

Universidade de Lisboa
Faculdade de Ciências
Departamento de Informática



AIDS/SIDA

Home assignment 3:

Interactome, Pathways and drug therapy targets

André Filipe Bernardes Oliveira, 45648

Mestrado em Informática (MI)

Report of **Bioinformática**

to teacher: André Falcão

1 Index

1	Index.....	1
2	Introduction.....	2
3	Interactome.....	2
4	Microarray analysis	3
5	Drug target discovery	4
6	Conclusion.....	5
7	Appendix.....	6
7.1	Review.....	6
7.2	Interactome.....	6
7.2.1	STRING	6
7.2.1	Pathways (STRING and Reactome)	12
7.3	Microarray analysis (ArrayExpress)	19
7.3.1	Protein Results (R).....	19
7.3.2	Gene Ontology.....	6
7.3.3	Pathways (STRING and Reactome)	11
7.4	Drug Therapy.....	22
7.4.1	DrugBank.....	22
7.4.2	Others.....	4

2 Introduction

Following the results of the previous reports, we will continue to explore AIDS disease. When developing a therapy, it is important to understand the main proteins that are related to a given characteristic (disease) and the proteins those protein interact with (their interactome). In previous reports, I already identified the proteins that were associated with Acquired Immunodeficiency Syndrome (AIDS) and HIV infection. Therefore, in this report, we focus on identifying their interactome and screen for possible targets of drugs therapies. In this work, I also analyze results of microarray available on ArrayExpress database in order to check the genes most related to this disease.

As starting point we should revisit the summary table (**Table 7.1**) from the first report where the main proteins related to AIDS are outlined.

3 Interactome

As already stated, we start by analyzing the previously identified proteins in STRING (<https://string-db.org>). In **Diagram 7.1** we can observe that the provided proteins are already associated with each other, and this result is expected from what was explained in the first report. The proteins from the first group (check **Table 7.1**) are all connected to each other and to *CXCL12*, in the other hand *CCL3L1* is only associated with β -chemokine (*CCR5* and *CCR2*). Proteins from group 3 are not related to each other nor to proteins in the remaining groups.

Then, we search for the interactome of the proteins of interest (**Diagram 7.2** and **Diagram 7.3**) and we can conclude that all these proteins are connected by some link (**Diagram 7.2**: 30 interactors in the first shell), but the network was further expanded (adding 15 interactors in the second shell) to retrieve most of the information available from the interactome.

With the final network (**Diagram 7.3**) we retrieve the pathways associated with that set of proteins, results were obtained from STRING (KEGG Pathways) - **Table 7.5** - and from Reactome (<http://www.reactome.org> using "Analyze Data" menu) - **Table 7.6**. Compiling information from both sources, we can postulate that the pathways more common (in quantity), in that set of proteins, are related to Immune System (more specifically Adaptive Immune System) and several types of signaling (Interferon Signaling, Cytokine Signaling, Signaling by Interleukins and Jak-STAT signaling pathway) as well as Cytokine-cytokine receptor interaction. These are the most common pathways for this set but also seem to be the most relevant ones (percentage of the total proteins that compose a pathway), which could also join the other pathways like general Signal Transduction, Metabolism of proteins, Post-translational protein modification, even Innate Immune System and lastly Disease. There were identified other pathways that seem interesting because they are related to HIV Infection, like HIV Life Cycle, Early Phase of HIV Life Cycle and

also Host Interactions of HIV factors. We can conclude that seems to be the right track to find targets so that a therapy can be developed.

These results make sense to what one would expect, so we can assume that on the develop network there might be a good target to exploit and develop a therapy to treat HIV or prevent AIDS. Also, it is normal that we see many signaling pathways as chemokines are involved in chemotaxis (response to chemical stimulus) and play a major role in inflammatory process. Moreover, there is many cytokines (category of proteins to which chemokines belongs) present which are important in cell signaling

Cytoscape software (<http://www.cytoscape.org>) was also used to compare the network results, but they are not show. It yields much bigger networks and since I could query all the proteins at once using STRING, Cytoscape did not seem necessary.

4 Microarray analysis

From ArrayExpress database were selected two studies of transcriptome analysis by microarray (**E-GEOD-57730** - *Microarray analysis of whole-blood in HIV-infected Viremic Non Progressor patients* and **E-GEOD-16363** - *Transcription profiling by array of human lymphatic tissue from HIV-1 infected individuals*) which seemed to be interesting because unlike others they provided general information about AIDS. That is, they allowed comparison between expression of individuals with a different AIDS stage and did not relate AIDS with other diseases like most of the studies available. Also, the array used in both studies (A-AFFY-44 - Affymetrix GeneChip Human Genome U133 Plus 2.0) allowed the analysis of the results with the tools used in the lectures.

I chose to present only the results for the second study (**E-GEOD-16363** - *Transcription profiling by array of human lymphatic tissue from HIV-1 infected individuals*) because despite being more hard to analyze and process the data (as there are much more rows than the first study, and more disease states) it yields more informative results and that can be related to the analysis performed until here. In this study several stages (control, asymptomatic HIV-1 infection, acute HIV-1 infection and AIDS) of the disease are compared which is an advantage compared to the other study (which only compared the progression to AIDS after the infection).

To make the analysis faster I created the design matrix loading the R script made available by the author, and then compare all other stages to the control, and between themselves. This will probably reveal proteins that affect each phase (like HIV infection, or progression to AIDS) in contrast to the first study, where such proteins did not appear.

The results outputted (list of UniProt ID's with differential expression - **Table 7.7**) from the R script seem to make sense. In the result set of proteins, it can be found some of the initial proteins like: *CCR5*, *IFNG* and *CCL3L1*. This makes sense, we have several sources corroborating and

stating that *CCR5* plays a major role on HIV infection and AIDS progression, also from the network analysis we can see that *IFNG* interacts with many proteins, and it is known that it has immunoregulatory functions and is an activator of macrophages. *CCL3L1* is affected which as well is expected since it interacts with *CCR5* and this one as we seen has differences in its expression. On the result list, we can also observe proteins that belong to the interactome that we discovered like: *CXCL10*, *IRF1*, *CCL5*, *STAT1*, *CCL4*, *IL2*, *CCL3* and *TBX21*. It should be noted that for comparison of results each gene symbol was transformed in the corresponding entry of SwissProt by adapting the script that provides the SwissProt IDs from the array.

Analyzing the pathways of the result set (using KEGG - **Table 7.9** - and Reactome - **Table 7.10**) we get similar results, that is the pathways are similar to the ones discovered of the interactome. To be more explicit those pathways are Cytokine-cytokine receptor interaction (related to the C-C and C-X-C), Natural killer cell mediated cytotoxicity (related with the way IFNG acts), Signal Transduction, Immune System, Metabolism, Innate Immune System, Adaptive Immune System and Disease. Also, there were some pathways that were not that relevant before, but seem to be relevant of this study and this include: Gene expression (Transcription), Ribosome and Proteasome. Proteasome pathways are especially interesting because it is related to programmed cell death, which can be related to death of immune cells (like macrophages and T cells) when the individual reaches the AIDS stage.

Since ProteinOn was not working, I got the annotation of the proteins from the result set from DAVID (**Table 7.8**). We can see that they are mostly cytosol proteins and associated with ribosomes (probably because they are involved in gene expression). The processes that they are involved with yield similar results to the analysis of pathways, like the following processes: defense response to virus, immune response and inflammatory response. The same is valid for molecular function, where we get: protein binding, receptor activity, chemokine activity and *CCR5* chemokine receptor binding, which as we seen (on this and previous report) is related to the signaling activity (for example of the chemokines).

5 Drug target discovery

Since AIDS and HIV infection are two highly studied diseases it is natural that there are several drugs therapies available. Searching DrugBank (<https://www.drugbank.ca/>) we can see that it identifies 3 targets related with AIDS: Chitosanase, Sodium/nucleoside cotransporter 1 and Integrin beta-7, being the last the most important as it allows the main trigger of AIDS. It also identifies several targets related with HIV. All this information is summarized at **Table 7.11**.

From the DrugBank research we can see that some of the proteins identified before (interactome and microarray analysis) are targets for drug therapies, this includes: *CCR5*, *CXCR4*, *CCR2* and others mentioned in the network. These targets have been used to develop several drugs each.

This allows me to conclude that the pathways they are being targeted are the same I already mentioned before, which will allow to use other proteins of those pathways in hope to get better results.

Likewise, a summary of information retrieved from FDA approved drugs (**Table 7.12**) is available stating some analogues for the drugs approved. An important one to highlight is Maraviroc which acts as antagonist of *CCR5*, which is being sold and used right now, this proves the importance of *CCR5* in HIV infection.

6 Conclusion

This final work gave some light to the investigation that I was doing related to the AIDS disease during this course. It proves some of my findings correct, corroborating the idea that the proteins selected could be potential targets to a drug therapy.

It allowed to analyze the interactome of my selected proteins in order to retrieve more proteins that could be relevant. It also provided the tools to analyze microarray data available in public databases, which can be useful get new information and prove or disprove one's findings.

Related to the drugs targets, it can be seen that, some of the identified proteins are also identified as targets. But no further conclusions were performed since this topic is confusing and was hard to find the pathways involved.

7 Appendix

7.1 Review

Table 7.1 - Human genes involved in AIDS with respective proteins names and IDs

Group	OMIM	Gene	Protein	UniProt
1	601373	CCR5	C-C chemokine receptor type 5	P51681
	162643	CCR2	C-C chemokine receptor type 2	P41597
	162643	CXCR4	C-X-C chemokine receptor type 4	P61073
	146929	CXCR1	C-X-C chemokine receptor type 1	P25024
2	601395	CCL3L1	C-C chemokine ligand 3-like 1	P16619
	600835	CXCL12	C-X-C Motif Chemokine Ligand 12 Stromal Cell-Derived Factor 1	P48061
3	147570	IFNG	Interferon- γ	P01579
	604946	KIR3DL1	Killer cell immunoglobulin-like receptor 3DL1 (Three Domains, Long cytoplasmic tail, 1)	P43629
	147781	IL4R	Interleukin 4 Receptor	P24394

7.2 Interactome

7.2.1 STRING

7.2.1.1 Query proteins

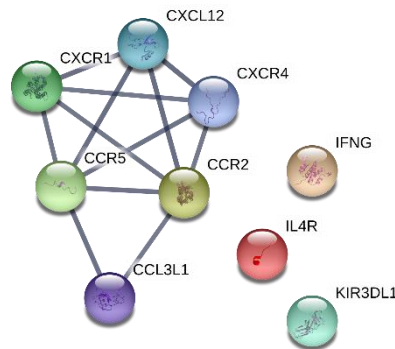


Diagram 7.1 - Network from STRING illustrating the associations between proteins of interest from **Table 7.1**. Results obtained using all sources, highest confidence for interaction score (0.9) and the edges represent confidence in the interaction: the ticker the line the stronger is data support.

Table 7.2 – Information about the proteins from **Table 7.1** available on STRING. UniProt (reviewed - Swiss-Prot) ID was obtain using the gene name in Bioconductor package for R.

Protein	Description	UniProt ID
CCL3L1	Chemokine (C-C motif) ligand 3-like 1; Chemotactic for lymphocytes and monocytes. Is a ligand for CCR1, CCR3 and CCR5. Is an inhibitor of HIV-1-infection. The processed form LD78-beta(3-70) shows a 20-fold to 30-fold higher chemotactic activity and is a very potent inhibitor of HIV-1- infection. LD78-beta(3-70) is also a ligand for CCR1, CCR3 and CCR5 (93 aa)	P16619

CCR2	Chemokine (C-C motif) receptor 2; Receptor for the CCL2, CCL7 and CCL13 chemokines. Transduces a signal by increasing intracellular calcium ion levels. Alternative coreceptor with CD4 for HIV-1 infection (374 aa)	P41597
CCR5	Chemokine (C-C motif) receptor 5 (gene/pseudogene); Receptor for a number of inflammatory CC-chemokines including MIP-1-alpha, MIP-1-beta and RANTES and subsequently transduces a signal by increasing the intracellular calcium ion level. May play a role in the control of granulocytic lineage proliferation or differentiation. Acts as a coreceptor (CD4 being the primary receptor) for HIV-1 R5 isolates (352 aa)	P51681
CXCL12	Chemokine (C-X-C motif) ligand 12; Chemoattractant active on T-lymphocytes, monocytes, but not neutrophils. Activates the C-X-C chemokine receptor CXCR4 to induce a rapid and transient rise in the level of intracellular calcium ions and chemotaxis. Also binds to atypical chemokine receptor ACKR3, which activates the beta-arrestin pathway and acts as a scavenger receptor for SDF-1. SDF-1-beta(3-72) and SDF-1- alpha(3-67) show a reduced chemotactic activity. Binding to cell surface proteoglycans seems to inhibit formation of SDF-1-alpha(3- 67) and thus to preserve activity on local sites [...] (140 aa)	P48061
CXCR1	Chemokine (C-X-C motif) receptor 1; Receptor to interleukin-8, which is a powerful neutrophils chemotactic factor. Binding of IL-8 to the receptor causes activation of neutrophils. This response is mediated via a G-protein that activate a phosphatidylinositol-calcium second messenger system. This receptor binds to IL-8 with a high affinity and to MGSA (GRO) with a low affinity (350 aa)	P25024
CXCR4	Chemokine (C-X-C motif) receptor 4; Receptor for the C-X-C chemokine CXCL12/SDF-1 that transduces a signal by increasing intracellular calcium ion levels and enhancing MAPK1/MAPK3 activation. Acts as a receptor for extracellular ubiquitin; leading to enhanced intracellular calcium ions and reduced cellular cAMP levels. Involved in hematopoiesis and in cardiac ventricular septum formation. Also plays an essential role in vascularization of the gastrointestinal tract, probably by regulating vascular branching and/or remodeling processes in endothelial cells. Involved in cerebellar develo [...] (356 aa)	P61073
IFNG	Interferon, gamma; Produced by lymphocytes activated by specific antigens or mitogens. IFN-gamma, in addition to having antiviral activity, has important immunoregulatory functions. It is a potent activator of macrophages, it has antiproliferative effects on transformed cells and it can potentiate the antiviral and antitumor effects of the type I interferons (166 aa)	P01579
IL4R	Interleukin 4 receptor; Receptor for both interleukin 4 and interleukin 13. Couples to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in promoting Th2 differentiation. The IL4/IL13 responses are involved in regulating IgE production and, chemokine and mucus production at sites of allergic inflammation. In certain cell types, can signal through activation of insulin receptor substrates, IRS1/IRS2 (825 aa)	P24394
KIR3DL1	Killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 1; Receptor on natural killer (NK) cells for HLA Bw4 allele. Inhibits the activity of NK cells thus preventing cell lysis (444 aa)	P43629

Table 7.3 - KEGG Pathways of the network displayed in **Diagram 7.1** (proteins from **Table 7.1**), results obtained from STRING.

Pathway ID	Pathway description	# genes	False discovery rate
4060	Cytokine-cytokine receptor interaction	8	1.56e-12
4062	Chemokine signaling pathway	6	4.7e-09
5323	Rheumatoid arthritis	3	0.000546
4144	Endocytosis	3	0.00471
5332	Graft-versus-host disease	2	0.00617
4672	Intestinal immune network for IgA production	2	0.00771
4612	Antigen processing and presentation	2	0.013
5321	Inflammatory bowel disease (IBD)	2	0.013
5132	Salmonella infection	2	0.0175

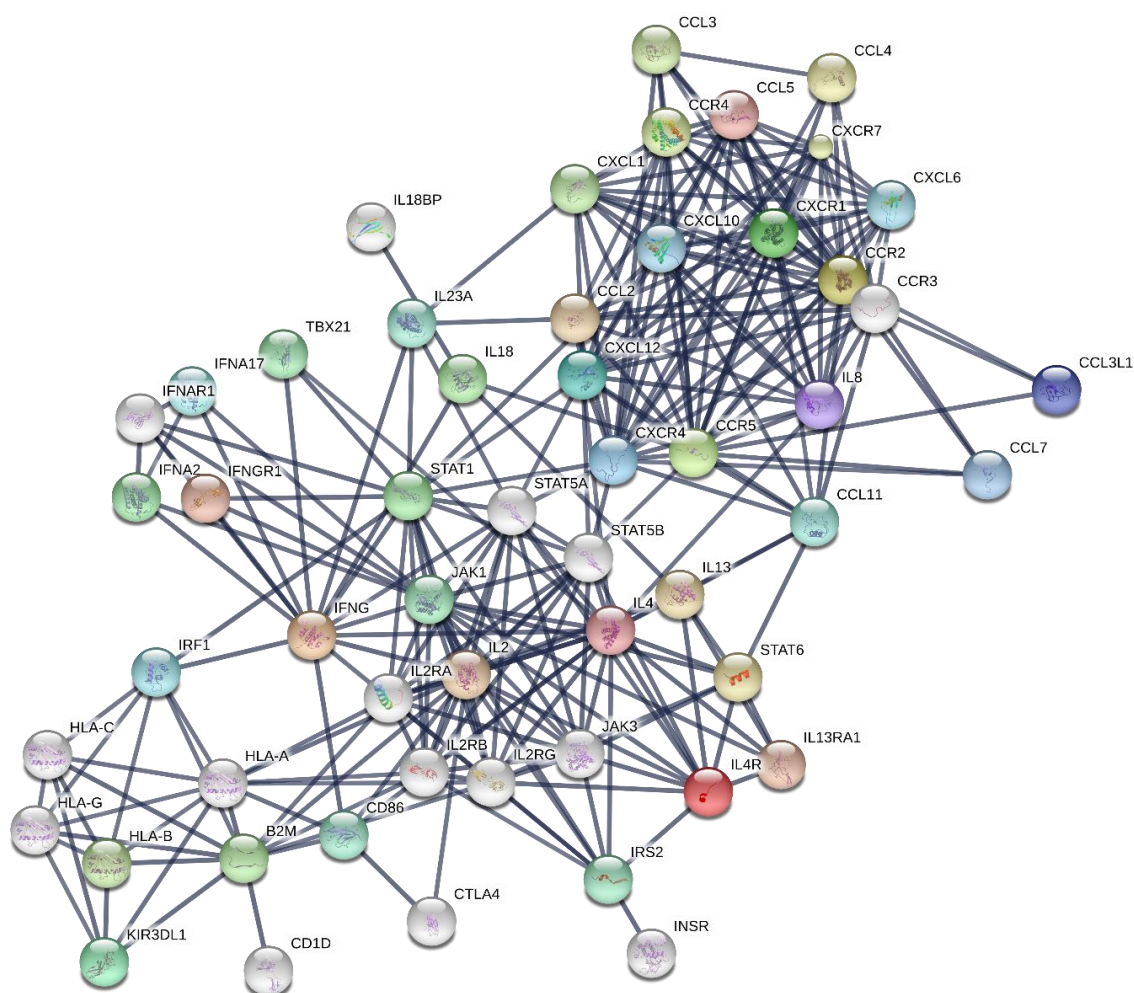


Table 7.4 – Interactors with proteins from **Table 7.1**, results collected from STRING (same as network shown in **Diagram 7.3**). Table displays protein name with respective description, results are sorted by score (confidence in interaction). UniProt (reviewed - Swiss-Prot) ID was obtain using the gene name in Bioconductor package for R.

Protein	Description	UniProt ID	Score
IL8	Interleukin 8; IL-8 is a chemotactic factor that attracts neutrophils, basophils, and T-cells, but not monocytes. It is also involved in neutrophil activation. It is released from several cell types in response to an inflammatory stimulus. IL-8(6-77) has a 5-10-fold higher activity on neutrophil activation, IL-8(5-77) has increased activity on neutrophil activation and IL-8(7-77) has a higher affinity to receptors CXCR1 and CXCR2 as compared to IL-8(1-77), respectively (99 aa)	P10145	0.998
IL4	Interleukin 4; Participates in at least several B-cell activation processes as well as of other cell types (PubMed-3016727). It is a costimulator of DNA-synthesis. It induces the expression of class II MHC molecules on resting B-cells. It enhances both secretion and cell surface expression of IgE and IgG1. It also regulates the expression of the low affinity Fc receptor for IgE (CD23) on both lymphocytes and monocytes. Positively regulates IL31RA expression in macrophages (By similarity) (153 aa)	P05112	0.998
CCL5	Chemokine (C-C motif) ligand 5; Chemoattractant for blood monocytes, memory T-helper cells and eosinophils. Causes the release of histamine from basophils and activates eosinophils. May activate several chemokine receptors including CCR1, CCR3, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant RANTES protein induces a	P13501	0.997

	dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV). The processed form RANTES(3-68) acts as a natural chemotaxis inhibitor and is a more potent inhibitor of HIV-1- infection. [...] (91 aa)		
IFNGR1	Interferon gamma receptor 1; Associates with IFNGR2 to form a receptor for the cytokine interferon gamma (IFNG) (PubMed-7615558, PubMed-2971451, PubMed-7617032, PubMed-10986460). Ligand binding stimulates activation of the JAK/STAT signaling pathway (PubMed-7673114) (489 aa)	P15260	0.996
IL13RA1	Interleukin 13 receptor, alpha 1; Binds with low affinity to interleukin-13 (IL13). Together with IL4RA can form a functional receptor for IL13. Also serves as an alternate accessory protein to the common cytokine receptor gamma chain for interleukin-4 (IL4) signaling, but cannot replace the function of IL2RG in allowing enhanced interleukin-2 (IL2) binding activity (427 aa)	P78552	0.996
IL2	Interleukin 2; Produced by T-cells in response to antigenic or mitogenic stimulation, this protein is required for T-cell proliferation and other activities crucial to regulation of the immune response. Can stimulate B-cells, monocytes, lymphokine- activated killer cells, natural killer cells, and glioma cells (153 aa)	P60568	0.995
CCL2	Chemokine (C-C motif) ligand 2; Chemotactic factor that attracts monocytes and basophils but not neutrophils or eosinophils. Augments monocyte anti-tumor activity. Has been implicated in the pathogenesis of diseases characterized by monocytic infiltrates, like psoriasis, rheumatoid arthritis or atherosclerosis. May be involved in the recruitment of monocytes into the arterial wall during the disease process of atherosclerosis (99 aa)	P13500	0.994
IL13	Interleukin 13; Cytokine (PubMed-8096327, PubMed-8097324). Inhibits inflammatory cytokine production (PubMed-8096327). Synergizes with IL2 in regulating interferon-gamma synthesis (PubMed-8096327). May be critical in regulating inflammatory and immune responses (PubMed-8096327, PubMed-8097324). Positively regulates IL31RA expression in macrophages (By similarity) (146 aa)	P35225	0.994
STAT6	Signal transducer and activator of transcription 6, interleukin-4 induced; Carries out a dual function- signal transduction and activation of transcription. Involved in IL4/interleukin-4- and IL3/interleukin-3-mediated signaling (847 aa)	P42226	0.993
CCL4	Chemokine (C-C motif) ligand 4; Monokine with inflammatory and chemokinetic properties. Binds to CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-beta induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV). The processed form MIP-1-beta(3-69) retains the abilities to induce down-modulation of surface expression of the chemokine receptor CCR5 and to inhibit the CCR5- mediated entry of HIV-1 in T-cells. MIP-1-beta(3-69) is also a ligand for CCR1 and CCR2 isoform B (92 aa)	P13236	0.991
CXCR7	Chemokine (C-X-C motif) receptor 7; Atypical chemokine receptor that controls chemokine levels and localization via high-affinity chemokine binding that is uncoupled from classic ligand-driven signal transduction cascades, resulting instead in chemokine sequestration, degradation, or transcytosis. Also known as interceptor (internalizing receptor) or chemokine-scavenging receptor or chemokine decoy receptor. Acts as a receptor for chemokines CXCL11 and CXCL12/SDF1. Chemokine binding does not activate G-protein- mediated signal transduction but instead induces beta-arrestin recruitment, [...] (362 aa)	P25106	0.990
CCR4	Chemokine (C-C motif) receptor 4; High affinity receptor for the C-C type chemokines CCL17/TARC, CCL22/MDC and CKLF isoform 1/CKLF1. The activity of this receptor is mediated by G(i) proteins which activate a phosphatidylinositol-calcium second messenger system. Can function as a chemoattractant homing receptor on circulating memory lymphocytes and as a coreceptor for some primary HIV-2 isolates. In the CNS, could mediate hippocampal-neuron survival (360 aa)	P51679	0.989
CCL3	Chemokine (C-C motif) ligand 3; Monokine with inflammatory and chemokinetic properties. Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV) (92 aa)	P10147	0.989
HLA-B	Major histocompatibility complex, class I, B; Involved in the presentation of foreign antigens to the immune system (362 aa)		0.987
CXCL1	Chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha); Has chemotactic activity for neutrophils. May play a role in inflammation and exerts its effects on endothelial cells in an autocrine fashion.	P09341	0.986

	In vitro, the processed forms GRO- alpha(4-73), GRO-alpha(5-73) and GRO-alpha(6-73) show a 30-fold higher chemotactic activity (107 aa)		
B2M	Beta-2-microglobulin; Component of the class I major histocompatibility complex (MHC). Involved in the presentation of peptide antigens to the immune system (119 aa)	P61769	0.986
IL18	Interleukin 18 (interferon-gamma-inducing factor); Augments natural killer cell activity in spleen cells and stimulates interferon gamma production in T-helper type I cells (193 aa)	Q14116	0.985
STAT1	Signal transducer and activator of transcription 1, 91kDa; Signal transducer and transcription activator that mediates cellular responses to interferons (IFNs), cytokine KITLG/SCF and other cytokines and other growth factors. Following type I IFN (IFN-alpha and IFN-beta) binding to cell surface receptors, signaling via protein kinases leads to activation of Jak kinases (TYK2 and JAK1) and to tyrosine phosphorylation of STAT1 and STAT2. The phosphorylated STATs dimerize and associate with ISGF3G/IRF-9 to form a complex termed ISGF3 transcription factor, that enters the nucleus. ISGF3 bi [...] (750 aa)	P42224	0.984
IFNA2	Interferon, alpha 2; Produced by macrophages, IFN-alpha have antiviral activities (188 aa)	P01563	0.984
TBX21	T-box 21; Transcription factor that controls the expression of the TH1 cytokine, interferon-gamma. Initiates TH1 lineage development from naive TH precursor cells both by activating TH1 genetic programs and by repressing the opposing TH2 programs (535 aa)	Q9UL17	0.984
JAK1	Janus kinase 1; Tyrosine kinase of the non-receptor type, involved in the IFN-alpha/beta/gamma signal pathway (PubMed-7615558). Kinase partner for the interleukin (IL)-2 receptor (PubMed-11909529) (1154 aa)	P23458	0.983
IRS2	Insulin receptor substrate 2; May mediate the control of various cellular processes by insulin (1338 aa)	Q9Y4H2	0.983
CD86	CD86 molecule; Receptor involved in the costimulatory signal essential for T-lymphocyte proliferation and interleukin-2 production, by binding CD28 or CTLA-4. May play a critical role in the early events of T-cell activation and costimulation of naive T-cells, such as deciding between immunity and anergy that is made by T- cells within 24 hours after activation. Isoform 2 interferes with the formation of CD86 clusters, and thus acts as a negative regulator of T-cell activation (329 aa)	P42081	0.982
IL23A	Interleukin 23, alpha subunit p19; Associates with IL12B to form the IL-23 interleukin, a heterodimeric cytokine which functions in innate and adaptive immunity. IL-23 may constitute with IL-17 an acute response to infection in peripheral tissues. IL-23 binds to a heterodimeric receptor complex composed of IL12RB1 and IL23R, activates the Jak- Stat signaling cascade, stimulates memory rather than naive T- cells and promotes production of proinflammatory cytokines. IL-23 induces autoimmune inflammation and thus may be responsible for autoimmune inflammatory diseases and may be important [...] (189 aa)	Q9NPF7	0.982
CCL11	Chemokine (C-C motif) ligand 11; In response to the presence of allergens, this protein directly promotes the accumulation of eosinophils, a prominent feature of allergic inflammatory reactions. Binds to CCR3 (97 aa)	P51671	0.982
IFNA17	Interferon, alpha 17; Produced by macrophages, IFN-alpha have antiviral activities. Interferon stimulates the production of two enzymes- a protein kinase and an oligoadenylate synthetase (189 aa)	P01571	0.982
IRF1	Interferon regulatory factor 1; Transcriptional regulator which displays a remarkable functional diversity in the regulation of cellular responses. These include the regulation of IFN and IFN-inducible genes, host response to viral and bacterial infections, regulation of many genes expressed during hematopoiesis, inflammation, immune responses and cell proliferation and differentiation, regulation of the cell cycle and induction of growth arrest and programmed cell death following DNA damage. Stimulates both innate and acquired immune responses through the activation of specific target [...] (325 aa)	P10914	0.982
CXCL6	Chemokine (C-X-C motif) ligand 6; Chemotactic for neutrophil granulocytes. Signals through binding and activation of its receptors (CXCR1 and CXCR2). In addition to its chemotactic and angiogenic properties, it has strong antibacterial activity against Gram-positive and Gram- negative bacteria (90-fold-higher when compared to CXCL5 and CXCL7) (114 aa)	P80162	0.981
CXCL10	Chemokine (C-X-C motif) ligand 10; Chemotactic for monocytes and T-lymphocytes. Binds to CXCR3 (98 aa)	P02778	0.979

CCL7	Chemokine (C-C motif) ligand 7; Chemotactic factor that attracts monocytes and eosinophils, but not neutrophils. Augments monocyte anti-tumor activity. Also induces the release of gelatinase B. This protein can bind heparin. Binds to CCR1, CCR2 and CCR3 (99 aa)	P80098	0.978
------	---	--------	-------

7.2.1 Pathways (STRING and Reactome)

Table 7.5 - KEGG Pathways of the network displayed in **Diagram 7.3**, results obtained from STRING.

Pathway ID	Pathway description	# genes	False discovery rate
4060	Cytokine-cytokine receptor interaction	34	2.77E-49
4062	Chemokine signaling pathway	21	9.33E-28
4630	Jak-STAT signaling pathway	20	2.36E-27
5162	Measles	16	2.96E-21
5323	Rheumatoid arthritis	13	2.34E-18
5321	Inflammatory bowel disease (IBD)	12	2.88E-18
5320	Autoimmune thyroid disease	10	2.12E-15
5168	Herpes simplex infection	13	2.28E-14
4620	Toll-like receptor signaling pathway	11	6.21E-14
5164	Influenza A	12	4.00E-13
5330	Allograft rejection	8	6.16E-13
5332	Graft-versus-host disease	8	9.37E-13
4650	Natural killer cell mediated cytotoxicity	10	1.80E-11
5203	Viral carcinogenesis	11	2.70E-11
5166	HTLV-I infection	12	3.55E-11
4940	Type I diabetes mellitus	7	1.86E-10
5132	Salmonella infection	8	6.43E-10
4151	PI3K-Akt signaling pathway	12	9.34E-10
4144	Endocytosis	10	1.06E-09
5161	Hepatitis B	9	1.40E-09
5142	Chagas disease (American trypanosomiasis)	8	2.08E-09
4612	Antigen processing and presentation	7	5.38E-09
4623	Cytosolic DNA-sensing pathway	6	1.57E-07
5152	Tuberculosis	8	1.73E-07
5160	Hepatitis C	7	5.07E-07
4672	Intestinal immune network for IgA production	5	1.18E-06
5416	Viral myocarditis	5	3.55E-06
4621	NOD-like receptor signaling pathway	5	3.75E-06
5169	Epstein-Barr virus infection	7	6.24E-06
5140	Leishmaniasis	5	1.00E-05
4514	Cell adhesion molecules (CAMs)	6	1.42E-05

5144	Malaria	4	5.84E-05
5145	Toxoplasmosis	5	9.99E-05
4380	Osteoclast differentiation	5	1.53E-04
5120	Epithelial cell signaling in Helicobacter pylori infection	4	2.14E-04
4622	RIG-I-like receptor signaling pathway	4	2.49E-04
4917	Prolactin signaling pathway	4	2.49E-04
5133	Pertussis	4	2.49E-04
5310	Asthma	3	4.00E-04
4640	Hematopoietic cell lineage	4	5.38E-04
4660	T cell receptor signaling pathway	4	9.12E-04
4140	Regulation of autophagy	3	1.02E-03
5146	Amoebiasis	4	1.09E-03
4668	TNF signaling pathway	4	1.15E-03
5134	Legionellosis	3	2.37E-03
4145	Phagosome	4	3.35E-03
5200	Pathways in cancer	5	9.36E-03
4064	NF-kappa B signaling pathway	3	9.74E-03
4066	HIF-1 signaling pathway	3	1.49E-02
5143	African trypanosomiasis	2	1.97E-02
5340	Primary immunodeficiency	2	2.17E-02
4930	Type II diabetes mellitus	2	3.48E-02
4932	Non-alcoholic fatty liver disease (NAFLD)	3	3.74E-02
5202	Transcriptional misregulation in cancer	3	4.85E-02
5221	Acute myeloid leukemia	2	4.85E-02

Table 7.6 - Reactome Pathways of the network displayed in **Diagram 7.3** results obtained from using “Analyze Data” menu from Reactome. Results are sorted in descending order by the ration of the number of entities found to the total number of entities of a pathway.

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-162582	Signal Transduction	26	2925	2.19E-01	2.34E-01
R-HSA-168256	Immune System	87	2616	1.95E-01	1.11E-16
R-HSA-392499	Metabolism of proteins	6	2266	1.69E-01	1.00E+00
R-HSA-168249	Innate Immune System	17	1540	1.15E-01	8.04E-02
R-HSA-597592	Post-translational protein modification	1	1524	1.14E-01	1.00E+00

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-372790	Signaling by GPCR	21	1509	1.13E-01	5.10E-03
R-HSA-1643685	Disease	6	1496	1.12E-01	9.78E-01
R-HSA-74160	Gene expression (Transcription)	1	1473	1.10E-01	1.00E+00
R-HSA-73857	RNA Polymerase II Transcription	1	1263	9.44E-02	1.00E+00
R-HSA-1266738	Developmental Biology	4	1164	8.70E-02	9.82E-01
R-HSA-388396	GPCR downstream signaling	19	1140	8.52E-02	1.06E-03
R-HSA-212436	Generic Transcription Pathway	1	1123	8.39E-02	1.00E+00
R-HSA-1280218	Adaptive Immune System	39	1086	8.11E-02	1.11E-16
R-HSA-1280215	Cytokine Signaling in Immune system	84	1006	7.52E-02	1.11E-16
R-HSA-109582	Hemostasis	7	798	5.96E-02	4.17E-01
R-HSA-8953854	Metabolism of RNA	1	782	5.84E-02	9.98E-01
R-HSA-449147	Signaling by Interleukins	40	688	5.14E-02	1.11E-16
R-HSA-422475	Axon guidance	3	603	4.51E-02	8.48E-01
R-HSA-500792	GPCR ligand binding	18	592	4.42E-02	6.19E-07
R-HSA-8953897	Cellular responses to external stimuli	2	592	4.42E-02	9.45E-01
R-HSA-5663205	Infectious disease	3	532	3.97E-02	7.81E-01
R-HSA-166520	Signalling by NGF	4	521	3.89E-02	5.72E-01
R-HSA-2262752	Cellular responses to stress	2	505	3.77E-02	9.04E-01
R-HSA-881907	Gastrin-CREB signalling pathway via PKC and MAPK	3	504	3.77E-02	7.49E-01
R-HSA-2454202	Fc epsilon receptor (FCERI) signaling	4	496	3.71E-02	5.33E-01
R-HSA-3700989	Transcriptional Regulation by TP53	1	485	3.62E-02	9.78E-01
R-HSA-6798695	Neutrophil degranulation	5	480	3.59E-02	3.10E-01
R-HSA-983169	Class I MHC mediated antigen processing & presentation	36	464	3.47E-02	1.11E-16
R-HSA-5663202	Diseases of signal transduction	3	463	3.46E-02	6.96E-01
R-HSA-187037	NGF signalling via TRKA from the plasma membrane	4	427	3.19E-02	4.18E-01
R-HSA-186797	Signaling by PDGF	6	420	3.14E-02	1.06E-01
R-HSA-2172127	DAP12 interactions	6	409	3.06E-02	9.63E-02

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-177929	Signaling by EGFR	4	402	3.00E-02	3.74E-01
R-HSA-373076	Class A/1 (Rhodopsin-like receptors)	18	401	3.00E-02	1.81E-09
R-HSA-2424491	DAP12 signaling	5	392	2.93E-02	1.85E-01
R-HSA-186763	Downstream signal transduction	6	389	2.91E-02	8.03E-02
R-HSA-194138	Signaling by VEGF	3	381	2.85E-02	5.64E-01
R-HSA-2871796	FCERI mediated MAPK activation	3	377	2.82E-02	5.57E-01
R-HSA-4420097	VEGFA-VEGFR2 Pathway	3	372	2.78E-02	5.48E-01
R-HSA-1433557	Signaling by SCF-KIT	6	367	2.74E-02	6.45E-02
R-HSA-74752	Signaling by Insulin receptor	3	349	2.61E-02	5.05E-01
R-HSA-448424	Interleukin-17 signaling	3	332	2.48E-02	4.72E-01
R-HSA-418594	G alpha (i) signalling events	17	329	2.46E-02	6.70E-10
R-HSA-2404192	Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R)	3	327	2.44E-02	4.62E-01
R-HSA-2428924	IGF1R signaling cascade	3	326	2.44E-02	4.60E-01
R-HSA-2428928	IRS-related events triggered by IGF1R	3	325	2.43E-02	4.58E-01
R-HSA-74751	Insulin receptor signalling cascade	3	324	2.42E-02	4.56E-01
R-HSA-5683057	MAPK family signaling cascades	3	324	2.42E-02	4.56E-01
R-HSA-983705	Signaling by the B Cell Receptor (BCR)	2	322	2.41E-02	7.12E-01
R-HSA-112399	IRS-mediated signalling	3	321	2.40E-02	4.50E-01
R-HSA-198933	Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell	37	316	2.36E-02	1.11E-16
R-HSA-375165	NCAM signaling for neurite out-growth	3	305	2.28E-02	4.17E-01
R-HSA-76002	Platelet activation, signaling and aggregation	2	305	2.28E-02	6.83E-01
R-HSA-512988	Interleukin-3, 5 and GM-CSF signaling	3	293	2.19E-02	3.93E-01
R-HSA-913531	Interferon Signaling	47	292	2.18E-02	1.11E-16
R-HSA-8853659	RET signaling	3	292	2.18E-02	3.91E-01
R-HSA-187687	Signalling to ERKs	3	287	2.14E-02	3.80E-01
R-HSA-5218921	VEGFR2 mediated cell proliferation	3	285	2.13E-02	3.76E-01
R-HSA-451927	Interleukin-2 signaling	3	284	2.12E-02	3.74E-01
R-HSA-167044	Signalling to RAS	3	278	2.08E-02	3.61E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-912526	Interleukin receptor SHC signaling	3	277	2.07E-02	3.59E-01
R-HSA-169893	Prolonged ERK activation events	3	276	2.06E-02	3.57E-01
R-HSA-2586552	Signaling by Leptin	3	275	2.05E-02	3.55E-01
R-HSA-5684996	MAPK1/MAPK3 signaling	3	274	2.05E-02	3.53E-01
R-HSA-170968	Frs2-mediated activation	3	274	2.05E-02	3.53E-01
R-HSA-187706	Signalling to p38 via RIT and RIN	3	272	2.03E-02	3.49E-01
R-HSA-170984	ARMS-mediated activation	3	272	2.03E-02	3.49E-01
R-HSA-112412	SOS-mediated signalling	3	267	1.99E-02	3.38E-01
R-HSA-5673001	RAF/MAP kinase cascade	3	267	1.99E-02	3.38E-01
R-HSA-179812	GRB2 events in EGFR signaling	3	267	1.99E-02	3.38E-01
R-HSA-180336	SHC1 events in EGFR signaling	3	267	1.99E-02	3.38E-01
R-HSA-162906	HIV Infection	3	256	1.91E-02	3.15E-01
R-HSA-2730905	Role of LAT2/NTAL/LAB on calcium mobilization	2	245	1.83E-02	5.64E-01
R-HSA-1168372	Downstream signaling events of B Cell Receptor (BCR)	2	225	1.68E-02	5.18E-01
R-HSA-6785807	Interleukin-4 and 13 signaling	18	212	1.58E-02	6.00E-14
R-HSA-2559583	Cellular Senescence	2	199	1.49E-02	4.54E-01
R-HSA-375276	Peptide ligand-binding receptors	18	194	1.45E-02	1.35E-14
R-HSA-1236975	Antigen processing-Cross presentation	36	186	1.39E-02	1.11E-16
R-HSA-983231	Factors involved in megakaryocyte development and platelet production	5	179	1.34E-02	1.27E-02
R-HSA-877300	Interferon gamma signaling	41	176	1.31E-02	1.11E-16
R-HSA-162587	HIV Life Cycle	2	171	1.28E-02	3.80E-01
R-HSA-1236974	ER-Phagosome pathway	36	164	1.23E-02	1.11E-16
R-HSA-381119	Unfolded Protein Response (UPR)	4	160	1.20E-02	3.56E-02
R-HSA-198203	PI3K/AKT activation	2	152	1.14E-02	3.27E-01
R-HSA-180292	GAB1 signalosome	2	152	1.14E-02	3.27E-01
R-HSA-1257604	PIP3 activates AKT signaling	2	149	1.11E-02	3.18E-01
R-HSA-162909	Host Interactions of HIV factors	1	148	1.11E-02	6.82E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-909733	Interferon alpha/beta signaling	43	141	1.05E-02	1.11E-16
R-HSA-6803157	Antimicrobial peptides	1	122	9.11E-03	6.11E-01
R-HSA-2219528	PI3K/AKT Signaling in Cancer	2	120	8.97E-03	2.36E-01
R-HSA-5617472	Activation of anterior HOX genes in hindbrain development during early embryogenesis	1	116	8.67E-03	5.92E-01
R-HSA-5619507	Activation of HOX genes during differentiation	1	116	8.67E-03	5.92E-01
R-HSA-199418	Negative regulation of the PI3K/AKT network	2	113	8.44E-03	2.16E-01
R-HSA-6811558	PI5P, PP2A and IER3 Regulate PI3K/AKT Signaling	2	105	7.84E-03	1.94E-01
R-HSA-983170	Antigen Presentation: Folding, assembly and peptide loading of class I MHC	36	102	7.62E-03	1.11E-16
R-HSA-446652	Interleukin-1 signaling	1	99	7.40E-03	5.35E-01
R-HSA-400253	Circadian Clock	1	99	7.40E-03	5.35E-01
R-HSA-109704	PI3K Cascade	1	98	7.32E-03	5.31E-01
R-HSA-388841	Costimulation by the CD28 family	1	97	7.25E-03	5.27E-01
R-HSA-1226099	Signaling by FGFR in disease	1	92	6.87E-03	5.09E-01
R-HSA-168928	RIG-I/MDA5 mediated induction of IFN-alpha/beta pathways	5	89	6.65E-03	6.63E-04
R-HSA-2219530	Constitutive Signaling by Aberrant PI3K in Cancer	2	89	6.65E-03	1.50E-01
R-HSA-2559582	Senescence-Associated Secretory Phenotype (SASP)	2	89	6.65E-03	1.50E-01
R-HSA-6783783	Interleukin-10 signaling	27	88	6.57E-03	1.11E-16
R-HSA-1834949	Cytosolic sensors of pathogen-associated DNA	1	88	6.57E-03	4.93E-01
R-HSA-1169408	ISG15 antiviral mechanism	2	83	6.20E-03	1.34E-01
R-HSA-1169410	Antiviral mechanism by IFN-stimulated genes	2	83	6.20E-03	1.34E-01
R-HSA-1236977	Endosomal/Vacuolar pathway	36	82	6.13E-03	1.11E-16
R-HSA-977225	Amyloid fiber formation	1	82	6.13E-03	4.69E-01
R-HSA-8852135	Protein ubiquitination	1	80	5.98E-03	4.61E-01
R-HSA-1368108	BMAL1:CLOCK,NPAS2 activates circadian gene expression	1	70	5.23E-03	4.17E-01
R-HSA-429914	Deadenylation-dependent mRNA decay	1	67	5.01E-03	4.04E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-6791312	TP53 Regulates Transcription of Cell Cycle Genes	1	65	4.86E-03	3.94E-01
R-HSA-114604	GPVI-mediated activation cascade	2	64	4.78E-03	8.76E-02
R-HSA-1236394	Signaling by ERBB4	2	59	4.41E-03	7.62E-02
R-HSA-397795	G-protein beta:gamma signalling	2	57	4.26E-03	7.19E-02
R-HSA-8866654	E3 ubiquitin ligases ubiquitinate target proteins	1	57	4.26E-03	3.56E-01
R-HSA-5655302	Signaling by FGFR1 in disease	1	57	4.26E-03	3.56E-01
R-HSA-392451	G beta:gamma signalling through PI3Kgamma	2	52	3.88E-03	6.13E-02
R-HSA-1461973	Defensins	1	50	3.74E-03	3.20E-01
R-HSA-380108	Chemokine receptors bind chemokines	18	48	3.59E-03	1.11E-16
R-HSA-1839124	FGFR1 mutant receptor activation	1	48	3.59E-03	3.09E-01
R-HSA-449836	Other interleukin signaling	1	43	3.21E-03	2.82E-01
R-HSA-389356	CD28 co-stimulation	1	40	2.99E-03	2.65E-01
R-HSA-1461957	Beta defensins	1	39	2.91E-03	2.60E-01
R-HSA-381042	PERK regulates gene expression	4	38	2.84E-03	2.30E-04
R-HSA-933541	TRAF6 mediated IRF7 activation	5	35	2.61E-03	8.65E-06
R-HSA-1251985	Nuclear signaling by ERBB4	2	33	2.47E-03	2.71E-02
R-HSA-380994	ATF4 activates genes	4	32	2.39E-03	1.20E-04
R-HSA-982772	Growth hormone receptor signaling	2	29	2.17E-03	2.13E-02
R-HSA-429947	Deadenylation of mRNA	1	29	2.17E-03	2.00E-01
R-HSA-164952	The role of Nef in HIV-1 replication and disease pathogenesis	1	29	2.17E-03	2.00E-01
R-HSA-912694	Regulation of IFNA signaling	7	28	2.09E-03	2.91E-09
R-HSA-112409	RAF-independent MAPK1/3 activation	1	28	2.09E-03	1.94E-01
R-HSA-6804115	TP53 regulates transcription of additional cell cycle genes whose exact role in the p53 pathway remain uncertain	1	28	2.09E-03	1.94E-01
R-HSA-6783589	Interleukin-6 family signaling	2	27	2.02E-03	1.87E-02
R-HSA-389513	CTLA4 inhibitory signaling	1	26	1.94E-03	1.81E-01
R-HSA-389357	CD28 dependent PI3K/Akt signaling	1	26	1.94E-03	1.81E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-1839117	Signaling by cytosolic FGFR1 fusion mutants	1	26	1.94E-03	1.81E-01
R-HSA-1834941	STING mediated induction of host immune responses	1	25	1.87E-03	1.75E-01
R-HSA-162594	Early Phase of HIV Life Cycle	2	23	1.72E-03	1.38E-02
R-HSA-164938	Nef-mediates down modulation of cell surface receptors by recruiting them to clathrin adapters	1	22	1.64E-03	1.56E-01
R-HSA-1266695	Interleukin-7 signaling	1	20	1.49E-03	1.43E-01
R-HSA-389359	CD28 dependent Vav1 pathway	1	18	1.34E-03	1.29E-01
R-HSA-877312	Regulation of IFNG signaling	4	16	1.20E-03	8.21E-06
R-HSA-6788467	IL-6-type cytokine receptor ligand interactions	1	15	1.12E-03	1.09E-01
R-HSA-173107	Binding and entry of HIV virion	2	13	9.71E-04	4.64E-03
R-HSA-447115	Interleukin-12 family signaling	2	13	9.71E-04	4.64E-03
R-HSA-110056	MAPK3 (ERK1) activation	1	13	9.71E-04	9.52E-02
R-HSA-112411	MAPK1 (ERK2) activation	1	12	8.97E-04	8.82E-02
R-HSA-164940	Nef mediated downregulation of MHC class I complex cell surface expression	1	11	8.22E-04	8.12E-02
R-HSA-74749	Signal attenuation	1	11	8.22E-04	8.12E-02
R-HSA-74713	IRS activation	1	7	5.23E-04	5.25E-02
R-HSA-448706	Interleukin-1 processing	1	7	5.23E-04	5.25E-02
R-HSA-3249367	STAT6-mediated induction of chemokines	1	5	3.74E-04	3.78E-02

7.3 Microarray analysis (ArrayExpress)

7.3.1 Protein Results (R)

Table 7.7 – Protein results of genes with differential expression output from the R script provided in the lectures. Study **E-GEOD-16363** - Transcription profiling by array of human lymphatic tissue from HIV-1 infected individuals, using array A-AFFY-44 - Affymetrix GeneChip Human Genome U133 Plus 2.0. Output of the script is UniProt ID, gene symbol retrieved with DAVID Gene Accession Conversion Tool.

UniProt ID	Gene Symbol	UniProt ID	Gene Symbol	UniProt ID	Gene Symbol
P00973	OAS1	Q8WXI9	GATAD2B	O75095	MEGF6
Q13765	NACA	Q86WA9	SLC26A11	Q6NT76	HMBOX1
Q71UM5	RPS27L	P01732	CD8A	O75582	RPS6KA5
Q9NTJ5	SACM1L	Q96FV3	TSPAN17	Q96AQ6	PBXIP1
Q4FZB7	KMT5B	Q13596	SNX1	P0C0L4	c4a
Q9BQ49	SMIM7	Q8IUI8	CRLF3	Q8IUK5	PLXDC1
P04733	Mt1f	A8MZ97	C2orf74	P0C0L5	C4B_2
Q92536	SLC7A6	Q13591	SEMA5A	P60228	EIF3E
Q9BYB4	GNB1L	Q99437	ATP6V0B	Q8WZ64	ARAP2
P31350	RRM2	Q9UGI6	KCNN3	P40305	IFI27
Q8N0W4	NLGN4X	Q13315	ATM	P40306	PSMB10
O95971	CD160	Q6J9G0	STYK1	Q7L8W6	DPH6
O95777	LSM8	O15091	KIAA0391	Q6UB99	ANKRD11
Q8IVG5	SAMD9L	B1AKI9	ISM1	Q96C92	SDCCAG3
P28062	PSMB8	P20591	MX1	Q96DX8	RTP4
A6NKT7	RGPD3	Q86VE9	SERINC5	P31941	APOBEC3A_B
O75558	STX11	P63208	SKP1	P47813	LOC107984923
Q96QP1	alpk1	Q8IVE3	PLEKHH2	Q06732	ZNF33B
Q96PP8	GBP5	Q5JUX0	SPIN3	Q9UJC3	HOOK1
Q9NRJ3	CCL28	Q5K651	SAMD9	Q5QGS0	KIAA2022
Q96PP9	GBP4	P01009	serpina1	Q9C002	C15ORF48
Q16822	PCK2	O75084	FZD7	Q06830	PRDX1
P28065	PSMB9	Q9UJA2	CRSL1	Q9HB21	PLEKHA1
P28066	PSMA5	Q13217	DNAJC3	Q8N8L6	ARL10
P06681	C2	P00813	ADA	Q9C000	NLRP1
Q96G42	KLHDC7B	Q13231	CHIT1	Q9BPX3	NCAPG
Q8NFU4	FDCSP	O15205	UBD	Q9BPX5	ARPC5L
P16260	SLC25A16	Q8WVK7	SKA2	A2RU30	TESPA1
Q9UKF7	PITPNC1	P21145	MAL	Q8NDX9	LY6G5B
Q8NCS7	SLC44A5	P24311	COX7B	Q49B96	cox19
Q8WXI2	CNKS2	O15204	ADAMDEC1	Q8N6M3	FITM2
Q96Q27	ASB2	Q9UGH3	SLC23A2	Q9NNX6	CD209
Q07325	CXCL9	P13056	NR2C1	O15063	KIAA0355
Q9BUV0	RSRP1	Q8IVF6	ANKRD18A	Q8IZL2	MAML2
O75563	SKAP2	P53804	TTC3	P21730	c5ar1
B4DU55	ZNF879	Q9H6L5	fam134b	P29017	CD1C
Q96L91	EP400	Q9BZW8	CD244	Q9Y3B9	RRP15
P14222	PRF1	P55085	F2RL1	Q8NHY6	ZFP28

UniProt ID	Gene Symbol
O15165	LDLRAD4
Q5VWK5	IL23R
P60900	PSMA6
Q9P2A4	ABI3
Q6NW40	RGMB
P57059	LOC102724428
Q6GPH4	XAF1
Q58EX7	PLEKHG4
P25787	PSMA2
Q6PKC3	TXNDC11
P21709	EPHA1
P27797	CALR
P51159	RAB27A
Q96MY1	NOL4L
Q8N6N3	C1orf52
Q9Y4C4	MFHAS1
Q9NRD1	FBXO6
O15243	LEPROT
Q460N5	PARP14
Q9Y2B2	PIGL
P05161	ISG15
Q8NEM8	AGBL3
O75182	SIN3B
O15432	SLC31A2
Q9UKA8	RCAN3
Q58EX2	SDK2
P01579	IFNG
O95727	CRTAM
O75444	MAF
B0YJ81	HACD1
P20674	Cox5a
Q16617	NKG7
O75446	SAP30
Q7L3V2	C22orf29
Q2NKJ3	CTC1
P21854	CD72
O15392	BIRC5
Q01469	FABP5
Q3KP44	ankrd55
P13639	EEF2
P51681	CCR5
P34810	CD68
Q9HAP2	MLXIP
P18077	RPL35A

UniProt ID	Gene Symbol
Q9Y2A4	ZNF443
Q10589	BST2
Q7L0R7	RNF44
Q9NQC7	CYLD
Q8WYQ9	ZCCHC14
Q7Z7K0	CMC1
P36402	TCF7
Q15004	KIAA0101
O00574	Cxcr6
Q6ICU9	SAT1
Q9NRB3	CHST12
Q96IX5	USMG5
Q96DE5	ANAPC16
P30793	GCH1
Q7Z3J3	RGPD4
Q8IXQ6	PARP9
Q13287	NMI
Q5T7M9	FAM69A
Q8IXQ9	ETFBKMT
E9PAV3	NACA
P17861	XBP1
Q8WWP7	GIMAP1
P50876	RNF144A
P61247	RPS3A
P48357	LEPR
P33552	CKS2
Q7LDG7	RASGRP2
P61313	RPL15
Q9C0K0	BCL11B
P13501	CCL5
P60059	SEC61G
Q96S94	CCNL2
Q00765	REEP5
Q9Y6R6	ZNF780B
Q96J88	EPSTI1
P80303	NUCB2
Q86W92	PPFIBP1
Q9BT67	NDFIP1
P51523	ZNF84
Q9H2C0	GAN
Q9H4B4	PLK3
P48060	GLIPR1
Q13009	TIAM1
O00764	PDXK

UniProt ID	Gene Symbol
Q13003	GRIK3
A4D1U4	KIAA1147
Q7Z5J4	RAI1
Q5TGI4	SAMD5
P39023	RPL3
Q9H173	SIL1
Q9Y603	etv7
P09912	IFI6
P11388	TOP2A
Q9H171	ZBP1
Q9BTX3	TMEM208
A6QL63	BTBD11
Q13017	ARHGAP5
Q9H825	METTL8
P53999	SUB1
Q9UNH5	CDC14A
Q96AZ6	ISG20
Q96RV3	PCNX1
P58335	ANTXR2
Q92619	ARHGAP45
Q13133	NR1H3
Q8IWB7	WDFY1
Q96DB9	FXDY5
Q9HAT8	PELI2
Q9BT88	SYT11
P07196	NEFL
Q96IU2	ZBED3
Q8WW43	APH1B
Q8TDB6	DTX3L
P10966	CD8B
Q76N32	CEP68
Q9UPQ0	LIMCH1
Q9Y5P2	CSAG3
Q9Y6P5	SESN1
Q8N3F0	MTURN
Q9HCJ1	ANKH
P42336	PIK3CA
Q6P5X7	TMEM71
P25445	FAS
O75509	TNFRSF21
P49721	PSMB2
Q14767	LTBP2
P40429	RPL13A
Q93038	TNFRSF25

UniProt ID	Gene Symbol
P02778	CXCL10
Q5VYK3	KIAA0368
P42224	STAT1
Q06643	LTB
P21462	FPR1
P48735	IDH2
P61009	SPCS3
O95936	EOMES
Q96RU2	USP28
Q92823	NRCAM
Q96HP4	OXNAD1
O95931	CBX7
P45954	ACADSB
Q92824	PCSK5
Q99457	NAP1L3
Q9Y2H0	DLGAP4
P27487	DPP4
Q16667	CDKN3
Q5EBM0	CMPK2
Q13241	KLRD1
P12838	DEFA4
Q53G44	IFI44L
Q8IZT6	ASPM
O60343	TBC1D4
O00522	KRIT1
Q12860	CNTN1
Q9Y6N5	SQRDL
O43566	RGS14
Q92830	KAT2A
P61925	PKIA
P62913	RPL11
P61927	RPL37
Q92637	FCGR1B
P48023	FASLG
Q9UNK4	PLA2G2D
Q92630	DYRK2
Q969Z0	TBRG4
Q13253	NOG
Q9UQ90	SPG7
Q9BQ16	SPOCK3
Q15398	DLGAP5
P37275	ZEB1
P10914	IRF1
Q9UK97	FBXO9

UniProt ID	Gene Symbol
Q68CP4	HGSNAT
Q8WVN6	SECTM1
P42681	TXK
P80217	IFI35
Q13261	IL15RA
P07992	ercc1
Q6IA86	ELP2
P22830	FECH
Q8N7A1	KLHDC1
Q99592	zbtb18
Q8NDQ6	ZNF540
P11473	VDR
Q9NSB8	HOMER2
P25490	YY1
Q9UK80	USP21
Q16566	CAMK4
Q96KC8	DNAJC1
Q2QGD7	ZXDC
Q9NWW6	NMRK1
Q7Z5H3	ARHGAP22
P32456	GBP2
P32455	gbp1
A6NJ69	IGIP
P51608	MECP2
Q9HCN8	SDF2L1
P42574	CASP3
P28838	LAP3
P29590	PML
Q9P021	CRIP1
P36578	RPL4
Q8N5W9	RFLNB
O60306	AQR
Q9NYL4	FKBP11
B4DX44	ZNF736
P42771	CDKN2A
P62753	RPS6
Q9HC16	APOBEC3G
Q15858	SCN9A
P23246	SFPQ
Q92673	SORL1
O14791	APOL1
P17900	GM2A
O43184	ADAM12
Q00987	MDM2

UniProt ID	Gene Symbol
Q99684	GFI1
P49792	RANBP2
P38606	ATP6V1A
Q86Y38	XYLT1
Q1L5Z9	LONRF2
Q9BQE5	APOL2
Q9UHL3	FAM153A
Q96SR6	ZNF382
Q9BQE4	SELENOS
Q9UJU2	LEF1
Q8WYH8	ING5
Q969F1	GTF3C6
P68104	EEF1A1
Q86V40	TRABD2A
Q00577	PURA
Q7Z388	DPY19L4
Q96DN0	erp27
Q8WTW2	NMI
Q96JB3	HIC2
Q9NR97	TLR8
P00558	PGK1
P10124	SRGN
Q6ZSS7	MFSD6
Q15723	ELF2
Q8TCG2	PI4K2B
Q5VWQ0	RSBN1
P55957	BID
Q8TAA5	grpel2
O43572	AKAP10
Q6PJW8	CNST
Q5JVG8	ZNF506
Q9Y547	HSPB11
Q4VX76	SYTL3
Q9NWX4	GPATCH2L
P17252	PRKCA
Q7Z3U7	MON2
Q92793	CREBBP
Q9H5X1	FAM96A
P11117	ACP2
Q96HL8	SH3YL1
Q8N413	SLC25A45
Q6P1R3	MSANTD2
Q8NEG7	DENND6B
Q99666	RGPD6

UniProt ID	Gene Symbol
P09769	FGR
P49863	GZMK
Q8WW59	spryd4
Q9ULJ7	ANKRD50
Q9NYI0	PSD3
Q01826	SATB1
P43007	SLC1A4
Q92783	STAM
Q9Y3M9	ZNF337
Q9NQV5	Prdm11
Q96F15	GIMAP5
O60928	KCNJ13
O95232	LUC7L3
Q9Y662	HS3ST3B1
Q96GE9	TMEM261
Q5JY77	GPRASP1
Q96FE7	PIK3IP1
Q8WUX9	CHMP7
P26374	CHML
Q8TBC5	ZSCAN18
O60337	march6
P13284	IFI30
P26373	RPL13
P23381	WARS
Q9UL17	TBX21
O94898	LRIG2
Q9UL19	RARRES3
Q8NHJ6	LILRB4
Q15811	ITSN1
P78509	RELN
Q96IJ6	GMPPA
P78508	KCNJ10
Q8IU68	tmc8
P62899	RPL31
Q9BZM1	PLA2G12A
Q5JSZ5	PRRC2B
Q15034	herc3
O00303	EIF3F
Q5VV63	ATRN1
Q9Y653	ADGRG1
P25105	ptafr
Q9BSN7	TMEM204
O94886	TMEM63A
Q14585	ZNF345

UniProt ID	Gene Symbol
Q15562	TEAD2
Q8TDP1	maseh2c
Q06323	PSME1
P05109	S100A8
O60551	NMT2
O00453	LST1
Q8WU39	MZB1
Q9NV12	TMEM140
P13498	CYBA
Q9Y5S9	RBM8A
Q3BBV1	NBPF9
Q86WW8	COA5
Q3BBV0	NBPF1
P06127	CD5
O00459	PIK3R2
P25116	F2R
Q96CJ1	EAF2
Q6P280	ZNF529
Q9Y3R0	GRIP1
Q53RD9	fbln7
P46777	RPL5
Q9UBN6	TNFRSF10D
P16871	IL7R
Q5T9C2	FAM102A
P67870	CSNK2B
Q13946	PDE7A
Q9NQ25	SLAMF7
Q86VP6	CAND1
P23588	EIF4B
O00421	CCRL2
Q6ICH7	ASPHD2
Q8TF01	PNISR
Q5VWP2	FAM46C
Q9BRL6	SRSF8
Q5VYY1	ANKRD22
Q86Y91	KIF18B
Q8N1L9	BATF2
P19971	TYMP
Q86WT6	TRIM69
P06280	GLA
Q8NEK5	ZNF548
P10747	CD28
P20062	TCN2
Q9BUM1	G6PC3

UniProt ID	Gene Symbol
Q96QD5	DEPDC7
Q9P0L0	VAPA
Q9NR31	SAR1A
Q9UL46	PSME2
Q4VXU2	PABPC1L
Q5MNZ9	WIP1
Q68D91	MBLAC2
Q9H2X8	IFI27L2
P51812	RPS6KA3
Q9NR34	MAN1C1
Q8NCD3	HJURP
O14879	IFIT3
O14777	NDC80
P50148	GNAQ
Q8IY45	AMN1
P13236	CCL4L1
P49639	HOXA1
P28907	CD38
P49641	MAN2A2
P62888	RPL30
Q15646	OASL
P10147	CCL3
Q99759	MAP3K3
A2RUB6	CCDC66
Q8NEL9	DDHD1
Q86T75	NBPF11
Q02252	ALDH6A1
Q9H3S5	PIGM
O00488	ZNF593
Q14141	SEPT6
O14513	NCKAP5
Q9Y228	TRAF3IP3
P19801	AOC1
O95450	ADAMTS2
Q9HBX8	LGR6
Q2VPA4	CR1L
Q96IF1	AJUBA
Q5H9K5	ZMAT1
O95070	YIF1A
O43708	GSTZ1
Q8TE68	EPS8L1
O43903	GAS2
P10415	BCL2
P19404	NDUFV2

UniProt ID	Gene Symbol
P12319	FCER1A
P12318	FCGR2A
O60880	SH2D1A
A8MQ14	ZNF850
Q4W5P6	TMEM155
P20248	CCNA2
Q9Y2T1	AXIN2
Q6N069	NAA16
Q6NT04	TIGD7
P12314	FCGR1A
Q2NKX9	c2orf68
Q9Y237	PIN4
Q86XK7	VSIG1
P42701	IL12RB1
O14715	RGPD8
Q92478	CLEC2B
O75132	zbed4
P08235	NR3C2
Q9UQD0	SCN8A
Q8N4N3	KLHL36
Q9H334	FOXP1
O00154	ACOT7
Q8TE56	ADAMTS17
P16619	CCL3L3
Q9NWH7	SPATA6
Q70EK8	USP53
Q9P0I2	EMC3
P62308	SNRPG
Q8IZC4	RTKN2
P23743	DGKA
O00463	TRAF5
Q5R3I4	TTC38
Q95460	MR1
O43825	B3GALT2
P08887	IL6R
Q9NZV6	MSRB1
Q719I0	AHSA2
Q02223	TNFRSF17
Q9Y244	POMP
P12544	GZMA
Q02224	CENPE
P51124	GZMM
O00268	TAF4
Q15782	CHI3L2

UniProt ID	Gene Symbol
O14639	ABLIM1
Q9H6A0	DENND2D
Q8NHL6	LILRB1
O14827	RASGRF2
P63279	UBE2I
Q9UGP8	SEC63
Q92482	AQP3
Q5SW96	LDLRAP1
Q9BRA2	TXNDC17
Q8N228	SCML4
O14933	UBE2L6
O14936	CASK
O00472	ELL2
P63162	SNRPN
O60669	SLC16A7
Q14154	KIAA0141
Q9Y262	EIF3L
P60568	IL2
P63172	DYNLT1
O43819	SCO2
P36222	CHI3L1
Q8N4L2	TMEM55A
A8MYP8	ODF3B
O14625	CXCL11
Q08380	LGALS3BP
Q86YW5	TREML1
Q96JP2	MYO15B
P26718	KLRC4-KLRK1
O60658	PDE8A
O14949	Uqcrq
O14948	TFEC
Q14626	il11ra
Q6ICB0	DESI1
Q6P1L5	FAM117B
Q9H3W5	LRRN3
P17039	ZNF30
Q9GZT3	SLIRP
Q17RY0	CPEB4
Q9C093	SPEF2
Q9BY50	SEC11C
A7E2F4	GOLGA8A
Q92563	SPOCK2
Q8N4S7	PAQR4
P62424	RPL7A

UniProt ID	Gene Symbol
Q9H204	MED28
O00244	ATOX1
Q8NI35	PATJ
P98198	ATP8B2
Q8N8U2	CDYL2
O96033	mocs2
Q9BWW8	APOL6
O75928	PIAS2
Q02543	RPL18A
A8MQT2	GOLGA8B
P18627	LAG3
Q9Y6X4	FAM169A
Q9ULY5	CLEC4E
P55345	PRMT2
Q8NFI3	ENGASE
Q9UKI2	CDC42EP3
P55145	MANF
O76096	CST7
O43147	SGSM2
Q9BZD6	PRRG4
Q8NEB9	PIK3C3
Q9Y6Y1	CAMTA1
Q9UBS5	GABBR1
P14550	AKR1A1
Q9Y4X0	AMMECR1
Q8TCT9	HM13
P78364	PHC1
Q9NS18	GLRX2
Q86Y07	VRK2
Q9BTC0	DIDO1
Q9BX74	TM2D1
P21673	SAT1
Q8NBZ7	UXS1
Q96RQ9	IL4I1
Q8N660	NBPF15
Q9Y297	BTRC
P35268	RPL22
O96007	mocs2
Q03519	tap2
Q9UHF7	TRPS1
P15812	CD1E
Q03518	TAP1
P20718	GZMH
O75023	LILRB5

UniProt ID	Gene Symbol	UniProt ID	Gene Symbol	UniProt ID	Gene Symbol
Q8N4Q0	ZADH2	Q9NRQ5	SMCO4	Q8TF71	SLC16A10
Q8N726	CDKN2A	O14979	HNRNPDL	Q8N268	C20orf197
Q8WYG1	RSAD2	Q96JQ2	CLMN	P35754	GLRX
Q9BY67	CADM1	Q96C19	EFHD2	Q6NSI8	KIAA1841
Q9NZ72	STMN3	Q9Y2Z0	SUGT1	Q96KP6	TNIP3
P55769	SNU13	Q96N16	JAKMIP1	Q96AB3	ISOC2
P23508	MCC	O95072	REC8	P32246	CCR1
Q9UKJ1	PILRA	O75015	FCGR3B	Q13609	DNASE1L3
P29965	CD40LG	Q495A1	Tigit	P32248	CCR7
Q6NSJ2	PHLDB3	Q9UH77	KLHL3	P16070	CD44
O95182	NDUFA7	Q96GA3	LTV1	P32241	VIPR1
O95183	VAMP5	P15531	NME1	O95486	sec24a

7.3.2 Gene Ontology

Table 7.8 – Gene Ontology results for the protein of **Table 7.7**. O – Ontology; # - number of proteins associated to the term; % - percentage of the total proteins know to have the term; FE - Fold Enrichment; B – Benjamini; FDR – False Discovery Rate

O	ID	Term	#	%	pValue	FE	B	FDR
Cellular Component	GO:0022625	cytosolic large ribosomal subunit	15	2.229	8.05E-08	6.271	3.74E-05	1.15E-04
	GO:0009897	external side of plasma membrane	25	3.715	5.07E-07	3.337	1.18E-04	7.23E-04
	GO:0005829	cytosol	163	24.220	3.10E-06	1.398	4.81E-04	4.42E-03
	GO:0005839	proteasome core complex	7	1.040	6.33E-05	9.477	7.33E-03	9.02E-02
	GO:0005840	ribosome	18	2.675	7.81E-05	3.083	7.24E-03	1.11E-01
	GO:0005737	cytoplasm	225	33.432	2.27E-04	1.225	1.74E-02	3.23E-01
	GO:0000502	proteasome complex	10	1.486	2.29E-04	4.738	1.51E-02	3.26E-01
	GO:0030529	intracellular ribonucleoprotein complex	13	1.932	3.06E-03	2.718	1.63E-01	4.28E+00
	GO:0030425	dendrite	23	3.418	3.74E-03	1.952	1.76E-01	5.21E+00
	GO:0005654	nucleoplasm	123	18.276	4.85E-03	1.256	2.02E-01	6.70E+00
	GO:0030176	integral component of endoplasmic reticulum membrane	10	1.486	1.09E-02	2.734	3.72E-01	1.45E+01
	GO:1990111	spermatoproteasome complex	3	0.446	1.15E-02	17.058	3.61E-01	1.52E+01
	GO:0043657	host cell	3	0.446	1.15E-02	17.058	3.61E-01	1.52E+01
	GO:0016020	membrane	97	14.413	1.37E-02	1.254	3.90E-01	1.79E+01

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:0031519	PcG protein complex	5	0.743	1.39E-02	5.265	3.72E-01	1.81E+01
	GO:0005887	integral component of plasma membrane	65	9.658	2.15E-02	1.306	4.90E-01	2.66E+01
	GO:0032587	ruffle membrane	8	1.189	2.51E-02	2.774	5.22E-01	3.04E+01
	GO:0019773	proteasome core complex, alpha-subunit complex	3	0.446	3.00E-02	10.661	5.65E-01	3.52E+01
	GO:0019005	SCF ubiquitin ligase complex	6	0.892	3.04E-02	3.412	5.49E-01	3.56E+01
	GO:0005794	Golgi apparatus	42	6.241	3.17E-02	1.384	5.46E-01	3.69E+01
	GO:0005634	nucleus	211	31.352	4.53E-02	1.108	6.60E-01	4.84E+01
	GO:0070062	extracellular exosome	115	17.088	5.16E-02	1.163	6.91E-01	5.30E+01
	GO:0016605	PML body	8	1.189	5.70E-02	2.321	7.11E-01	5.67E+01
	GO:0005789	endoplasmic reticulum membrane	40	5.944	6.38E-02	1.319	7.36E-01	6.09E+01
	GO:0072536	interleukin-23 receptor complex	2	0.297	6.90E-02	28.431	7.50E-01	6.39E+01
	GO:0005956	protein kinase CK2 complex	2	0.297	6.90E-02	28.431	7.50E-01	6.39E+01
	GO:0005783	endoplasmic reticulum	38	5.646	7.62E-02	1.305	7.71E-01	6.77E+01
	GO:0043202	lysosomal lumen	7	1.040	7.83E-02	2.341	7.68E-01	6.87E+01
	GO:0043235	receptor complex	9	1.337	7.90E-02	2.015	7.57E-01	6.90E+01
	GO:0005576	extracellular region	68	10.104	8.14E-02	1.201	7.56E-01	7.02E+01
	GO:0005942	phosphatidylinositol 3-kinase complex	3	0.446	8.48E-02	6.092	7.59E-01	7.17E+01
	GO:0043025	neuronal cell body	17	2.526	9.10E-02	1.534	7.72E-01	7.43E+01
	GO:0033290	eukaryotic 48S preinitiation complex	3	0.446	9.57E-02	5.686	7.79E-01	7.61E+01
	GO:0016282	eukaryotic 43S preinitiation complex	3	0.446	9.57E-02	5.686	7.79E-01	7.61E+01
	GO:0005925	focal adhesion	20	2.972	9.67E-02	1.454	7.72E-01	7.65E+01
Molecular Function	GO:0005515	protein binding	365	54.235	9.19E-06	1.167	6.90E-03	1.40E-02
	GO:0004872	receptor activity	22	3.269	3.23E-05	2.848	1.21E-02	4.91E-02
	GO:0042288	MHC class I protein binding	7	1.040	3.59E-05	10.348	8.98E-03	5.47E-02
	GO:0004298	threonine-type endopeptidase activity	7	1.040	6.76E-05	9.363	1.27E-02	1.03E-01
	GO:0003735	structural constituent of ribosome	20	2.972	3.75E-04	2.530	5.50E-02	5.70E-01
	GO:0016301	kinase activity	21	3.120	3.94E-04	2.448	4.83E-02	5.98E-01
	GO:0004896	cytokine receptor activity	7	1.040	1.54E-03	5.462	1.53E-01	2.32E+00
	GO:0008009	chemokine activity	8	1.189	1.62E-03	4.586	1.42E-01	2.45E+00

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:0019789	SUMO transferase activity	5	0.743	2.04E-03	8.778	1.58E-01	3.07E+00
	GO:0031730	CCR5 chemokine receptor binding	4	0.594	2.19E-03	14.044	1.52E-01	3.28E+00
	GO:0015026	coreceptor activity	6	0.892	3.80E-03	5.618	2.30E-01	5.64E+00
	GO:0030246	carbohydrate binding	16	2.377	4.41E-03	2.293	2.42E-01	6.51E+00
	GO:0019864	IgG binding	4	0.594	5.95E-03	10.214	2.93E-01	8.69E+00
	GO:0003723	RNA binding	32	4.755	7.35E-03	1.643	3.28E-01	1.06E+01
	GO:0008097	5S rRNA binding	3	0.446	1.17E-02	16.853	4.48E-01	1.65E+01
	GO:0048248	CXCR3 chemokine receptor binding	3	0.446	1.17E-02	16.853	4.48E-01	1.65E+01
	GO:0050681	androgen receptor binding	6	0.892	1.31E-02	4.213	4.64E-01	1.82E+01
	GO:0032393	MHC class I receptor activity	3	0.446	1.72E-02	14.044	5.37E-01	2.32E+01
	GO:0008270	zinc ion binding	56	8.321	1.99E-02	1.346	5.70E-01	2.64E+01
	GO:0016004	phospholipase activator activity	3	0.446	2.35E-02	12.038	6.11E-01	3.04E+01
	GO:0004568	chitinase activity	3	0.446	2.35E-02	12.038	6.11E-01	3.04E+01
	GO:0031726	CCR1 chemokine receptor binding	3	0.446	2.35E-02	12.038	6.11E-01	3.04E+01
	GO:0019901	protein kinase binding	22	3.269	2.78E-02	1.643	6.55E-01	3.49E+01
	GO:0008061	chitin binding	3	0.446	3.06E-02	10.533	6.73E-01	3.77E+01
	GO:0044822	poly(A) RNA binding	53	7.875	3.30E-02	1.319	6.83E-01	4.00E+01
	GO:0008017	microtubule binding	14	2.080	3.51E-02	1.891	6.90E-01	4.20E+01
	GO:0004842	ubiquitin-protein transferase activity	19	2.823	4.66E-02	1.622	7.77E-01	5.16E+01
	GO:0000900	translation repressor activity, nucleic acid binding	3	0.446	4.70E-02	8.426	7.66E-01	5.19E+01
	GO:0005102	receptor binding	20	2.972	4.79E-02	1.591	7.59E-01	5.26E+01
	GO:0005031	tumor necrosis factor-activated receptor activity	4	0.594	5.20E-02	4.681	7.75E-01	5.56E+01
	GO:0016740	transferase activity	8	1.189	5.48E-02	2.341	7.81E-01	5.76E+01
	GO:0003713	transcription coactivator activity	15	2.229	5.95E-02	1.699	7.97E-01	6.07E+01
	GO:0016493	C-C chemokine receptor activity	3	0.446	6.58E-02	7.022	8.19E-01	6.45E+01
	GO:0001191	transcriptional repressor activity, RNA polymerase II transcription factor binding	3	0.446	6.58E-02	7.022	8.19E-01	6.45E+01
	GO:0003682	chromatin binding	21	3.120	6.59E-02	1.509	8.09E-01	6.46E+01

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:0042803	protein homodimerization activity	35	5.201	6.66E-02	1.347	8.03E-01	6.50E+01
	GO:0051087	chaperone binding	7	1.040	6.82E-02	2.427	8.01E-01	6.59E+01
	GO:0015038	glutathione disulfide oxidoreductase activity	2	0.297	6.98E-02	28.088	7.99E-01	6.68E+01
	GO:0042019	interleukin-23 binding	2	0.297	6.98E-02	28.088	7.99E-01	6.68E+01
	GO:0071791	chemokine (C-C motif) ligand 5 binding	2	0.297	6.98E-02	28.088	7.99E-01	6.68E+01
	GO:0042020	interleukin-23 receptor activity	2	0.297	6.98E-02	28.088	7.99E-01	6.68E+01
	GO:0005164	tumor necrosis factor receptor binding	4	0.594	8.25E-02	3.874	8.44E-01	7.31E+01
	GO:0042043	neurexin family protein binding	3	0.446	8.66E-02	6.019	8.50E-01	7.48E+01
	GO:0004553	hydrolase activity, hydrolyzing O-glycosyl compounds	4	0.594	8.94E-02	3.745	8.52E-01	7.60E+01
	GO:0002039	p53 binding	6	0.892	8.95E-02	2.515	8.44E-01	7.60E+01
	GO:0005525	GTP binding	20	2.972	9.15E-02	1.463	8.44E-01	7.68E+01
Biological Process	GO:0051607	defense response to virus	26	3.863	1.08E-09	4.381	2.81E-06	1.92E-06
	GO:0006955	immune response	43	6.389	2.24E-09	2.840	2.92E-06	3.97E-06
	GO:0060337	type I interferon signaling pathway	16	2.377	5.60E-09	6.950	4.86E-06	9.92E-06
	GO:0002250	adaptive immune response	22	3.269	7.54E-08	4.133	4.90E-05	1.34E-04
	GO:0006413	translational initiation	21	3.120	9.52E-08	4.262	4.95E-05	1.69E-04
	GO:0006954	inflammatory response	37	5.498	1.11E-07	2.714	4.81E-05	1.97E-04
	GO:0033209	tumor necrosis factor-mediated signaling pathway	19	2.823	2.12E-07	4.476	7.86E-05	3.75E-04
	GO:0006614	SRP-dependent cotranslational protein targeting to membrane	17	2.526	2.14E-07	5.028	6.95E-05	3.79E-04
	GO:0000184	nuclear-transcribed mRNA catabolic process, nonsense-mediated decay	18	2.675	1.19E-06	4.205	3.43E-04	2.10E-03
	GO:0060333	interferon-gamma-mediated signaling pathway	14	2.080	1.24E-06	5.482	3.23E-04	2.20E-03
	GO:0019083	viral transcription	17	2.526	2.44E-06	4.220	5.76E-04	4.32E-03
	GO:0002223	stimulatory C-type lectin receptor signaling pathway	16	2.377	5.01E-06	4.236	1.09E-03	8.88E-03

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:0045071	negative regulation of viral genome replication	10	1.486	9.44E-06	6.950	1.89E-03	1.67E-02
	GO:0006364	rRNA processing	23	3.418	9.58E-06	2.988	1.78E-03	1.70E-02
	GO:0002479	antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-dependent	12	1.783	1.32E-05	5.295	2.28E-03	2.33E-02
	GO:0009615	response to virus	15	2.229	3.91E-05	3.791	6.34E-03	6.93E-02
	GO:0097190	apoptotic signaling pathway	12	1.783	4.23E-05	4.699	6.45E-03	7.49E-02
	GO:0051437	positive regulation of ubiquitin-protein ligase activity involved in regulation of mitotic cell cycle transition	12	1.783	8.04E-05	4.390	1.16E-02	1.42E-01
	GO:0050852	T cell receptor signaling pathway	17	2.526	8.49E-05	3.193	1.16E-02	1.50E-01
	GO:0032496	response to lipopolysaccharide	18	2.675	8.73E-05	3.051	1.13E-02	1.55E-01
	GO:0038061	NIK/NF-kappaB signaling	11	1.634	1.14E-04	4.634	1.40E-02	2.02E-01
	GO:0006935	chemotaxis	15	2.229	1.23E-04	3.418	1.44E-02	2.17E-01
	GO:0006412	translation	23	3.418	1.24E-04	2.527	1.39E-02	2.19E-01
	GO:0070098	chemokine-mediated signaling pathway	11	1.634	2.12E-04	4.307	2.27E-02	3.75E-01
	GO:0000209	protein polyubiquitination	18	2.675	3.51E-04	2.720	3.59E-02	6.20E-01
	GO:0045087	innate immune response	31	4.606	4.24E-04	2.004	4.16E-02	7.49E-01
	GO:0006521	regulation of cellular amino acid metabolic process	9	1.337	4.30E-04	4.906	4.06E-02	7.59E-01
	GO:0060326	cell chemotaxis	10	1.486	4.97E-04	4.277	4.51E-02	8.77E-01
	GO:0006919	activation of cysteine-type endopeptidase activity involved in apoptotic process	11	1.634	7.61E-04	3.685	6.60E-02	1.34E+00
	GO:0023052	signaling	4	0.594	8.50E-04	18.534	7.11E-02	1.50E+00
	GO:0046632	alpha-beta T cell differentiation	4	0.594	8.50E-04	18.534	7.11E-02	1.50E+00
	GO:0051436	negative regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle	10	1.486	9.57E-04	3.916	7.72E-02	1.68E+00
	GO:0090263	positive regulation of canonical Wnt signaling pathway	13	1.932	1.27E-03	3.012	9.83E-02	2.23E+00

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:0051603	proteolysis involved in cellular protein catabolic process	8	1.189	1.52E-03	4.634	1.13E-01	2.66E+00
	GO:0060071	Wnt signaling pathway, planar cell polarity pathway	11	1.634	1.69E-03	3.324	1.22E-01	2.96E+00
	GO:0007165	signal transduction	62	9.212	1.77E-03	1.485	1.24E-01	3.10E+00
	GO:0031145	anaphase-promoting complex-dependent catabolic process	10	1.486	2.05E-03	3.519	1.38E-01	3.58E+00
	GO:0048304	positive regulation of isotype switching to IgG isotypes	4	0.594	2.25E-03	13.901	1.47E-01	3.92E+00
	GO:0045954	positive regulation of natural killer cell mediated cytotoxicity	5	0.743	3.37E-03	7.723	2.06E-01	5.81E+00
	GO:0002690	positive regulation of leukocyte chemotaxis	5	0.743	3.37E-03	7.723	2.06E-01	5.81E+00
	GO:0006915	apoptotic process	34	5.052	4.56E-03	1.667	2.63E-01	7.77E+00
	GO:0050776	regulation of immune response	15	2.229	5.02E-03	2.343	2.79E-01	8.54E+00
	GO:0000042	protein targeting to Golgi	5	0.743	5.04E-03	6.950	2.74E-01	8.57E+00
	GO:0050850	positive regulation of calcium-mediated signaling	5	0.743	5.04E-03	6.950	2.74E-01	8.57E+00
	GO:0043123	positive regulation of I-kappaB kinase/NF-kappaB signaling	14	2.080	5.41E-03	2.418	2.86E-01	9.17E+00
	GO:0090090	negative regulation of canonical Wnt signaling pathway	14	2.080	6.00E-03	2.388	3.05E-01	1.01E+01
	GO:0019835	cytolysis	5	0.743	6.05E-03	6.619	3.02E-01	1.02E+01
	GO:0051402	neuron apoptotic process	6	0.892	6.06E-03	5.055	2.96E-01	1.02E+01
	GO:0042127	regulation of cell proliferation	15	2.229	7.01E-03	2.254	3.28E-01	1.17E+01
	GO:0002230	positive regulation of defense response to virus by host	5	0.743	7.19E-03	6.318	3.29E-01	1.20E+01
	GO:0071222	cellular response to lipopolysaccharide	11	1.634	7.48E-03	2.706	3.34E-01	1.25E+01
	GO:0071353	cellular response to interleukin-4	5	0.743	9.87E-03	5.792	4.10E-01	1.61E+01
	GO:0007059	chromosome segregation	8	1.189	1.09E-02	3.271	4.33E-01	1.76E+01
	GO:0008625	extrinsic apoptotic signaling pathway via death domain receptors	6	0.892	1.11E-02	4.390	4.33E-01	1.79E+01
	GO:0002181	cytoplasmic translation	5	0.743	1.14E-02	5.560	4.37E-01	1.84E+01

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:0043488	regulation of mRNA stability	10	1.486	1.18E-02	2.699	4.41E-01	1.89E+01
	GO:0019060	intracellular transport of viral protein in host cell	3	0.446	1.20E-02	16.681	4.40E-01	1.92E+01
	GO:0033153	T cell receptor V(D)J recombination	3	0.446	1.20E-02	16.681	4.40E-01	1.92E+01
	GO:0038095	Fc-epsilon receptor signaling pathway	14	2.080	1.21E-02	2.187	4.39E-01	1.94E+01
	GO:0006605	protein targeting	6	0.892	1.23E-02	4.277	4.38E-01	1.97E+01
	GO:0051928	positive regulation of calcium ion transport	5	0.743	1.31E-02	5.346	4.53E-01	2.09E+01
	GO:0043161	proteasome-mediated ubiquitin-dependent protein catabolic process	15	2.229	1.51E-02	2.054	4.94E-01	2.36E+01
	GO:0071346	cellular response to interferon-gamma	7	1.040	1.61E-02	3.414	5.11E-01	2.50E+01
	GO:0006959	humoral immune response	7	1.040	1.61E-02	3.414	5.11E-01	2.50E+01
	GO:0030816	positive regulation of cAMP metabolic process	3	0.446	1.75E-02	13.901	5.36E-01	2.69E+01
	GO:0045084	positive regulation of interleukin-12 biosynthetic process	3	0.446	1.75E-02	13.901	5.36E-01	2.69E+01
	GO:0000122	negative regulation of transcription from RNA polymerase II promoter	38	5.646	1.85E-02	1.467	5.48E-01	2.81E+01
	GO:0071407	cellular response to organic cyclic compound	7	1.040	1.88E-02	3.298	5.50E-01	2.86E+01
	GO:0045893	positive regulation of transcription, DNA-templated	29	4.309	1.96E-02	1.566	5.59E-01	2.96E+01
	GO:0045454	cell redox homeostasis	8	1.189	2.05E-02	2.888	5.69E-01	3.07E+01
	GO:0002474	antigen processing and presentation of peptide antigen via MHC class I	5	0.743	2.15E-02	4.634	5.81E-01	3.20E+01
	GO:0002407	dendritic cell chemotaxis	4	0.594	2.15E-02	6.541	5.76E-01	3.20E+01
	GO:0071310	cellular response to organic substance	4	0.594	2.15E-02	6.541	5.76E-01	3.20E+01
	GO:0006968	cellular defense response	7	1.040	2.35E-02	3.139	6.03E-01	3.44E+01
	GO:2000503	positive regulation of natural killer cell chemotaxis	3	0.446	2.40E-02	11.915	6.05E-01	3.50E+01
	GO:0006032	chitin catabolic process	3	0.446	2.40E-02	11.915	6.05E-01	3.50E+01

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:2000427	positive regulation of apoptotic cell clearance	3	0.446	2.40E-02	11.915	6.05E-01	3.50E+01
	GO:0050798	activated T cell proliferation	3	0.446	2.40E-02	11.915	6.05E-01	3.50E+01
	GO:0070374	positive regulation of ERK1 and ERK2 cascade	13	1.932	2.42E-02	2.065	6.04E-01	3.53E+01
	GO:0030593	neutrophil chemotaxis	7	1.040	3.08E-02	2.949	6.88E-01	4.26E+01
	GO:0050862	positive regulation of T cell receptor signaling pathway	3	0.446	3.12E-02	10.425	6.87E-01	4.30E+01
	GO:0010818	T cell chemotaxis	3	0.446	3.12E-02	10.425	6.87E-01	4.30E+01
	GO:0009636	response to toxic substance	8	1.189	3.30E-02	2.617	7.03E-01	4.48E+01
	GO:0030335	positive regulation of cell migration	13	1.932	3.39E-02	1.964	7.08E-01	4.58E+01
	GO:0042542	response to hydrogen peroxide	6	0.892	3.55E-02	3.271	7.20E-01	4.73E+01
	GO:0031648	protein destabilization	5	0.743	3.57E-02	3.972	7.17E-01	4.75E+01
	GO:0007166	cell surface receptor signaling pathway	17	2.526	3.91E-02	1.725	7.45E-01	5.07E+01
	GO:0010389	regulation of G2/M transition of mitotic cell cycle	3	0.446	3.92E-02	9.267	7.41E-01	5.08E+01
	GO:0035456	response to interferon-beta	3	0.446	3.92E-02	9.267	7.41E-01	5.08E+01
	GO:0031647	regulation of protein stability	7	1.040	3.95E-02	2.780	7.40E-01	5.11E+01
	GO:0007267	cell-cell signaling	16	2.377	4.13E-02	1.751	7.50E-01	5.26E+01
	GO:0016032	viral process	18	2.675	4.23E-02	1.674	7.55E-01	5.35E+01
	GO:0008037	cell recognition	4	0.594	4.27E-02	5.055	7.54E-01	5.39E+01
	GO:0071356	cellular response to tumor necrosis factor	9	1.337	4.45E-02	2.275	7.64E-01	5.54E+01
	GO:0019882	antigen processing and presentation	6	0.892	4.69E-02	3.033	7.78E-01	5.73E+01
	GO:0033089	positive regulation of T cell differentiation in thymus	3	0.446	4.79E-02	8.340	7.81E-01	5.81E+01
	GO:0001731	formation of translation preinitiation complex	4	0.594	4.79E-02	4.835	7.77E-01	5.81E+01
	GO:0043524	negative regulation of neuron apoptotic process	10	1.486	4.85E-02	2.106	7.78E-01	5.85E+01
	GO:0000165	MAPK cascade	16	2.377	5.15E-02	1.698	7.94E-01	6.08E+01
	GO:0007204	positive regulation of cytosolic calcium ion concentration	10	1.486	5.24E-02	2.075	7.97E-01	6.15E+01

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:0034341	response to interferon-gamma	4	0.594	5.33E-02	4.634	7.98E-01	6.21E+01
	GO:0031146	SCF-dependent proteasomal ubiquitin-dependent protein catabolic process	4	0.594	5.33E-02	4.634	7.98E-01	6.21E+01
	GO:0045184	establishment of protein localization	5	0.743	5.43E-02	3.475	8.01E-01	6.28E+01
	GO:0006661	phosphatidylinositol biosynthetic process	6	0.892	5.67E-02	2.876	8.11E-01	6.44E+01
	GO:0045060	negative thymic T cell selection	3	0.446	5.71E-02	7.582	8.11E-01	6.47E+01
	GO:0034145	positive regulation of toll-like receptor 4 signaling pathway	3	0.446	5.71E-02	7.582	8.11E-01	6.47E+01
	GO:0001501	skeletal system development	10	1.486	5.87E-02	2.029	8.16E-01	6.58E+01
	GO:0034612	response to tumor necrosis factor	4	0.594	5.90E-02	4.448	8.14E-01	6.60E+01
	GO:0032735	positive regulation of interleukin-12 production	4	0.594	5.90E-02	4.448	8.14E-01	6.60E+01
	GO:0050715	positive regulation of cytokine secretion	4	0.594	5.90E-02	4.448	8.14E-01	6.60E+01
	GO:0001816	cytokine production	4	0.594	5.90E-02	4.448	8.14E-01	6.60E+01
	GO:0006465	signal peptide processing	4	0.594	5.90E-02	4.448	8.14E-01	6.60E+01
	GO:0016925	protein sumoylation	9	1.337	5.99E-02	2.139	8.16E-01	6.65E+01
	GO:0036498	IRE1-mediated unfolded protein response	6	0.892	6.02E-02	2.827	8.14E-01	6.67E+01
	GO:0002548	monocyte chemotaxis	5	0.743	6.30E-02	3.310	8.25E-01	6.84E+01
	GO:0097191	extrinsic apoptotic signaling pathway	5	0.743	6.30E-02	3.310	8.25E-01	6.84E+01
	GO:0048661	positive regulation of smooth muscle cell proliferation	6	0.892	6.38E-02	2.780	8.26E-01	6.89E+01
	GO:0060394	negative regulation of pathway-restricted SMAD protein phosphorylation	3	0.446	6.70E-02	6.950	8.38E-01	7.07E+01
	GO:0043950	positive regulation of cAMP-mediated signaling	3	0.446	6.70E-02	6.950	8.38E-01	7.07E+01
	GO:0090399	replicative senescence	3	0.446	6.70E-02	6.950	8.38E-01	7.07E+01
	GO:0031328	positive regulation of cellular biosynthetic process	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:1900424	regulation of defense response to bacterium	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0051606	detection of stimulus	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0006925	inflammatory cell apoptotic process	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0050706	regulation of interleukin-1 beta secretion	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0002302	CD8-positive, alpha-beta T cell differentiation involved in immune response	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0046967	cytosol to ER transport	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0021873	forebrain neuroblast division	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0055092	sterol homeostasis	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0038155	interleukin-23-mediated signaling pathway	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0035926	chemokine (C-C motif) ligand 2 secretion	2	0.297	7.05E-02	27.801	8.51E-01	7.26E+01
	GO:0033077	T cell differentiation in thymus	4	0.594	7.12E-02	4.119	8.51E-01	7.30E+01
	GO:0051281	positive regulation of release of sequestered calcium ion into cytosol	4	0.594	7.12E-02	4.119	8.51E-01	7.30E+01
	GO:0055007	cardiac muscle cell differentiation	4	0.594	7.12E-02	4.119	8.51E-01	7.30E+01
	GO:0034975	protein folding in endoplasmic reticulum	3	0.446	7.73E-02	6.416	8.72E-01	7.60E+01
	GO:2000484	positive regulation of interleukin-8 secretion	3	0.446	7.73E-02	6.416	8.72E-01	7.60E+01
	GO:0031274	positive regulation of pseudopodium assembly	3	0.446	7.73E-02	6.416	8.72E-01	7.60E+01
	GO:0006878	cellular copper ion homeostasis	3	0.446	7.73E-02	6.416	8.72E-01	7.60E+01
	GO:0043922	negative regulation by host of viral transcription	3	0.446	7.73E-02	6.416	8.72E-01	7.60E+01
	GO:0016358	dendrite development	4	0.594	7.77E-02	3.972	8.71E-01	7.62E+01
	GO:0007616	long-term memory	4	0.594	7.77E-02	3.972	8.71E-01	7.62E+01
	GO:0051897	positive regulation of protein kinase B signaling	7	1.040	8.14E-02	2.317	8.80E-01	7.78E+01

O	ID	Term	#	%	pValue	FE	B	FDR
	GO:0030307	positive regulation of cell growth	7	1.040	8.14E-02	2.317	8.80E-01	7.78E+01
	GO:0032729	positive regulation of interferon-gamma production	5	0.743	8.23E-02	3.022	8.81E-01	7.82E+01
	GO:0042981	regulation of apoptotic process	13	1.932	8.25E-02	1.697	8.79E-01	7.83E+01
	GO:0014068	positive regulation of phosphatidylinositol 3-kinase signaling	6	0.892	8.37E-02	2.566	8.81E-01	7.88E+01
	GO:0042149	cellular response to glucose starvation	4	0.594	8.45E-02	3.835	8.81E-01	7.91E+01
	GO:0030889	negative regulation of B cell proliferation	3	0.446	8.81E-02	5.957	8.89E-01	8.05E+01
	GO:2000353	positive regulation of endothelial cell apoptotic process	3	0.446	8.81E-02	5.957	8.89E-01	8.05E+01
	GO:0045892	negative regulation of transcription, DNA-templated	25	3.715	9.02E-02	1.393	8.93E-01	8.13E+01
	GO:0030217	T cell differentiation	4	0.594	9.15E-02	3.707	8.95E-01	8.17E+01
	GO:0030449	regulation of complement activation	4	0.594	9.15E-02	3.707	8.95E-01	8.17E+01
	GO:0060325	face morphogenesis	4	0.594	9.15E-02	3.707	8.95E-01	8.17E+01
	GO:0042752	regulation of circadian rhythm	5	0.743	9.84E-02	2.837	9.10E-01	8.41E+01
	GO:0042771	intrinsic apoptotic signaling pathway in response to DNA damage by p53 class mediator	4	0.594	9.87E-02	3.587	9.09E-01	8.42E+01
	GO:0000470	maturation of LSU-rRNA	3	0.446	9.93E-02	5.560	9.08E-01	8.43E+01
	GO:0030502	negative regulation of bone mineralization	3	0.446	9.93E-02	5.560	9.08E-01	8.43E+01
	GO:0006825	copper ion transport	3	0.446	9.93E-02	5.560	9.08E-01	8.43E+01

7.3.3 Pathways (STRING and Reactome)

7.3.3.1 STRING

Table 7.9 - KEGG Pathways obtained from STRING, using query proteins from obtained in **Table 7.7**.

Pathway ID	Pathway description	# genes	False discovery rate
4060	Cytokine-cytokine receptor interaction	27	3.65E-05
3010	Ribosome	17	8.97E-05
3050	Proteasome	10	8.97E-05
4650	Natural killer cell mediated cytotoxicity	14	0.00356

5143	African trypanosomiasis	7	0.00448
5330	Allograft rejection	7	0.00457
5332	Graft-versus-host disease	7	0.00575
4062	Chemokine signaling pathway	16	0.00804
5150	Staphylococcus aureus infection	8	0.00804
4612	Antigen processing and presentation	9	0.00806
4932	Non-alcoholic fatty liver disease (NAFLD)	14	0.00873
5164	Influenza A	15	0.0088
4640	Hematopoietic cell lineage	10	0.00981
4380	Osteoclast differentiation	12	0.0144
4141	Protein processing in endoplasmic reticulum	14	0.0159
5340	Primary immunodeficiency	6	0.0159
4115	p53 signaling pathway	8	0.0225
5152	Tuberculosis	14	0.0225
4630	Jak-STAT signaling pathway	13	0.0241
4940	Type I diabetes mellitus	6	0.0241
5168	Herpes simplex infection	14	0.0241
5210	Colorectal cancer	7	0.0321
5206	MicroRNAs in cancer	12	0.0322
4672	Intestinal immune network for IgA production	6	0.0348
5162	Measles	11	0.0389
5321	Inflammatory bowel disease (IBD)	7	0.0439
5142	Chagas disease (American trypanosomiasis)	9	0.0441
5200	Pathways in cancer	20	0.0455
3060	Protein export	4	0.0493
5320	Autoimmune thyroid disease	6	0.0493

7.3.3.2 Reactome

Table 7.10 - Reactome Pathways of the proteins in **Table 7.7**, results obtained from using “Analyze Data” menu from Reactome. Top 300 results are sorted in descending order by the ration of the number of entities found to the total number of entities of a pathway.

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-162582	Signal Transduction	96	2601	2.38E-01	1.00E+00
R-HSA-168256	Immune System	155	2352	2.15E-01	2.98E-01
R-HSA-1430728	Metabolism	98	2125	1.94E-01	1.00E+00

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-392499	Metabolism of proteins	102	1908	1.74E-01	9.75E-01
R-HSA-168249	Innate Immune System	82	1419	1.30E-01	8.25E-01
R-HSA-597592	Post-translational protein modification	64	1355	1.24E-01	9.96E-01
R-HSA-372790	Signaling by GPCR	46	1354	1.24E-01	1.00E+00
R-HSA-74160	Gene expression (Transcription)	65	1275	1.17E-01	9.75E-01
R-HSA-1643685	Disease	61	1134	1.04E-01	9.22E-01
R-HSA-73857	RNA Polymerase II Transcription	61	1084	9.91E-02	8.49E-01
R-HSA-1266738	Developmental Biology	39	1071	9.79E-02	1.00E+00
R-HSA-1280218	Adaptive Immune System	53	1027	9.39E-02	9.52E-01
R-HSA-388396	GPCR downstream signaling	31	1019	9.32E-02	1.00E+00
R-HSA-212436	Generic Transcription Pathway	57	963	8.81E-02	7.20E-01
R-HSA-1280215	Cytokine Signaling in Immune system	74	862	7.88E-02	5.10E-03
R-HSA-382551	Transport of small molecules	27	792	7.24E-02	1.00E+00
R-HSA-5653656	Vesicle-mediated transport	18	758	6.93E-02	1.00E+00
R-HSA-109582	Hemostasis	22	743	6.79E-02	1.00E+00
R-HSA-556833	Metabolism of lipids	27	740	6.77E-02	1.00E+00
R-HSA-8953854	Metabolism of RNA	38	648	5.93E-02	7.08E-01
R-HSA-199991	Membrane Trafficking	16	632	5.78E-02	1.00E+00
R-HSA-1640170	Cell Cycle	34	615	5.62E-02	8.13E-01
R-HSA-422475	Axon guidance	32	583	5.33E-02	8.18E-01
R-HSA-449147	Signaling by Interleukins	44	549	5.02E-02	6.74E-02
R-HSA-69278	Cell Cycle, Mitotic	27	508	4.65E-02	8.47E-01
R-HSA-166520	Signalling by NGF	26	488	4.46E-02	8.39E-01
R-HSA-6798695	Neutrophil degranulation	34	480	4.39E-02	2.75E-01
R-HSA-8953897	Cellular responses to external stimuli	30	476	4.35E-02	5.35E-01
R-HSA-2454202	Fc epsilon receptor (FCERI) signaling	22	467	4.27E-02	9.40E-01
R-HSA-500792	GPCR ligand binding	18	461	4.22E-02	9.91E-01
R-HSA-5663205	Infectious disease	44	454	4.15E-02	4.02E-03
R-HSA-881907	Gastrin-CREB signalling pathway via PKC and MAPK	23	452	4.13E-02	8.81E-01
R-HSA-983169	Class I MHC mediated antigen processing & presentation	28	440	4.02E-02	5.15E-01
R-HSA-381753	Olfactory Signaling Pathway	2	432	3.95E-02	1.00E+00
R-HSA-194315	Signaling by Rho GTPases	16	408	3.73E-02	9.86E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-2262752	Cellular responses to stress	26	399	3.65E-02	4.67E-01
R-HSA-187037	NGF signalling via TRKA from the plasma membrane	21	397	3.63E-02	8.26E-01
R-HSA-186797	Signaling by PDGF	20	390	3.57E-02	8.57E-01
R-HSA-1852241	Organelle biogenesis and maintenance	4	390	3.57E-02	1.00E+00
R-HSA-5663202	Diseases of signal transduction	20	384	3.51E-02	8.39E-01
R-HSA-2172127	DAP12 interactions	21	381	3.48E-02	7.69E-01
R-HSA-177929	Signaling by EGFR	21	373	3.41E-02	7.36E-01
R-HSA-3700989	Transcriptional Regulation by TP53	22	366	3.35E-02	6.26E-01
R-HSA-71291	Metabolism of amino acids and derivatives	33	364	3.33E-02	2.72E-02
R-HSA-2424491	DAP12 signaling	21	364	3.33E-02	6.96E-01
R-HSA-2871796	FCERI mediated MAPK activation	14	362	3.31E-02	9.83E-01
R-HSA-186763	Downstream signal transduction	20	361	3.30E-02	7.56E-01
R-HSA-112316	Neuronal System	16	360	3.29E-02	9.46E-01
R-HSA-194138	Signaling by VEGF	17	347	3.17E-02	8.85E-01
R-HSA-1433557	Signaling by SCF-KIT	20	346	3.16E-02	6.90E-01
R-HSA-4420097	VEGFA-VEGFR2 Pathway	17	338	3.09E-02	8.60E-01
R-HSA-74752	Signaling by Insulin receptor	20	330	3.02E-02	6.08E-01
R-HSA-373076	Class A/1 (Rhodopsin-like receptors)	15	324	2.96E-02	9.16E-01
R-HSA-448424	Interleukin-17 signaling	19	316	2.89E-02	6.21E-01
R-HSA-983168	Antigen processing: Ubiquitination & Proteasome degradation	20	309	2.83E-02	4.90E-01
R-HSA-2404192	Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R)	18	309	2.83E-02	6.71E-01
R-HSA-2428924	IGF1R signaling cascade	18	308	2.82E-02	6.66E-01
R-HSA-2428928	IRS-related events triggered by IGF1R	18	307	2.81E-02	6.60E-01
R-HSA-74751	Insulin receptor signalling cascade	18	306	2.80E-02	6.55E-01
R-HSA-112399	IRS-mediated signalling	18	303	2.77E-02	6.39E-01
R-HSA-71387	Metabolism of carbohydrates	11	303	2.77E-02	9.84E-01
R-HSA-983705	Signaling by the B Cell Receptor (BCR)	15	301	2.75E-02	8.56E-01
R-HSA-1474244	Extracellular matrix organization	8	301	2.75E-02	9.99E-01
R-HSA-68886	M Phase	19	300	2.74E-02	5.30E-01
R-HSA-5683057	MAPK family signaling cascades	17	298	2.72E-02	7.00E-01
R-HSA-446203	Asparagine N-linked glycosylation	8	298	2.72E-02	9.99E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-195721	Signaling by Wnt	19	297	2.72E-02	5.13E-01
R-HSA-198933	Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell	17	297	2.72E-02	6.95E-01
R-HSA-73894	DNA Repair	9	294	2.69E-02	9.95E-01
R-HSA-375165	NCAM signaling for neurite out-growth	14	290	2.65E-02	8.78E-01
R-HSA-425407	SLC-mediated transmembrane transport	8	290	2.65E-02	9.98E-01
R-HSA-913531	Interferon Signaling	30	284	2.60E-02	5.22E-03
R-HSA-5688426	Deubiquitination	19	282	2.58E-02	4.23E-01
R-HSA-512988	Interleukin-3, 5 and GM-CSF signaling	15	279	2.55E-02	7.72E-01
R-HSA-76002	Platelet activation, signaling and aggregation	12	279	2.55E-02	9.38E-01
R-HSA-8853659	RET signaling	16	278	2.54E-02	6.83E-01
R-HSA-195258	RHO GTPase Effectors	7	277	2.53E-02	9.99E-01
R-HSA-187687	Signalling to ERKs	13	272	2.49E-02	8.78E-01
R-HSA-451927	Interleukin-2 signaling	15	270	2.47E-02	7.29E-01
R-HSA-5218921	VEGFR2 mediated cell proliferation	14	266	2.43E-02	7.91E-01
R-HSA-167044	Signalling to RAS	13	264	2.41E-02	8.53E-01
R-HSA-912526	Interleukin receptor SHC signaling	15	263	2.40E-02	6.92E-01
R-HSA-2586552	Signaling by Leptin	14	261	2.39E-02	7.69E-01
R-HSA-169893	Prolonged ERK activation events	13	261	2.39E-02	8.42E-01
R-HSA-5684996	MAPK1/MAPK3 signaling	15	260	2.38E-02	6.76E-01
R-HSA-170968	Frs2-mediated activation	13	259	2.37E-02	8.34E-01
R-HSA-187706	Signalling to p38 via RIT and RIN	13	257	2.35E-02	8.27E-01
R-HSA-170984	ARMS-mediated activation	13	257	2.35E-02	8.27E-01
R-HSA-5673001	RAF/MAP kinase cascade	13	253	2.31E-02	8.11E-01
R-HSA-112412	SOS-mediated signalling	13	253	2.31E-02	8.11E-01
R-HSA-179812	GRB2 events in EGFR signaling	13	253	2.31E-02	8.11E-01
R-HSA-180336	SHC1 events in EGFR signaling	13	253	2.31E-02	8.11E-01
R-HSA-418594	G alpha (i) signalling events	13	247	2.26E-02	7.84E-01
R-HSA-202733	Cell surface interactions at the vascular wall	6	245	2.24E-02	9.98E-01
R-HSA-162906	HIV Infection	20	243	2.22E-02	1.44E-01
R-HSA-72203	Processing of Capped Intron-Containing Pre-mRNA	7	242	2.21E-02	9.94E-01
R-HSA-3247509	Chromatin modifying enzymes	8	241	2.20E-02	9.85E-01
R-HSA-4839726	Chromatin organization	8	241	2.20E-02	9.85E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-8951664	Neddylolation	19	236	2.16E-02	1.74E-01
R-HSA-2730905	Role of LAT2/NTAL/LAB on calcium mobilization	5	230	2.10E-02	9.99E-01
R-HSA-211859	Biological oxidations	3	223	2.04E-02	1.00E+00
R-HSA-112315	Transmission across Chemical Synapses	11	213	1.95E-02	7.90E-01
R-HSA-1483257	Phospholipid metabolism	13	211	1.93E-02	5.76E-01
R-HSA-983712	Ion channel transport	3	210	1.92E-02	1.00E+00
R-HSA-1168372	Downstream signaling events of B Cell Receptor (BCR)	15	206	1.88E-02	3.28E-01
R-HSA-5689880	Ub-specific processing proteases	16	205	1.87E-02	2.32E-01
R-HSA-397014	Muscle contraction	2	203	1.86E-02	1.00E+00
R-HSA-201681	TCF dependent signaling in response to WNT	16	202	1.85E-02	2.16E-01
R-HSA-5617833	Cilium Assembly	1	201	1.84E-02	1.00E+00
R-HSA-72766	Translation	28	200	1.83E-02	1.12E-04
R-HSA-453274	Mitotic G2-G2/M phases	13	199	1.82E-02	4.92E-01
R-HSA-6811442	Intra-Golgi and retrograde Golgi-to-ER traffic	4	199	1.82E-02	9.99E-01
R-HSA-2555396	Mitotic Metaphase and Anaphase	16	197	1.80E-02	1.89E-01
R-HSA-69275	G2/M Transition	13	197	1.80E-02	4.78E-01
R-HSA-68882	Mitotic Anaphase	16	196	1.79E-02	1.84E-01
R-HSA-72312	rRNA processing	20	193	1.76E-02	2.38E-02
R-HSA-416476	G alpha (q) signalling events	8	193	1.76E-02	9.21E-01
R-HSA-375276	Peptide ligand-binding receptors	14	189	1.73E-02	3.13E-01
R-HSA-72172	mRNA Splicing	6	188	1.72E-02	9.79E-01
R-HSA-69620	Cell Cycle Checkpoints	14	185	1.69E-02	2.87E-01
R-HSA-2467813	Separation of Sister Chromatids	15	184	1.68E-02	1.95E-01
R-HSA-8868773	rRNA processing in the nucleus and cytosol	19	183	1.67E-02	2.67E-02
R-HSA-196854	Metabolism of vitamins and cofactors	10	183	1.67E-02	7.21E-01
R-HSA-72163	mRNA Splicing - Major Pathway	6	180	1.65E-02	9.71E-01
R-HSA-948021	Transport to the Golgi and subsequent modification	4	179	1.64E-02	9.96E-01
R-HSA-8978868	Fatty acid metabolism	2	179	1.64E-02	1.00E+00
R-HSA-5357801	Programmed Cell Death	14	174	1.59E-02	2.18E-01
R-HSA-2029480	Fcgamma receptor (FCGR) dependent phagocytosis	5	174	1.59E-02	9.86E-01
R-HSA-5621481	C-type lectin receptors (CLRs)	15	173	1.58E-02	1.40E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-6791226	Major pathway of rRNA processing in the nucleolus and cytosol	19	172	1.57E-02	1.53E-02
R-HSA-877300	Interferon gamma signaling	15	172	1.57E-02	1.36E-01
R-HSA-109581	Apoptosis	14	169	1.55E-02	1.90E-01
R-HSA-1428517	The citric acid (TCA) cycle and respiratory electron transport	7	169	1.55E-02	9.10E-01
R-HSA-1236975	Antigen processing-Cross presentation	16	168	1.54E-02	7.27E-02
R-HSA-168254	Influenza Infection	21	167	1.53E-02	2.77E-03
R-HSA-2871837	FCERI mediated NF-kB activation	13	167	1.53E-02	2.64E-01
R-HSA-2559583	Cellular Senescence	9	164	1.50E-02	7.10E-01
R-HSA-983231	Factors involved in megakaryocyte development and platelet production	5	163	1.49E-02	9.77E-01
R-HSA-162587	HIV Life Cycle	5	160	1.46E-02	9.74E-01
R-HSA-5633007	Regulation of TP53 Activity	11	159	1.45E-02	4.25E-01
R-HSA-168255	Influenza Life Cycle	20	156	1.43E-02	2.79E-03
R-HSA-168898	Toll-Like Receptors Cascades	8	155	1.42E-02	7.64E-01
R-HSA-1236974	ER-Phagosome pathway	13	152	1.39E-02	1.72E-01
R-HSA-69481	G2/M Checkpoints	10	151	1.38E-02	4.86E-01
R-HSA-168273	Influenza Viral RNA Transcription and Replication	19	149	1.36E-02	3.71E-03
R-HSA-5619115	Disorders of transmembrane transporters	9	149	1.36E-02	6.01E-01
R-HSA-162599	Late Phase of HIV Life Cycle	4	149	1.36E-02	9.85E-01
R-HSA-2029482	Regulation of actin dynamics for phagocytic cup formation	2	149	1.36E-02	9.99E-01
R-HSA-5358351	Signaling by Hedgehog	11	148	1.35E-02	3.38E-01
R-HSA-5693532	DNA Double-Strand Break Repair	4	148	1.35E-02	9.84E-01
R-HSA-199977	ER to Golgi Anterograde Transport	2	148	1.35E-02	9.99E-01
R-HSA-8957322	Metabolism of steroids	2	148	1.35E-02	9.99E-01
R-HSA-453279	Mitotic G1-G1/S phases	14	146	1.34E-02	8.51E-02
R-HSA-166658	Complement cascade	5	146	1.34E-02	9.54E-01
R-HSA-418555	G alpha (s) signalling events	3	146	1.34E-02	9.95E-01
R-HSA-3858494	Beta-catenin independent WNT signaling	13	143	1.31E-02	1.26E-01
R-HSA-162909	Host Interactions of HIV factors	16	142	1.30E-02	2.10E-02
R-HSA-112314	Neurotransmitter receptors and postsynaptic signal transmission	10	142	1.30E-02	4.11E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-1500931	Cell-Cell communication	7	142	1.30E-02	7.94E-01
R-HSA-194840	Rho GTPase cycle	9	141	1.29E-02	5.35E-01
R-HSA-1474228	Degradation of the extracellular matrix	3	140	1.28E-02	9.93E-01
R-HSA-5576891	Cardiac conduction	2	140	1.28E-02	9.99E-01
R-HSA-69242	S Phase	11	139	1.27E-02	2.69E-01
R-HSA-3781865	Diseases of glycosylation	3	139	1.27E-02	9.93E-01
R-HSA-8856828	Clathrin-mediated endocytosis	4	138	1.26E-02	9.75E-01
R-HSA-198203	PI3K/AKT activation	4	138	1.26E-02	9.75E-01
R-HSA-180292	GAB1 signalosome	4	138	1.26E-02	9.75E-01
R-HSA-909733	Interferon alpha/beta signaling	17	137	1.25E-02	7.55E-03
R-HSA-202403	TCR signaling	13	137	1.25E-02	1.00E-01
R-HSA-2132295	MHC class II antigen presentation	4	136	1.24E-02	9.73E-01
R-HSA-977606	Regulation of Complement cascade	4	135	1.23E-02	9.71E-01
R-HSA-1257604	PIP3 activates AKT signaling	4	135	1.23E-02	9.71E-01
R-HSA-76005	Response to elevated platelet cytosolic Ca ²⁺	5	133	1.22E-02	9.23E-01
R-HSA-5663220	RHO GTPases Activate Formins	5	133	1.22E-02	9.23E-01
R-HSA-8856688	Golgi-to-ER retrograde transport	2	130	1.19E-02	9.98E-01
R-HSA-166016	Toll Like Receptor 4 (TLR4) Cascade	5	129	1.18E-02	9.11E-01
R-HSA-2173782	Binding and Uptake of Ligands by Scavenger Receptors	2	129	1.18E-02	9.97E-01
R-HSA-69206	G1/S Transition	12	128	1.17E-02	1.18E-01
R-HSA-68877	Mitotic Prometaphase	7	128	1.17E-02	7.00E-01
R-HSA-1483206	Glycerophospholipid biosynthesis	7	128	1.17E-02	7.00E-01
R-HSA-114608	Platelet degranulation	4	128	1.17E-02	9.61E-01
R-HSA-196849	Metabolism of water-soluble vitamins and cofactors	10	126	1.15E-02	2.79E-01
R-HSA-163200	Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins.	6	124	1.13E-02	7.96E-01
R-HSA-381426	Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs)	5	124	1.13E-02	8.93E-01
R-HSA-1630316	Glycosaminoglycan metabolism	5	124	1.13E-02	8.93E-01
R-HSA-400206	Regulation of lipid metabolism by Peroxisome proliferator-activated receptor alpha (PPARalpha)	6	123	1.12E-02	7.90E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-2990846	SUMOylation	11	122	1.12E-02	1.56E-01
R-HSA-72613	Eukaryotic Translation Initiation	22	120	1.10E-02	1.34E-05
R-HSA-72737	Cap-dependent Translation Initiation	22	120	1.10E-02	1.34E-05
R-HSA-373760	L1CAM interactions	7	120	1.10E-02	6.36E-01
R-HSA-1989781	PPARA activates gene expression	5	120	1.10E-02	8.76E-01
R-HSA-2500257	Resolution of Sister Chromatid Cohesion	5	120	1.10E-02	8.76E-01
R-HSA-5693538	Homology Directed Repair	4	120	1.10E-02	9.45E-01
R-HSA-2408522	Selenoamino acid metabolism	17	118	1.08E-02	1.76E-03
R-HSA-927802	Nonsense-Mediated Decay (NMD)	18	117	1.07E-02	6.32E-04
R-HSA-975957	Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)	18	117	1.07E-02	6.32E-04
R-HSA-212165	Epigenetic regulation of gene expression	4	117	1.07E-02	9.38E-01
R-HSA-2871809	FCERI mediated Ca+2 mobilization	2	117	1.07E-02	9.95E-01
R-HSA-202424	Downstream TCR signaling	13	116	1.06E-02	3.63E-02
R-HSA-3108232	SUMO E3 ligases SUMOylate target proteins	11	116	1.06E-02	1.23E-01
R-HSA-68875	Mitotic Prophase	3	116	1.06E-02	9.78E-01
R-HSA-166054	Activated TLR4 signalling	5	115	1.05E-02	8.52E-01
R-HSA-5173105	O-linked glycosylation	3	115	1.05E-02	9.76E-01
R-HSA-5693567	HDR through Homologous Recombination (HR) or Single Strand Annealing (SSA)	4	114	1.04E-02	9.30E-01
R-HSA-2029485	Role of phospholipids in phagocytosis	4	114	1.04E-02	9.30E-01
R-HSA-72706	GTP hydrolysis and joining of the 60S ribosomal subunit	22	113	1.03E-02	5.37E-06
R-HSA-1799339	SRP-dependent cotranslational protein targeting to membrane	20	113	1.03E-02	5.26E-05
R-HSA-5610787	Hedgehog 'off' state	11	113	1.03E-02	1.08E-01
R-HSA-156827	L13a-mediated translational silencing of Ceruloplasmin expression	22	112	1.02E-02	4.68E-06
R-HSA-6785807	Interleukin-4 and 13 signaling	7	111	1.01E-02	5.55E-01
R-HSA-157118	Signaling by NOTCH	6	111	1.01E-02	7.04E-01
R-HSA-166663	Initial triggering of complement	4	111	1.01E-02	9.21E-01
R-HSA-163685	Integration of energy metabolism	2	111	1.01E-02	9.93E-01
R-HSA-5696398	Nucleotide Excision Repair	4	110	1.01E-02	9.17E-01
R-HSA-72306	tRNA processing	2	110	1.01E-02	9.93E-01
R-HSA-156580	Phase II - Conjugation of compounds	2	110	1.01E-02	9.93E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-8878159	Transcriptional regulation by RUNX3	17	109	9.97E-03	7.63E-04
R-HSA-69306	DNA Replication	10	108	9.88E-03	1.52E-01
R-HSA-3214847	HATs acetylate histones	5	108	9.88E-03	8.13E-01
R-HSA-8957275	Post-translational protein phosphorylation	4	107	9.78E-03	9.07E-01
R-HSA-425393	Transport of inorganic cations/anions and amino acids/oligopeptides	4	107	9.78E-03	9.07E-01
R-HSA-211000	Gene Silencing by RNA	1	107	9.78E-03	9.99E-01
R-HSA-211945	Phase I - Functionalization of compounds	1	106	9.69E-03	9.99E-01
R-HSA-15869	Metabolism of nucleotides	5	105	9.60E-03	7.93E-01
R-HSA-5668914	Diseases of metabolism	3	105	9.60E-03	9.62E-01
R-HSA-425366	Transport of glucose and other sugars, bile salts and organic acids, metal ions and amine compounds	2	105	9.60E-03	9.90E-01
R-HSA-382556	ABC-family proteins mediated transport	9	104	9.51E-03	2.17E-01
R-HSA-8978870	Fatty acid synthesis	1	104	9.51E-03	9.99E-01
R-HSA-199418	Negative regulation of the PI3K/AKT network	3	103	9.42E-03	9.58E-01
R-HSA-72689	Formation of a pool of free 40S subunits	21	102	9.33E-03	3.79E-06
R-HSA-5668541	TNFR2 non-canonical NF-kB pathway	15	102	9.33E-03	2.63E-03
R-HSA-6811434	COPI-dependent Golgi-to-ER retrograde traffic	2	102	9.33E-03	9.89E-01
R-HSA-192823	Viral mRNA Translation	18	101	9.24E-03	1.12E-04
R-HSA-611105	Respiratory electron transport	6	101	9.24E-03	6.16E-01
R-HSA-2219528	PI3K/AKT Signaling in Cancer	4	101	9.24E-03	8.82E-01
R-HSA-2029481	FCGR activation	3	101	9.24E-03	9.54E-01
R-HSA-391251	Protein folding	2	101	9.24E-03	9.88E-01
R-HSA-69239	Synthesis of DNA	10	100	9.14E-03	1.07E-01
R-HSA-937061	TRIF-mediated TLR3/TLR4 signaling	4	100	9.14E-03	8.77E-01
R-HSA-166166	MyD88-independent TLR3/TLR4 cascade	4	100	9.14E-03	8.77E-01
R-HSA-168164	Toll Like Receptor 3 (TLR3) Cascade	4	100	9.14E-03	8.77E-01
R-HSA-1296071	Potassium Channels	3	99	9.05E-03	9.50E-01
R-HSA-2187338	Visual phototransduction	2	99	9.05E-03	9.86E-01
R-HSA-2168880	Scavenging of heme from plasma	1	99	9.05E-03	9.98E-01
R-HSA-5607764	CLEC7A (Dectin-1) signaling	11	98	8.96E-03	5.07E-02
R-HSA-168179	Toll Like Receptor TLR1:TLR2 Cascade	5	98	8.96E-03	7.42E-01
R-HSA-181438	Toll Like Receptor 2 (TLR2) Cascade	5	98	8.96E-03	7.42E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-193704	p75 NTR receptor-mediated signalling	5	98	8.96E-03	7.42E-01
R-HSA-8856825	Cargo recognition for clathrin-mediated endocytosis	4	98	8.96E-03	8.67E-01
R-HSA-373080	Class B/2 (Secretin family receptors)	2	97	8.87E-03	9.85E-01
R-HSA-975956	Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC)	17	96	8.78E-03	1.85E-04
R-HSA-5689603	UCH proteinases	10	96	8.78E-03	8.82E-02
R-HSA-168138	Toll Like Receptor 9 (TLR9) Cascade	7	96	8.78E-03	4.06E-01
R-HSA-6811558	PI5P, PP2A and IER3 Regulate PI3K/AKT Signaling	3	96	8.78E-03	9.42E-01
R-HSA-156842	Eukaryotic Translation Elongation	19	95	8.69E-03	1.60E-05
R-HSA-446652	Interleukin-1 signaling	13	95	8.69E-03	8.66E-03
R-HSA-381119	Unfolded Protein Response (UPR)	7	95	8.69E-03	3.96E-01
R-HSA-166058	MyD88:Mal cascade initiated on plasma membrane	5	95	8.69E-03	7.18E-01
R-HSA-168188	Toll Like Receptor TLR6:TLR2 Cascade	5	95	8.69E-03	7.18E-01
R-HSA-2682334	EPH-Ephrin signaling	4	95	8.69E-03	8.51E-01
R-HSA-390466	Chaperonin-mediated protein folding	2	95	8.69E-03	9.83E-01
R-HSA-72764	Eukaryotic Translation Termination	17	94	8.60E-03	1.45E-04
R-HSA-2408557	Selenocysteine synthesis	17	94	8.60E-03	1.45E-04
R-HSA-2559580	Oxidative Stress Induced Senescence	4	94	8.60E-03	8.45E-01
R-HSA-6803157	Antimicrobial peptides	3	94	8.60E-03	9.36E-01
R-HSA-190236	Signaling by FGFR	1	94	8.60E-03	9.97E-01
R-HSA-168181	Toll Like Receptor 7/8 (TLR7/8) Cascade	6	93	8.50E-03	5.36E-01
R-HSA-975155	MyD88 dependent cascade initiated on endosome	6	93	8.50E-03	5.36E-01
R-HSA-983170	Antigen Presentation: Folding, assembly and peptide loading of class I MHC	4	93	8.50E-03	8.39E-01
R-HSA-3371556	Cellular response to heat stress	4	93	8.50E-03	8.39E-01
R-HSA-163125	Post-translational modification: synthesis of GPI-anchored proteins	3	93	8.50E-03	9.33E-01
R-HSA-4086400	PCP/CE pathway	11	92	8.41E-03	3.50E-02
R-HSA-446728	Cell junction organization	3	92	8.41E-03	9.30E-01
R-HSA-6804756	Regulation of TP53 Activity through Phosphorylation	7	91	8.32E-03	3.55E-01

Pathway ID	Pathway description	# Entities	# Total	Ratio	pValue
R-HSA-975138	TRAF6 mediated induction of NFkB and MAP kinases upon TLR7/8 or 9 activation	6	91	8.32E-03	5.15E-01
R-HSA-6794362	Protein-protein interactions at synapses	5	91	8.32E-03	6.82E-01
R-HSA-5617472	Activation of anterior HOX genes in hindbrain development during early embryogenesis	5	91	8.32E-03	6.82E-01
R-HSA-5619507	Activation of HOX genes during differentiation	5	91	8.32E-03	6.82E-01
R-HSA-156902	Peptide chain elongation	19	90	8.23E-03	7.67E-06
R-HSA-8876198	RAB GEFs exchange GTP for GDP on RABs	4	90	8.23E-03	8.21E-01
R-HSA-428157	Sphingolipid metabolism	3	90	8.23E-03	9.24E-01
R-HSA-73886	Chromosome Maintenance	1	90	8.23E-03	9.97E-01
R-HSA-418346	Platelet homeostasis	1	90	8.23E-03	9.97E-01
R-HSA-1474290	Collagen formation	1	90	8.23E-03	9.97E-01
R-HSA-2980736	Peptide hormone metabolism	5	89	8.14E-03	6.64E-01
R-HSA-388841	Costimulation by the CD28 family	3	89	8.14E-03	9.20E-01
R-HSA-5687128	MAPK6/MAPK4 signaling	11	88	8.05E-03	2.67E-02
R-HSA-450531	Regulation of mRNA stability by proteins that bind AU-rich elements	10	88	8.05E-03	5.67E-02
R-HSA-5628897	TP53 Regulates Metabolic Genes	6	88	8.05E-03	4.83E-01
R-HSA-1500620	Meiosis	4	88	8.05E-03	8.07E-01
R-HSA-416482	G alpha (12/13) signalling events	5	87	7.96E-03	6.44E-01
R-HSA-2565942	Regulation of PLK1 Activity at G2/M Transition	3	87	7.96E-03	9.13E-01
R-HSA-174143	APC/C-mediated degradation of cell cycle proteins	14	86	7.86E-03	1.46E-03
R-HSA-453276	Regulation of mitotic cell cycle	14	86	7.86E-03	1.46E-03
R-HSA-109704	PI3K Cascade	5	86	7.86E-03	6.34E-01
R-HSA-216083	Integrin cell surface interactions	1	86	7.86E-03	9.96E-01
R-HSA-351202	Metabolism of polyamines	10	85	7.77E-03	4.70E-02
R-HSA-68874	M/G1 Transition	9	85	7.77E-03	9.48E-02
R-HSA-69002	DNA Replication Pre-Initiation	9	85	7.77E-03	9.48E-02

7.4 Drug Therapy

7.4.1 DrugBank

Table 7.11 – Most of the results obtained from DrugBank searching for targets related with HIV or AIDS

Target	DrugBank ID	Name	Drug group	Actions
60S ribosomal protein L3	DB02494	Alpha-Hydroxy-Beta-Phenyl-Propionic Acid	experimental	
	DB04865	Omacetaxine mepesuccinate	approved	antagonist
	DB07374	Anisomycin	experimental	
	DB08437	Puromycin	experimental	
	DB02709	Resveratrol	experimental, investigational	
Casein kinase II subunit alpha	DB03127	Benzamidine	experimental	
	DB04395	Phosphoaminophosphonic Acid-Adenylate Ester	experimental	
	DB07715	Emodin	investigational	
C-C chemokine receptor type 2	DB08846	Ellagic Acid	investigational	inhibitor
	DB05130	INCB3284	investigational	
	DB05159	CCX915	investigational	
	DB05486	MLN-1202	investigational	
	DB04835	Maraviroc	approved, investigational	antagonist
C-C chemokine receptor type 5	DB05062	INCB9471	investigational	
	DB05501	AMD-070	investigational	
C-C chemokine receptor type 9	DB05005	CCX282	investigational	
C-C motif chemokine 3	DB05364	ROX-888	investigational	
Chitosanase	DB01296	Glucosamine	approved	
Complement component 1 Q subcomponent-binding protein, mitochondrial	DB08818	Hyaluronic acid	approved, vet_approved	binder
C-X-C chemokine receptor type 4	DB00452	Framycetin	approved	antagonist
	DB05501	AMD-070	investigational	
	DB06809	Plerixafor	approved	antagonist
Envelope glycoprotein gp160	DB04639	Biphenylalanine	experimental	
	DB05658	SPL-7013	investigational	
	DB05342	SP-01A	investigational	
	DB05398	C31G	investigational	
	DB05871	UC-781	investigational	
Gag polyprotein	DB06039	PA-1050040	investigational	
	DB06414	Etravirine	approved	
	DB07885	Talviraline	investigational	
	DB08639	Dapivirine	investigational	
Genome polyprotein	DB01720	(2Z)-2-(Benzoylamino)-3-	experimental	

Target	DrugBank ID	Name	Drug group	Actions
		[4-(2-Bromophenoxy)Phenyl]-2-Propenoic Acid		
	DB04005	Uridine 5'-Triphosphate	experimental	
	DB05868	Ciluprevir	investigational	
	DB06038	ITMN-191	investigational	
	DB06058	XTL-6865	investigational	
	DB07238	Nesbuvir	investigational	
		N-[(2R,3S)-1-((2S)-2- {[(CYCLOPENTYLAMINO) CARBONYL]AMINO}-3- METHYLBUTANOYL)-2- (1-FORMYL-1- CYCLOBUTYL)PYRROLIDINYL] CYCLOPROPANECARBOXAMIDE	experimental	
	DB01992	Coenzyme A	nutraceutical	
	DB01992	Coenzyme A	nutraceutical	
Histone acetyltransferase KAT2A	DB08186	(3E)-4-(1-METHYL-1H-INDOL-3-YL) BUT-3-EN-2-ONE	experimental	
	DB08291	N-(3-AMINOPROPYL)-2- NITROBENZENAMINE	experimental	
Histone acetyltransferase KAT5	DB01992	Coenzyme A	nutraceutical	
	DB02039	S-Acetyl-Cysteine	experimental	
HIV-1 protease	DB00220	Nelfinavir	approved	inhibitor
Integrin alpha-V	DB00098	Anti-thymocyte Globulin (Rabbit)	approved	
Integrin beta-1	DB00098	Anti-thymocyte Globulin (Rabbit)	approved	
	DB00054	Abciximab	approved	antagonist
	DB00063	Eptifibatide	approved, investigational	
Integrin beta-3	DB00098	Anti-thymocyte Globulin (Rabbit)	approved	
	DB00775	Tirofiban	approved	antagonist
	DB04863	Lefradafiban	investigational	
	DB05787	LM-609	investigational	
	DB05122	R1295	investigational	
Integrin beta-7	DB05802	MLN-02	investigational	
	DB09033	Vedolizumab	approved	antibody
	DB00786	Marimastat	approved, investigational	inhibitor
Interstitial collagenase	DB07556	N-HYDROXY-2(R)-[[[4- METHOXYPHENYL]SULFONYL] (3-PICOLYL)AMINO]-3- METHYLBUTANAMIDE HYDROCHLORIDE	experimental	

Target	DrugBank ID	Name	Drug group	Actions
	DB07926	N-[3-(N'-HYDROXYCARBOXAMIDO)-2-(2-METHYLPROPYL)-PROPANOYL]-O-TYROSINE-N-METHYLAMIDE	experimental	
	DB08403	METHYLAMINO-PHENYLALANYL-LEUCYL-HYDROXAMIC ACID	experimental	
	DB08482	[[1-[N-HYDROXY-ACETAMIDYL]-3-METHYL-BUTYL]-CARBONYL-LEUCINYL]-ALANINE ETHYL ESTER	experimental	
	DB08491	N-HYDROXY-2-[4-(4-PHENOXY-BENZENESULFONYL)-TETRAHYDRO-PYRAN-4-YL]-ACETAMIDE	experimental	
Low-density lipoprotein receptor	DB00707	Porfimer	approved, investigational	
Lysine--tRNA ligase	DB00123	L-Lysine	approved, nutraceutical	
NAD-dependent protein deacetylase sirtuin-1	DB05073	SRT501	investigational	
Nuclear factor NF-kappa-B	DB00945	Acetylsalicylic acid	approved, vet_approved	antagonist
	DB01296	Glucosamine	approved	antagonist
	DB05212	HE3286	investigational	
Nuclear factor NF-kappa-B p100 subunit	DB05451	P54	investigational	
	DB05464	NOX-700	investigational	
	DB05471	SGN-30	investigational	
	DB05487	CC-8490	investigational	
	DB05767	HMPL-004	investigational	
Sodium/nucleoside cotransporter 1	DB00441	Gemcitabine	approved	
	DB00495	Zidovudine	approved	
	DB00649	Stavudine	approved, investigational	
T-cell surface glycoprotein CD4	DB00098	Anti-thymocyte Globulin (Rabbit)	approved	

7.4.2 Others

Table 7.12 – Summary of recent drugs approved by the FDA related with HIV or AIDS.

Compound	ChEMBL ID	Brand Name	Drug Class	Target Predictions	Organism	Analogues
Abacavir	CHEMBL1380	Ziagen	Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	Adenosine A1, A2a, A3 receptors	<i>Homo sapiens</i>	Dundee; LINT
Nevirapine	CHEMBL57	Viramune	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	HIV1 reverse transcriptase	HIV1	

Darunavir	CHEMBL1323	Prezista	Protease Inhibitors	HIV1 protease	HIV1	7
Maraviroc	CHEMBL1201187	Selzentry	Entry Inhibitors	C-C chemokine receptor type 5	Homo sapiens	MLSMR