Alcott: A Convolutional Neural Network to Predict Multimeric Interactions in HIV-1 Neural Infection

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Microglial cells have the ability to engulf HIV-1 infected glial cells by binding to neuronal blebs, effectively stopping the subsequent encephalopathy. However, two HIV-1 accessory proteins –Nef and Fyn– can relocalize the Th cell recruiting protein CD59 to the cell membrane, limiting its function and inciting immune evasion. This is achieved via the formation of a Nef/Fyn polyproline helix utilizing glycine rich motifs, similar to how spider silk is twisted by golden orb weaver spiders. This experiment aimed to investigate if the enzymes used by golden orb weaver spiders to untwist their silk could be used to limit the Nef-Fyn complex function. First, a convolutional neural network was created in order to determine binding affinity from peptide alignment motifs based on sequence oligomerization capacity and degree of conservation. The oligomerization capacity was determined via the logP sum of each tokenized amino acid to determine solubility, and entropy was a function of the peptide's Gibbs Free Energy. The binding affinity (k-score) was ultimately determined through the generation of a confusion matrix. The system was trained on 5,000 data points and showed a 0.83 accuracy. From this, the enzyme Cathepsin L was determined to have the highest binding affinity to Nef (0.95 functional alignment), and gel electrophoresis was used to measure the degradation of Nef when digested with Cathepsin L, which was shown to be significant in glycine rich alignment motifs. Therefore, binding affinity predicted based on alignment motifs could be useful in improving enzyme therapy success rates and Cathepsin L could be used as a low-cost treatment component for reducing HIV-1 neural proliferation.

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