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Overview - doc.funds "Molecular Metabolism" (MOBILES) (uni-graz.at)
Structural Biology - Institute of Molecular Biosciences (uni-graz.at)
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I have an open position for a PhD student to fill at the Institute of Molecular Biosciences, University of Graz, Austria.

This PhD position is advertised in the frame of the SFB Lipid Hydrolysis: Cellular Lipid Degradation Pathways in Health and Disease, a research network between the Medical University of Graz, the University of Graz, the Medical University of Vienna, and the Technische Universität Wien.

The working language of my international research group is English. The selected student will receive salary, healthcare and social benefits according to the FWF-guidelines (https://www.fwf.ac.at/en/research-funding/personnel-costs).

Applications for the selection process takes place vie the following webpage at the Medical University of Graz:General information (medunigraz.at)

Application deadline: September 21, 2023

Please pass it on to potentially interested candidates for an exciting opportunity to carry out a PhD program at the interface of Structural Biology, Biochemistry, Molecular Biology and Biophysics. The project description is appended below and can also be found online (p16 of the pdf-file): Med_Uni_Graz_Application_Call2_2023_Projektbeschreibungen.pdf (medunigraz.at).

Project Title: Structure-function relationship of lipolytic regulation

Background:

Over the last decades, the number of obese individuals has drastically increased and with it the risk for susceptibility to cardiovascular diseases, type 2 diabetes, non-alcoholic fatty liver disease (NAFLD), and cancer. For potential therapeutic intervention, it is of immense importance to identify the players involved in lipid hydrolysis and lipid synthesis and to understand their dynamic interplay in detail. Our work focuses on expanding our knowledge of key mammalian lipid hydrolases at the molecular level. In adipose tissue, neutral lipolysis is primarily carried out by consecutive action of adipose triglyceride lipase (ATGL), hormone

sensitive lipase, and monoacylglycerol lipase [1]. ATGL initiates intracellular lipid mobilization, yet has also newly discovered functions as a transacylase in the biosynthesis of lipids with anti-diabetic and anti-inflammatory effects [2]. Insights in ATGL regulation have been emerging over the last years of intensive research from different laboratories worldwide along with significant contributions from the Oberer-group [3–6].

Hypothesis and Objective:

Our work focuses on expanding our knowledge of ATGL, and its regulation by proteins at the molecular level. These include its co-activator comparative gene identification-58 (CGI-58), officially annotated as ABHD5, and its inhibitory protein G0/G1 switch protein (G0S2). Biochemical studies with variants of ATGL, CGI-58 and G0S2 will identify individual residues that are essential for co-activation and inhibition as evaluated by activity and interaction assays. MS-based approaches will be used to experimentally map the protein-protein interfaces of ATGL. *In-vitro* and *in-silico* approaches are carried out to characterize the proteins in lipid droplets and lipid-droplet-mimicking systems. We will continue to optimize protein production of highest quality suitable for structural studies using cryoEM and protein crystallography.

Methodology:

The PhD student of this project will predominantly focus on lipases that are involved neutral lipid hydrolysis and its interaction with regulatory proteins. Plasmids encoding proteins, expression protocols for bacteria and the mammalian Expi293F™ system, as well as purification protocls using ÄKTA chromoatography systems are already available in the group [3,4]. Biochemical activity/inhibition assays will be performed partly also with isotope-labelled substrates. The PhD student will also carry out biophysical methods (e.g., circular dichroism spectroscopy, small-angle X-ray scattering, dynamic light scattering, mass-spectrometry). Protein crystallization setups will be done with manual set-ups or robotic equipment. Cryo-EM studies are carried out in an international collaboration (United States). The PhD student will perform most of the work in the international Structural Biology group at the IMB at the University of Graz, where 6 PIs and their groups have been working together in a “laboratory without walls” concept with shared knowledge, seminars and equipment since many years. We will continue collaboration within the SFB Lipid Hydrolysis and especially with the groups of Dr. R. Zimmermann, Dr. K. Gruber, Dr. R. Schreiber at the University of Graz, Dr. R. Birner-Grünberger at TU-Vienna, and Dr. A. Winkler at TU Graz.

References:

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