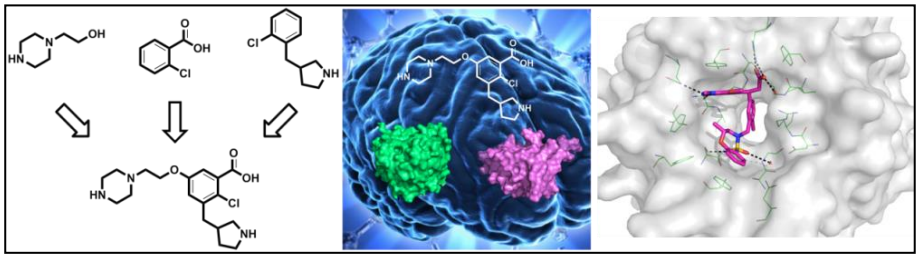
University of Copenhagen

Master Thesis Projects in Bach Group



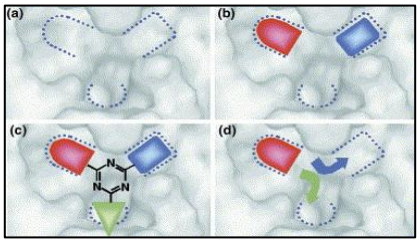
Are you interested in doing a master thesis project within drug discovery?

In the ***Bach Group*** we develop biological active small-molecule inhibitors against proteins in the brain. These compounds can be used as chemical probes for pharmacological studies and for identifying new therapeutic principles against e.g. ischemic stroke and brain cancer. We apply ***fragment-based drug discovery (FBDD)*** by screening fragments (small substructures of druglike molecules) and optimize the hits by organic chemical synthesis and medicinal chemistry. We have projects within following areas:

1. Screening fragments and biostructural studies of hits (X-ray crystallography):

Project A: You will setup biochemical and biophysical assays such as fluorescence polarization (***FP***) and surface plasmon resonance (***SPR***), and screen our fragment library against the proteins. Following this you will validate the hits from the screen by FP/SPR in order to characterize the binding-site and affinity, which is important for evaluating the hits as lead compounds for further drug design.

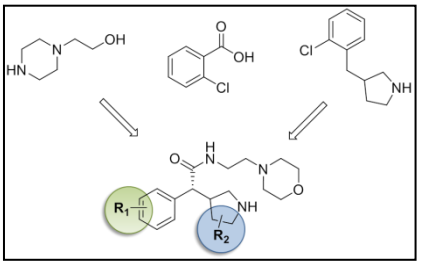
Project B: With the aim of determining the three-dimensional structure of the fragment-hits in the protein binding pocket, the compounds are tested using ***X-ray crystallography*** (e.g. crystal soaking). This will provide basis for optimization by fragment growing/linking in order to rationally design potent molecules towards the CNS proteins.



- In these projects you will learn how to ***express and purify proteins*** and acquire experience with innovative ***biophysical techniques*** frequently used in drug discovery projects both in academia and industry.

2. Medicinal Chemistry:

Here, you will ***design and synthesize*** new small-molecules against our protein targets. You may work on fragment-hits and optimize these into more potent molecules; or you could do ***structure-activity relationship (SAR)*** studies of known inhibitors. The aim would be to design potent compounds that are also able to enter the brain. Design is guided by X-ray crystallography and/or computational docking studies.



- As a master student you will be part of the Bach Group and its on-going research. You will be guided by a postdoc or PhD student involved in the project. Depending on your interests and project status your project can comprise one or more of above topics.

- For more information, contact associate professor Anders Bach (Dept. Drug Design & Pharmacology, Medicinal Chemistry Research): anders.bach@sund.ku.dk