Proteomics Final Project

Akash Nagapurkar

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**Research Goal:** The goal of this project was to determine if interactions with opsins receptors and immune ligands were significant given a list of predicted protein-protein interactions from “Systematic prediction of human membrane receptor interactions” (Ashburner et al., 2000). Supplementary Figure 6 was used.

**Methods:** To examine this, opsin receptors in the human body were sourced from the HUGO Gene Nomenclature Committee (HGNC) Database. The immune ligands were sourced from the Gene Ontology database using the following search terms: chemokines, cytokines, toll, tumor necrosis factor, bone morphogenic proteins, interferons, interleukins, tachykinin, and endothelins. These were chosen as the HGNC database indicated that they all have a large

involvement in the immune system. This was also checked when pulling the data as the filters that were applied were that the genes needed to be Homo sapiens genes, they needed to be involved in regulation of the immune system, and they needed to be UniProt ID genes (so as to avoid including duplicates from different ID systems).

After gene list extraction, the tables were pre-processed to ensure that the genes in each system were unique and only one count of each existed. The genes from the gene lists were then used to see if opsin receptors and immune ligands had any predicted interactions with one another in the predicted interactions data from the aforementioned paper. Following this, the expected interactions between opsin receptors and immune ligands were calculated. The formulas for these calculation are included in the Jupyter Notebook.

To check for the significance of the interactions, a chi square test was used to see if the associations between immune ligands and opsin receptors were indeed significant. The observed and expected values for immune ligand and opsin receptor interactions were thus fed into this analysis to perform the significance test. Finally, a network graph was created in the same Jupyter Notebook to visualize the observed interactions and determine which receptors and ligands had shared and different networks.

**Results:** The chi square test was completed using critical values and p-values. Both methods yielded a rejection of the null hypothesis and a conclusion that the associations observed were not due to random chance. Overall, there were 10 predicted interactions between immune ligands and opsin receptors that were found.

**Discussion:** Examining the graph below, we can see that there aren't very many interactions between the Opsin Receptor and Ligands, but based on the significance tests conducted beforehand, their interactions are significant. We can see that OPN3 is a very well-interacted-with receptor, having connections with immune ligand genes such as PTPN1, PTPN11, PTPRC, PTPN6, and PTPRS. These genes are Protein Tyrosine Phosphatase genes and are often involved in immune system regulation by interacting with interleukins and other immune system related molecules. We can also see that CD80, a molecule that plays a role in T cell activation, interacts with RHO which is the gene responsible for making rhodopsin. Another interesting view in the network graph is that PTPRS binds to both OPN3 and RGR which shows that there is non-specific binding occurring between those molecules. This means that there is a potential for there to be even more non-specific binding and protein-protein interactions if the list of predicted interactions used for this analysis was extended to include Scores below 1.

**Chart

Description automatically generated**

**Sources:**

Ashburner M, Ball CA, Blake JA, Botstein D, Butler H, Cherry JM, Davis AP, Dolinski K,

Dwight SS, Eppig JT, Harris MA, Hill DP, Issel-Tarver L, Kasarskis A, Lewis S, Matese JC, Richardson JE, Ringwald M, Rubin GM, Sherlock G. Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. Nat Genet. 2000 May;25(1):25-9. doi: 10.1038/75556. PMID: 10802651; PMCID: PMC3037419.

Gene Ontology Consortium. The Gene Ontology resource: enriching a GOld mine. Nucleic

Acids Res. 2021 Jan 8;49(D1):D325-D334. doi: 10.1093/nar/gkaa1113. PMID: 33290552; MCID: PMC7779012.

Qi Y, Dhiman HK, Bhola N, Budyak I, Kar S, Man D, Dutta A, Tirupula K, Carr BI, Grandis J,

Bar-Joseph Z, Klein-Seetharaman J. Systematic prediction of human membrane receptor interactions. Proteomics. 2009 Dec;9(23):5243-55. doi: 10.1002/pmic.200900259. PMID: 19798668; PMCID: PMC3076061.

Seal RL, Braschi B, Gray K, Jones TEM, Tweedie S, Haim-Vilmovsky L, Bruford EA.

Genenames.org: the HGNC resources in 2023. Nucleic Acids Res. 2023 Jan 6;51(D1):D1003-D1009. doi: 10.1093/nar/gkac888. PMID: 36243972; PMCID: PMC9825485.