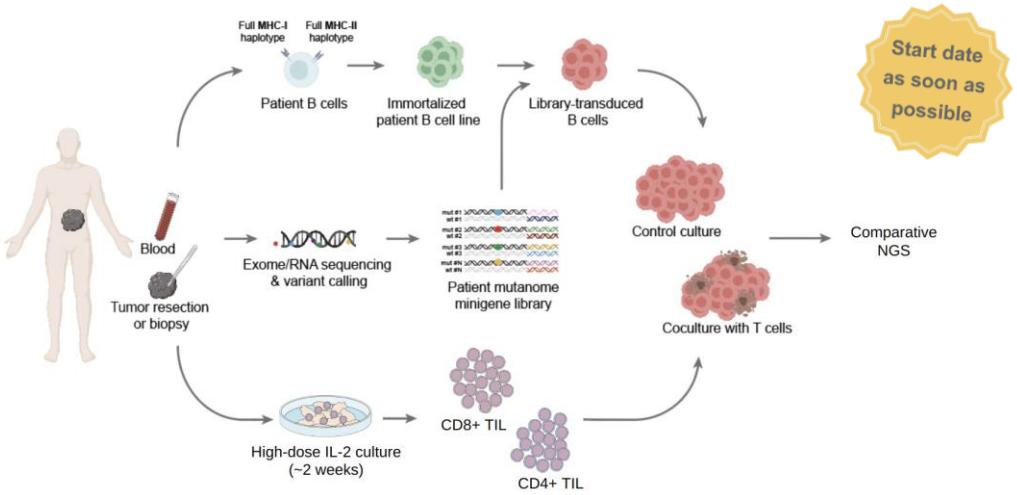
Master Thesis Opportunity in Molecular Medicine: Adoptive Cell Therapy and T-Cell Epitope Recognition (computational)

Are you passionate about cutting-edge cancer research and bioinformatics? Join our research group for a **Master's Thesis in Molecular Medicine**, focusing on **Adoptive Cell Therapy**!



The Challenge:

Adoptive cell therapy involves enriching and reinfusing T-cells into cancer patients, but identifying which T-cells target specific cancer-related neoantigens remains a "black box." In research with our experimental collaborators, we sequence cancer patients' genomes to identify potential neoantigens and T-cell receptor (TCR) sequences. These neoantigens are then tested in a **co-culture system** with T-cells harboring patient-specific TCRs, allowing us to understand which neoantigens are recognized and eliminated by which T-cells.

Your Role:

We are a **bioinformatics-focused research group** using the **R programming language** to develop tools that analyze data from these co-culture experiments. The goal of this Master's thesis project is to **further develop and optimize these tools** to analyze and interpret the intricate relationships between neoantigens and TCRs, contributing to advancements in personalized cancer therapies.

What You'll Gain:

- Hands-on experience with bioinformatics and cancer immunotherapy.
- Develop skills in R programming and data analysis for immunological applications.
- Contribute to the advancement of precision medicine in cancer treatment.

If you're excited to bridge the gap between cancer immunology and bioinformatics, please contact Asst. Prof. Michael Schubert (m.schubert@i-med.ac.at) stating your background, skills, and when you are planning to work on your thesis project!

2x Master Thesis Announcements

Are you excited about decision-making?

Interested in interspecies modeling of psychiatric conditions?

The Passecker Lab is seeking enthusiastic Master Students interested in pushing the frontiers of decision-making research. The lab studies the neuronal basis of Decision-Making and Reinforcement Learning in both health and disease. More information about the lab can be found at https://lab.jpassecker.com/ or through the Institute of Neurobiochemistry of the Medical University Innsbruck, Austria

The Projects:

We offer two new collaborative and highly multidisciplinary projects ***with partners of the University of Innsbruck***. Both projects aim to establish and test new decision-making paradigms in our highly flexible and scalable behavioral toolbox system. A system that allows the investigation of AI or human-based decision tasks in rodents for increased translational validity to investigate neurobiological foundations of decision-making. The first project aims to establish a new paradigm on how subjects overcome short-term negativity for higher long-term gains. The second project investigates how we can increase the inter-species modelling of inductive biases.

Background & Environment:

We are looking for students holding a BSc in biology, psychology, computer science, or a related subject. The ideal candidate should be highly motivated, creative, detail-oriented, have initiative and innovation abilities and oral and written communication skills in English. Previous experience with coding/comp. modeling or animal-based research is advantageous, but not required.

You can expect:

- A fun, multicultural and collaborative team.
- A multidisciplinary working atmosphere for gaining hands-on experience alongside your studies;
- The chance to develop your skills in planning and designing a research project;
- To get familiarized with the modern techniques currently used in behavioral, systems and computational neuroscience;
- Support and guidance for next steps in your career.

Applications for the above should be sent to johannes.passecker@i-med.ac.at and include a 1) full CV, 2) a short motivation letter stating your research interests, experience and potential career goals. **Starting Date:** positions are open until filled during 2024, starting date is negotiable. Date of issue: 01.02.2024

Topic

Role of PKN in neuronal energy metabolism and stroke

Advisor *Gabriele Baier and Stephanie zur Nedden (Institute of Neurobiochemistry)*

Contact gabriele.baier-bitterlich@i-med.ac.at
stephanie.zur-nedden@i-med.ac.at

Start *asap*

Project.

Stroke is a major global cause of death and permanent disability. Due to its stringent selection criteria only a small percentage of stroke patients qualify for the only FDA-approved treatment, tissueplasminogen-activator. Therefore, ongoing research into cerebroprotective mechanisms aim to uncover novel therapeutic approaches that improve the functional recovery after a stroke and would eventually be available to a greater percentage of stroke patients. We have recently established that protein kinase N (PKN), an enzyme mapped at the heart of signaling networks governing differentiation and cell survival, acts as a critical gatekeeper of the AKT prosurvival-signaling pathway during brain development (zur Nedden *et al*., 2018, Journal of Clinical Investigation, Safari et al, 2021, Frontiers in Synaptic Neuroscience).

Additionally, we found that PKN regulates protective signaling cascades related to energy metabolism after ischemic stroke, and may therefore serve as a novel target for cerebroprotective interventions (zur Nedden *et al*., Manuscript in prep). We are currently studying the role of PKN in neuronal energy metabolism particularly focusing on brain areas with a high energy demand, such as the retina and the hippocampus.

We seek a master/diploma student who performs biochemical, functional as well as metabolic analysis of brain tissue derived from WT and *Pkn1*$^{-/-}$ mice. The prospective candidate will be trained in a whole range of state-of-the-art-methods including molecular and biochemical techniques, metabolite extraction and analysis as well as metabolic phenotyping. Furthermore, the student will get experience in widely used neuroscientific model systems such as primary cell cultures, retinal whole mounts and acute hippocampal brain slices.

Topic

Measuring the glycoprotein afamin in a large cohort of chronic kidney disease patients with subsequent statistical data analyses

Advisor *Florian Kronenberg, Barbara Kollerits, Hans Dieplinger, Cathrin Pfurtscheller, (Institute of Genetic Epidemiology)*

Contact *florian.kronenberg@i-med.ac.at, barbara.kollerits@i-med.ac.at*

Start *Any time from now onwards*

Project (Background)
Afamin is a human vitamin E-binding glycoprotein primarily expressed in liver but also in kidney. Small proteomic and case control studies identified urinary afamin as a marker of kidney disease. In earlier studies, we described strong associations of plasma afamin concentrations with metabolic syndrome and diabetes mellitus. Analyses in >5000 CKD patients (i.e. mild to severe CKD, mostly stage G3) of the prospective German Chronic Kidney Disease (GCKD) cohort study provide evidence that elevated serum afamin concentrations are strongly and independently associated with a reduced risk for kidney failure.

The main aim of the current project will be to measure afamin in urine in >5000 CKD patients of the GCKD study. An ELISA will be established for these measurements. This ELISA is a double-antibody sandwich ELISA using two different anti-human afamin monoclonal antibodies for coating 96-well microtitre plates and, in peroxidase-conjugated form, for detection.

Possible additional project to work on: A discovery-driven approach will be applied to identify metabolites and metabolite-pair ratios associated with serum and urine afamin concentrations. As serum afamin is strongly associated with T2D and kidney failure, and should also urine afamin and the urine afamin-creatinine ratio be associated with CKD progression, then it could be expected that afamin will be associated with some known metabolites for CKD. This will help to illuminate the pathways linking afamin to chronic conditions such as CKD. The master student will have the possibility to additionally work on this project resulting in the possibility to write a manuscript and publish these results.

The ideal candidate for this Master position should have the following skills and competences:
Interest in work with proteins and applying/establishing a lab method (ELISA) for measurement. Interest in statistical data analyses and application of appropriate methods of the field. Excellent knowledge of English.

References:
*Kronenberg F, Kollerits B, Kiechl S, et al. Circ Cardiovasc Genet. 7: 822-9, 2014 (doi: 10.1161/ CIRCGENETICS.113.0006)
*Kronenberg F AND Dieplinger H. Clin. Lipidol. 10: 207-10, 2015 (https://doi.org/10.2217/clp.15.9)
*Kollerits B, Lamina C, Huth C, et al. Diabetes Care. 40: 1386-1393, 2017 (doi: 10.2337/dc17-0201)
*Pang, L, Duan, N, Xu, D et al. *Biomark Med,* 12**:** 1241-1249, 2018 (doi: 10.2217/bmm-2018-0126)

Topic

Open traineeship position in the Experimental Urology Department

Advisor *Chiara ANDOLFI (Experimental Urology Department)*

Contact chiara.andolfi@i-med.ac.at

Start *Oct 2023*

Outline

My team and I are looking for an enthusiastic student to join us in the study of the **Mediator complex** in the modulation of **prostate cancer metabolism**.
Eligible candidates are **Master students** looking for a **thesis project** or **recently graduated students** looking for a post-graduation traineeship.
The traineeship time should be at least 6 months.
If interested, please send your **CV** and a brief **introductory email.**
We are looking forward to your applications!

Project proposal

Role of MED12 in the modulation of metabolism in prostate cancer (PCa) cells

The mediator complex is a multi-subunit protein that regulates gene expression by molecularly bridging RNA polymerase II with transcription factors. Our team is studying its subunit called MED12, which plays a structural role within its kinase module. Perner et al. first showed that MED12 knockdown decreases the cell proliferation of PCa cell lines. We found out that MED12 knockdown dramatically decreases c-MYC mRNA and protein expression in our PCa cell lines, thus significantly reducing its downstream signalling. Since c-MYC is a main driver of PCa cell growth and proliferation, we believe that this is a key event in the MED12-mediated effects in cell proliferation. Interestingly, our pathway analysis also related MED12 knockdown to the inhibition of oxidative phosphorylation (OXPHOS), suggesting that its impact in cell proliferation might occur through metabolic reprogramming.
Therefore, this project aims at exploring the involvement of MED12 in the modulation of PCa cell metabolism. By inhibiting MED12 in our PCa cell lines, we will study its effects on the glycolysis and OXPHOS pathways. Moreover, we plan to inhibit the kinase activity of the mediator complex and analyse the downstream effects on PCa cell metabolism. In this way, we could assess if MED12 knockdown affects cell metabolism through its structural role within the kinase module of the mediator complex or independently from it.

Topic

Immunomodulation by endogenous retroelements in cancer

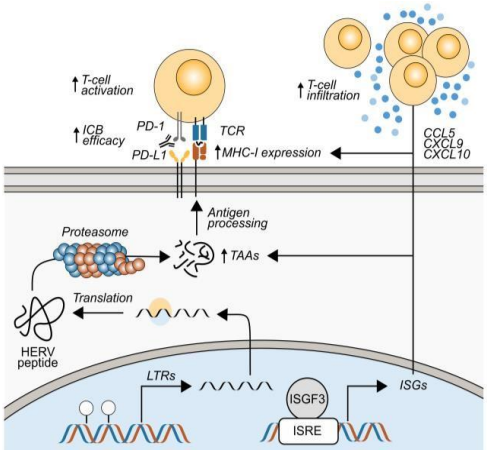
Advisor *Hubert Hackl (Institute of Bioinformatics, Biocenter, http://icbi.at/cbio/)*

Contact *hubert.hackl@i-med.ac.at*

Start: *March 2023 onwards*

Project

The aim of this project is to determine immunomodulatory effects of endogenous retroelements, which are specific in tumor compared to normal tissue or can be activated by epigenetic or radiotherapy. Thereby viral mimicry encompasses innate and adaptive immune responses triggered by endogenous sources of cytosolic RNA/DNA or tumor associated antigens encoded by human endogenous retroviruses.



The analyses might involve:

1) Identification of differentially expressed genes and transposable elements in tumor versus normal cells, by epigenetic or radiotherapy
2) Immunopeptidomics data analysis and prediction of tumor associated antigens
3) Identification of active antiviral and immune response triggered by endogenous stimuli Computational analysis of single-cell sequencing data (scRNAseq, TCRseq, Decode-seq)

Candidate

We are looking for a motivated student of Molecular Medicine or Medicine at the Medical University Innsbruck for a combined computational-experimental approach with a strong background/interest in bioinformatics data analyses (R/Python) as well as wet lab experiments. In our research group (CBIO) we also offer a longer-term collaboration (e.g. PhD position).

References

Chen R, et al. Endogenous retroelements and the viral mimicry response in cancer therapy and cellular homeostasis. ***Cancer Discov***. 2021. 11:2707-2725. doi: 10.1158/2159-8290.CD21-0506.

Bonaventura P, et al. Identification of shared tumor epitopes from endogenous retroviruses inducing high-avidity cytotoxic T cells for cancer immunotherapy. ***Sci Adv***. 2022. 8:eabj3671. doi: 10.1126/sciadv.abj3671

Natoli M, et al. Transcriptional analysis of multiple ovarian cancer cohorts reveals prognostic and immunomodulatory consequences of ERV expression. ***J Immunother Cancer***. 2021. 9:e001519. doi: 10.1136/jitc-2020-001519

Topic

Functional implications of LAMTOR1 phosphorylation

Advisor *Prof Lukas A. Huber and MSc Isabel Singer (Institute of Cell Biology, Biocenter MUI, https://cellbiology.i-med.ac.at/)*

Contact *lukas.huber@i-med.ac.at; isabel.singer@i-med.ac.at*

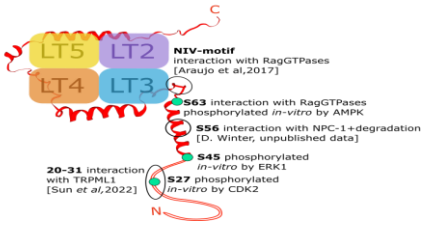
Start: *Any time from March 2023 onwards*

Project

In recent years, the view of lysosomes as a cellular garbage disposal system has been extended by data underlying its importance in orchestrating cellular metabolism. Lysosomes are crucial for cell growth, proliferation, differentiation and cell-type specific processes, rendering proper lysosomal function indispensable for cellular homeostasis.

Lysosomes harbor a complex nutrient sensing machinery that integrates information about extra- and intracellular nutrient availability and activates corresponding signaling pathways, causing changes in the cell's metabolic program. The LAMTOR [late endosomal/lysosomal adaptor and MAPK (mitogenactivated protein kinase) and mTOR (mechanistic target of Rapamycin) activator] complex plays a central role in these processes by recruiting and/or activating AMPK (AMP-activated protein kinase), MAPK and mTOR on the lysosomal surface.

In order to regulate these processes, LAMTOR associates with a number of partners including the RagGTPases, SLC38A9, the lysosomal v-ATPase, MEK, BORC, AXIN, LKB1, and many more. We know that some of these associations are mutually exclusive, whereas others occur under the same physiological conditions. We could show in previous work, that phosphorylation of the N-terminus of LAMTOR1 plays a role in regulating these interactions, however the functional trigger(s) for these events and their physiological consequences for the cell remain largely unknown.



The aim of this Master thesis, is to investigate these phosphorylation sites functionally. A large number of cell lines with different mutations are available for this purpose. Methods to be used include biochemical analysis, high resolution microscopy and basic molecular biology techniques.

Requirements:

We are looking for motivated young scientists to join our lab at the CCB Innsbruck for their Master thesis. We offer a collaborative lab atmosphere and thorough training in molecular cell biology, protein biochemistry and microscopy.

Topic

A comparative analysis of different mTORopathies

Advisor *Mariana Eca Guimaraes de Araujo (Institute of Cell Biology, Biocenter MUI, https://cellbiology.i-med.ac.at/)*

Contact *mariana.araujo@i-med.ac.at*

Start: *Any time from March 2023 onwards*

Project

Most organisms have mechanisms for efficiently transitioning between anabolic and catabolic states, allowing them to survive and grow in environments in which nutrient availability is limited. In mammals, an example of such a mechanism is the signaling network coordinated by mTOR (Mechanistic target of rapamycin). Because mTORC1 triggers a rather resource-intensive anabolic program (growth/mass accumulation and proliferation), cells have evolved mechanisms to ensure that it becomes active only when sufficient resources are available. As such, lysosomal mTORC1 is activated as a coordinated response to amino acids, cholesterol and glucose availability. Despite decades of research, we are only now beginning to unravel the intricate cascade of events that control this cellular gatekeeper.

mTOR is involved in a wide variety of diseases, including cancer, obesity, type 2 diabetes, and neurodegeneration. Moreover, mutations in genes encoding for mTOR regulators (TSC1, TSC2, PTEN, AKT, GATOR and KICSTOR components) result in a collection of neurodevel-opmental disorders commonly known as mTORopathies. These diseases can affect multiple organs, but all have distinct neurological clinical presentations, including mental retardation, autism, and epilepsy.

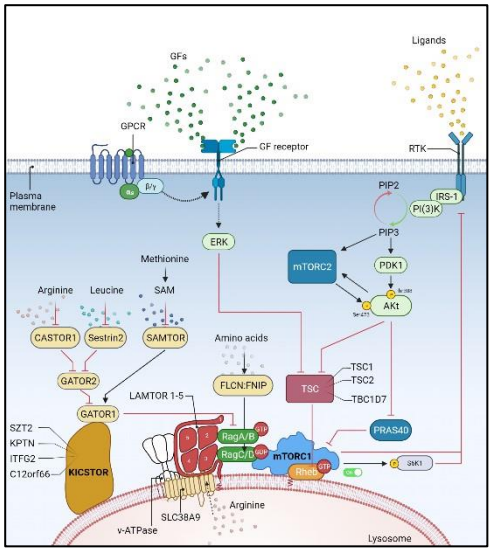


Fig1. Upstream regulators of mTORC1

Despit e the mentioned similarities, there are obvious differences between the identified mTORopathies and it remains unclear if these arise from the degree of mTOR hyperactivation or if other deregulated pathways also contribute to the specific phenotypes

The aim of this project is, to perform a detailed comparative characterization of patient fibroblasts with mutations in different mTOR regulators. The analysis will include biochemical, molecular biology and fluorescence imaging methods.

Requirements: We are looking for a highly motivated student with an interest in understanding the pathological mechanisms underlying rare human diseases. We offer a collaborative lab atmosphere and thorough training in molecular cell biology, protein biochemistry and microscopy.

Master Thesis Announcement

Are you excited about the brain?
Interested in interspecies modeling of psychiatric conditions?

The Passecker Lab is seeking an enthusiastic Master's Student interested in studying and mapping the connectivity and function of different cell types involved in the neuronal circuitry that mediate cognitive control of behavior in healthy and psychiatric conditions. The lab studies the neuronal basis of Decision-Making and Reinforcement Learning in both health and disease. More information about the lab can be found at https://lab.jpassecker.com/ or through the Institute of Neurobiochemistry of the Medical University Innsbruck, Austria

The Project:
The DiGeorge Syndrome is a debilitating genetic disease that causes learning disabilities and cognitive dysfunction. While global neuronal disconnectivity patterns are reported in humans and non-human models, we have yet no understand how the connectivity between two key regions for higher cognitive function are affected. We ask whether a deficit in connectivity could be the cause for inefficient information processing leading to the observed behavioural deficits. To address this question, the main research aim of the thesis is to determine the changes in neuronal connectivity between the prefrontal cortex and the striatum in a genetic mouse model of the syndrome.

Background & Environment:
We are looking for students holding a BSc in biology, biochemistry, computer science, mathematics, medicine, psychology or a related subject. The ideal candidate should be highly motivated, creative, detail-oriented, have initiative and innovation abilities and oral and written communication skills in English. Previous experience with coding/programming, rodent studies, histological assays or microscopy analysis is a bonus, but not required.
You can expect a fun, multicultural and collaborative team of scientists. A multidisciplinary working atmosphere for gaining hands-on experience alongside your studies; The chance to develop your skills in planning and designing a research project; Get familiarized with the modern techniques currently used in behavioral, systems and computational neuroscience; Support and guidance for next steps in your career.

Applications for the above should be sent to johannes.passecker@i-med.ac.at and include a 1) full CV, 2) Motivation letter stating your neuroscience research interests, lab experience and career goals. **Starting Date: position is open until filled during 2023, starting date is negotiable. Date of issue: 20.01.2**