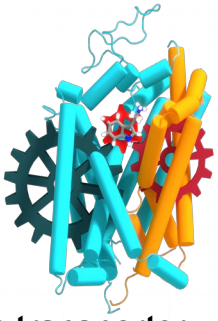
CENTER FOR PHYSIOLOGY
AND PHARMACOLOGY
MEDICAL UNIVERSITY OF VIENNA
Institute of Pharmacology



Project for Master -/ Diploma Thesis

Characterization of the hydrophobic gate of the human serotonin transporter

Medical University of Vienna
Institute for Physiology and Pharmacology
Department of Pharmacology and Toxicology

Supervisors: Assoc.- Prof. Dr. Thomas Stockner, Mag. Ralph Gradisch

About the project:
The human serotonin transporter (SERT) is a secondary active transporter that is abundantly expressed on presynaptic neurons of the central nervous system, but also in the gastrointestinal tract. It's function is to terminate serotoninergic neurotransmission, thereby shaping amplitude and frequency of inter-neuron signalling. Dysfunction and dysregulation are associated with several neuropsychiatric diseases, highlighting the importance of SERT as pharmacological target.
Substrate transport by SERT is energized by the transmembrane electrochemical gradient and functionally described by the alternating access model, which states that the substrate binding site located in the core of this transmembrane protein is always accessible to only one side of the membrane. During the transport cycle, accessibility to the substrate binding site alternates between access from the extracellular site to bind substrates and intracellular access to release the transported substrate to the cytosol. High resolution structures of 3 state of the transport cycle are available, forming an excellent basis for studies designed to query transporter function.
An essential step of substrate transport is the occlusion of bound substrate, when substrate becomes inaccessible from both sides of the membrane due to conformational changes. **The main aim of this thesis is the study of the functional importance of the hydrophobic gate that is essential for substrate occlusion and consist of highly conserved residues.**

What we offer:
Excellent interdisciplinary research environment of molecular biologists, physicians, pharmacologists and biophysicists.
Broad spectrum of experimental approaches, most importantly:
- Cell culture and mutagenesis
- Radio-labelled substrate transport and inhibitor assays
- Electrophysiology
- Fluorescent-activated cell sorting (FACS)

Insights into computational approaches (Molecular modelling and molecular dynamics simulations)
Possibility to be part of a peer-reviewed publication

Your qualifications:
- Student in the life science field with a passion for science
- Experiences in cell culture and wet lab
- English skills

Duration: At least 6-9 month. Position to be filled as soon as possible.
If this project grasps your attention, you are interested in structure-function relationship and open-minded to learn new approaches, please contact us. If you would like to apply, please send an application including a motivation letter and a CV to:
thomas.stockner@meduniwien.ac.at & ralph.gradisch@meduniwien.ac.at

We are looking forward to receive your application

Thomas Stockner and Ralph Gradisch