endocytosis (GO:0006898)	Localisation	Mucus Healthy + CRS	0.00025	IGKV1-5;ALB;HBB;IGHA1;JCHAIN
regulation of acute inflammatory response (GO:0002673)	Response to stimulus	Mucus CRS	0.00033	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;GSTP1;IGHV3-23;IGLC1
regulation of apoptotic process (GO:0042981)	Cell death	Mucosa CRS	0.01647	HSPA9;FABP1;HSPA5;GSTP1;GLO1;TAOK1;HSPD1
regulation of apoptotic process (GO:0042981)	Cell death	Mucosa Healthy + CRS	0.00197	PRDX2;ANXA1;ARHGDI3;CAT;NME4;PARK7;TPT1;HSP90B1;TXNDC5;SOD1
regulation of B cell activation (GO:0050864)	Cell activation	Mucus CRS	0.00001	IGHG3;IGHM;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;IGHA2
regulation of complement activation (GO:0030449)	Immune system process	Mucus CRS	0.00137	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
regulation of endopeptidase activity (GO:0052548)	Regulation of molecular function	Mucus CRS	0.00009	SERPINB3;SERPINA3;SERPINB4;SERPINB12;SERPINA1;AHSG;GAPDH
regulation of humoral immune response (GO:0002920)	Immune system process	Mucus CRS	0.00165	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
regulation of immune effector process (GO:0002697)	Immune system process	Mucus CRS	0.00170	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
regulation of peptidase activity (GO:0052547)	Regulation of molecular function	Mucus CRS	0.00085	SERPINB3;SERPINB4;CSTB;CSTA
regulation of protein activation cascade (GO:2000257)	Metabolic process	Mucus CRS	0.00133	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
regulation of protein processing (GO:0070613)	Metabolic process	Mucus CRS	0.00327	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
regulation of proteolysis (GO:0030162)	Metabolic process	Mucus CRS	0.00828	SERPINB3;SERPINB4;CSTB;CSTA;CST4
regulation of respiratory burst (GO:0060263)	Metabolic process	Mucus Healthy + CRS	0.01001	IGHA1;JCHAIN

Biological Process	Classification	Source	Adjusted P-value	Genes
regulation of water loss via skin (GO:0033561)	Biological regulation	Mucus CRS	0.00058	FLG;KRT16;SFN;HRNR
removal of superoxide radicals (GO:0019430)	Cellular response to chemical stimulus	Mucosa Healthy + CRS	0.04334	PRDX2;SOD1
renal filtration (GO:0097205)	System process	Mucus Healthy + CRS	0.01129	IGHA1;JCHAIN
response to hydrogen peroxide (GO:0042542)	Response to stimulus	Mucosa Healthy + CRS	0.04154	CAT;PARK7;SOD1
response to unfolded protein (GO:0006986)	Response to stimulus	Mucosa CRS	0.02186	HSPA9;HSPA5;HSPD1
retina homeostasis (GO:0001895)	Tissue homeostasis	Mucus CRS	0.00000	IGHG3;PIGR;AZGP1;IGKC;PIP;HSPB1;LCN1;B2M;IGHA2;ACTB;CST4
retina homeostasis (GO:0001895)	Tissue homeostasis	Mucus Healthy + CRS	0.00000	TF;ALB;LYZ;IGHA1;JCHAIN;LTF
retina homeostasis (GO:0001895)	Tissue homeostasis	Mucosa Healthy + CRS	0.03245	ACTB;ACTG1;SOD1
sensory perception of bitter taste (GO:0050913)	Sensory perception	Mucus CRS	0.01951	PIGR;AZGP1;PIP;CST4
skin development (GO:0043588)	System development	Mucus CRS	0.00000	DSP;FLG;CSTA;ANXA1;KRT10;ASPRV1;KRT9;HRNR;COL1A1;COL1A2;KRT16;SFN;SPRR2B;SPRR1A;TGM3;IVL;SPRR1B;S100A7

### Molecular function

Molecular Function	Classification	Group	Adjusted P-value	Genes
cadherin binding (GO:0045296)	Binding	Mucus CRS	0.00294	LDHA;ANXA1;PKM;JUP;ANXA2;MYH9;SFN;ENO1;ALDOA;YWHAZ;S100A11
cadherin binding involved in cell-cell adhesion (GO:0098641)	Binding	Mucus CRS	0.03519	ANXA1;ANXA2;S100A11
cysteine-type endopeptidase inhibitor activity (GO:0004869)	Molecular function regulator	Mucus CRS	0.00625	SERPINB3;CSTB;CSTA;LCN1;CST4
endopeptidase activity (GO:0004175)	Catalytic activity	Mucus CRS	0.02312	IGHG3;IGHG4;CASP14;IGHG1;IGHG2;IGKC;PIP;IGHV3-23;IGLC1;ASPRV1
endopeptidase inhibitor activity (GO:0004866)	Molecular function regulator	Mucus CRS	0.00000	SERPINB3;SERPINA3;SERPINB4;CSTB;SERPINB12;CSTA;SERPINA1;AHSG;LCN1;GAPDH;CST4
immunoglobulin receptor binding (GO:0034987)	Binding	Mucus CRS	0.00000	IGHG3;IGHM;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1;IGHA2
intermediate filament binding (GO:0019215)	Binding	Mucus CRS	0.00802	KRT14;PKP1;VIM
protease binding (GO:0002020)	Binding	Mucus CRS	0.00000	COL1A1;SERPINB3;SERPINB4;CSTB;CSTA;COL1A2;SERPINA1;ANXA2;SEMG2;UBC;CST4
protein binding involved in cell-cell adhesion (GO:0098632)	Binding	Mucus CRS	0.04508	ANXA1;ANXA2;S100A11
serine-type endopeptidase activity (GO:0004252)	Catalytic activity	Mucus CRS	0.04657	IGHG3;IGHG4;IGHG1;IGHG2;IGKC;IGHV3-23;IGLC1
serine-type endopeptidase inhibitor activity (GO:0004867)	Molecular function regulator	Mucus CRS	0.00817	SERPINB3;SERPINA3;SERPINB4;SERPINB12;SERPINA1
signal recognition particle binding (GO:0005047)	Binding	Mucus Healthy + CRS	0.01688	TF;LTF