Observations of Drug Synergy Mechanisms to Target Intrinsically Disordered Proteins in Viruses

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An intrinsically disordered protein (IDP) is a protein that lacks a stable tertiary structure. A key aspect of such a protein is that it goes against the traditional dogma that protein structure determines protein function. IDPs, despite their unstable structure, have many applications in biology and biochemistry. Molecular recognition features (MoRFs) are regions in intrinsically disordered proteins that undergo disorder-to-order transitions by binding to different partners. There are many hurdles to using conventional experimental methods to find drugs that can target intrinsically disordered proteins. For instance, IDPs cannot be crystallized due to their unpredictable tertiary structure. However, computational modeling provides an efficient alternative to laboratory testing for drugs. In this project, past data on MoRFs and IDPs was used to determine drug synergy mechanisms to target MoRFs and their binding partners, alongside looking at aspects of MoRFs such as biomimicry and three-dimensional similarity. Machine learning was conducted in R, and further aspects of IDPs were used to train the binary classifier. The predicted drugs proved to be more effective than current antiviral drugs, as the predicted drugs had a higher binding affinity towards their targeted binding site as opposed to their commercial counterparts. ROC curves and one-sample t-tests were used to validate the accuracy of the binary classifier. This system of drug screening can be used in the future and be applied to any disease or condition that involves a genome that codes for IDPs.

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