Improving the druggability of Aquaporin-1 for future drug discovery campaigns

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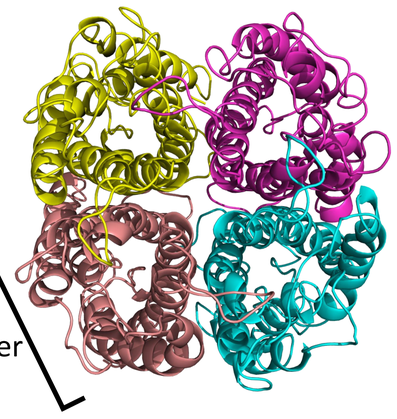
Introduction

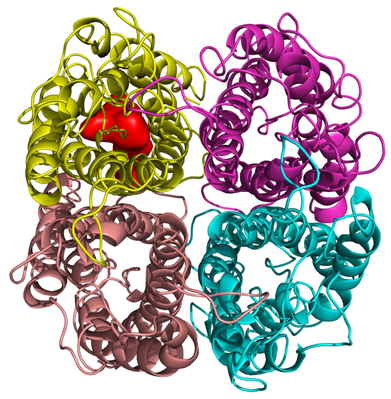
- Aquaporins (AQPs) are integral membrane proteins, whose function is to facilitate the passive transport of water across the plasma membrane of the cell. [1]
- These proteins have been proven to be over-expressed in tumors, when compared to normal tissues. [2]
- They can work as potential diagnostic and therapeutic targets in anticancer treatment. [2]
- The hit rate for the identification of small-molecule AQP modulators appears to be very low. [3]



- The growth of structure-function knowledge on AQPs, makes them promising therapeutic target to be used in future computational drug discovery campaigns. [1]

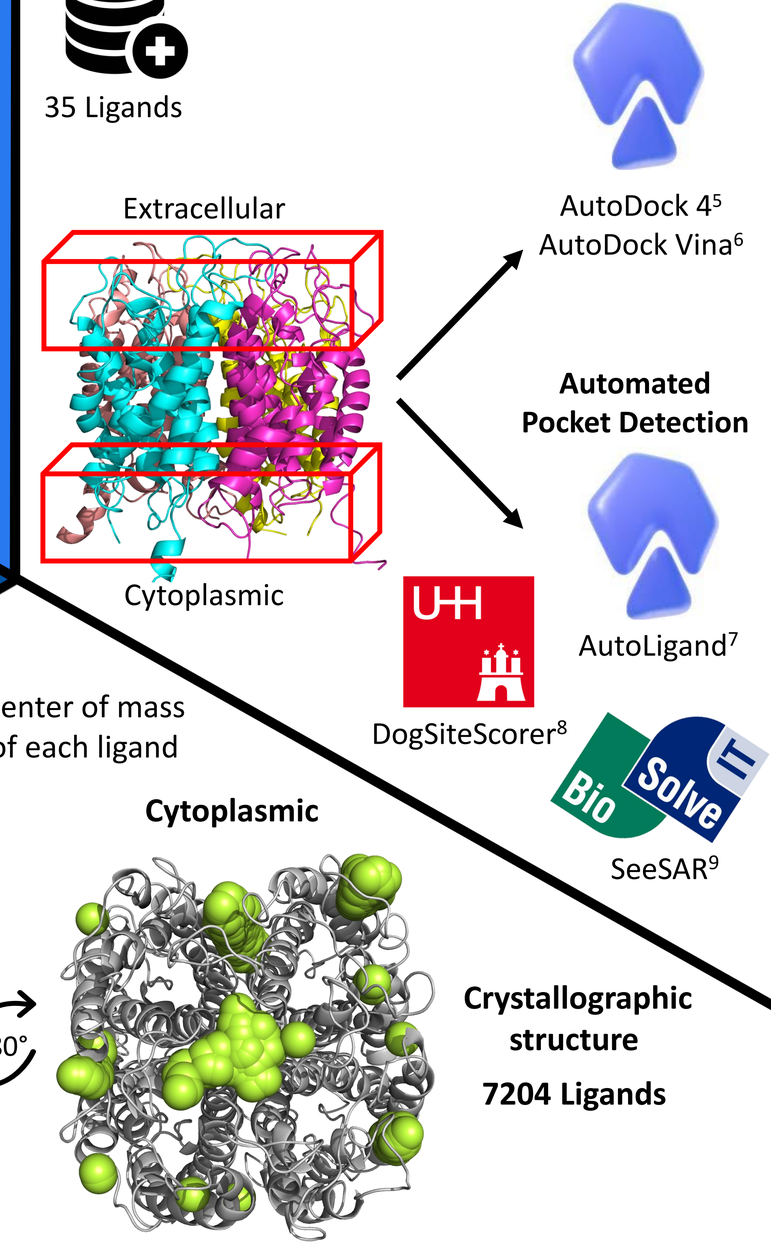
Objectives

- In this project, we are developing a new computational workflow based on several methods that combine innovative **ligand** and **structure-based** approaches to identify new AQP-1 modulators.
- **Ligand-based**: identification of new AQP modulators based on the chemical characteristics of the available ones.



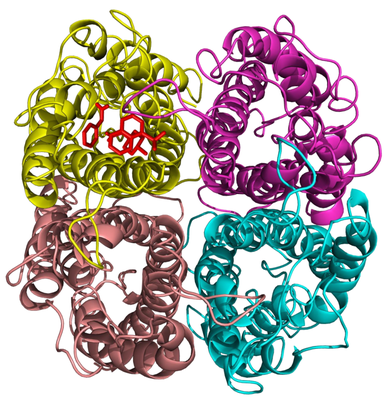
- **Structure-based**: pharmacophore and molecular docking, together with virtual screening.
- Our goal is the identification of the most promising binding pockets of the protein for future drug discovery campaigns.

Methods



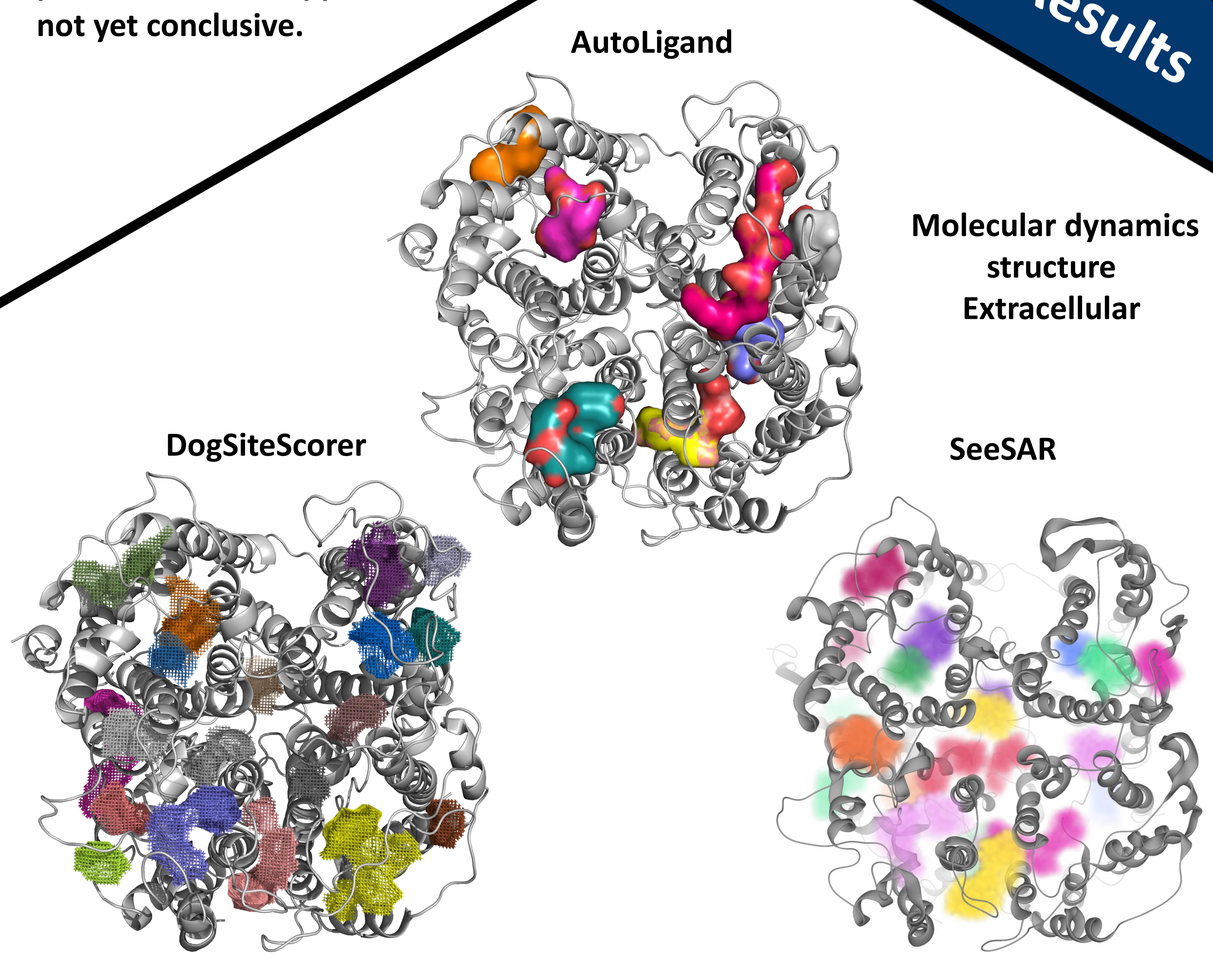
Docking Results

- **Using solely the crystallographic structure in this type of studies is not recommended.**
- **The use of additional conformations is what distinguishes our work.**



- **The use of MD snapshots allowed us to identify additional probable binding pockets in AQP-1 not found in the crystallographic structure.**
- **The results obtained with Automated pocket detection approach are not yet conclusive.**

Pocket Results



Conclusions

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