Mining Common Structural Features of Aggregating Proteins in Neurodegenerative Diseases

Zhang, Shuwen (School: Vivian Webb School)

I set out to find the similarities between different aggregating proteins' amino acid sequences and 3D conformations in neurodegenerative diseases (NDDs) using computational methods. Using the found similarities, I then pinpointed drug targets between some proteins, which may become useful references for future NDD therapeutics. Because the amino acid sequences and the crystallography structures of most NDD-related proteins are publicly available on Protein Database (PDB), I used the derived PDB files and FASTA sequence files to conduct several computational analyses. First, I used tools such as BLAST and Topmatch to align the amino acid sequences of the proteins to see how similar the sequences are. Then, I employed algorithms such as FATCAT and Dali to search for similarities between their 3D structures. From the most similar pairs of aggregating proteins, I then used icn3d to hone in on specific similar sequences between Transportin-1 and Tau, the most similar protein pair. Though I found no significant similarities between the amino acid sequences of aggregating proteins, there were six significant structural alignments found during my research. Of these six pairs, three (Transportin-1 and Tau, Transportin-1 and APP, and APP and Tau) had a significant structural similarity. I then used the obtained binding sites for Trn1 and Tau to determine respective drug targets since there are no drugs that target both simultaneously. Possible future targets to be tested for Tau are S-Adenosylmethionine (DB00118) and Sirolimus (DB00877). A potential drug that could be repurposed to target Trn1 is Acetic acid (DB03166).