Deciphering the drug discovery puzzle: unveiling the interaction of Galectin proteins

Drug discovery is akin to solving a complex puzzle, with the protein acting as the mold and the ligand structure representing the pieces. The pursuit of therapeutic drugs to counter diseases is a time-consuming and complex process. At the start of this endeavor lies the identification of a protein that is associated with the disease – finding the target protein. The end objective of a successful drug is to “turn off” the target protein, thus halting the progression of the disease. This is often achieved by providing a more attractive interaction partner in the form of the administered drug, effectively preventing any other interaction of the protein.

Amongst the numerous proteins implied in disease progression, galectin-3 and galectin-8 is the focal point of this project. To create a potent drug, a viable starting point is essential – a small fragment with the potential to evolve into an effective ligand. The thesis presents drug development efforts in both the early stages of discovering new potent starting points for development, as well as testing out new pieces added to already well established ligands. The results offer new potential avenues for future disease treatment.

X-ray crystallography was employed in order to elucidate the interplay between these molecules and their protein counterpart. In this work the technique was utilized to visualize never before seen interactions in molecular structures with atomic precision. The knowledge gained from these detailed structural models provide salient insight into the puzzle of protein-ligand binding of galectins. With the new discoveries obtained in this thesis, another piece is added; aiding in the effort of optimizing these drug precursors. In sum, further additions and alterations offer new possibilities for interaction between the protein and ligand, closing in on a functional drug.