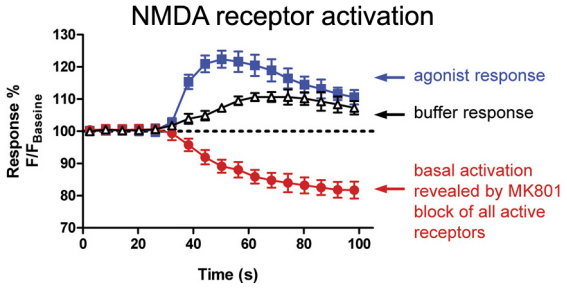
MSc projects in the MOLECULAR PHARMACOLOGY group

Molecular pharmacology

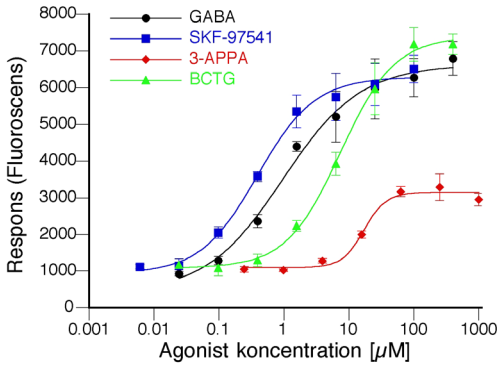
Molecular pharmacology is used to investigate cloned receptors and transporters, including their interaction with ligands and their molecular mechanism-of-action. Usually we apply a combination of techniques such as molecular biology (e.g. cloning and mutagenesis), cell culture and pharmacological assays (e.g. concentration-response curves and development of novel assays).



Supervisors: *Hans Bräuner-Osborne* (hbo@sund.ku.dk)
Anders A. Jensen (aaj@sund.ku.dk)
Petrine Wellendorph (pw@sund.ku.dk).
Website:https://drug.ku.dk/disciplines/molecular-and-cellular-pharmacology/molecular_pharmacology/

Pharmacological testing

Most receptors and transporters belong to families of targets for which the endogenous ligand activate several subtypes. For example, 24 glutamate receptors and 5 glutamate transporters have been identified. Therapeutically, it is often desired to only activate/inhibit one or few of the subtypes to e.g. avoid side-effects. By testing ligands on the receptor/transporter subtypes individually expressed in cell lines, it is possible to determine the potency, efficacy and subtype selectivity of the ligands, and thereby generate structure-activity-relationships. Such studies are performed in close collaboration with medicinal chemists and computational chemists to rationally generate subtype selective compounds with improved potency/selectivity for the target of interest.

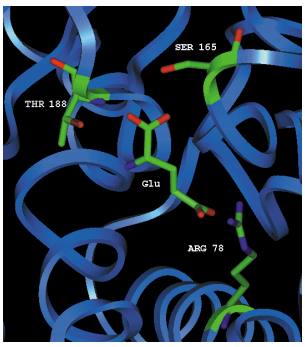


Screening for new lead structures

For some targets it is desired to discover new lead structures which can then be developed into novel pharmacological tool compounds as described above. For these receptor/transporter targets we perform pharmacological screening of compound libraries using either a general library of diverse compounds available in the group or focused target libraries generated by e.g. chemogenomics or virtual screening. Such projects will typically involve optimization of pharmacological assays to enable high-throughput screening assays before actually engaging in the screening.

Investigations of binding sites and mechanism-of-action

Often it is of interest to get increased insight into the ligand binding site and mechanism-of-action. Combined with computational chemists we generate models of the binding sites and subsequently test these models by generation of mutations which are predicted to e.g. influence ligand binding or subtype selectivity. Such information can be applied to structure-based design of novel ligands with improved pharmacological properties. Along the same lines we investigate the mechanism-of-action of e.g. agonist induced receptor activation by introducing mutations predicted to influence receptor activation.



MSc project examples

- Pharmacological characterization of ligands on cloned receptors and transporters
- Screening of compound libraries for novel pharmacological lead structures
- Development of novel pharmacological assays
- Generation and characterization of mutated receptors and transporters

Please contact one of the supervisors to discuss more concrete projects possibilities. We also have a strong network with Danish companies and foreign universities and can facilitate projects outside University of Copenhagen.