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Decoding *Hippophae rhamnoides*' action of mechanism in Sjögren's syndrome: A network pharmacology and molecular docking study

Lu-yun Xia[1†], Zheng Luo[1†], Han-piao Xu[1†], Liu Liu[1], Wen-ying Huai[1], Jun Xia[1], Qiao-zhi Yin[2], Tian-e Zhang[1,2*], Yun-hui Chen[1]

[1]*College of Basic Medicine/College of International Education, Chengdu University of Traditional Chinese Medicine, Chengdu, China;* [2]*Key Biology Laboratory for TCM Viscera-Manifestation Research of Sichuan University, Chinese Medical Center of Chengdu University of TCM, Chengdu, China*

[†]These authors contributed equally to this work.

***Corresponding authors:** Tian-e Zhang and Yun-hui Chen, College of Basic Medicine/College of International Education, Chengdu University of Traditional Chinese Medicine, Chengdu, China. Emails: zhte2003@cdutcm.edu.cn; chenyunhui@cdutcm.edu.cn

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Abstract

This study aimed to decode the potential bioactive compounds and action mechanism of *Hippophae rhamnoides* in treating Sjögren's syndrome using network pharmacology and molecular docking approach. The Traditional Chinese Medicine Systematic Pharmacology Database and Analysis Platform (TCMSP) and HERB (a High-throughput Experiment- and Reference-guided database of TCM) database were used to identify the active components of *Hippophae rhamnoides* and their targets. Databases, including GeneCards, Online Mendelian Inheritance (OMIM), and DisGeNET, were used to acquire the major targets of action in Sjögren's syndrome. Venn diagrams were constructed to identify the compound gene targets. Then the Search Tool for the Retrieval of Interacting genes/proteins database (STRING) platform was used to build a protein–protein interaction (PPI) network to analyze the potential protein functional modules. Analysis of Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) was performed through the Metascape platform to predict their biological processes and decipher the mechanism of action. The drug component–target–action pathway network was constructed through the Cytoscape 3.8.2 software. Furthermore, the AutoDock Vina software was used to perform molecular docking of core components and key targets, validating binding affinity between potential core components and key targets. Twenty-two *Hippophae rhamnoide* candidate compounds and 208 potential targets for Sjögren's syndrome were acquired. The network analysis showed that the core active ingredients of *Hippophae rhamnoides* in regulating Sjögren's syndrome were quercetin, kaempferol, and beta-sitosterol (β-sitosterol). Core targets included albumin (*ALB*), epidermal growth factor receptor (*EGFR*), Caspase-3 (*CASP3*), peroxisome proliferator-activated receptor gamma (*PPAR*-gamma or *PPARG*), estrogen receptor (ER) *ESR1*, heat shock protein HSP 90-alpha, EC 3.6.4.10 (*HSP90AA1*), plasminogen, EC 3.4.21.7 (*PLG*), *MAPK14*, *MAPK8*, and *MAPK1.* The KEGG analyses demonstrated that *Hippophae rhamnoides* could exert their functioning against Sjögren's syndrome by reacting with the lipid and atherosclerosis signaling pathway and tumor necrosis factor (TNF) signaling pathway. Further, molecular docking analysis suggested that 10 compounds of *Hippophae rhamnoides* could be effective to treat Sjögren's syndrome by matching five core genes to docking pockets. This study indicated that *Hippophae rhamnoides*' functioning effects on Sjögren's syndrome could be attributed to the regulation of a network comprising multi-targets, multi-compounds, and multi-pathways.

Keywords: Hippophae rhamnoides; Sjögren's syndrome; network pharmacology; molecular docking

Introduction

Sjögren's syndrome (SS) is a chronic autoimmune disease characterized by dysfunction and destruction of salivary and lacrimal glands associated with a wide range of systemic manifestations (Bombardieri *et al.*, 2020). Males are 10 times more affected by this disease, and the reported mean age of onset is between 50 and 60 years. Various glandular manifestations are also observed in 30–50% of patients. The prevalence of primary Sjögren's syndrome is inconsistent at around 1:1000–1:100 (Qin *et al.*, 2015). In spite of all the efforts made, its pathogenesis remains poorly understood, and no well-acknowledged therapy that halts the progression of Sjögren's syndrome has been available (Vivino *et al.*, 2016). Therefore, there is an urgent need for research to develop novel pharmacological interventions.

Traditional Chinese medicine (TCM) contains various active ingredients and carries complex mechanisms of action to treat and prevent diseases. In the Chinese Pharmacopoeia 2020 edition, *Hippophae rhamnoides* has been described as a dried fruit of Hippophae rhamnoides L. that can strengthen the spleen, help digestion, arrest cough, eliminate phlegm, activate blood circulation, and disperse blood stasis. This edible medicinal fruit is of a food and medicine continuum and contains a wide variety of active ingredients, such as flavonoids, tannins, terpenoids, polysaccharides, and vitamins. These pharmacological ingredients exert a wide range of pharmacological activities, including anti-inflammatory, antioxidant, hepato-protective, anti-obesity, anti-cardiovascular disorder properties as well as anti-bacterial potency (Gao-Shuang *et al.*, 2121; Heinrich *et al.*, 2021). Further, an increasing number of studies have reported that *Hippophae rhamnoides* may exert desirable therapeutic effects on Sjögren's syndrome. However, its potential active ingredients and underlying mechanism remain elusive.

Network pharmacology has been considered a new approach to identify the mechanism of herb–ingredient–target multimolecular synergy at the systemic level (Li and Zhang, 2013). Furthermore, the research strategy of network pharmacology embodies the TCM's holistic view of the disease, providing new ideas and methods for relative research. Therefore, this study aimed at deciphering the *Hippophae rhamnoides* targets and potential signaling pathways in the treatment of Sjögren's syndrome by performing network pharmacologic and molecular docking study. The flow chart of the docking study is presented in Figure 1.

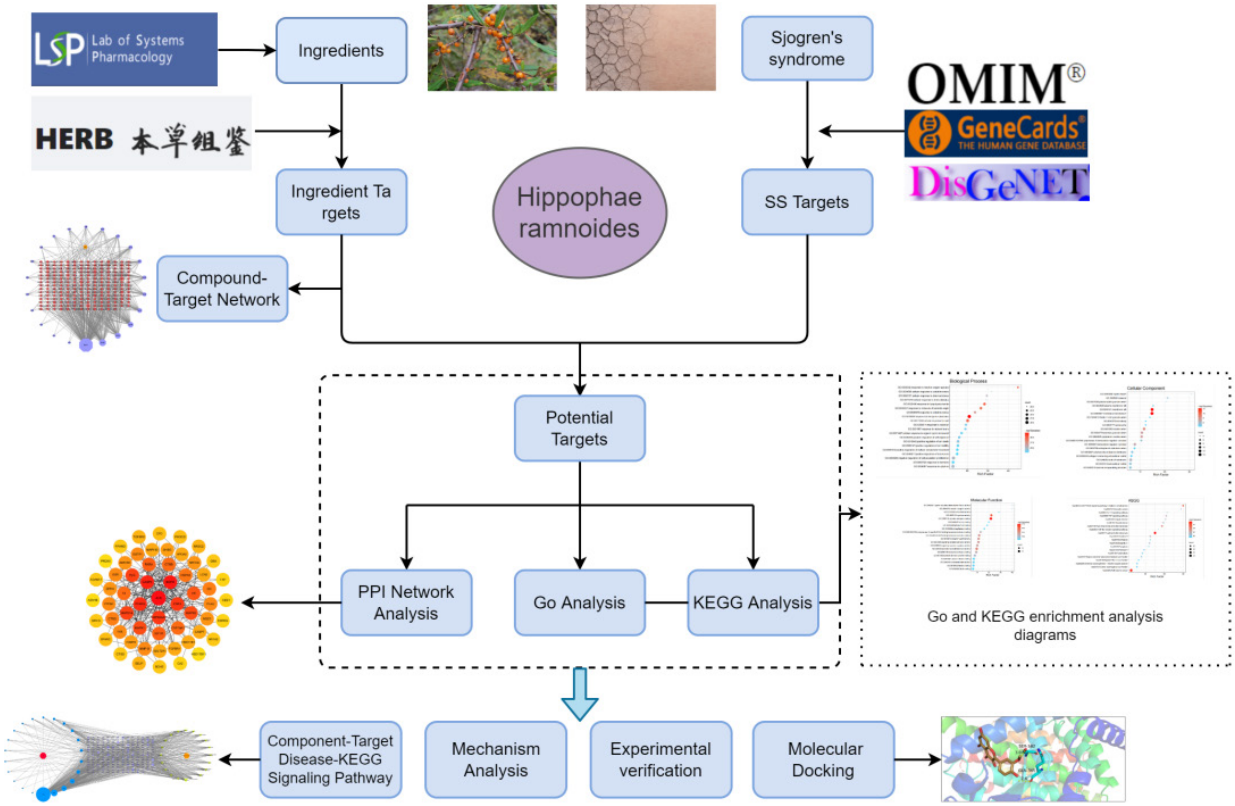

Figure 1. Flowchart of the study design.

Materials and methods

Hippophae rhamnoides' chemical composition search and screening

The Traditional Chinese Medicine Systematic Pharmacology Database and Analysis Platform (TCMSP) (http://tcmspw.com/tcmsp.php) is an online database used to filter the related targets and active ingredients of *Hippophae rhamnoides*. This database comprises 499 Chinese medicinal species and provides data about the absorption, distribution, metabolism, and excretion (ADME) properties of various ingredients (Ru *et al.*, 2014). Oral bioavailability (OB) and drug-like (DL) properties are the foremost pharmacokinetic indicators (Huang *et al.*, 2017). Oral bioavailability (OB) and drug-like (DL) properties are the foremost pharmacokinetic indicators (Huang *et al.*, 2017). In this study, compounds with OB ndicatorinal speciesfrom *Hippophae rhamnoides* were selected as candidate components, and their corresponding target proteins were predicted by searching the HERB (High-throughput Experiment- and Reference-guided database of TCM; http://herb.ac.cn) database (Fang *et al.*, 2021).

Construction of target networks of Hippophae rhamnoides' components

Initially, active ingredients and targets of *Hippophae rhamnoides* were imported into the network visualization software Cytoscape 3.8.2 (Shannon *et al.*, 2003). A network map of active ingredients and targets was constructed, and the core ingredients of *Hippophae rhamnoides* were screened.

Screening of Sjögren's syndrome-related targets

The Online Mendelian Inheritance (OMIM; http://www.omim.org), the Human Gene Database (GeneCards; https://www.genecards.org), and DisGeNET (http://www.disgenet.org/) databases were screened using "Sjögren's Syndrome" as keywords to identify the disease-related targets. After deduplication, a Venn diagram was drawn using active ingredient targets of *Hippophae rhamnoides*. Similarly, a Venn diagram was constructed using the disease targets of Sjögren's syndrome with the microbiology letter online mapping tool (www.bioinformatics.com.cn) to obtain crossover genes as candidate genes.

Protein–protein interaction (PPI) network construction

A PPI network was constructed by importing the processed dataset into the Search Tool for the Retrieval of Interacting Genes/Proteins 11.5 (STRING) online database (https://string-db.org) and the Cytoscape 3.8.2 software. The Cytohubba plug-in of Cytoscape was utilized to screen out key genes.

Functional enrichment analysis

Gene ontology (GO) enrichment analysis was performed on target proteins obtained after network merging in the Metascape database (Zhou *et al.*, 2019), and the R language toolkit was used to visualize biological processes, cellular components, molecular functions, and signaling pathways.

Compound–Target–Pathway (C-T-P) network construction

To further investigate the therapeutic mechanism of *Hippophae rhamnoides* in Sjögren's syndrome, a C-T-P network was created using Cytoscape 3.8.2.

Molecular docking

Molecular docking was used to assess the binding activity of core compounds to key targets. Using core compounds as ligands and core target genes obtained from PPI network topology analysis as receptors, the AutoDock Vina 1.5.7 software developed by Olson's research group in Scripps Research Institute (CA, USA) was applied for molecular docking (Trott and Olson, 2010). The top five targets of the PPI network and the top 10 core compounds of *Hippophae rhamnoides* were selected and downloaded from the RCSB PDB database (http://www.rcsb.org/) (Goodsell *et al.*, 2020), while their chemical structures were downloaded from the TCMSP platform. The candidate compounds were converted to Program Database (PDB) format using AutoDock tools. The protein crystal structures of core target genes were preprocessed by dehydration, hydrogenation, modeling the missing loop regions, calculation of protein ionization, and protonation of protein structures. The compounds and proteins were converted into Protein Data Bank, Partial Charge (Q), & Atom Type (T) (PDBQT) format using AutoDock tool, and the position of each protein or its ligand was determined to figure out the active pocket of the protein. When the binding energy value is zero, the molecular proteins are considered to bind and interact spontaneously. Therefore, the lower the binding energy required for docking, the more stable the molecular conformation, and the best receptor-ligand binding complex is selected for visualization.

Results

Composition prediction of Hippophae rhamnoides

In all, 33 active compounds were screened using the requirements of OB ≥ 30% and DL ≥ 0; 18 and 22 active ingredients were obtained after deleting duplicates by searching the TCMSP database (Table 1). The active ingredients were entered into HERB to acquire drug target names, and 208 gene targets were obtained after removing duplications.

Construction of target networks for Hippophae rhamnoides components

The network comprised 231 nodes (22 nodes for compounds, 208 nodes for targets, and one node for the herb) and 538 edges (Figure 2). Quercetin was connected to 161 targets with the highest degree of network connectivity, followed by kaempferol with 65 targets and β-sitosterol with 48 targets. The properties of this network were suitable for presenting complex compounds with multiple targets and compound–target interactions. The OBs of the three above-mentioned compounds were 46.43%, 41.88%, and 36.91%, respectively, suggesting that Quercetin, kaempferol, and β-sitosterol might be the potential key active compounds. Detailed information on the complex target network is provided in Supplementary Table S1.

Collection of Sjögren's syndrome-related targets

A total of 2,185 Sjögren's syndrome targets were integrated from multiple databases, including 643 targets from OMIM, 1,061 targets from GeneCards, and 481 targets from DisGeNET. After removing duplicates, a final list of 1,876 Sjögren's syndrome-related targets was obtained (Table S2). In this study, 87 cross-targets were identified and collected for further mechanistic studies (Figure 3 and Table S3).

Potential target PPI network analysis

The STRING database was utilized to obtain the PPI network topology by importing 87 potential targets of *Hippophae rhamnoides* for improving Sjögren's syndrome. The first 58 targets of the PPI network are shown in Figure 4. The network had 58 nodes and 269 edges with an average node degree of 9.276 and an average local clustering coefficient of 0.597. The built-in Network Analyzer function in Cytoscape 3.8.2 demonstrated that

Table 1. Potential active compounds of *Hippophae rhamnoides.*

No.	Molecular ID	Molecular name	OB (%)	DL (%)	Drug attribution
SJ1	MOL001004	Pelargonidin	37.99	0.21	*Hippophae rhamnoides*
SJ2	MOL010211	14,15-Dimethyl-alpha-sitosterol	43.14	0.78	*Hippophae rhamnoides*
SJ3	MOL010212	14-Methyl-alpha-sitosterol	43.49	0.78	*Hippophae rhamnoides*
SJ4	MOL010230	ST5330591	48.08	0.84	*Hippophae rhamnoides*
SJ5	MOL010240	Ergosta-7-en-3-beta-ol	38.76	0.83	*Hippophae rhamnoides*
SJ6	MOL010241	Ergostenol	35.41	0.71	*Hippophae rhamnoides*
SJ7	MOL001979	LAN	42.12	0.75	*Hippophae rhamnoides*
SJ8	MOL001420	ZINC04073977	38.00	0.76	*Hippophae rhamnoides*
SJ9	MOL001494	Mandenol	42.00	0.19	*Hippophae rhamnoides*
SJ10	MOL001510	24-Epicampesterol	37.58	0.71	*Hippophae rhamnoides*
SJ11	MOL002268	Rhein	47.07	0.28	*Hippophae rhamnoides*
SJ12	MOL002773	Beta-carotene	37.18	0.58	*Hippophae rhamnoides*
SJ13	MOL000354	Isorhamnetin	49.60	0.31	*Hippophae rhamnoides*
SJ14	MOL000358	Beta-sitosterol	36.91	0.75	*Hippophae rhamnoides*
SJ15	MOL000359	Sitosterol	36.91	0.75	*Hippophae rhamnoides*
SJ16	MOL000422	Kaempferol	41.88	0.24	*Hippophae rhamnoides*
SJ17	MOL000098	Quercetin	46.43	0.28	*Hippophae rhamnoides*
SJ18	MOL000433	Ferulic acid (FA)	68.96	0.71	*Hippophae rhamnoides*
SJ19	MOL000492	(+)-Catechin	54.83	0.24	*Hippophae rhamnoides*
SJ20	MOL006756	Schottenol	37.42	0.75	*Hippophae rhamnoides*
SJ21	MOL000073	Ent-Epicatechin	48.96	0.24	*Hippophae rhamnoides*
SJ22	MOL000953	CLR	37.87	0.68	*Hippophae rhamnoides*

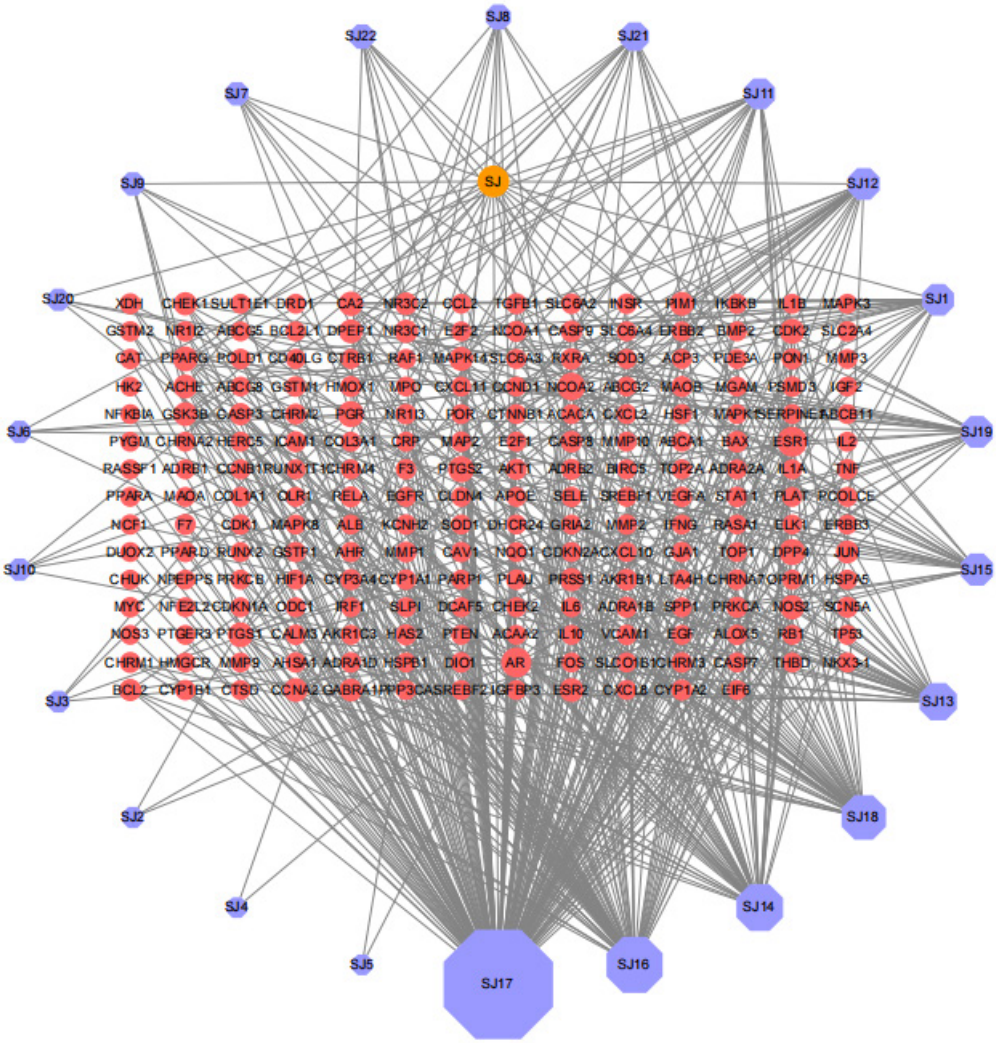

Figure 2. Compound–target network. Yellow circles represent *Hippophae rhamnoides*, purple hexagons represent its active compounds, and red circles represent its related targets (IDs of the components are presented in Table 1).

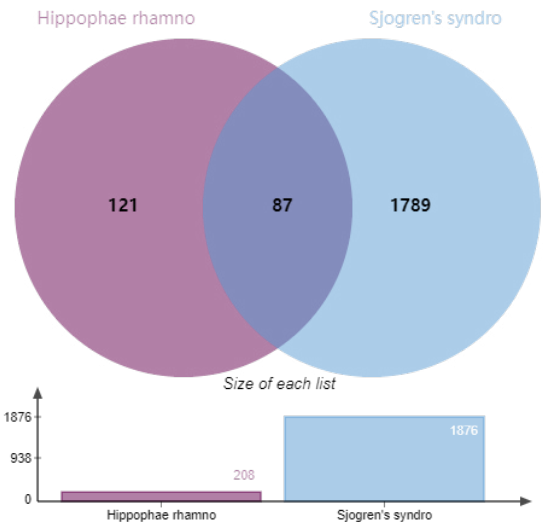

Figure 3. Venn diagram of intersection targets of *Hippophae rhamnoides* and Sjögren's syndrome.

ALB, epidermal growth factor receptor (*EGFR*), epidermal growth factor receptor/Caspase-3 (*CASP3*), peroxisome proliferator-activated receptor gamma (*PPARG*), and estrogen receptor (*ESR1*) were the targets with large values and were of 43°, 28°, 25°, 24°, and 22°, respectively. It suggested that the efficacy mechanism of *Hippophae rhamnoides* in treating Sjögren's syndrome could be closely related to these proteins.

Potential targets of GO and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway-enrichment analysis

The Metascape database and the R language toolkit were adopted to perform the GO and KEGG pathway-enrichment analysis of *Hippophae rhamnoides* in treating Sjögren's syndrome. The biological processes (BP) involved in the GO-enrichment results were mainly responses to inorganic substances and

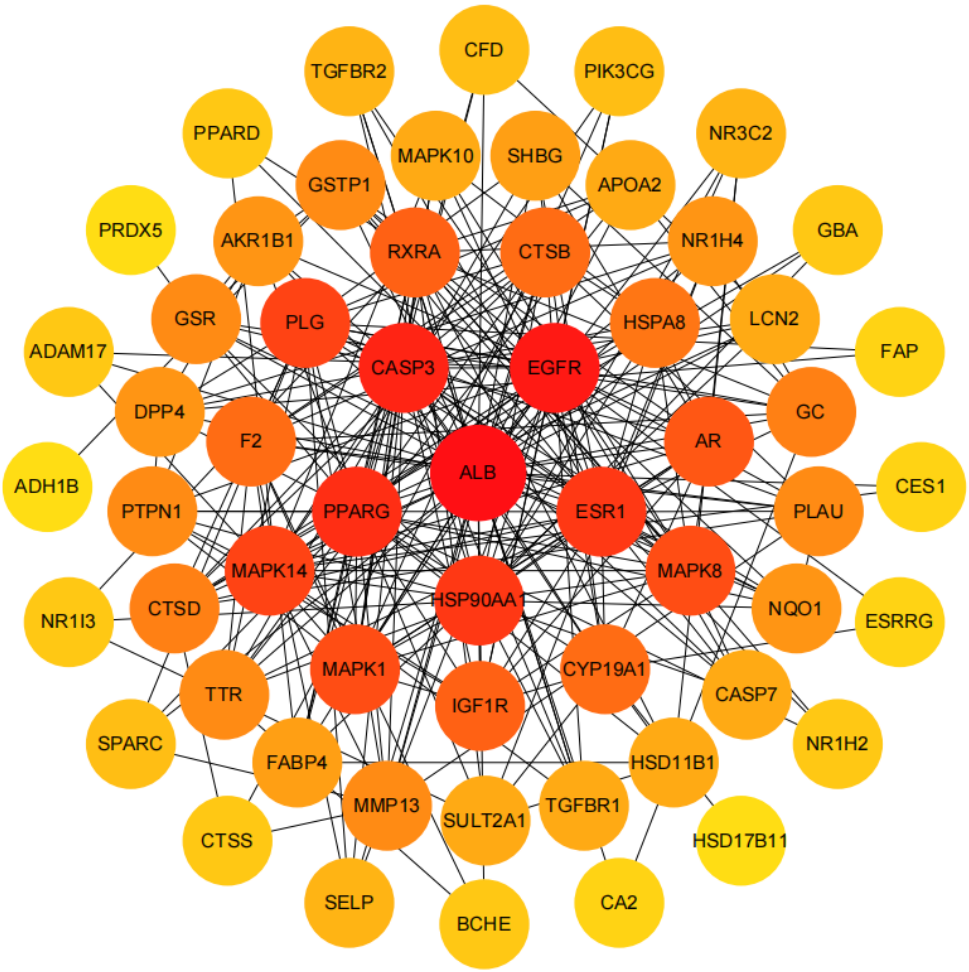

Figure 4. Protein–protein interaction network of *Hippophae rhamnoides* for Sjögren's syndrome.

lipopolysaccharides, negative regulation of cell population proliferation, positive regulation of cell death and cell migration, response to radiation and nutrient levels, and cellular response to organic cyclic compounds (Figure 5A). Relevant cellular components (CC) included were membrane raft, vesicle lumen, transcription regulator complex, side of membrane, extracellular matrix, myelin sheath, and endocytic vesicle (Figure 5B). The molecular functions (MF) involved cytokine receptor binding, protein homodimerization activity, DNA-binding transcription factor binding, protein structure, transcription factor binding, protein domain-specific binding, and oxidoreductase activity (Figure 5C). The KEGG pathway analysis suggested that 171 KEGG pathways were significantly enriched with the potential therapeutic targets of *Hippophae rhamnoides*. Key pathways with high *P*-values and literature of relative diseases were extracted, and the 14 pathways closely associated with Sjögren's syndrome were displayed, with lipid and atherosclerosis, and tumor necrosis factor (TNF) signaling pathway as the top two pathways (Figure 5D).

The component–target–pathway network diagram

The network analysis revealed that the top five targets in the highest degree were transcription factor p65 (*RELA*), *AKT1*, *CASP8*, *CASP3*, and transcription factor Jun (*JUN*), and the top five active ingredients in the highest degree were quercetin, kaempferol, β-sitosterol, folic acid, and isorhamnetin (Figure 6). It was indicated that these were the important components and targets of *Hippophae rhamnoides* for its potential therapeutic effect on Sjögren's syndrome.

Molecular docking

The top 10 active compounds obtained from the analysis of component target network were docked with the five potential core targets, *ALB*, *EGFR*, *CASP3*, *PPARG*, and *ESR1*, obtained from the PPT network analysis. Detailed information on compounds and targets is demonstrated in Table 2 and Figure 7. Binding

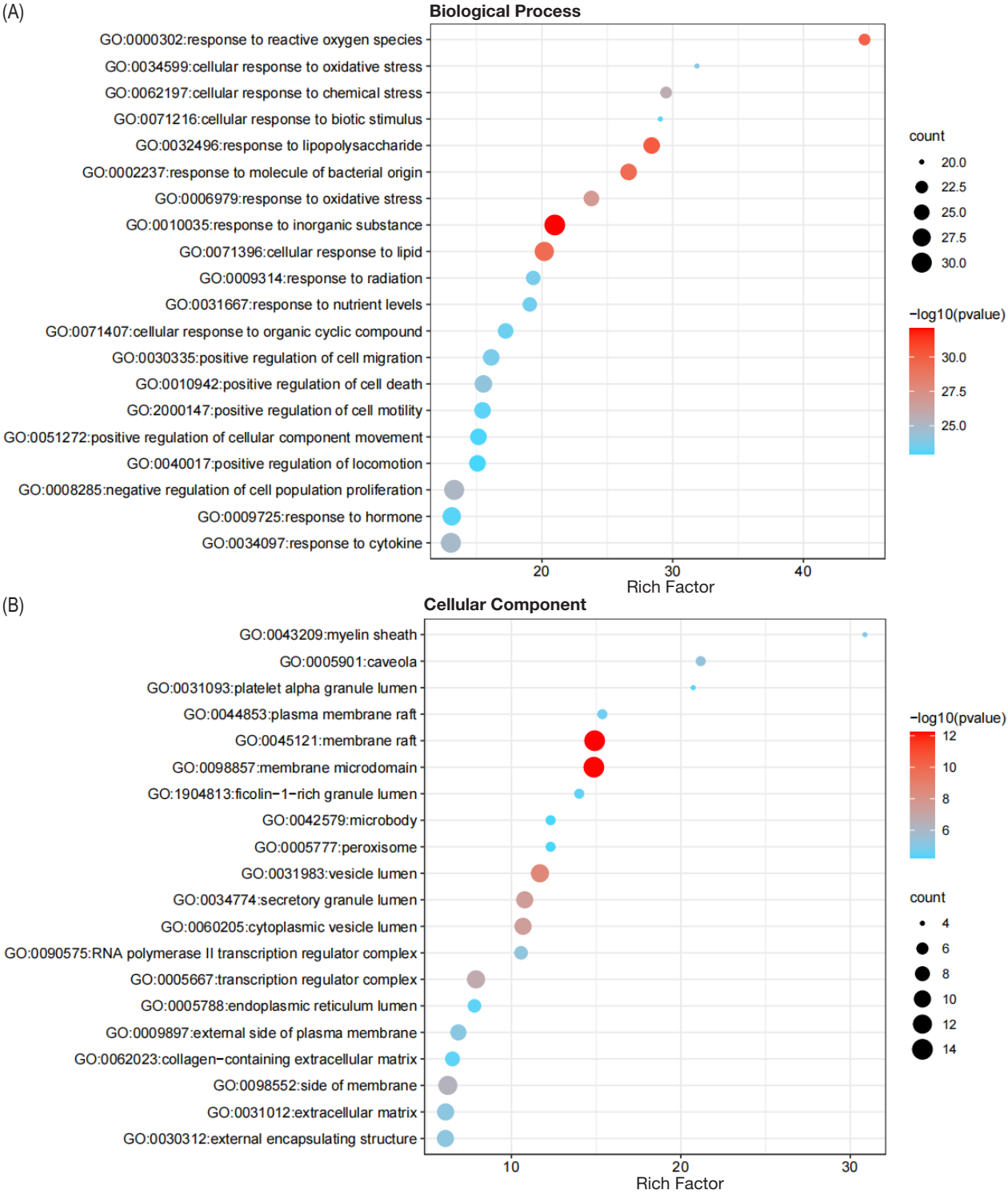

Figure 5. Gene ontology analysis for (A) BP, (B) CC, and (C) MF and pathway enrichment. (D) KEGG analysis of *Hippophae rhamnoides*–Sjögren's syndrome overlapping target genes.

energies are presented in Table 3. When the binding activity was less than 0, the ligand molecule could spontaneously bind to the receptor protein. The ligand molecule had the desired binding affinity if the binding energy was less than −5.0 kJ-mol^{-1} (Yang *et al.*, 2021). It was observed that all compound–target pairs had zero binding energy, suggesting that each core compound had good binding affinities for the first five targets. Docking pattern analysis was also performed for strong docking binding activity, as shown in Figure 8. The docking predictions might provide an initial basis for further drug target studies.

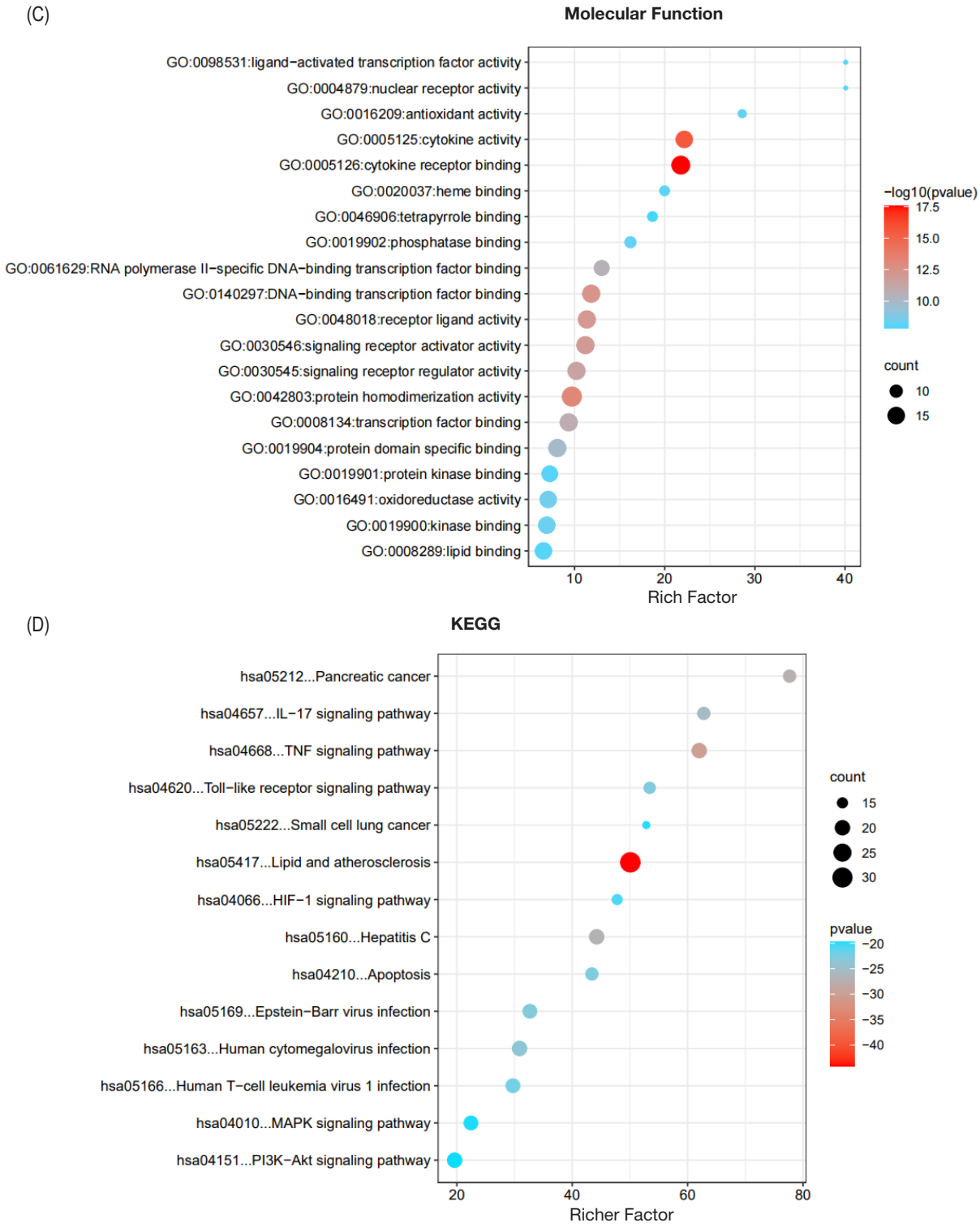

Figure 5. (Continued)

Discussion

Owing to complexity, heterogeneity, and poorly defined active parameters of Sjögren's syndrome, only a few treatment options are available, although it is one of the most common collagen diseases. TCM has demonstrated a desirable therapeutical potential for Sjögren's syndrome, and the edible medicinal *Hippophae rhamnoides* has a variety of active ingredients with substantial anti-inflammatory, antioxidant, and immunity-enhancing properties. However, the composition of TCM is complicated, and its active ingredients are unclear in

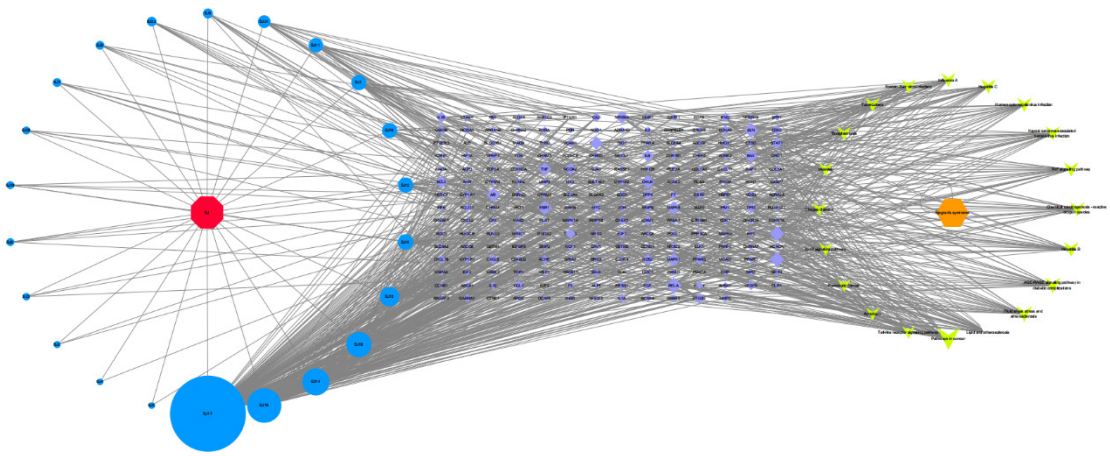

Figure 6. Component–target–pathway network. Blue circles represent active ingredients of *Hippophae rhamnoides*; green circles represent signaling pathways of Sjögren's syndrome; and purple circles represent the targets.

Table 2. Core active compounds of *Hippophae rhamnoides*.

Molecule ID	Molecule name	Degree	Source
MOL000098	Quercetin	162	SJ17
MOL000422	Kaempferol	66	SJ16
MOL000358	Beta_sitosterol	49	SJ14
MOL000433	Ferulic acid (FA)	43	SJ18
MOL000354	Isorhamnetin	32	SJ13
MOL000359	Sitosterol	22	SJ15
MOL000073	Ent_Epicatechin	22	SJ21
MOL002773	Beta_carotene	22	SJ12
MOL001004	Pelargonidin	20	SJ1
MOL002268	Rhein	16	SJ11

pharmacology and clinical practice, as specific target genes or proteins for drug action have not been identified completely. Network pharmacology combines system network analysis and pharmacology and may facilitate the systematic molecular study of effective components, targets, and pathways of herbs.

In the present study, the TCM active component–target network analysis revealed that quercetin, kaempferol, β-sitosterol, FA, and isorhamnetin could act on multiple targets in the network, indicating that these components of *Hippophae rhamnoides* may exert therapeutic effects on Sjögren's syndrome. Quercetin has been reported to exert significant improving effects on the loss of saliva flow, salivary gland damage, and inflammatory response in non-obese diabetic (NOD)/Ltj mice. Furthermore, it blocked the increased expression of obesity receptors and its downstream Janus kinase 2/signal transducer and activator of transcription 3 signaling in the salivary glands (Chang *et al.*, 2022). Kaempferol inhibits the nuclear factor kappa B (NF-κB) binding activity of DNA and myeloid differentiation factor 88 and suppresses the release of interleukin 6 (IL-6), IL-1β, IL-18, and TNF-α, enhancing messenger RNA (mRNA) and protein expression of nuclear factor erythroid 2-related factor 2 (Nrf2)-regulated genes, and restraining the toll-like receptor 4 (Nam *et al.*, 2017; Saw *et al.*, 2014; Tang *et al.*, 2015; Zhang *et al.*, 2017). β-sitosterol may treat Sjogren's syndrome with an improved prognosis by enhancing the expression of cholinergic receptor muscarinic 3 (*CHRM3*) and stimulating salivary secretion (Wu *et al.*, 2022). Isorhamnetin can significantly improve innate immunity (Wang *et al.*, 2012) and effectively down-regulate TNF-α, IL-6, and IL-1β and up-regulate IL-10 to reduce inflammatory responses (Zhang *et al.*, 2017).

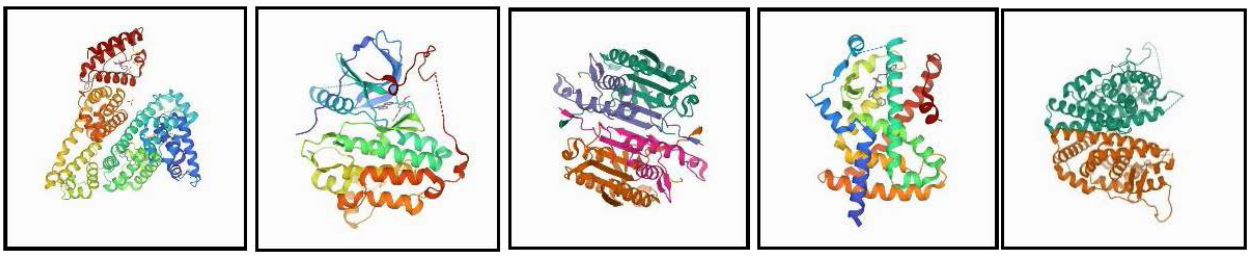

Figure 7. Three-dimensional (3D) structural diagram of the top five target proteins.

Table 3. The binding energy values of core compounds of *Hippophae rhamnoides* and core targets.

Molecule name	*ALB* (*6r7s*) binding affinity (KJ-mol^{-1})	EGFR (*6lud*) binding affinity (KJ-mol^{-1})	CASP3 (*7rnd*) binding affinity (KJ-mol^{-1})	*PPARG* (*7jqg*) binding affinity (KJ-mol^{-1})	ESR1 (*6vgh*) binding affinity (KJ-mol^{-1})
Kaempferol	–8.2	–6.9	–7.4	–7.2	–7.1
Ferulic acid (FA)	–8.4	–6.7	–8.0	–7.6	–7.7
Isorhamnetin	–8.2	–5.6	–7.6	–7.8	–6.8
Pelargonidin	–7.5	–5.9	–7.1	–7.2	–7.3

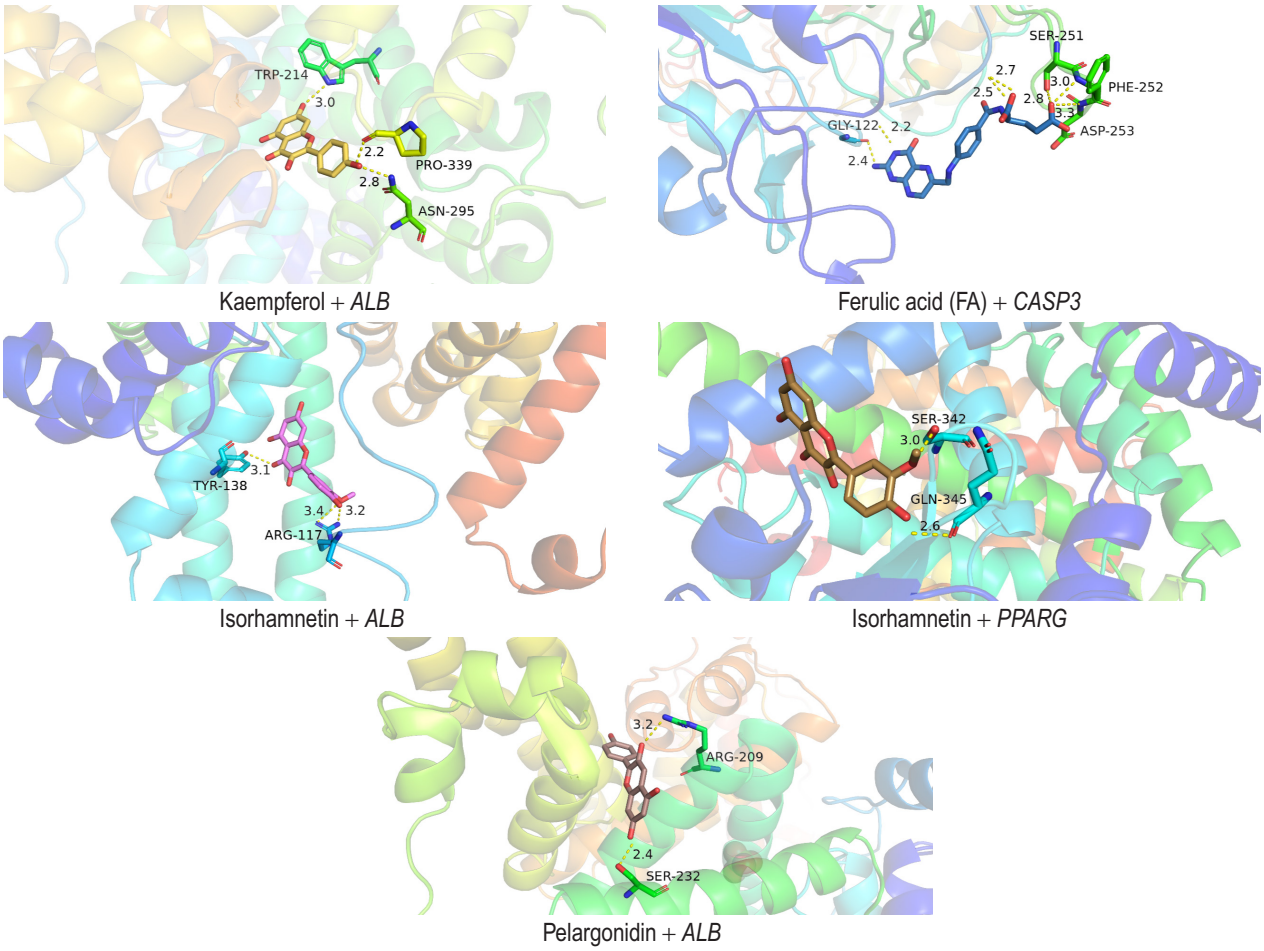

Figure 8. Molecular docking patterns of active components with *ALB, CASP3*, and *PPARG.*

In the PPI network, 58 targets of *Hippophae rhamnoides* were identified to act in Sjögren's syndrome, and the top 10 targets based on node degree were *ALB*, *EGFR*, *CASP3*, *PPARG*, *ESR1*, *HSP90AA1*, *PLG*, *MAPK14*, *MAPK8*, and *MAPK1.* These core proteins have potent therapeutic effects in Sjögren's syndrome. Among them, increasing evidence has suggested that the *EGFR* pathway could have a significant impact on the inflammatory/immune reactions of epithelial cells. The *EGFR*-extracellular-signal-regulated kinase pathway plays a role in the pro-inflammatory responses mounted by Sjögren's syndrome salivary gland epithelial cells (Sisto *et al.*, 2015). While *CASP3* is closely linked with autoimmunity (Lin *et al.*, 2011), various studies have suggested that *PPAR*-γ agonists might exert anti-inflammatory activities by inhibiting production of cytokines in a variety of mouse models in chronic inflammatory and autoimmune diseases. Beauregard and Brandt (2003) found that *PPAR*-α and *PPAR*-γ can inhibit IL-1β-induced production of nitric oxide (NO) in cultured lacrimal gland acinar cells, suggesting *PPAR* agonists as useful therapeutic agents for preventing dry eye disease because of NO-mediated lacrimal gland damage. Results of the above research highlight that *Hippophae rhamnoides* may exert anti-Sjögren's syndrome activity by modulating such core targets as *EGFR, CASP3,* and *PPARG.*

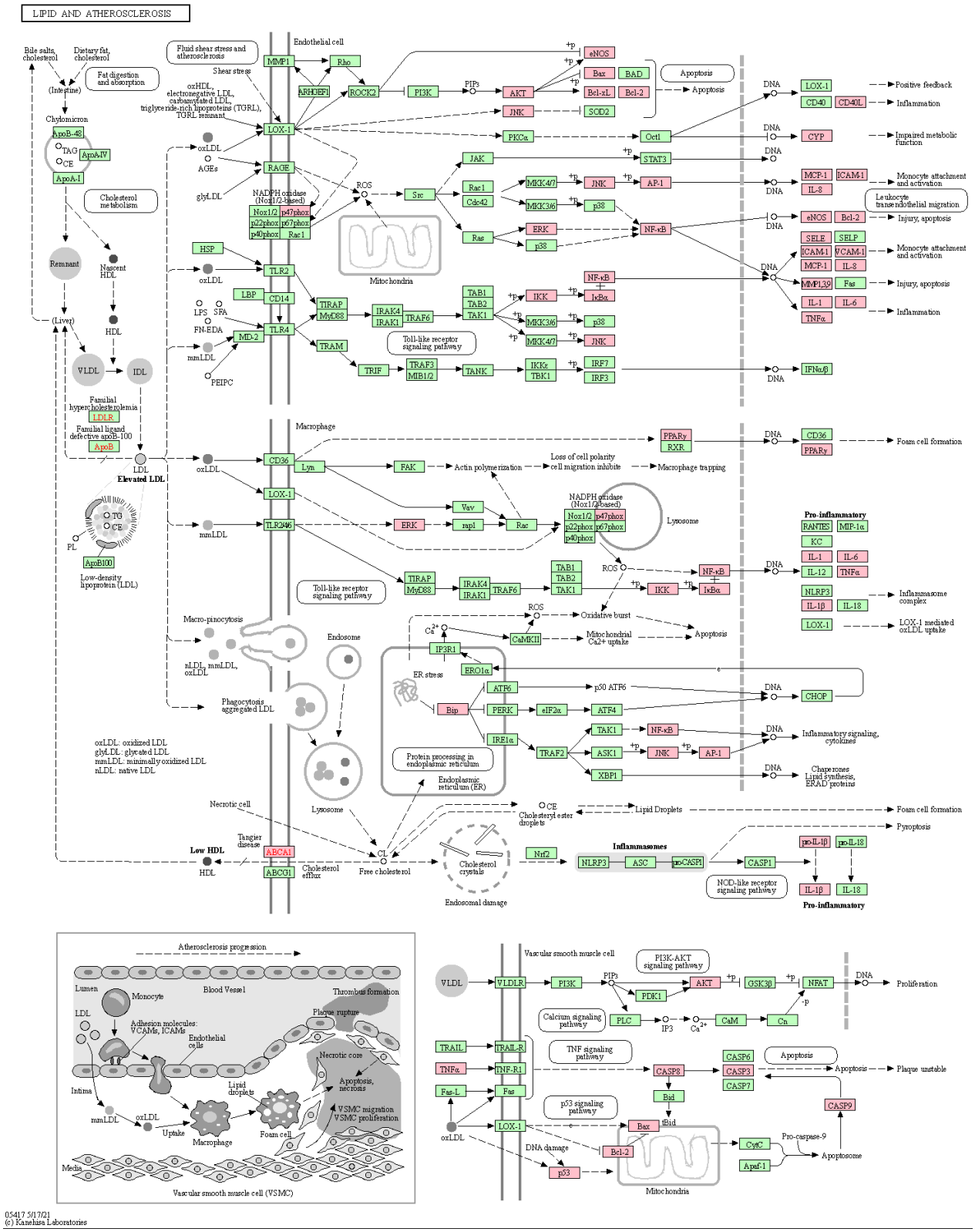

Figure 9. Potential target proteins of *Hippophae rhamnoides* regulating Sjögren's syndrome on the predicted pathways (pink nodes are potential target proteins of *Hippophae rhamnoides*, and green nodes are relevant targets in the pathway).

Gene ontology and KEGG-enrichment analysis of the 87 potential targets were performed to predict the mechanism underlying the therapeutic effect of *Hippophae rhamnoides* in Sjögren's syndrome. The results showed that the 20 most significantly enriched BP terms were mainly responses to inorganic substances, lipopolysaccharides, and reactive oxygen species. Numerous studies have proposed that the onset and development of Sjögren's syndrome are related to the activated immune system and the epithelial cells, targets, and players of autoimmune responses (Bombardieri *et al.*, 2020). The enriched MFs included cytokine receptor binding, transcription factor, mitogen-activated protein kinase (MAPK), and integrin; heme-binding cytokine receptor binding, DNA-binding transcription factor binding, endo-peptidase activity, protein homo-dimerization activity, and protein structure. Further, the enriched CCs covered membrane raft, vesicle lumen, transcription regulator complex, side of membrane, extracellular matrix, and myelin sheath. These findings also illustrate the complexity of the pathological mechanism of Sjögren's syndrome. To decode the potential mechanism of *Hippophae rhamnoides* in treating Sjögren's syndrome, KEGG analysis of the 87 potential targets of *Hippophae rhamnoides* was conducted. The pathways related to Sjögren's syndrome involved lipid and atherosclerosis, TNF-signaling pathway, and pancreatic cancer. Atherosclerosis is a major cause of cardiovascular disease involving autoimmune reactions and inflammation in its pathogenesis. During the early onset of atherosclerosis, inflammatory cells (monocytes, macrophages, dendritic cells, and T- and B-cells), and cytokines can be identified in the lesion area, and these cells may provoke cell-mediated immune reactions that (i) modulate the development of atherosclerosis and may (ii) predetermine its progression (Frostegård, 2002; Jonasson *et al.*, 1997). TNF-α is mainly activated by macrophages and lymphocytes, and generated in salivary epithelial cells (Sisto *et al.*, 2009). Several studies indicated that TNF-α plays an important role in the pathogenesis of Sjögren's syndrome, as it is up-regulated in both plasma and salivary glands of patients with Sjögren's syndrome as well as major salivary glands of animal models of Sjögren's syndrome (Humphreys-Beher *et al.*, 1994, 1998). These studies also propose that *Hippophae rhamnoides* can act on Sjögren's syndrome at multiple levels through signaling pathway networks that are mediated by direct or indirect targets (Figure 9).

According to the herb-active ingredient-target network and PPI network results, we selected five active ingredients and five key target genes for docking. The docking results showed that these compounds could bind stably to the active pocket of key protein, suggesting that *Hippophae rhamnoides* may treat Sjögren's syndrome by inhibiting *ALB, EGFR, CASP3, PPARG,* and *ESR1* (Figure 9).

Conclusion

This study deciphered the potential mechanism of *Hippophae rhamnoides* in treating Sjögren's syndrome based on network pharmacology and molecular docking approach. Compounds such as quercetin, kaempferol, and β-sitosterol may play a critical role in treating Sjögren's syndrome by affecting *ALB, EGFR, CASP3, PPARG,* and *ESR1*. Furthermore, the molecular docking study also demonstrated that the active components of *Hippophae rhamnoides* might dock well with *ALB, EGFR, CASP3, PPARG,* and *ESR1*. However, owing to the limitations of network pharmacology, further experimental investigations and verifications are warranted.

Author Contributions

TEZ, YHC, and LUX: conceptualization. ZL,YHC, and HPX: methodology and visualization. WYH, LL, XJ, and QZY: software. YHC , XLY and ZL: writing-original draft. YHC and TEZ: writing-review and editing. TEZ and QZY: supervision and project administration. All authors have read and agreed to the published version of the manuscript.

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Supplementary

Table S1. Chemical composition

Mol ID	Molecule Name	MW	AlogP	Hdon	Hacc	OB(%)	DL	FASA-	HL
MOL001004	Pelargonidin	271.26	1.933	4	5	37.99	0.21	94.05999756	0.479802
MOL010211	14,15-dimethyl-alpha-sitosterol	454.86	8.611	1	1	43.14	0.78	20.22999954	5.899813
MOL010212	14-methyl-alpha-sitosterol	440.83	8.36	1	1	43.49	0.78	20.22999954	6.040801
MOL010227	Canthaxanthine	564.92	9.716	0	2	41.59	0.56	34.13999939	3.866396
MOL010228	carotenoid	568.96	9.465	2	2	40.76	0.55	40.45999908	4.912507
MOL010230	ST5330591	490.84	9.419	0	2	48.08	0.84	26.29999924	8.119666
MOL010232	cislycopene	536.96	12.761	0	0	45.51	0.54	0	6.574152
MOL010234	delta-Carotene	536.96	12.185	0	0	31.80	0.55	0	2.616793
MOL010240	ergosta-7-en-3-beta-ol	472.96	9.76	0	1	38.76	0.83	9.229999542	3.496122
MOL010241	ergostenol	400.76	7.822	1	1	35.41	0.71	20.22999954	4.490605
MOL010247	(2R,6S,7aR)-2-[(1E,3E,5E,7E,9E,11E,13E,15E)-16-[(1R,4R)-4-hydroxy-2,6,6-trimethyl-1-cyclohex-2-enyl]-1,5,10,14-tetramethyl hexadeca-1,3,5,7,9,11,13,15-octaenyl]-2,4,4,7a-tetramethyl-6,7-dihydro-5H-benzofuran-6-ol	598.99	8.447	2	3	57.88	0.53	49.68999863	16.66617
MOL010248	gamma-carotene	536.96	12.38	0	0	30.98	0.55	0	3.972945
MOL001979	LAN	426.8	8.12	1	1	42.12	0.75	20.22999954	5.835494
MOL010267	LYC	536.96	12.761	0	0	32.57	0.51	0	3.423468
MOL010283	ZINC03831331	450.77	10.251	0	2	47.60	0.65	34.13999939	28.4009
MOL001420	ZINC04073977	412.77	7.758	0	1	38.00	0.76	17.06999969	5.450883
MOL001494	Mandenol	308.56	6.991	0	2	42.00	0.19	26.29999924	5.385969
MOL001510	24-epicampesterol	400.76	7.628	1	1	37.58	0.71	20.22999954	4.496849
MOL002268		284.23	1.878	3	6	47.07	0.28	111.9000015	32.11726
MOL002588	(3S,5R,10S,13R,14R,17R)-17-[(1R)-1,5-dimethyl-4-methylenehexyl]-4,4,10,13,14-pentamethyl-2,3,5,6,7,11,12,15,16,17-decahydro-1H-cyclopenta[a]phenanthren-3-ol	440.83	8.426	1	1	42.37	0.77	20.22999954	5.408929
MOL002773	beta-carotene	536.96	11.999	0	0	37.18	0.58	0	4.357938
MOL000354	isorhamnetin	316.28	1.755	4	7	49.60	0.31	120.3600006	14.33926
MOL000358	beta-sitosterol	414.79	8.084	1	1	36.91	0.75	20.22999954	5.355491
MOL000359	sitosterol	414.79	8.084	1	1	36.91	0.75	20.22999954	5.371091
MOL000422	kaempferol	286.25	1.771	4	6	41.88	0.24	111.1299973	14.74337
MOL000433	FA	441.45	0.007	7	13	68.96	0.71	213.2799988	24.81124
MOL000449	Stigmasterol	412.77	7.64	1	1	43.83	0.76	20.22999954	5.574595
MOL000492	(+)-catechin	290.29	1.92	5	6	54.83	0.24	110.3799973	0.609577
MOL005100	5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)chroman-4-one	302.3	2.281	3	6	47.74	0.27	96.22000122	16.51482
MOL006756	Schottenol	414.79	8.084	1	1	37.42	0.75	20.22999954	5.632795
MOL000073	ent-Epicatechin	290.29	1.92	5	6	48.96	0.24	110.3799973	0.626389
MOL000953	CLR	386.73	7.376	1	1	37.87	0.68	20.22999954	4.518834
MOL000098	Quercetin	302.25	1.504	5	7	46.43	0.28	131.3600006	14.4005

(Continues)

Table S1. (Continued)
Drug target

MOLID	ID	Genename
MOL001004	SJ1	ACHE
MOL001004	SJ1	AR
MOL001004	SJ1	CA2
MOL001004	SJ1	NR3C1
MOL001004	SJ1	NR3C2
MOL001004	SJ1	NOS2
MOL001004	SJ1	PGR
MOL001004	SJ1	PTGS1
MOL001004	SJ1	PTGS2
MOL001004	SJ1	RXRA
MOL001004	SJ1	NCOA1
MOL001004	SJ1	NCOA2
MOL001004	SJ1	MAPK14
MOL001004	SJ1	CHEK1
MOL001004	SJ1	CDK2
MOL001004	SJ1	PPARG
MOL001004	SJ1	DPP4
MOL001004	SJ1	ESR1
MOL001004	SJ1	CCNA2
MOL001004	SJ1	ESR2
MOL001004	SJ1	PIM1
MOL010211	SJ2	ESR1
MOL010211	SJ2	AR
MOL010212	SJ3	PGR
MOL010212	SJ3	ESR1
MOL010212	SJ3	AR
MOL010230	SJ4	ESR1
MOL010240	SJ5	AR
MOL010241	SJ6	PGR
MOL010241	SJ6	NCOA2
MOL010241	SJ6	AR
MOL010241	SJ6	ESR1
MOL001979	SJ7	NR3C2
MOL001979	SJ7	PGR
MOL001979	SJ7	NCOA2
MOL001979	SJ7	NR3C1
MOL001979	SJ7	AR
MOL001979	SJ7	ESR1
MOL001420	SJ8	PGR
MOL001420	SJ8	PTGS2
MOL001420	SJ8	NR3C1
MOL001420	SJ8	PRSS1
MOL001420	SJ8	DPP4
MOL001420	SJ8	ESR1
MOL001420	SJ8	AR
MOL001420	SJ8	GABRA1

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL001420	SJ8	ACHE
MOL001494	SJ9	PTGS1
MOL001494	SJ9	PTGS2
MOL001494	SJ9	ACHE
MOL001494	SJ9	PPARG
MOL001494	SJ9	NCOA2
MOL001494	SJ9	DPP4
MOL001510	SJ10	PGR
MOL001510	SJ10	AR
MOL001510	SJ10	ESR1
MOL001510	SJ10	NCOA2
MOL002268	SJ11	AKR1B1
MOL002268	SJ11	JUN
MOL002268	SJ11	PTGS1
MOL002268	SJ11	PTGS2
MOL002268	SJ11	PPARG
MOL002268	SJ11	NCOA2
MOL002268	SJ11	CHEK1
MOL002268	SJ11	AR
MOL002268	SJ11	DPP4
MOL002268	SJ11	ESR2
MOL002268	SJ11	ESR1
MOL002268	SJ11	DPEP1
MOL002268	SJ11	CDK2
MOL002268	SJ11	MAPK14
MOL002268	SJ11	NOS2
MOL002268	SJ11	CCNA2
MOL002268	SJ11	GSK3B
MOL002268	SJ11	CA2
MOL002268	SJ11	PIM1
MOL002773	SJ12	AKT1
MOL002773	SJ12	ALB
MOL002773	SJ12	BCL2
MOL002773	SJ12	CASP3
MOL002773	SJ12	CASP7
MOL002773	SJ12	CASP8
MOL002773	SJ12	CASP9
MOL002773	SJ12	CAV1
MOL002773	SJ12	CTNNB1
MOL002773	SJ12	CYP1A2
MOL002773	SJ12	CYP3A4
MOL002773	SJ12	F3
MOL002773	SJ12	GJA1
MOL002773	SJ12	HMOX1
MOL002773	SJ12	JUN
MOL002773	SJ12	MMP1
MOL002773	SJ12	MMP2

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL002773	SJ12	MMP10
MOL002773	SJ12	MYC
MOL002773	SJ12	PTGS2
MOL002773	SJ12	VEGFA
MOL000354	SJ13	NOS2
MOL000354	SJ13	OLR1
MOL000354	SJ13	RELA
MOL000354	SJ13	XDH
MOL000354	SJ13	NCF1
MOL000354	SJ13	DPEP1
MOL000354	SJ13	MAPK14
MOL000354	SJ13	PTGS2
MOL000354	SJ13	PIM1
MOL000354	SJ13	PPARD
MOL000354	SJ13	F7
MOL000354	SJ13	PRSS1
MOL000354	SJ13	ESR1
MOL000354	SJ13	ESR2
MOL000354	SJ13	MAOB
MOL000354	SJ13	GABRA1
MOL000354	SJ13	CA2
MOL000354	SJ13	GSK3B
MOL000354	SJ13	NCOA1
MOL000354	SJ13	CCNA2
MOL000354	SJ13	CHEK1
MOL000354	SJ13	PYGM
MOL000354	SJ13	AKR1B1
MOL000354	SJ13	AR
MOL000354	SJ13	PTGS1
MOL000354	SJ13	CDK2
MOL000354	SJ13	PPARG
MOL000354	SJ13	GRIA2
MOL000354	SJ13	NCOA2
MOL000354	SJ13	DPP4
MOL000354	SJ13	ACHE
MOL000358	SJ14	BAX
MOL000358	SJ14	BCL2
MOL000358	SJ14	CASP3
MOL000358	SJ14	CASP8
MOL000358	SJ14	CASP9
MOL000358	SJ14	JUN
MOL000358	SJ14	MAP2
MOL000358	SJ14	PON1
MOL000358	SJ14	PRKCA
MOL000358	SJ14	TGFB1
MOL000358	SJ14	ACHE
MOL000358	SJ14	CHRM4

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000358	SJ14	DRD1
MOL000358	SJ14	NR3C1
MOL000358	SJ14	CHRM1
MOL000358	SJ14	NCOA2
MOL000358	SJ14	DPP4
MOL000358	SJ14	CHRNA2
MOL000358	SJ14	CHRNA7
MOL000358	SJ14	GSK3B
MOL000358	SJ14	CCNA2
MOL000358	SJ14	SCN5A
MOL000358	SJ14	CHRM3
MOL000358	SJ14	PDE3A
MOL000358	SJ14	PGR
MOL000358	SJ14	CDK2
MOL000358	SJ14	CA2
MOL000358	SJ14	ESR1
MOL000358	SJ14	PPARG
MOL000358	SJ14	PRSS1
MOL000358	SJ14	ADRB2
MOL000358	SJ14	AR
MOL000358	SJ14	NOS2
MOL000358	SJ14	PTGS1
MOL000358	SJ14	PIM1
MOL000358	SJ14	DPEP1
MOL000358	SJ14	CHEK1
MOL000358	SJ14	GABRA1
MOL000358	SJ14	SLC6A4
MOL000358	SJ14	PTGS2
MOL000358	SJ14	NR3C2
MOL000358	SJ14	OPRM1
MOL000358	SJ14	MAPK14
MOL000358	SJ14	ADRA1B
MOL000358	SJ14	KCNH2
MOL000358	SJ14	CHRM2
MOL000358	SJ14	ADRA1D
MOL000358	SJ14	ESR2
MOL000359	SJ15	APOE
MOL000359	SJ15	BAX
MOL000359	SJ15	BCL2
MOL000359	SJ15	CASP3
MOL000359	SJ15	CASP8
MOL000359	SJ15	CASP9
MOL000359	SJ15	DHCR24
MOL000359	SJ15	ICAM1
MOL000359	SJ15	JUN
MOL000359	SJ15	MAP2
MOL000359	SJ15	NR3C2

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000359	SJ15	PGR
MOL000359	SJ15	PON1
MOL000359	SJ15	PRKCA
MOL000359	SJ15	SREBF1
MOL000359	SJ15	SREBF2
MOL000359	SJ15	TGFB1
MOL000359	SJ15	ABCB11
MOL000359	SJ15	NR3C1
MOL000359	SJ15	ESR1
MOL000359	SJ15	NCOA2
MOL000359	SJ15	AR
MOL000422	SJ16	ACHE
MOL000422	SJ16	AHR
MOL000422	SJ16	AKT1
MOL000422	SJ16	ALOX5
MOL000422	SJ16	AR
MOL000422	SJ16	BAX
MOL000422	SJ16	BCL2
MOL000422	SJ16	CALM3
MOL000422	SJ16	CASP3
MOL000422	SJ16	CHRM1
MOL000422	SJ16	CYP1A1
MOL000422	SJ16	CYP1A2
MOL000422	SJ16	CYP1B1
MOL000422	SJ16	CYP3A4
MOL000422	SJ16	DIO1
MOL000422	SJ16	ESR1
MOL000422	SJ16	ESR2
MOL000422	SJ16	GSTM1
MOL000422	SJ16	GSTM2
MOL000422	SJ16	GSTP1
MOL000422	SJ16	HAS2
MOL000422	SJ16	HMOX1
MOL000422	SJ16	ICAM1
MOL000422	SJ16	IKBKB
MOL000422	SJ16	INSR
MOL000422	SJ16	JUN
MOL000422	SJ16	MMP1
MOL000422	SJ16	NOS2
MOL000422	SJ16	PGR
MOL000422	SJ16	POLD1
MOL000422	SJ16	PPARG
MOL000422	SJ16	PPP3CA
MOL000422	SJ16	MAPK8
MOL000422	SJ16	PRSS1
MOL000422	SJ16	PSMD3
MOL000422	SJ16	PTGS1

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000422	SJ16	PTGS2
MOL000422	SJ16	RELA
MOL000422	SJ16	SELE
MOL000422	SJ16	SLC2A4
MOL000422	SJ16	SLC6A2
MOL000422	SJ16	SLPI
MOL000422	SJ16	STAT1
MOL000422	SJ16	TNF
MOL000422	SJ16	VCAM1
MOL000422	SJ16	XDH
MOL000422	SJ16	AKR1C3
MOL000422	SJ16	NR1I2
MOL000422	SJ16	NR1I3
MOL000422	SJ16	AHSA1
MOL000422	SJ16	F7
MOL000422	SJ16	GABRA1
MOL000422	SJ16	PIM1
MOL000422	SJ16	MAPK14
MOL000422	SJ16	CDK1
MOL000422	SJ16	NCOA2
MOL000422	SJ16	DPEP1
MOL000422	SJ16	CDK2
MOL000422	SJ16	ADRA1B
MOL000422	SJ16	GSK3B
MOL000422	SJ16	CHRM2
MOL000422	SJ16	CCNA2
MOL000422	SJ16	CA2
MOL000422	SJ16	CHEK1
MOL000422	SJ16	DPP4
MOL000433	SJ18	CDK2
MOL000433	SJ18	GSK3B
MOL000433	SJ18	ABCA1
MOL000433	SJ18	HMGCR
MOL000433	SJ18	SLCO1B1
MOL000433	SJ18	ABCG5
MOL000433	SJ18	ABCG8
MOL000433	SJ18	CHRM1
MOL000433	SJ18	CHRM2
MOL000433	SJ18	AR
MOL000433	SJ18	LTA4H
MOL000433	SJ18	ESR1
MOL000433	SJ18	MAOB
MOL000433	SJ18	PRSS1
MOL000433	SJ18	MAOA
MOL000433	SJ18	CTRB1
MOL000433	SJ18	ADRA1B
MOL000433	SJ18	SCN5A

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000433	SJ18	RXRA
MOL000433	SJ18	CDK2
MOL000433	SJ18	DPEP1
MOL000433	SJ18	SLC6A3
MOL000433	SJ18	ADRA1D
MOL000433	SJ18	PPARG
MOL000433	SJ18	PLAU
MOL000433	SJ18	CHRNA7
MOL000433	SJ18	PGR
MOL000433	SJ18	NR3C2
MOL000433	SJ18	ADRB2
MOL000433	SJ18	ADRB1
MOL000433	SJ18	NCOA2
MOL000433	SJ18	ADRA2A
MOL000433	SJ18	PTGS2
MOL000433	SJ18	NCOA1
MOL000433	SJ18	CHRM3
MOL000433	SJ18	CA2
MOL000433	SJ18	NOS2
MOL000433	SJ18	DPP4
MOL000433	SJ18	PTGS1
MOL000433	SJ18	SLC6A2
MOL000433	SJ18	ACHE
MOL000433	SJ18	NR3C1
MOL000433	SJ18	AKR1B1
MOL000433	SJ18	GABRA1
MOL000492	SJ19	CALM3
MOL000492	SJ19	CAT
MOL000492	SJ19	ESR1
MOL000492	SJ19	HAS2
MOL000492	SJ19	PTGS1
MOL000492	SJ19	PTGS2
MOL000492	SJ19	RXRA
MOL000492	SJ19	CA2
MOL000492	SJ19	DPEP1
MOL000492	SJ19	GSK3B
MOL000492	SJ19	DPP4
MOL000492	SJ19	CHEK1
MOL000492	SJ19	NOS2
MOL000492	SJ19	ESR2
MOL000492	SJ19	PPARG
MOL000492	SJ19	PIM1
MOL000492	SJ19	CCNA2
MOL000492	SJ19	MAPK14
MOL000492	SJ19	NCOA2
MOL000492	SJ19	CDK2
MOL000492	SJ19	AR

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL006756	SJ20	PGR
MOL006756	SJ20	AR
MOL006756	SJ20	NCOA2
MOL006756	SJ20	ESR1
MOL000073	SJ21	ESR1
MOL000073	SJ21	PTGS1
MOL000073	SJ21	PTGS2
MOL000073	SJ21	DPEP1
MOL000073	SJ21	MAPK14
MOL000073	SJ21	PPARG
MOL000073	SJ21	ESR2
MOL000073	SJ21	CCNA2
MOL000073	SJ21	CDK2
MOL000073	SJ21	PIM1
MOL000073	SJ21	DPP4
MOL000073	SJ21	AR
MOL000073	SJ21	CA2
MOL000073	SJ21	NOS2
MOL000073	SJ21	GSK3B
MOL000953	SJ22	NR3C2
MOL000953	SJ22	PGR
MOL000953	SJ22	NCOA2
MOL000953	SJ22	DPP4
MOL000953	SJ22	ESR1
MOL000953	SJ22	AR
MOL000953	SJ22	NR3C1
MOL000953	SJ22	PRSS1
MOL000098	SJ17	ACACA
MOL000098	SJ17	ACHE
MOL000098	SJ17	ACP3
MOL000098	SJ17	PARP1
MOL000098	SJ17	ADRB2
MOL000098	SJ17	AHR
MOL000098	SJ17	AKT1
MOL000098	SJ17	AKR1B1
MOL000098	SJ17	ALOX5
MOL000098	SJ17	BIRC5
MOL000098	SJ17	AR
MOL000098	SJ17	BAX
MOL000098	SJ17	CCND1
MOL000098	SJ17	BCL2
MOL000098	SJ17	BCL2L1
MOL000098	SJ17	BMP2
MOL000098	SJ17	CASP3
MOL000098	SJ17	CASP8
MOL000098	SJ17	CASP9
MOL000098	SJ17	CAT

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000098	SJ17	CAV1
MOL000098	SJ17	RUNX2
MOL000098	SJ17	RUNX1T1
MOL000098	SJ17	CCNB1
MOL000098	SJ17	CD40LG
MOL000098	SJ17	CDKN1A
MOL000098	SJ17	CDKN2A
MOL000098	SJ17	CHUK
MOL000098	SJ17	COL1A1
MOL000098	SJ17	COL3A1
MOL000098	SJ17	CLDN4
MOL000098	SJ17	CRP
MOL000098	SJ17	CTSD
MOL000098	SJ17	CYP1A1
MOL000098	SJ17	CYP1A2
MOL000098	SJ17	CYP1B1
MOL000098	SJ17	CYP3A4
MOL000098	SJ17	NQO1
MOL000098	SJ17	DIO1
MOL000098	SJ17	E2F1
MOL000098	SJ17	E2F2
MOL000098	SJ17	EGF
MOL000098	SJ17	EGFR
MOL000098	SJ17	ELK1
MOL000098	SJ17	ERBB2
MOL000098	SJ17	ERBB3
MOL000098	SJ17	ESR1
MOL000098	SJ17	ESR2
MOL000098	SJ17	F3
MOL000098	SJ17	FOS
MOL000098	SJ17	GJA1
MOL000098	SJ17	CXCL2
MOL000098	SJ17	GSK3B
MOL000098	SJ17	GSTM1
MOL000098	SJ17	GSTM2
MOL000098	SJ17	GSTP1
MOL000098	SJ17	HAS2
MOL000098	SJ17	HIF1A
MOL000098	SJ17	HK2
MOL000098	SJ17	HMOX1
MOL000098	SJ17	HSF1
MOL000098	SJ17	HSPA5
MOL000098	SJ17	HSPB1
MOL000098	SJ17	ICAM1
MOL000098	SJ17	IFNG
MOL000098	SJ17	IGF2
MOL000098	SJ17	IGFBP3

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000098	SJ17	IL1A
MOL000098	SJ17	IL1B
MOL000098	SJ17	IL2
MOL000098	SJ17	IL6
MOL000098	SJ17	CXCL8
MOL000098	SJ17	IL10
MOL000098	SJ17	CXCL10
MOL000098	SJ17	INSR
MOL000098	SJ17	IRF1
MOL000098	SJ17	EIF6
MOL000098	SJ17	JUN
MOL000098	SJ17	KCNH2
MOL000098	SJ17	MAOB
MOL000098	SJ17	MMP1
MOL000098	SJ17	MMP2
MOL000098	SJ17	MMP3
MOL000098	SJ17	MMP9
MOL000098	SJ17	MPO
MOL000098	SJ17	MYC
MOL000098	SJ17	NFE2L2
MOL000098	SJ17	NFKBIA
MOL000098	SJ17	NKX3-1
MOL000098	SJ17	NOS2
MOL000098	SJ17	NOS3
MOL000098	SJ17	ODC1
MOL000098	SJ17	SERPINE1
MOL000098	SJ17	PCOLCE
MOL000098	SJ17	PLAT
MOL000098	SJ17	PLAU
MOL000098	SJ17	POLD1
MOL000098	SJ17	PON1
MOL000098	SJ17	POR
MOL000098	SJ17	PPARA
MOL000098	SJ17	PPARD
MOL000098	SJ17	PPARG
MOL000098	SJ17	PRKCA
MOL000098	SJ17	PRKCB
MOL000098	SJ17	MAPK1
MOL000098	SJ17	MAPK3
MOL000098	SJ17	PRSS1
MOL000098	SJ17	PSMD3
MOL000098	SJ17	PTEN
MOL000098	SJ17	PTGER3
MOL000098	SJ17	PTGS1
MOL000098	SJ17	PTGS2
MOL000098	SJ17	RAF1
MOL000098	SJ17	RASA1

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000098	SJ17	RB1
MOL000098	SJ17	RELA
MOL000098	SJ17	RXRA
MOL000098	SJ17	SCN5A
MOL000098	SJ17	CCL2
MOL000098	SJ17	CXCL11
MOL000098	SJ17	SELE
MOL000098	SJ17	SLC2A4
MOL000098	SJ17	SOD1
MOL000098	SJ17	SOD3
MOL000098	SJ17	SPP1
MOL000098	SJ17	STAT1
MOL000098	SJ17	SULT1E1
MOL000098	SJ17	TGFB1
MOL000098	SJ17	THBD
MOL000098	SJ17	TNF
MOL000098	SJ17	TOP1
MOL000098	SJ17	TOP2A
MOL000098	SJ17	TP53
MOL000098	SJ17	VCAM1
MOL000098	SJ17	VEGFA
MOL000098	SJ17	XDH
MOL000098	SJ17	DCAF5
MOL000098	SJ17	NR1I2
MOL000098	SJ17	MGAM
MOL000098	SJ17	ABCG2
MOL000098	SJ17	NPEPPS
MOL000098	SJ17	NR1I3
MOL000098	SJ17	ACAA2
MOL000098	SJ17	AHSA1
MOL000098	SJ17	RASSF1
MOL000098	SJ17	CHEK2
MOL000098	SJ17	DUOX2
MOL000098	SJ17	HERC5
MOL000098	SJ17	NCF1
MOL000098	SJ17	PIM1
MOL000098	SJ17	F7
MOL000098	SJ17	DPEP1
MOL000098	SJ17	GABRA1
MOL000098	SJ17	CDK1
MOL000098	SJ17	DPP4
MOL000098	SJ17	CA2
MOL000098	SJ17	MAPK14
MOL000098	SJ17	CDK2
MOL000098	SJ17	CCNA2
MOL000098	SJ17	CHEK1
MOL000098	SJ17	NCOA2

(Continues)

Table S1. (Continued)
Duplicate removal

MOLID	ID	Genename
MOL001004	SJ1	ACHE
MOL001004	SJ1	AR
MOL001004	SJ1	CA2
MOL001004	SJ1	NR3C1
MOL001004	SJ1	NR3C2
MOL001004	SJ1	NOS2
MOL001004	SJ1	PGR
MOL001004	SJ1	PTGS1
MOL001004	SJ1	PTGS2
MOL001004	SJ1	RXRA
MOL001004	SJ1	NCOA1
MOL001004	SJ1	NCOA2
MOL001004	SJ1	MAPK14
MOL001004	SJ1	CHEK1
MOL001004	SJ1	CDK2
MOL001004	SJ1	PPARG
MOL001004	SJ1	DPP4
MOL001004	SJ1	ESR1
MOL001004	SJ1	CCNA2
MOL001004	SJ1	ESR2
MOL001004	SJ1	PIM1
MOL001420	SJ2	PRSS1
MOL001420	SJ2	GABRA1
MOL002268	SJ3	AKR1B1
MOL002268	SJ3	JUN
MOL002268	SJ3	DPEP1
MOL002268	SJ3	GSK3B
MOL002773	SJ4	AKT1
MOL002773	SJ4	ALB
MOL002773	SJ4	BCL2
MOL002773	SJ4	CASP3
MOL002773	SJ4	CASP7
MOL002773	SJ4	CASP8
MOL002773	SJ4	CASP9
MOL002773	SJ4	CAV1
MOL002773	SJ4	CTNNB1
MOL002773	SJ4	CYP1A2
MOL002773	SJ4	CYP3A4
MOL002773	SJ4	F3
MOL002773	SJ4	GJA1
MOL002773	SJ4	HMOX1
MOL002773	SJ4	MMP1
MOL002773	SJ4	MMP2
MOL002773	SJ4	MMP10
MOL002773	SJ4	MYC
MOL002773	SJ4	VEGFA

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000354	SJ5	OLR1
MOL000354	SJ5	RELA
MOL000354	SJ5	XDH
MOL000354	SJ5	NCF1
MOL000354	SJ5	PPARD
MOL000354	SJ5	F7
MOL000354	SJ5	MAOB
MOL000354	SJ5	PYGM
MOL000354	SJ5	GRIA2
MOL000358	SJ6	BAX
MOL000358	SJ6	MAP2
MOL000358	SJ6	PON1
MOL000358	SJ6	PRKCA
MOL000358	SJ6	TGFB1
MOL000358	SJ6	CHRM4
MOL000358	SJ6	DRD1
MOL000358	SJ6	CHRM1
MOL000358	SJ6	CHRNA2
MOL000358	SJ6	CHRNA7
MOL000358	SJ6	SCN5A
MOL000358	SJ6	CHRM3
MOL000358	SJ6	PDE3A
MOL000358	SJ6	ADRB2
MOL000358	SJ6	SLC6A4
MOL000358	SJ6	OPRM1
MOL000358	SJ6	ADRA1B
MOL000358	SJ6	KCNH2
MOL000358	SJ6	CHRM2
MOL000358	SJ6	ADRA1D
MOL000359	SJ7	APOE
MOL000359	SJ7	DHCR24
MOL000359	SJ7	ICAM1
MOL000359	SJ7	SREBF1
MOL000359	SJ7	SREBF2
MOL000359	SJ7	ABCB11
MOL000422	SJ8	AHR
MOL000422	SJ8	ALOX5
MOL000422	SJ8	CALM3
MOL000422	SJ8	CYP1A1
MOL000422	SJ8	CYP1B1
MOL000422	SJ8	DIO1
MOL000422	SJ8	GSTM1
MOL000422	SJ8	GSTM2
MOL000422	SJ8	GSTP1
MOL000422	SJ8	HAS2
MOL000422	SJ8	IKBKB
MOL000422	SJ8	INSR

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000422	SJ8	POLD1
MOL000422	SJ8	PPP3CA
MOL000422	SJ8	MAPK8
MOL000422	SJ8	PSMD3
MOL000422	SJ8	SELE
MOL000422	SJ8	SLC2A4
MOL000422	SJ8	SLC6A2
MOL000422	SJ8	SLPI
MOL000422	SJ8	STAT1
MOL000422	SJ8	TNF
MOL000422	SJ8	VCAM1
MOL000422	SJ8	AKR1C3
MOL000422	SJ8	NR1I2
MOL000422	SJ8	NR1I3
MOL000422	SJ8	AHSA1
MOL000422	SJ8	CDK1
MOL000433	SJ9	ABCA1
MOL000433	SJ9	HMGCR
MOL000433	SJ9	SLCO1B1
MOL000433	SJ9	ABCG5
MOL000433	SJ9	ABCG8
MOL000433	SJ9	LTA4H
MOL000433	SJ9	MAOA
MOL000433	SJ9	CTRB1
MOL000433	SJ9	SLC6A3
MOL000433	SJ9	PLAU
MOL000433	SJ9	ADRB1
MOL000433	SJ9	ADRA2A
MOL000492	SJ10	CAT
MOL000098	SJ11	ACACA
MOL000098	SJ11	ACP3
MOL000098	SJ11	PARP1
MOL000098	SJ11	BIRC5
MOL000098	SJ11	CCND1
MOL000098	SJ11	BCL2L1
MOL000098	SJ11	BMP2
MOL000098	SJ11	RUNX2
MOL000098	SJ11	RUNX1T1
MOL000098	SJ11	CCNB1
MOL000098	SJ11	CD40LG
MOL000098	SJ11	CDKN1A
MOL000098	SJ11	CDKN2A
MOL000098	SJ11	CHUK
MOL000098	SJ11	COL1A1
MOL000098	SJ11	COL3A1
MOL000098	SJ11	CLDN4
MOL000098	SJ11	CRP

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000098	SJ11	CTSD
MOL000098	SJ11	NQO1
MOL000098	SJ11	E2F1
MOL000098	SJ11	E2F2
MOL000098	SJ11	EGF
MOL000098	SJ11	EGFR
MOL000098	SJ11	ELK1
MOL000098	SJ11	ERBB2
MOL000098	SJ11	ERBB3
MOL000098	SJ11	FOS
MOL000098	SJ11	CXCL2
MOL000098	SJ11	HIF1A
MOL000098	SJ11	HK2
MOL000098	SJ11	HSF1
MOL000098	SJ11	HSPA5
MOL000098	SJ11	HSPB1
MOL000098	SJ11	IFNG
MOL000098	SJ11	IGF2
MOL000098	SJ11	IGFBP3
MOL000098	SJ11	IL1A
MOL000098	SJ11	IL1B
MOL000098	SJ11	IL2
MOL000098	SJ11	IL6
MOL000098	SJ11	CXCL8
MOL000098	SJ11	IL10
MOL000098	SJ11	CXCL10
MOL000098	SJ11	IRF1
MOL000098	SJ11	EIF6
MOL000098	SJ11	MMP3
MOL000098	SJ11	MMP9
MOL000098	SJ11	MPO
MOL000098	SJ11	NFE2L2
MOL000098	SJ11	NFKBIA
MOL000098	SJ11	NKX3-1
MOL000098	SJ11	NOS3
MOL000098	SJ11	ODC1
MOL000098	SJ11	SERPINE1
MOL000098	SJ11	PCOLCE
MOL000098	SJ11	PLAT
MOL000098	SJ11	POR
MOL000098	SJ11	PPARA
MOL000098	SJ11	PRKCB
MOL000098	SJ11	MAPK1
MOL000098	SJ11	MAPK3
MOL000098	SJ11	PTEN
MOL000098	SJ11	PTGER3
MOL000098	SJ11	RAF1

(Continues)

Table S1. (Continued)

MOLID	ID	Genename
MOL000098	SJ11	RASA1
MOL000098	SJ11	RB1
MOL000098	SJ11	CCL2
MOL000098	SJ11	CXCL11
MOL000098	SJ11	SOD1
MOL000098	SJ11	SOD3
MOL000098	SJ11	SPP1
MOL000098	SJ11	SULT1E1
MOL000098	SJ11	THBD
MOL000098	SJ11	TOP1
MOL000098	SJ11	TOP2A
MOL000098	SJ11	TP53
MOL000098	SJ11	DCAF5
MOL000098	SJ11	MGAM
MOL000098	SJ11	ABCG2
MOL000098	SJ11	NPEPPS
MOL000098	SJ11	ACAA2
MOL000098	SJ11	RASSF1
MOL000098	SJ11	CHEK2
MOL000098	SJ11	DUOX2
MOL000098	SJ11	HERC5

Table S2

OMIM	Genecards	Disgenet
ACTG2	FBN1	STAT4
ADAR	TP53	TNFAIP3
AFF3	PTEN	TNIP1
AGRN	MECP2	GTF2I
AHDC1	FGFR2	IL12A
AKT3	ALDH3A2	PRDM1
ALG14	HSPG2	NCF1
ALMS1	CDH1	DGKQ
ANAPC1	RET	PHIP
ANTXR1	SIL1	TNFSF13B
ARID1A	COL4A3	IRAK1BP1
ASPG3	LMNA	ITSN2
ASXL2	COL1A2	FCGR2A
ATAD3A	POLG	PTTG1
ATP13A2	FAS	TNF
B3GALT6	TGFBR2	THBS1
BBS5	CFH	IL4
BCL10	PAX6	IL2RA
BCL11A	IL10	IL2
BOLA3	INSR	TGFB1
BOS2	AIRE	AIRE
BSND	AKT1	CYP19A1

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
C1DELp35	STAT3	CCR7
CALM2	CD40LG	NFKBIA
CCDC28B	TNFRSF1A	ST14
CCDC88A	SLC12A3	TRAF3IP2
CDC42	RELN	FAS
CDC73	C3	ID3
CDCA7	CAV3	E2F1
CELA2A	TNF	MAP3K14
CENPF	PITX2	HMOX1
CEP104	FOXP3	RORC
CFH	PDGFRA	IRF5
CFHR1	SSB	BLK
CFHR3	FASLG	RELN
CHN1	CD46	HLA-DPB1
CHRM3	SPTAN1	COL11A2P1
CHRNA1	IL6	SSB
CKAP2L	ALB	SHISA9
CLCNKA	INS	TNPO3
CLCNKB	PNPLA6	IL17A
CNNM4	TREX1	IFNG
COL11A1	COL11A2	RO60
COL3A1	FOXC1	TRIM21
COL9A2	COL18A1	IL12A-AS1
COLEC11	CYLD	KLRG1
CXCR4	ATP13A2	IL6
DCAF17	BDNF	ATN1
DCTN1	PRKCD	IL10
DDR2	SMAD3	CALR
DDX59	HLA-B	HLA-DRA
DEL1p36	ELN	IL1B
DEL1q21	NOTCH2	AQP5
DEL1q41q42	CTSC	CXCL13
DEL2p12p11.2	ERCC5	CXCL10
DEL2p16.1-p15	HLA-DRB1	BPIFA2
DEL2p21	IL1B	HLA-DRB1
DEL2q31	TH	CTSS
DGUOK	CTLA4	LILRA3
DNMT3A	FGF10	MIR146A
DPYSL5	PSMB8	RBM45
DUP1q21	LEP	CA6
DUP2q31.1	FERMT1	MUC1
DVL1	MAPK1	CXCL8
EIF2AK2	XIAP	IL18
EIF2AK3	KIT	IFNA1
EN1	CRP	EGF
ENDOVESL	FLNB	MMP9
ESPN	MEFV	IL22

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
F5	STIM1	CXCL12
FASLG	INPP5K	IL23A
FLG2	TRIM21	HMGB1
FSHR	ZNRD2	REG1A
FWS	IFNG	BCL2
GATAD2B	TNFAIP3	IL21
GGPS1	TAP2	HT
GLI2	XK	HLA-A
GNAI3	TGM5	CXCR5
GNB1	SCO2	IFNB1
GPSM2	EGFR	SPTAN1
GRHL3	MTHFR	BMP6
H3F3A	H19	CNTN2
HAAO	TGFB1	TRAF6
HADHA	MPZ	IL7
HHAT	ZMPSTE24	TRBV20OR9-2
HOXD13	APOH	ICAM1
HS2ST1	PPARG	IL13
HSPG2	TNXB	MYDGF
IBA57	CFB	TXLNA
IFIH1	CP	OAS1
IFT172	B2M	NLRP3
IL6R	GTF2IRD1	ACR
IRF6	NAGLU	CHRM3
KCND3	ADIPOQ	LINC02605
KCNH1	GTF2I	TNFSF13
KCNJ10	SSNA1	CRISP3
KCNN3	CHRM3	MUC5AC
KIF14	CASP8	CASP3
KIRREL1	TAP1	VCAM1
KONDS	FRAXA	IFNA13
KYNU	APOE	RTEL1
LBR	RO60	CCL21
LMNA	MDM2	ADIPOQ
LMOD1	C4A	ISG20
LOR	IGF1	FOXP3
LRIG2	ITPR1	PSPN
LRP2	GNAQ	AQP4
LYST	COLQ	MYD88
MCP	TLR4	CXCL1
MDM4	LAMA3	PSMB9
MDS2	IL2RA	CXCL9
MPV17	CD40	HLA-DQA1
MPZ	EDN1	NGF
MSH2	PLOD2	HLA-B
MSH6	VEGFA	IL17D
MTOR	RNU4ATAC	GZMA

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
MTX2	HOXD13	TLR7
MYCN	NDN	GSTT1
MYSM1	AICDA	GSN
NBAS	SGSH	PAX6
NECTIN4	ACE	GSTM1
NFU1	TNFSF13B	MSMB
NLRC4	CXCL8	PSPH
NLRP3	STAT4	AREG
NOS1AP	HFE	IL1A
NOTCH2	C1S	ITPR1
NPHP1	ATP6V1B2	ITGB2
NPHP4	KITLG	ITGAL
NRAS	F2	IL27
NRXN1	POMC	ITGAE
NUP133	CRYAA	IL5
ODC1	BSCL2	ITPR3
ORC1	CLN3	CXCL11
ORC4	CYP19A1	IGH
PADI3	CD27	LTA
PBX1	CCL2	HRES1
PDCN	IL4	ICA1
PER3	GATA4	PTEN
PHGDH	CD79A	ASCL2
PIGF	PRL	CCL18
PIGV	NOS3	PRL
PIK3CD	HLA-DQB1	MDK
PKP1	AMHR2	MBL2
PLOD1	IL17A	RAB4A
POGZ	LBR	RBBP4
POLR1B	ADA	AQP1
POU3F3	GDNF	AGER
PPP1CB	SLC6A4	CTLA4
PREPL	IL1RN	IL23R
PRG4	IL2	CD40
PSMB4	CXCR4	CCR9
PTCH2	SHBG	C3
RAB3GAP1	OPA3	ALB
RAB3GAP2	ALDH2	MTOR
RBM8A	RNF125	TP53
RC3H1	NR3C1	TXN
RFX5	CASR	RIDA
RIT1	SERPINA1	LOC102723407
RLS7	HLA-A	XBP1
RNF2	CYP21A2	EGFR
RNU4ATAC	MMP9	IL33
RYR2	DHODH	TRIM38
SCN1A	PSMB9	CDKN2A

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
SDCCAG8	PIK3C2A	VIP
SIAT9	CYP17A1	VEGFA
SKI	CALR	LOC102724971
SLC19A2	CA8	MALT1
SLC25A24	CCR6	BTG3
SLC2A1	IL18	PUF60
SLC5A7	BIVM-ERCC5	IL17F
SLC9A1	PTPN22	ADAM17
SOS1	KRT14	CXCR3
SOX11	SLC12A2	TAP2
SPEN	H2AC18	TREX1
SPRED2	GAD1	STXBP3
SPRTN	RETN	IGHV3-52
STAMBP	HCCS	STAT1
SUCLG1	APTX	SYT1
SYT2	FLT3	RELA
TBCE	IRF5	TRIM27
TBX15	CSF3	CD27
TCHH	CD4	CD14
TET3	SIAE	PSMB8
TGFB2	PLA2G6	BCL6
TMCO1	PUF60	MUC16
TPRKB	OCLN	CD9
TTC7A	MIR146A	CD8A
USH2A	ESR1	MSC
VANGL1	C2	PTPN2
WDPCP	EGF	BAX
WDR26	COL7A1	PVT1
WIPF1	VWF	CD2
WLS	PRTN3	PSS
WNT4	GMPPB	PLAAT4
WS2B	IL13	MIR146B
YRDC	IL12A	NRP1
YY1AP1	ELANE	PTN
ZEB2	HADHA	IL18R1
C1DUPp36.33	PHF21A	AICDA
DUP1p36.33	CSF2	CD4
2ADUB	FCGR3B	RETN
ACDP4	LTF	ABCG2
ACHRD	IL23R	CD44
ACTA3	IL7R	PRKAA1
AGS2	MIR155	IKBKE
ALPS4	IL6R	RNPC3
ALSS	MPO	CD68
AMSH	HESX1	IL17RB
APC1	COG4	MIR448
APDS	IL33	NUDT15

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
ARCND1	CFTR	NAT10
BABS	STAT1	TRIM68
BMFS6	ICAM1	CD69
C1DELp36	ETV6	MFN2
C1DELq21	CA2	RNF125
C1DELq41q42	ACSL4	TET2
C1DUPq21	CXCL13	PRKAA2
C1orf4	LPL	CD40LG
C1orf69	HP	PRTN3
C20orf37	PLAG1	TNFRSF8
C2DELp12p11.2	FGF3	CHST3
C2DELp161-p15	ISCA1	ATG5
C2DELp21	HLA-C	ATF7IP
C2DUPq31.1	FN1	EIF2AK2
C2orf86	CCL5	MAP2K7
CACP	AQP5	RAB3D
CAKUHED	HTR2A	MAPK8
CAPON	ABHD5	MAPK1
CARD12	CDKN3	CLOCK
CCCAP	IL1A	VAC14
CD46	DNMT1	APOBEC3B
CFSMR	GUSB	PRKAB1
CHN	SLC17A5	PPBP
CHS1	CRH	EDA2R
CHT1	NGF	SSRP1
CIAS1	CHUK	C4A
CILD31	IFNA1	TRPM2
CLK1	TPO	TTR
CMS15	CASP3	WNK1
CMS7A	CXCL12	MUC5B
CMS8	IKZF1	IL25
CMT1B	CTDP1	GORASP1
COCA1	TNFRSF1B	UBTF
CRMP5	ETS1	SPTBN1
CTIP1	SELE	UVRAG
D2S201E	CD55	CX3CL1
DBS	CD28	VDR
DEL1p35	SPP1	ROBO3
DGK	AMPH	SELE
DRADA	IL7	TPMT
DRS2	CCL3	SLC17A1
DVC1	SOD1	TNFRSF1A
EAG	SATB1	STAT3
EDM2	ENSG00000259505	STIM1
EDSFS	ENSG00000234586	SPRR2A
EDSVASC	ENSG00000244429	TAC1
ELA2A	MSTO1	TAP1

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
ENDOVESLB	CYP11A1	SPRR1B
FASPS3	CALCA	SOAT1
FHR1	SELP	TARBP1
FHR3	ERBB2	MIR551B
FRAP1	COQ8A	SLPI
GAMOS5	MBL2	BTK
GEFSP2	IL1R1	TSPO
GGPPS1	PHIP	SLC22A1
GINGF	PON1	CLDN5
GLUT1	CCR1	VIPR2
GLYBP	HLA-DQA1	TRPV1
GPR177	ABCA1	CASP1
GTBP	NCF1	FAM167A
H3F3	VCAM1	HMCN1
HAYOS	CD8A	NT5C1A
HF1	TLR2	SEMA7A
HIRIP	IL5	USO1
HMN7B	ALDH3A1	SATB1
HOX4I	EDA	S100A9
HPE9	TG	S100A8
HPMRS1	PDE8B	TP63
HRPT2	HIF1A	BDNF
IFPS	C4B	MIR483
IL6RQ	FOXP2	RPE65
IMD37	AGPAT2	VAMP8
IRIP	CCN2	CAST
JPO1	CXCL10	TAM
KCND3S	VIP	CCL5
KCS	SOCS1	NAPB
KIAA0042	CCL11	XBP1P1
KIAA0401	GJA8	XDH
KIAA0436	EYS	CA1
KIAA0461	SYP	CA2
KIAA1150	GAST	LAPTM5
KIAA1212	IL12A-AS1	CXCR4
KIAA1685	CCR5	NR1I3
KIAA2025	CYCS	CCL25
KYNUU	TGM1	CCL22
LAF4	LIPC	DHX40
LDS4	FCGR2A	ASRGL1
LGN	BCL2	MAP1LC3B
LH1	MIF	CCL17
LIG2	TLR3	TNFSF14
LMN1	CXCR2	PPARG
LQT15	TPH1	CTSD
MART2	LTA	ERV3-1
MDA5	PHYH	ESR1

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
MDPS	ATP1A2	ALCAM
MGC1203	NFKB1	F9
MINT	GAD2	NR1I4
MMDS2	TFRC	ATF6
MRD27	PERP	CUL9
MRD42	FADD	FLNB
MTDPS6	ITGB2	FMR1
MTPA	TNFSF4	EPHB2
NAG	NOS2	ELN
NEPH1	IL3	CX3CR1
NFSRA	HGF	CYP1A1
NHE1	HLA-DRA	IFNLR1
NLS1	PDPN	NUDT10
NMYC	BAX	DLAT
NPH1	AQP4	DNASE1
NPHS18	BCL6	EDA
NPHS2	BMP6	ABCA1
NS14	RNPC3	EDNRA
NSLH2	CLN5	KCNH3
NTRKR3	MUC1	ARHGAP45
ODG1	CCK	SEC14L2
OFD5	DNASE1L3	AMH
OORS	SELL	ACAD8
ORC1L	GSTM1	CHIA
ORC4L	NR4A2	PDLIM3
PARK9	LOC110806262	AMY1A
PBS	CYP2U1	AMY1B
PEK	VDR	AMY1C
PHA	LTBP1	GOLGA1
PKBG	NPY	GOLGA4
PLC	PCNA	HEYL
PRAAS3	HSPA5	GNL3
PRKR	CST3	PADI4
PTHSL2	CXCR5	FPR2
PVRL4	ACE2	DDX58
RAB3GAP150	OTOA	ALPP
RADMIS	NR3C2	FUCA1
RBM8B	STS	FUCA2
RING2	S100A9	NCR3
RIT	SPTBN2	ATRNL1
RP39	KIR3DL1	MYCBP
SCAMC1	IRF1	GOT2
SEMDJL1	CLU	ADA
SERKAL	GGT1	TRIM22
SESAME	CXCR3	ABCA7
SGS	MME	SEMA3A
SK3	BLK	NOD1

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
SKDEAS	MCAM	NXF1
SLB	ATXN2	PERCC1
SLSN4	SERPINA3	CENPB
SMLMOD	RELA	GRAP
SNIBFIS	ITGAM	CFTR
SOM	SAA1	CDKN2D
ST3GALV	ACP1	CDK2AP2
STBM2	ENO2	AKT3
STL2	JUN	MIR1248
SUCLA1	FLG	MIR1207
TBRS	ANXA5	OCLN
TCS4	TOR1A	MIR4695
TEM8	IL15	MIR4484
THH	MMP3	IFNG-AS1
THPH2	NFKBIA	EBI3
THTR1	KRT1	PRG4
TKS	THBS1	CCL27
TNFSF6	ALOXE3	SUB1
TTC7	IRAK1	TMED2
U4ATAC	DIABLO	TNFRSF13C
UHS1	IFNG-AS1	CLN3
USH1M	PARP1	TMEM132D
VCRL1	CAVIN1	CNN3
VTSIP	MYD88	CP
VWS1	HSPD1	CR2
WARBM1	CX3CR1	CRP
WASPIP	MAPK10	NRSN1
XIGIS	SYK	CST3
YAP	CXCR2P1	H3P19
ZFHX1B	PAX5	H3P8
1D	LINC00426	CKAP4
3MC2	LINC02384	DSTN
AGS7	HMGB1	TPPP
AHUS2	FGF7	RPP14
AOMS4	DDHD2	WDHD1
APNH	BCL10	CHP1
APT1LG1	VIM	DBA2
ARHGAP2	CASP1	SLC26A9
ARVD2	NFIB	H3P13
ATR	SPTBN1	CTSB
B120	ICOSLG	LTBR
BBS15	FLNC	MMP2
BEFAHRS	TLR9	MMP3
BRYLIB1	ACADVL	MPO
C1orf124	BTNL2	MS
C1orf28	CLDN4	MIAT
CJS	KCND2	MSH5

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
CLAN	TNFRSF13B	MSN
CMS1B	IRAK1BP1	MUC4
CMS22	DDC	MYC
CMT2EE	MAG	STS
CMTDID	DNAJC3	MIR34C
CRAM	TOP1	LTF
CSS9	IL2RB	LY9
DFNA37	MERTK	LYZ
DSH	IL17F	MIR130A
EDSSPD2	XDH	MIR155
EGBRS	LEF1	MIR181A2
EMD2	DAB1	MIR200B
EVI	SFTPD	MIR223
EVI9	MIR200B	MIR31
FCC1	ITGAL	ATD
FCU	GSTT1	NCL
GAMOS10	CD274	ATHS
GAMOS8	IFNB1	SF3B6
GF1	SRD5A1	SERPINA1
HCCA2	S100A8	PIK3CA
HESJAS	SCT	PIK3CB
HFL1	SAR1B	PIK3CD
HJCYS	EZR	PIK3CG
HKRP1	PPT1	DNAJC10
HLF4	CENPB	UGT2B28
HMN7A	LCN2	POU2F1
HNPCC5	ATP6AP1	PDCD1
HTLVR	MUC16	LEF1
HUS	CCL4	NFKB1
ICF3	NTRK1	NFKBIL1
IDDEBF	PDCD1	NR4A2
IL6QTL	GZMB	MIR377
IMD14A	PROP1	OXTR
IMDSHY	XRCC5	P2RX7
KCND3L	MLN	PAEP
KCS1	HLA-DPB1	PAX3
KIAA0328	CENPC	TRAT1
KIAA0464	MIR145	PPARA
KIAA0562	CTSD	MUC19
KIAA0806	CD44	HIF1A
KIAA1140	SUMF1	HLA-DRB3
KIAA1179	AQP2	HLA-H
KIAA1915	M6PR	HOXC6
KINS	STAT5A	HSPA4
KRPPD	XRCC6	LINC01139
LEUDEN	ALPP	IFI16
LLH	NCAM1	IFI27

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
LPS	CYP1A2	CCN1
MDHLO	FAM167A	GSTM2
MDS	HSPB1	CD274
MICCAP	ELOVL4	TRBV6-2
MKS12	RNASE3	TRBV5-6
MMDS1	HMGCR	GPT
MMDS3	FURIN	LAMTOR2
MOPD1	ITGA4	GRN
MPPH2	CCR7	GRIN2A
MRD25	TGFA	NR3C1
MRD37	MICB	PYCARD
MSF	LAMB1	TBK1
MTDPS3	MUC19	APOH
MTDPS9	TACR1	RBPJ
MYSPC	KIR2DS4	IL1RN
NPHS23	CAT	IRAK1
NPY3R	GAPDH	IRF1
NS6	ATP7B	IRF2
ODED	CR1	KDR
P130	NR1H2	KRT6B
p150	CD70	LCN1
p68	ATF6	LEP
PERK	DDHD1	LEPR
PHASK	CFLAR	PRAMEF13
PHGDHD	ADCYAP1	INSRR
PHRINL	MX1	ILF3
PINS	GBA2	FASLG
PMGEDSV	TBK1	IL6R
PRR4	IRF3	IL7R
PSS6	RAX	CXCR1
RING1B	FA2H	CXCR2
ROC1	LYZ	IL12RB1
RPRGL1	GOLGA1	AQP3
SCZD17	KRT7	TNFRSF9
SHAPNS	CR2	ILF2
SHARP	ATP6V1B1	LPL
SJS	MIA2	
SKCA3	ITGA2	
SKI1	ALDH16A1	
SKS	C5AR1	
SLSN1	GRP	
SLSN7	ADAM17	
SMADIP1	BAMBI	
SMEI	FCGR3A	
SOPH	NOS1	
SPD1	RNF170	
SPDRS	CD59	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
SRN1	TNFRSF10A	
STL5	CXCL9	
STROMS	KCTD7	
TAR	MUC5AC	
TFCP2L4	TLR7	
THL	HLA-DRB5	
TKT	FBL	
TMBTS	PTGS1	
TRMA	CLN6	
VCRL2	C3AR1	
VSCM1	CHI3L1	
WIP	TNFRSF13C	
ALGAZ	IL23A	
ARMD4	DNASE1	
ARVC2	EWSR1	
BBS16	IL1RL1	
BDSD	SIGLEC5	
BMFS4	COL17A1	
C1DELq21.1	TNIP1	
CFHL1	MCOLN1	
CFHL3	KIR2DL1	
CHDTHP	KCNC3	
CMNS	AGER	
CMS1A	KRT16	
CMS20	ALOX5	
CMS7B	EXOSC10	
DFNB82	SLC4A1	
DSRAD	AGMO	
DSS	EEF1A1	
DYT18	PLA2G7	
DYT33	CD80	
EDSKCL1	TFEB	
EDSS1	IRF7	
FASL	LCN1	
FCAS1	PF4	
FEB3A	BCL2L1	
FPLD2	TPP1	
GANDS	MAPK8	
GAPO	TRB	
GIRDIN	CCL17	
GRNG	OGDH	
HGF	IL12B	
HIAA0929	ADIPOR1	
HIES5	CATSPER1	
HIPI3	MICA	
HNPCC1	KRT19	
HRD	SULT1A3	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
ILFS2	IL17RA	
IMD14B	CASP9	
IPAF	PPOX	
JBTS25	CA4	
JBTS4	CTSG	
KIAA0839	MASP2	
KIAA1809	HLA-DMA	
LIKNS	TNFSF10	
MARTS2	PLIN1	
MCPH20	MUC5B	
MEPCA	IL22	
MINAT	CYP27B1	
MMIHS3	IRF4	
MMIHS5	SPINK1	
MMRCS3	MIR31	
MODED	VIPR2	
NNMS	MIR142	
NPHS22	CTSB	
NS8	RORA	
PEOB4	TNFRSF4	
PIT	KLRK1	
RHOGAP2	ADIPOR2	
RJALS	TNFSF13	
RTSC4	CLN8	
SCA19	GC	
SGMRT1	CD244	
SIP1	CYP21A1P	
SJA	HRH2	
SMARCF1	LGALS3	
SPG74	AXL	
SPG78	HMCN1	
SRTD10	ITGB1	
SZP	ITSN2	
TALS	MKI67	
THMD1	TXN	
TRHY	ATG5	
UFS2	GFRA1	
VWS2	ALDH4A1	
WAS2	HYOU1	
WHIMS1	PRDM1	
WHSUS	KRT5	
WRCN	TRAF6	
WRS	CLDN3	
ZKS	ICA1	
ZLS1	HNRNPH1	
ZLS3	CTSH	
AHUS1	CBX5	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
AIFEC	SLPI	
ALPS1B	TRAPPC10	
APE	ARHGAP6	
CHN2	TGM2	
CMCS	RAP1A	
CMD1A	NFAT5	
DEE6A	AQP1	
DEL1q21.1	IFNAR1	
DILOS	DNAJC5	
DING	FUCA1	
DURS2	CXCL1	
GIDID	KLHL12	
HAPO	ITPR3	
IFI4	TNFRSF8	
MMRCS2	AMBP	
MRD14	MALT1	
NALP3	PNPLA1	
NCMS	P4HTM	
NCPH1	FAM89B	
NS4	ELAVL4	
PEAMO	ALDH1B1	
PED	PRRG4	
PPS1	NFKBIL1	
RATARS	NCR3	
RFMN	TNFRSF6B	
ROCHIS	ARMS2	
RP71	KRT6B	
SCA22	ARMC8	
SJS1	PPBP	
UHS3	TJP1	
VACRDS	ARL9	
WARBM2	A2M	
BAP1	EDC4	
BBS20	CA6	
BRGDA9	TNFSF12	
CSS2	CCL21	
DRVT	ACSL6	
FCAS4	RECK	
G1P1	ID3	
GIV	CCDC174	
GLUT1DS	SEPSECS	
HGPS	SSBL5P	
LWS	SSBL2P	
MARTS1	SSBL3P	
OFC6	TLR1	
PYPAF1	CLEC7A	
AGS6	KIR2DL3	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
DFNA34	BANK1	
EIG12	ITGA1	
FHM3	IL9	
LUSYAM	BRD2	
PEHOL	MIR130A	
DEE6B	XBP1	
DYT9	TNPO3	
KEFH	MIR125B2	
SDCHCN	GAL	
C2DELp12p11.2	CX3CL1	
	IL21	
	PADI4	
	AQP3	
	IL37	
	ITPR2	
	CD86	
	MIR30A	
	SOCS3	
	S100A6	
	CD2	
	RAB3D	
	GPI	
	HLA-DPA1	
	CCN1	
	MSMB	
	HLA-DRB3	
	GZMA	
	ACSL3	
	GLS	
	ABCA7	
	MUC4	
	GAS6	
	SDR9C7	
	H2AC4	
	MIR125B1	
	GRAP	
	CXCL11	
	IFI16	
	LINC00871	
	SNRNP70	
	TNFRSF18	
	HLA-DQA2	
	IL1RL2	
	TYRO3	
	IL18BP	
	ATP10B	
	PTTG1	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
	IGHG1	
	PLA2G10	
	PRLR	
	TNFRSF25	
	RPLP0	
	EDA2R	
	IGHM	
	CD72	
	TNFSF15	
	PRCC	
	HLA-DMB	
	GRIP2	
	HLA-DOA	
	HCP5	
	SPDEF	
	HOOK1	
	REG1A	
	B3GAT1	
	DDIT3	
	CIDEC	
	PEAR1	
	ANO1	
	HLA-DQB2	
	ITGAX	
	MFSD8	
	PHC1	
	GADD45A	
	TLX1	
	PIP	
	SUMO4	
	IMMP1L	
	KIR3DS1	
	CCR4	
	SERPINH1	
	CCL3L1	
	FCRL4	
	TPI1	
	LTB	
	TRIM27	
	CD52	
	ERLIN1	
	GOLGA4	
	KIR2DS5	
	CASP2	
	NCOA1	
	PRRC2A	
	TLR8	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
	SAFB	
	DNAJC24	
	TRAF3IP2	
	KIR2DS1	
	KIR2DS3	
	DEFB1	
	MUC7	
	LTBR	
	CD247	
	VAV1	
	CKAP4	
	CD58	
	HLA-DOB	
	MAP2K4	
	TSLP	
	AGPAT1	
	KIR2DL2	
	EPX	
	PSMB1	
	CARD16	
	CD276	
	TNRC6A	
	CXCR6	
	YIF1A	
	CCL22	
	LGALS1	
	FLNC-AS1	
	ATP6V1F	
	BAK1	
	DEFB4A	
	MIP	
	NTRK3	
	AZGP1	
	RNY1	
	ASCL2	
	CAPN1	
	ANGPTL2	
	CD200	
	TASL	
	BLVRB	
	NXF1	
	IGKC	
	RBMS3	
	FABP5	
	H4C2	
	ICAM3	
	TRIM68	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
	CDKL2	
	DDX39B	
	APAF1	
	PRKAB1	
	H2BC3	
	WWTR1	
	AP4B1-AS1	
	RPS6KA5	
	RSAD2	
	PKM	
	C8B	
	IL32	
	MIR744	
	POLR3K	
	ATP6V0A4	
	BLZF1	
	MIR4695	
	TFF3	
	SSRP1	
	S1PR1	
	CHRM1	
	MIR1207	
	VARS1	
	PEBP1	
	B3GALT5	
	CTSF	
	MS4A1	
	HRH1	
	KIR2DS2	
	CCL20	
	PSIP1	
	TSIX	
	CLEC4A	
	TIGIT	
	SHISA9	
	PTN	
	VPS52	
	AREG	
	TNFRSF17	
	DCD	
	HLA-DRB6	
	HLA-DQB1-AS1	
	SPHK1	
	PRSS2	
	PINX1	
	KCNIP3	
	NAB1	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
	MDK	
	IGSF10	
	ALDH9A1	
	PSME1	
	SIGLEC1	
	RAB11FIP5	
	RBBP4	
	STK19	
	LY6G5B	
	HDGF	
	CRISP3	
	AHCYL1	
	KLRG1	
	HACL1	
	IQGAP2	
	BOD1	
	TRIM38	
	CA1	
	IVL	
	CCN6	
	KCP	
	DHFRP2	
	EBI3	
	CCL27	
	ALDH3B1	
	FAM98A	
	CD226	
	PMVK	
	BTN2A1	
	ATF6B	
	TSBP1-AS1	
	MTCO3P1	
	TSSK1B	
	IL22RA1	
	ACSL1	
	ZNF646	
	MAML2	
	TSBP1	
	TCP1	
	CCL18	
	OAS1	
	C4BPA	
	FPR2	
	ARHGEF11	
	RASGRP3	
	NISCH	
	DLAT	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
	CTSS	
	EPSTI1	
	RPL7	
	SH2D2A	
	TSPAN33	
	HLA-DQB3	
	lnc-HLA-DQB1-2	
	HSALNG0049436	
	LPO	
	P2RX7	
	DEFB103B	
	ALDH3B2	
	CRTC1	
	SLU7	
	SLC20A1	
	IL27	
	H1-1	
	CCL28	
	HNRNPDL	
	LILRA3	
	GRIN3B	
	AKNA	
	DGKQ	
	CPEB4	
	MIS18BP1	
	TRIM63	
	LAMP3	
	GNL3	
	IL36A	
	MRPL24	
	SULT1A1	
	LGALS9	
	RXRB	
	SLAMF7	
	PIGR	
	GPSM3	
	C3orf80	
	HCG23	
	LOC101929290	
	RNU6-959P	
	ENSG00000269918	
	HSALNG0021150	
	RF00026-588	
	lnc-IL12A-2	
	IL34	
	CLEC2B	
	INSRR	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
	NR6A1	
	C4BPB	
	ZFPM1	
	CCR9	
	TPI1P2	
	CRTC3	
	FAM228A	
	IL1F10	
	DNAJC10	
	FBLN7	
	ARHGAP45	
	ISG20L2	
	NACC2	
	BTLA	
	COIL	
	PSME3	
	CREBRF	
	C3orf20	
	LRRC71	
	DEFB136	
	METTL25B	
	MIR9-1HG	
	MIR765	
	SATB1-AS1	
	MIR3142HG	
	LINC01485	
	LINC01117	
	WAKMAR2	
	LINC00562	
	PTMAP5	
	LINC02539	
	ENSG00000269954	
	ALG1L11P	
	GNG5P5	
	ENSG00000223356	
	ENSG00000271553	
	ENSG00000257105	
	COL11A2P1	
	BTF3L4P3	
	RN7SL700P	
	RNU6-187P	
	lnc-IRF5-3	
	lnc-LTBP1-1	
	NONHSAG044958.2	
	lnc-BTNL2-2	
	LOC107986649	
	ENSG00000242162	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
	lnc-PTTG1-5	
	MN297643	
	NONHSAG045793.2	
	lnc-SLC35G5-2	
	lnc-HLA-DRB1-8	
	ENSG00000224163	
	HSALNG0014115	
	HSALNG0049429	
	HSALNG0061260	
	HSALNG0061261	
	HSALNG0049404	
	HSALNG0063445	
	ENSG00000288064	
	piR-35674-092	
	MN298231	
	HSALNG0109667	
	HSALNG0046729	
	HSALNG0049428	
	HSALNG0007635	
	HSALNG0007636	
	HSALNG0046730	
	HSALNG0049427	
	piR-52910	
	RF00017-5040	
	piR-61240-151	
	LOC105370283	
	LOC105374329	
	HSALNG0013607	
	piR-50437-359	
	IL25	
	SLC17A3	
	IFN1@	
	ATP6V0D2	
	DEFA1	
	WFDC2	
	SCGB2A1	
	CCL23	
	BIRC7	
	ACSL5	
	AQP7	
	CHIA	
	TRBV16	
	TNFSF18	
	ORM2	
	C2-AS1	
	ADAD1	
	SNRPD3	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
	POU2F1	
	IGK	
	STATH	
	ALDH8A1	
	APOF	
	BPIFA2	
	SEPTIN7	
	DUT	
	SNRPD1	
	ATP6V1C2	
	CCR8	
	DPP7	
	F11R	
	CD6	
	H1-5	
	EBF1	
	VTCN1	
	GTF2I-AS1	
	CD180	
	ACCS	
	MFSD6	
	SPRR2A	
	FOXN2	
	MIR5100	
	MIR5572	
	MIR4524B	
	MIR5571	
	H2AC6	
	IGHV3-71	
	FGL1	
	SPRR1B	
	BHLHA15	
	HRES1	
	ASGR2	
	TXLNA	
	APOBEC3A	
	GTF2F1	
	VGLL3	
	BTN2A2	
	CST1	
	AQP6	
	BTN3A1	
	SLC17A2	
	BTN3A2	
	BTN3A3	
	HMGN4	
	AAK1	

(Continues)

Table S2. (Continued)

OMIM	Genecards	Disgenet
	H3C2	
	H2BC4	
	SOCS6	
	H1-6	
	LOC116158548	

O+G+D
ACTG2
ADAR
AFF3
AGRN
AHDC1
AKT3
ALG14
ALMS1
ANAPC1
ANTXR1
ARID1A
ASPG3
ASXL2
ATAD3A
ATP13A2
B3GALT6
BBS5
BCL10
BCL11A
BOLA3
BOS2
BSND
C1DELp35
CALM2
CCDC28B
CCDC88A
CDC42
CDC73
CDCA7
CELA2A
CENPF
CEP104
CFH
CFHR1
CFHR3
CHN1
CHRM3
CHRNA1
CKAP2L

O+G+D
CLCNKA
CLCNKB
CNNM4
COL11A1
COL3A1
COL9A2
COLEC11
CXCR4
DCAF17
DCTN1
DDR2
DDX59
DEL1p36
DEL1q21
DEL1q41q42
DEL2p12p11.2
DEL2p16.1-p15
DEL2p21
DEL2q31
DGUOK
DNMT3A
DPYSL5
DUP1q21
DUP2q31.1
DVL1
EIF2AK2
EIF2AK3
EN1
ENDOVESL
ESPN
F5
FASLG
FLG2
FSHR
FWS
GATAD2B
GGPS1
GLI2
GNAI3

O+G+D
GNB1
GPSM2
GRHL3
H3F3A
HAAO
HADHA
HHAT
HOXD13
HS2ST1
HSPG2
IBA57
IFIH1
IFT172
IL6R
IRF6
KCND3
KCNH1
KCNJ10
KCNN3
KIF14
KIRREL1
KONDS
KYNU
LBR
LMNA
LMOD1
LOR
LRIG2
LRP2
LYST
MCP
MDM4
MDS2
MPV17
MPZ
MSH2
MSH6
MTOR
MTX2
MYCN
MYSM1
NBAS
NECTIN4
NFU1
NLRC4
NLRP3
NOS1AP

O+G+D
NOTCH2
NPHP1
NPHP4
NRAS
NRXN1
NUP133
ODC1
ORC1
ORC4
PADI3
PBX1
PDCN
PER3
PHGDH
PIGF
PIGV
PIK3CD
PKP1
PLOD1
POGZ
POLR1B
POU3F3
PPP1CB
PREPL
PRG4
PSMB4
PTCH2
RAB3GAP1
RAB3GAP2
RBM8A
RC3H1
RFX5
RIT1
RLS7
RNF2
RNU4ATAC
RYR2
SCN1A
SDCCAG8
SIAT9
SKI
SLC19A2
SLC25A24
SLC2A1
SLC5A7
SLC9A1
SOS1

(Continues)

Table S2. (Continued)

O+G+D	O+G+D	O+G+D	O+G+D
SOX11	C20orf37	GLUT1	NEPH1
SPEN	C2DELp12p11.2	GLYBP	NFSRA
SPRED2	C2DELp161-p15	GPR177	NHE1
SPRTN	C2DELp21	GTBP	NLS1
STAMBP	C2DUPq31.1	H3F3	NMYC
SUCLG1	C2orf86	HAYOS	NPH1
SYT2	CACP	HF1	NPHS18
TBCE	CAKUHED	HIRIP	NPHS2
TBX15	CAPON	HMN7B	NS14
TCHH	CARD12	HOX4I	NSLH2
TET3	CCCAP	HPE9	NTRKR3
TGFB2	CD46	HPMRS1	ODG1
TMCO1	CFSMR	HRPT2	OFD5
TPRKB	CHN	IFPS	OORS
TTC7A	CHS1	IL6RQ	ORC1L
USH2A	CHT1	IMD37	ORC4L
VANGL1	CIAS1	IRIP	PARK9
WDPCP	CILD31	JPO1	PBS
WDR26	CLK1	KCND3S	PEK
WIPF1	CMS15	KCS	PHA
WLS	CMS7A	KIAA0042	PKBG
WNT4	CMS8	KIAA0401	PLC
WS2B	CMT1B	KIAA0436	PRAAS3
YRDC	COCA1	KIAA0461	PRKR
YY1AP1	CRMP5	KIAA1150	PTHSL2
ZEB2	CTIP1	KIAA1212	PVRL4
C1DUPp36.33	D2S201E	KIAA1685	RAB3GAP150
DUP1p36.33	DBS	KIAA2025	RADMIS
2ADUB	DEL1p35	KYNUU	RBM8B
ACDP4	DGK	LAF4	RING2
ACHRD	DRADA	LDS4	RIT
ACTA3	DRS2	LGN	RP39
AGS2	DVC1	LH1	SCAMC1
ALPS4	EAG	LIG2	SEMDJL1
ALSS	EDM2	LMN1	SERKAL
AMSH	EDSFS	LQT15	SESAME
APC1	EDSVASC	MART2	SGS
APDS	ELA2A	MDA5	SK3
ARCND1	ENDOVESLB	MDPS	SKDEAS
BABS	FASPS3	MGC1203	SLB
BMFS6	FHR1	MINT	SLSN4
C1DELp36	FHR3	MMDS2	SMLMOD
C1DELq21	FRAP1	MRD27	SNIBFIS
C1DELq41q42	GAMOS5	MRD42	SOM
C1DUPq21	GEFSP2	MTDPS6	ST3GALV
C1orf4	GGPPS1	MTPA	STBM2
C1orf69	GINGF	NAG	STL2

(Continues)

Table S2. (Continued)

O+G+D	O+G+D	O+G+D	O+G+D
SUCLA1	EDSSPD2	MRD25	VCRL2
TBRS	EGBRS	MRD37	VSCM1
TCS4	EMD2	MSF	WIP
TEM8	EVI	MTDPS3	ALGAZ
THH	EVI9	MTDPS9	ARMD4
THPH2	FCC1	MYSPC	ARVC2
THTR1	FCU	NPHS23	BBS16
TKS	GAMOS10	NPY3R	BDSD
TNFSF6	GAMOS8	NS6	BMFS4
TTC7	GF1	ODED	C1DELq21.1
U4ATAC	HCCA2	P130	CFHL1
UHS1	HESJAS	p150	CFHL3
USH1M	HFL1	p68	CHDTHP
VCRL1	HJCYS	PERK	CMNS
VTSIP	HKRP1	PHASK	CMS1A
VWS1	HLF4	PHGDHD	CMS20
WARBM1	HMN7A	PHRINL	CMS7B
WASPIP	HNPCC5	PINS	DFNB82
XIGIS	HTLVR	PMGEDSV	DSRAD
YAP	HUS	PRR4	DSS
ZFHX1B	ICF3	PSS6	DYT18
1D	IDDEBF	RING1B	DYT33
3MC2	IL6QTL	ROC1	EDSKCL1
AGS7	IMD14A	RPRGL1	EDSS1
AHUS2	IMDSHY	SCZD17	FASL
AOMS4	KCND3L	SHAPNS	FCAS1
APNH	KCS1	SHARP	FEB3A
APT1LG1	KIAA0328	SJS	FPLD2
ARHGAP2	KIAA0464	SKCA3	GANDS
ARVD2	KIAA0562	SKI1	GAPO
ATR	KIAA0806	SKS	GIRDIN
B120	KIAA1140	SLSN1	GRNG
BBS15	KIAA1179	SLSN7	HGF
BEFAHRS	KIAA1915	SMADIP1	HIAA0929
BRYLIB1	KINS	SMEI	HIES5
C1orf124	KRPPD	SOPH	HIPI3
C1orf28	LEUDEN	SPD1	HNPCC1
CJS	LLH	SPDRS	HRD
CLAN	LPS	SRN1	ILFS2
CMS1B	MDHLO	STL5	IMD14B
CMS22	MDS	STROMS	IPAF
CMT2EE	MICCAP	TAR	JBTS25
CMTDID	MKS12	TFCP2L4	JBTS4
CRAM	MMDS1	THL	KIAA0839
CSS9	MMDS3	TKT	KIAA1809
DFNA37	MOPD1	TMBTS	LIKNS
DSH	MPPH2	TRMA	MARTS2

(Continues)

Table S2. (Continued)

O+G+D	O+G+D	O+G+D	O+G+D
MCPH20	DING	FBN1	ERCC5
MEPCA	DURS2	TP53	HLA-DRB1
MINAT	GIDID	PTEN	IL1B
MMIHS3	HAPO	MECP2	TH
MMIHS5	IFI4	FGFR2	CTLA4
MMRCS3	MMRCS2	ALDH3A2	FGF10
MODED	MRD14	CDH1	PSMB8
NNMS	NALP3	RET	LEP
NPHS22	NCMS	SIL1	FERMT1
NS8	NCPH1	COL4A3	MAPK1
PEOB4	NS4	COL1A2	XIAP
PIT	PEAMO	POLG	KIT
RHOGAP2	PED	FAS	CRP
RJALS	PPS1	TGFBR2	FLNB
RTSC4	RATARS	PAX6	MEFV
SCA19	RFMN	IL10	STIM1
SGMRT1	ROCHIS	INSR	INPP5K
SIP1	RP71	AIRE	TRIM21
SJA	SCA22	AKT1	ZNRD2
SMARCF1	SJS1	STAT3	IFNG
SPG74	UHS3	CD40LG	TNFAIP3
SPG78	VACRDS	TNFRSF1A	TAP2
SRTD10	WARBM2	SLC12A3	XK
SZP	BAP1	RELN	TGM5
TALS	BBS20	C3	SCO2
THMD1	BRGDA9	CAV3	EGFR
TRHY	CSS2	TNF	MTHFR
UFS2	DRVT	PITX2	H19
VWS2	FCAS4	FOXP3	TGFB1
WAS2	G1P1	PDGFRA	ZMPSTE24
WHIMS1	GIV	SSB	APOH
WHSUS	GLUT1DS	SPTAN1	PPARG
WRCN	HGPS	IL6	TNXB
WRS	LWS	ALB	CFB
ZKS	MARTS1	INS	CP
ZLS1	OFC6	PNPLA6	B2M
ZLS3	PYPAF1	TREX1	GTF2IRD1
AHUS1	AGS6	COL11A2	NAGLU
AIFEC	DFNA34	FOXC1	ADIPOQ
ALPS1B	EIG12	COL18A1	GTF2I
APE	FHM3	CYLD	SSNA1
CHN2	LUSYAM	BDNF	CASP8
CMCS	PEHOL	PRKCD	TAP1
CMD1A	DEE6B	SMAD3	FRAXA
DEE6A	DYT9	HLA-B	APOE
DEL1q21.1	KEFH	ELN	RO60
DILOS	SDCHCN	CTSC	MDM2

(Continues)

Table S2. (Continued)

O+G+D	O+G+D	O+G+D	O+G+D
C4A	RNF125	IL23R	CCL3
IGF1	NR3C1	IL7R	SOD1
ITPR1	CASR	MIR155	SATB1
GNAQ	SERPINA1	MPO	ENSG00000259505
COLQ	HLA-A	HESX1	ENSG00000234586
TLR4	CYP21A2	COG4	ENSG00000244429
LAMA3	MMP9	IL33	MSTO1
IL2RA	DHODH	CFTR	CYP11A1
CD40	PSMB9	STAT1	CALCA
EDN1	PIK3C2A	ICAM1	SELP
PLOD2	CYP17A1	ETV6	ERBB2
VEGFA	CALR	CA2	COQ8A
NDN	CA8	ACSL4	MBL2
AICDA	CCR6	CXCL13	IL1R1
SGSH	IL18	LPL	PHIP
ACE	BIVM-ERCC5	HP	PON1
TNFSF13B	PTPN22	PLAG1	CCR1
CXCL8	KRT14	FGF3	HLA-DQA1
STAT4	SLC12A2	ISCA1	ABCA1
HFE	H2AC18	HLA-C	NCF1
C1S	GAD1	FN1	VCAM1
ATP6V1B2	RETN	CCL5	CD8A
KITLG	HCCS	AQP5	TLR2
F2	APTX	HTR2A	IL5
POMC	FLT3	ABHD5	ALDH3A1
CRYAA	IRF5	CDKN3	EDA
BSCL2	CSF3	IL1A	TG
CLN3	CD4	DNMT1	PDE8B
CYP19A1	SIAE	GUSB	HIF1A
CD27	PLA2G6	SLC17A5	C4B
CCL2	PUF60	CRH	FOXP2
IL4	OCLN	NGF	AGPAT2
GATA4	MIR146A	CHUK	CCN2
CD79A	ESR1	IFNA1	CXCL10
PRL	C2	TPO	VIP
NOS3	EGF	CASP3	SOCS1
HLA-DQB1	COL7A1	CXCL12	CCL11
AMHR2	VWF	IKZF1	GJA8
IL17A	PRTN3	CTDP1	EYS
ADA	GMPPB	TNFRSF1B	SYP
GDNF	IL13	ETS1	GAST
SLC6A4	IL12A	SELE	IL12A-AS1
IL1RN	ELANE	CD55	CCR5
IL2	PHF21A	CD28	CYCS
SHBG	CSF2	SPP1	TGM1
OPA3	FCGR3B	AMPH	LIPC
ALDH2	LTF	IL7	FCGR2A

(Continues)

Table S2. (Continued)

O+G+D	O+G+D	O+G+D	O+G+D
BCL2	IRF1	TLR9	M6PR
MIF	CLU	ACADVL	STAT5A
TLR3	GGT1	BTNL2	XRCC6
CXCR2	CXCR3	CLDN4	ALPP
TPH1	MME	KCND2	NCAM1
LTA	BLK	TNFRSF13B	CYP1A2
PHYH	MCAM	IRAK1BP1	FAM167A
ATP1A2	ATXN2	DDC	HSPB1
NFKB1	SERPINA3	MAG	ELOVL4
GAD2	RELA	DNAJC3	RNASE3
TFRC	ITGAM	TOP1	HMGCR
PERP	SAA1	IL2RB	FURIN
FADD	ACP1	MERTK	ITGA4
ITGB2	ENO2	IL17F	CCR7
TNFSF4	JUN	XDH	TGFA
NOS2	FLG	LEF1	MICB
IL3	ANXA5	DAB1	LAMB1
HLA-DRA	TOR1A	SFTPD	MUC19
PDPN	IL15	MIR200B	TACR1
BAX	MMP3	ITGAL	KIR2DS4
AQP4	NFKBIA	GSTT1	CAT
BCL6	KRT1	CD274	GAPDH
BMP6	THBS1	IFNB1	ATP7B
RNPC3	ALOXE3	SRD5A1	CR1
CLN5	IRAK1	S100A8	NR1H2
MUC1	DIABLO	SCT	CD70
CCK	IFNG-AS1	SAR1B	ATF6
DNASE1L3	PARP1	EZR	DDHD1
SELL	CAVIN1	PPT1	CFLAR
GSTM1	MYD88	CENPB	ADCYAP1
NR4A2	HSPD1	LCN2	MX1
LOC110806262	CX3CR1	ATP6AP1	GBA2
CYP2U1	MAPK10	MUC16	TBK1
VDR	SYK	CCL4	IRF3
LTBP1	CXCR2P1	NTRK1	RAX
NPY	PAX5	PDCD1	FA2H
PCNA	LINC00426	GZMB	LYZ
HSPA5	LINC02384	PROP1	GOLGA1
CST3	HMGB1	XRCC5	KRT7
CXCR5	FGF7	MLN	CR2
ACE2	DDHD2	HLA-DPB1	ATP6V1B1
OTOA	VIM	CENPC	MIA2
NR3C2	CASP1	MIR145	ITGA2
STS	NFIB	CTSD	ALDH16A1
S100A9	SPTBN1	CD44	C5AR1
SPTBN2	ICOSLG	SUMF1	GRP
KIR3DL1	FLNC	AQP2	ADAM17

(Continues)

Table S2. (Continued)

O+G+D	O+G+D	O+G+D	O+G+D
BAMBI	ADIPOR1	CLDN3	SSBL2P
FCGR3A	CATSPER1	ICA1	SSBL3P
NOS1	MICA	HNRNPH1	TLR1
RNF170	KRT19	CTSH	CLEC7A
CD59	SULT1A3	CBX5	KIR2DL3
TNFRSF10A	IL17RA	SLPI	BANK1
CXCL9	CASP9	TRAPPC10	ITGA1
KCTD7	PPOX	ARHGAP6	IL9
MUC5AC	CA4	TGM2	BRD2
TLR7	CTSG	RAP1A	MIR130A
HLA-DRB5	MASP2	NFAT5	XBP1
FBL	HLA-DMA	AQP1	TNPO3
PTGS1	TNFSF10	IFNAR1	MIR125B2
CLN6	PLIN1	DNAJC5	GAL
C3AR1	MUC5B	FUCA1	CX3CL1
CHI3L1	IL22	CXCL1	IL21
TNFRSF13C	CYP27B1	KLHL12	PADI4
IL23A	IRF4	ITPR3	AQP3
DNASE1	SPINK1	TNFRSF8	IL37
EWSR1	MIR31	AMBP	ITPR2
IL1RL1	VIPR2	MALT1	CD86
SIGLEC5	MIR142	PNPLA1	MIR30A
COL17A1	CTSB	P4HTM	SOCS3
TNIP1	RORA	FAM89B	S100A6
MCOLN1	TNFRSF4	ELAVL4	CD2
KIR2DL1	KLRK1	ALDH1B1	RAB3D
KCNC3	ADIPOR2	PRRG4	GPI
AGER	TNFSF13	NFKBIL1	HLA-DPA1
KRT16	CLN8	NCR3	CCN1
ALOX5	GC	TNFRSF6B	MSMB
EXOSC10	CD244	ARMS2	HLA-DRB3
SLC4A1	CYP21A1P	KRT6B	GZMA
AGMO	HRH2	ARMC8	ACSL3
EEF1A1	LGALS3	PPBP	GLS
PLA2G7	AXL	TJP1	ABCA7
CD80	HMCN1	ARL9	MUC4
TFEB	ITGB1	A2M	GAS6
IRF7	ITSN2	EDC4	SDR9C7
LCN1	MKI67	CA6	H2AC4
PF4	TXN	TNFSF12	MIR125B1
BCL2L1	ATG5	CCL21	GRAP
TPP1	GFRA1	ACSL6	CXCL11
MAPK8	ALDH4A1	RECK	IFI16
TRB	HYOU1	ID3	LINC00871
CCL17	PRDM1	CCDC174	SNRNP70
OGDH	KRT5	SEPSECS	TNFRSF18
IL12B	TRAF6	SSBL5P	HLA-DQA2

(Continues)

Table S2. (Continued)

O+G+D	O+G+D	O+G+D	O+G+D
IL1RL2	KIR2DS5	RBMS3	SPHK1
TYRO3	CASP2	FABP5	PRSS2
IL18BP	NCOA1	H4C2	PINX1
ATP10B	PRRC2A	ICAM3	KCNIP3
PTTG1	TLR8	TRIM68	NAB1
IGHG1	SAFB	CDKL2	MDK
PLA2G10	DNAJC24	DDX39B	IGSF10
PRLR	TRAF3IP2	APAF1	ALDH9A1
TNFRSF25	KIR2DS1	PRKAB1	PSME1
RPLP0	KIR2DS3	H2BC3	SIGLEC1
EDA2R	DEFB1	WWTR1	RAB11FIP5
IGHM	MUC7	AP4B1-AS1	RBBP4
CD72	LTBR	RPS6KA5	STK19
TNFSF15	CD247	RSAD2	LY6G5B
PRCC	VAV1	PKM	HDGF
HLA-DMB	CKAP4	C8B	CRISP3
GRIP2	CD58	IL32	AHCYL1
HLA-DOA	HLA-DOB	MIR744	KLRG1
HCP5	MAP2K4	POLR3K	HACL1
SPDEF	TSLP	ATP6V0A4	IQGAP2
HOOK1	AGPAT1	BLZF1	BOD1
REG1A	KIR2DL2	MIR4695	TRIM38
B3GAT1	EPX	TFF3	CA1
DDIT3	PSMB1	SSRP1	IVL
CIDEC	CARD16	S1PR1	CCN6
PEAR1	CD276	CHRM1	KCP
ANO1	TNRC6A	MIR1207	DHFRP2
HLA-DQB2	CXCR6	VARS1	EBI3
ITGAX	YIF1A	PEBP1	CCL27
MFSD8	CCL22	B3GALT5	ALDH3B1
PHC1	LGALS1	CTSF	FAM98A
GADD45A	FLNC-AS1	MS4A1	CD226
TLX1	ATP6V1F	HRH1	PMVK
PIP	BAK1	KIR2DS2	BTN2A1
SUMO4	DEFB4A	CCL20	ATF6B
IMMP1L	MIP	PSIP1	TSBP1-AS1
KIR3DS1	NTRK3	TSIX	MTCO3P1
CCR4	AZGP1	CLEC4A	TSSK1B
SERPINH1	RNY1	TIGIT	IL22RA1
CCL3L1	ASCL2	SHISA9	ACSL1
FCRL4	CAPN1	PTN	ZNF646
TPI1	ANGPTL2	VPS52	MAML2
LTB	CD200	AREG	TSBP1
TRIM27	TASL	TNFRSF17	TCP1
CD52	BLVRB	DCD	CCL18
ERLIN1	NXF1	HLA-DRB6	OAS1
GOLGA4	IGKC	HLA-DQB1-AS1	C4BPA

(Continues)

Table S2. (Continued)

O+G+D	O+G+D	O+G+D	O+G+D
FPR2	RF00026-588	lnc-LTBP1-1	TNFSF18
ARHGEF11	lnc-IL12A-2	NONHSAG044958.2	ORM2
RASGRP3	IL34	lnc-BTNL2-2	C2-AS1
NISCH	CLEC2B	LOC107986649	ADAD1
DLAT	INSRR	ENSG00000242162	SNRPD3
CTSS	NR6A1	lnc-PTTG1-5	POU2F1
EPSTI1	C4BPB	MN297643	IGK
RPL7	ZFPM1	NONHSAG045793.2	STATH
SH2D2A	CCR9	lnc-SLC35G5-2	ALDH8A1
TSPAN33	TPI1P2	lnc-HLA-DRB1-8	APOF
HLA-DQB3	CRTC3	ENSG00000224163	BPIFA2
lnc-HLA-DQB1-2	FAM228A	HSALNG0014115	SEPTIN7
HSALNG0049436	IL1F10	HSALNG0049429	DUT
LPO	DNAJC10	HSALNG0061260	SNRPD1
P2RX7	FBLN7	HSALNG0061261	ATP6V1C2
DEFB103B	ARHGAP45	HSALNG0049404	CCR8
ALDH3B2	ISG20L2	HSALNG0063445	DPP7
CRTC1	NACC2	ENSG00000288064	F11R
SLU7	BTLA	piR-35674-092	CD6
SLC20A1	COIL	MN298231	H1-5
IL27	PSME3	HSALNG0109667	EBF1
H1-1	CREBRF	HSALNG0046729	VTCN1
CCL28	C3orf20	HSALNG0049428	GTF2I-AS1
HNRNPDL	LRRC71	HSALNG0007635	CD180
LILRA3	DEFB136	HSALNG0007636	ACCS
GRIN3B	METTL25B	HSALNG0046730	MFSD6
AKNA	MIR9-1HG	HSALNG0049427	SPRR2A
DGKQ	MIR765	piR-52910	FOXN2
CPEB4	SATB1-AS1	RF00017-5040	MIR5100
MIS18BP1	MIR3142HG	piR-61240-151	MIR5572
TRIM63	LINC01485	LOC105370283	MIR4524B
LAMP3	LINC01117	LOC105374329	MIR5571
GNL3	WAKMAR2	HSALNG0013607	H2AC6
IL36A	LINC00562	piR-50437-359	IGHV3-71
MRPL24	PTMAP5	IL25	FGL1
SULT1A1	LINC02539	SLC17A3	SPRR1B
LGALS9	ENSG00000269954	IFN1@	BHLHA15
RXRB	ALG1L11P	ATP6V0D2	HRES1
SLAMF7	GNG5P5	DEFA1	ASGR2
PIGR	ENSG00000223356	WFDC2	TXLNA
GPSM3	ENSG00000271553	SCGB2A1	APOBEC3A
C3orf80	ENSG00000257105	CCL23	GTF2F1
HCG23	COL11A2P1	BIRC7	VGLL3
LOC101929290	BTF3L4P3	ACSL5	BTN2A2
RNU6-959P	RN7SL700P	AQP7	CST1
ENSG00000269918	RNU6-187P	CHIA	AQP6
HSALNG0021150	lnc-IRF5-3	TRBV16	BTN3A1

(Continues)

Table S2. (Continued)

O+G+D	O+G+D	O+G+D	O+G+D
SLC17A2	PLAAT4	CAST	CNN3
BTN3A2	MIR146B	TAM	NRSN1
BTN3A3	NRP1	NAPB	H3P19
HMGN4	IL18R1	XBP1P1	H3P8
AAK1	ABCG2	LAPTM5	DSTN
H3C2	PRKAA1	NR1I3	TPPP
H2BC4	IKBKE	CCL25	RPP14
SOCS6	CD68	DHX40	WDHD1
H1-6	IL17RB	ASRGL1	CHP1
LOC116158548	MIR448	MAP1LC3B	DBA2
ST14	NUDT15	TNFSF14	SLC26A9
E2F1	NAT10	ERV3-1	H3P13
MAP3K14	CD69	ALCAM	MMP2
HMOX1	MFN2	F9	MS
RORC	TET2	NR1I4	MIAT
ATN1	PRKAA2	CUL9	MSH5
RBM45	CHST3	FMR1	MSN
HT	ATF7IP	EPHB2	MYC
CNTN2	MAP2K7	CYP1A1	MIR34C
TRBV20OR9-2	CLOCK	IFNLR1	LY9
MYDGF	VAC14	NUDT10	MIR181A2
ACR	APOBEC3B	EDNRA	MIR223
LINC02605	TRPM2	KCNH3	ATD
IFNA13	TTR	SEC14L2	NCL
RTEL1	WNK1	AMH	ATHS
ISG20	GORASP1	ACAD8	SF3B6
PSPN	UBTF	PDLIM3	PIK3CA
IL17D	UVRAG	AMY1A	PIK3CB
GSN	ROBO3	AMY1B	PIK3CG
PSPH	TPMT	AMY1C	UGT2B28
ITGAE	SLC17A1	HEYL	MIR377
IGH	TAC1	DDX58	OXTR
RAB4A	SOAT1	FUCA2	PAEP
RIDA	TARBP1	ATRNL1	PAX3
LOC102723407	MIR551B	MYCBP	TRAT1
CDKN2A	BTK	GOT2	PPARA
LOC102724971	TSPO	TRIM22	HLA-H
BTG3	SLC22A1	SEMA3A	HOXC6
STXBP3	CLDN5	NOD1	HSPA4
IGHV3-52	TRPV1	PERCC1	LINC01139
SYT1	NT5C1A	CDKN2D	IFI27
CD14	SEMA7A	CDK2AP2	GSTM2
CD9	USO1	MIR1248	TRBV6-2
MSC	TP63	MIR4484	TRBV5-6
PTPN2	MIR483	SUB1	GPT
PVT1	RPE65	TMED2	LAMTOR2
PSS	VAMP8	TMEM132D	GRN

(Continues)

Table S2. (Continued)

O+G+D
GRIN2A
PYCARD
RBPJ
IRF2
KDR
LEPR
PRAMEF13
ILF3
CXCR1
IL12RB1
TNFRSF9
ILF2

Table S3

Intersection target	Intersection target	Intersection target
CA2	APOE	ERBB2
NR3C1	ICAM1	HIF1A
NR3C2	ALOX5	HSPA5
NOS2	CYP1A1	HSPB1
PTGS1	GSTM1	IFNG
NCOA1	GSTM2	IL1A
PPARG	INSR	IL1B
ESR1	MAPK8	IL2
JUN	SELE	IL6
AKT1	SLPI	CXCL8
ALB	STAT1	IL10
BCL2	TNF	CXCL10
CASP3	VCAM1	IRF1
CASP8	NR1I3	MMP3
CASP9	ABCA1	MMP9
CYP1A2	HMGCR	MPO
HMOX1	CAT	NFKBIA
MMP2	PARP1	NOS3
MYC	BCL2L1	ODC1
VEGFA	CD40LG	PPARA
RELA	CDKN2A	MAPK1
XDH	CHUK	PTEN
NCF1	COL3A1	CCL2
BAX	CLDN4	CXCL11
PON1	CRP	SOD1
TGFB1	CTSD	SPP1
CHRM1	E2F1	TOP1
CHRM3	EGF	TP53
SLC6A4	EGFR	ABCG2