Modeling human cytokine–receptor complexes as a first step towards predicting novel small molecules

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Cytokines are a family of small proteins that act as chemical messengers between cells, playing an essential role in orchestrating and regulating the immune response. They can have pro-inflammatory or anti-inflammatory effects and bind to their specific target receptors. Due to their essential role in the immune system, an imbalance in their expression or regulation can lead to the pathophysiology of various inflammatory and autoimmune diseases, making them major therapeutic targets [1–3].

Biological agents such as monoclonal anti-cytokine antibodies are already commercially available for a minority of these proteins, but small molecules could represent a complementary asset [4]. Therefore, our objective is to develop an open access *in silico* tool for predicting new small molecules targeting cytokines.

The first step of this project was the construction of a relational database dedicated to cytokines structures and ligands. We retrieved all the experimental and computational structures already available in the Protein Data Bank for each cytokine, linked to their UniProt code and extracted the necessary data. The next step is the identification of the different receptors associated with each cytokine. The corresponding complexes are currently being predicted, including all the domains of the cytokine receptors, using Boltz-2 [5]. These structural complexes will subsequently be used to identify potential binding sites for small molecules. Indeed, protein-protein interfaces will be of particular interest in the case of cytokines.

Bibliography:

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