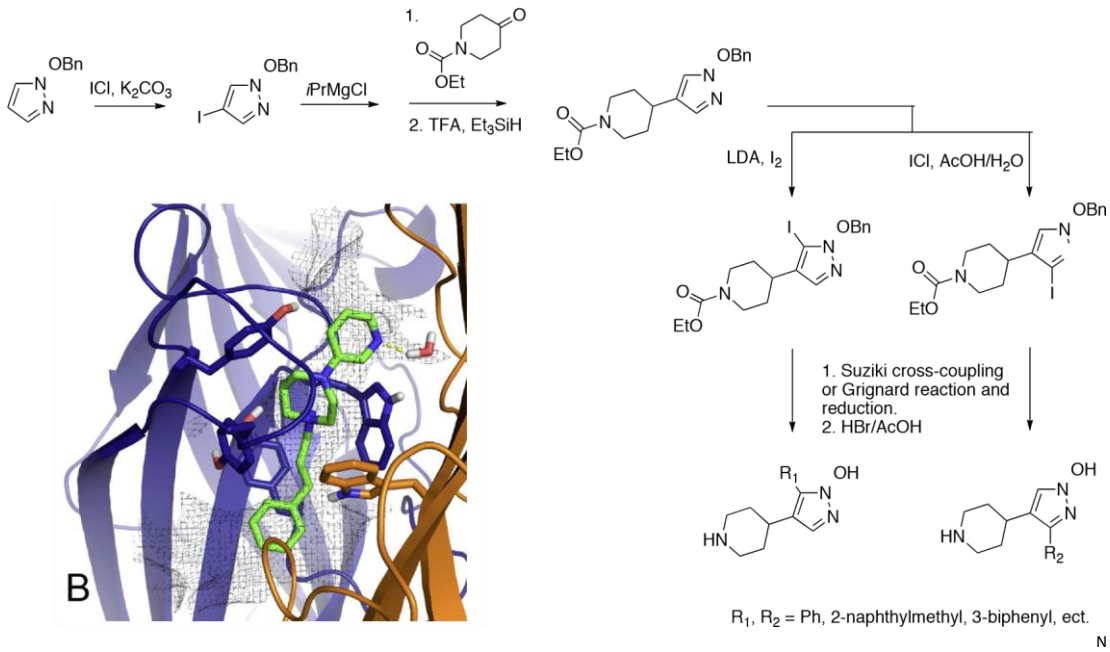
Design and synthesis of ligands for studying the GABAA or nicotinic acetylcholine receptors

The $GABA_A$ and nicotinic acetylcholine (nACh) receptors, which are structural very similar, are both important drug targets in a number of neurological and psychiatric disorders such as Alzheimer's Disease, Parkinson's Disease, epilepsy, schizophrenia and depression.

The aim of the overall project is to design and synthesize selective ligands that can be used for studying the architecture, localization and function of the $GABA_A$ or nACh receptors.

There exist a number of subtypes within each of the receptor groups differentiating in amino acid sequence, regional location and function. This opens up for subtype selective targeting, and thereby development of ligands with potential optimised therapeutic properties. Since no 3D-structure of the native $GABA_A$ and nACh receptors has been reported, our studies are based on homology receptor models and structure-activity studies of known ligands mainly developed at The Department of Drug Design and Pharmacology.

The project will cover design and synthesis of potential subtype selective ligands to be used for exploring the binding pockets of the receptors, in search for the structural basis for subtype selective targeting. The ligands will include labeling ligands, such as fluorescent, photoaffinity and photoswitches but also ligands for structure-activity studies. These studies are done in close collaboration with colleagues mastering molecular modelling and molecular pharmacology at The Department of Drug Design and Pharmacology.



Ref: ex. Bach et al, *Eur. J. Med.Chem.*, 2015, 102, 425-444, Krall et al, *ChemMedChem*, 2016, 2299–2310, Giraudo et al, *J. Med.Chem.*, 2019, 62, 5797-5809, L'Estrade et al, *ACSOMEGA*, 2019, 4, 8846-8851.

As a Master student you will be part of the ongoing research at the actual stage for the start of the master project, guided by a post doc or PhD student involved in the project. For the student the present project will involve literature study, experimental organic synthesis, spectroscopic characterisation and structure-activity studies. Furthermore, the molecular pharmacology and computer modelling relevant for the project can be followed.

For further information, please contact Bente Frølund, Department of Drug Design and Pharmacology, bfr@sund.ku.dk, room 203.