EISENBERG Tobias (MetAGE Key Researcher)

University of Graz

Harnessing Lipostasis and Autophagy for Healthy Aging

Background: Aging is associated with a decline of both lipostasis (the control of lipid breakdown and formation) and proteostasis (the control of protein degradation and synthesis). Intriguingly, it appears that these two processes are mechanistically linked. Recent research in yeast has highlighted the need for sufficient lipid flux to fuel autophagic membrane biogenesis, suggesting that autophagy-mediated proteostasis depends on functional lipid metabolism. Understanding the regulatory framework of this link has broad implications for healthy aging as well as aging-associated diseases with features of disturbed lipostasis, such as obesity, fatty liver disease and cardiometabolic complications.

Hypothesis and Objectives: We hypothesize that lipostasis is essential for maintaining cellular autophagic capacity during aging. Our objectives are to (i) understand how aging-associated changes in lipid metabolism affect the autophagic competence of cells and tissues, (ii) explore how this impacts cellular and systemic functions, including mitochondrial function, energy metabolism, and inflammatory processes, and (iii) investigate how this process can be leveraged to enhance healthspan.

Methodology: As part of a research group embedded within the Cluster of Excellence MetAGE, you will genetically and pharmacologically manipulate lipid metabolism in established mouse models of aging and dietary interventions. You will investigate the interaction of lipostasis with autophagy using a range of assays to monitor autophagy (including assessment of autophagic flux with flow cytometry), along with biochemical and omics analyses of metabolites, lipids, and autophagy-signaling. Through collaboration within the MetAGE consortium, you will have access to human samples from observational studies to translate preclinical findings to humans.

References:

1. Gross AS, Zimmermann A, Pendl T, Schroeder S, [et al.], and Eisenberg T (2019). Acetyl-CoA carboxylase 1-dependent lipogenesis promotes autophagy downstream of AMPK. J Biol Chem. 294(32): 12020–12039. doi: 10.1074/jbc.RA118.007020.
2. Eisenberg T, Abdellatif M, et al. (2016). Cardioprotection and lifespan extension by the natural polyamine spermidine. Nat Med. 22(12): 1428–1438. doi: 10.1038/nm.4222.

GRAIER Wolfgang (MetAGE Key Researcher)

Medical University of Graz

Targeting mitochondria against aging

Background: Mitochondria are essential for cellular energy metabolism, but their function declines with age, contributing to age-related diseases. The exact mechanisms behind this decline are still not fully understood but involve impaired ATP production and oxidative stress that damages mitochondrial components[1]. Aging also affects inter-organelle communication and Ca^{2+} signaling, making senescent cells vulnerable to mitochondrial Ca^{2+} overload[2], which leads to increased production of reactive oxygen species. However, these cells have developed protective mechanisms, such as desensitized mitochondrial Ca^{2+} uptake machinery[3] and the utilization of hexokinase 1 as an energy stress sensor to regulate mitochondrial shape, connectivity, and metabolic activity[4].

Hypothesis and Objectives: We recently discovered a key process of mitochondrial aging, which we hypothesize to serve as a potential target for the development of *senolytics* - compounds that selectively kill senescent cells. AI-based structure-functions prediction (e.g., with AlphaFold, Schrödinger) will be used to develop lead substances that interact selectively with key processes of mitochondrial bioenergetics in senescent cells (Aim 1). Subsequently, these lead substances will be tested for their potency against cellular and animal aging (Aim 2). In addition, we will search for natural compounds with comparable lead motifs in corresponding databases (e.g., NERDD) (AIM 3), and test their potency against aging (AIM 4).

Methodology: Human cells/organoids and non-mammalian animal models of aging will be used. In addition to state-of-the-art biochemical and molecular biology techniques, we will employ biosensor-based multi-channel (sub-)cellular, multicellular, and intravital recordings of, cell metabolism & function, transcription, and signaling using super-/high-resolution microscopes (SIM, LSM, LS).

Specific position requirements: The ideal candidate holds a PhD in molecular biology, structural chemistry, or similar. The candidate ideally has experience in drug discovery using AI-based structural prediction algorithms (e.g., AlphaFold, Schrödinger) and the analysis of cellular processes and single-cell-based transcription.

References:

1. Amorim, J. A. *et al.* Mitochondrial and metabolic dysfunction in ageing and age-related diseases. *Nat Rev Endocrinol* 1–16 (2022) doi:10.1038/s41574-021-00626-7.
2. Madreiter-Sokolowski, C. T. *et al.* Enhanced inter-compartmental Ca^{2+} flux modulates mitochondrial metabolism and apoptotic threshold during aging. *Redox biology* **20**, (2018). doi: 10.1016/j.redox.2018.11.003
3. Madreiter-Sokolowski, C. T. *et al.* PRMT1-mediated methylation of MICU1 determines the UCP2/3 dependency of mitochondrial Ca^{2+} uptake in immortalized cells. *Nat Commun* **7**, 12897 (2016). doi:10.1038/ncomms12897
4. Pilic, J. *et al.* Hexokinase 1 forms rings that regulate mitochondrial fission during energy stress. *Mol. Cell* (2024) doi:10.1016/j.molcel.2024.06.009.

MADEO Frank (MetAGE Key Researcher & Director of Research)

University of Graz

Polyamine metabolism as an integrator of lipostasis and proteostasis in nutritional aging interventions

Background: The polyamine spermidine is a ubiquitous molecule linked to various health benefits. We have recently shown that polyamine biosynthesis is essential for the beneficial effects of fasting, suggesting that the polyamine pathway represents a key node of nutritional anti-aging interventions. Mechanistically, polyamines are required for proteostasis, especially autophagy and we speculate that an upregulation of polyamine metabolism enables both rapid and sustained activation of autophagy through metabolic and post-translational means, respectively. In addition, recent data suggests crosstalk of polyamine metabolism to lipostasis, the coordinated control of lipid formation and breakdown.

Hypothesis and Objectives: We hypothesize that the crosstalk of polyamines to proteostasis and lipostasis is a key component for interventions against obesity- or metabolic syndrome-related disorders. Our objectives are to (i) measure polyamines and related metabolites under different dietary conditions in humans and mice, (ii) link polyamine metabolism to lipostasis control upon nutritional or pharmacological interventions, and (iii) modulate polyamine metabolism in mice to explore the casuality of this pathway for counteracting obesity-related aging.

Methodology: You will work in a flourishing research environment embedded in the Cluster of Excellence MetAGE consortium, which offers access to both preclinical models and clinical biospecimen. You will plan and supervise polyamine analytics as well as metabolic and post-translational downstream targets of polyamine metabolism in close collaboration with a dedicated data science platform. You will plan and conduct in vivo experiments addressing the role of polyamine metabolism in different nutritional and pharmacological interventions.

References:

1. Madeo, F., Eisenberg, T., Pietrocola, F. & Kroemer, G. Spermidine in health and disease. *Science* **359**, eaan2788 (2018).
2. Eisenberg, T. *et al.* Cardioprotection and lifespan extension by the natural polyamine spermidine. *Nat Med* **22**, 1428–1438 (2016).
3. Hofer, S. et al. Spermidine is essential for fasting-mediated autophagy and longevity. *Nat Cell Biol* accepted (2024)

MADEO Frank (MetAGE Key Researcher & Director of Research)

University of Graz

Omics-based molecular aging clocks as quantitative indicators of healthspan-promoting interventions

Background: The interpretation of aging intervention trials in humans is curbed by the lack of defined, quantitative outcomes and a standardized definition of biological age. In the recent years, so-called “aging clocks” based on different biomarkers, e.g., DNA methylation or inflammation markers, were developed to predict life expectancy. While each individual clock provides a good estimate for biological age, they are limited when it comes to intervention trials aiming at decelerating biological aging.

Hypothesis and Objectives: We hypothesize that a combination of omics-based aging clocks can predict biological age beyond the current state-of-the-art, and allow a quantitative interpretation of the efficacy of anti-aging interventions. The main objective is the implementation of existing aging clocks in the Cluster of Excellence MetAGE human and animal trials and the exploration of novel, omics-based clock combinations for refined biological age estimation.

Methodology: You will be part of an interdisciplinary team in the Cluster of Excellence MetAGE conducting translational aging research and apply various methods of biological age estimation. Among your duties will be the standardized integration of omics workflows (e.g., proteomics, metabolomics, including sample preparation techniques) in the MetAGE consortium. You will lead the implementation of established and novel biological clock analysis pipelines using open-source scripts for linear and non-linear prediction models combined with advanced statistical methods.

References:

1. Moqri M, et al. (2024). Validation of biomarkers of aging. Nat Med. 30(2): 360–372. doi: 10.1038/s41591-023-02784-9.

PERTSCHY Brigitte (MetAGE Key Researcher)

University of Graz

The Role of Ribosome Biogenesis in Aging and its Interplay with Autophagy

Background: Ribosome biogenesis, the process of creating new ribosomes, has been implicated in the aging process, as opposed to the anti-aging role of protein degradation through autophagy. Inhibition of ribosome biogenesis extends the life span of various model organisms, including yeast, flies and worms. However, systematic studies identifying which steps of ribosome biogenesis are linked to lifespan extension are still lacking. Many anti-aging interventions act through autophagy activation, but it remains unclear whether the life-span extension observed upon inhibiting ribosome biogenesis is dependent on autophagy or occurs through an authophagy-independent mechanism.

Hypothesis and Objectives: We hypothesize that ribosome biogenesis is directly connected to aging through a currently unknown mechanism. The objectives of this project are to (i) pinpoint the specific steps in ribosome biogenesis that influence aging and identify the proteins regulating this interplay, and (ii) investigate whether the lifespan extension mediated by ribosome biogenesis inhibition is dependent on autophagy and explore the potential of targeting both pathways simultaneously.

Methodology: In this MetAGE project, you will genetically and chemically manipulate ribosome biogenesis in yeast (primary model), *C. elegans,* and mammalian cells, but also analyse samples from a human clinical study, and investigate phenotypes related to ribosome biogenesis, autophagy and aging. You will use various assays including growth and survival tests, qRT PCR and fluorescence in situ hybridization to detect rRNA intermediates, affinity purification and characterization of ribosome biogenesis intermediates, immunoblotting to detect ribosome biogenesis/autophagy factors, and fluorescence microscopy to visualize nuceoli and autophagosomes.

References:

1. MacInnes AW (2016). The role of the ribosome in the regulation of longevity and lifespan extension. Wiley Interdiscip Rev RNA. 7(2): 198–212. doi: 10.1002/wrna.1325.
2. Tiku V et al. (2017). Small nucleoli are a cellular hallmark of longevity. Nat Commun. 8(1): 16083. doi: 10.1038/ncomms16083.
3. Steffen KK et al. (2008). Yeast life span extension by depletion of 60s ribosomal subunits is mediated by Gcn4. Cell. 133(2): 292–302. doi: 10.1016/j.cell.2008.02.037.
4. Turi Z et al. (2019). Impaired ribosome biogenesis: mechanisms and relevance to cancer and aging. Aging. 11(8): 2512–2540. doi: 10.18632/aging.101922.

MetAGE Cluster of Excellence Postdoc Program

PERTSCHY Brigitte (MetAGE Key Researcher)

University of Graz

The Interplay between Ribosome Biogenesis and Polyamines in Aging

Background: Polyamines are abundant positively charged molecules that prolong lifespan by activating autophagy. Inhibition of polyamine synthesis not only prevents fasting-mediated lifespan extension but also specifically blocks the nuclear steps of large ribosomal subunit synthesis. In contrast, small ribosomal subunit synthesis remains unaffected by polyamine synthesis inhibition. S-adenosylmethionine, a precursor for polyamine synthesis, also serves as a methyl donor for cellular methylation reactions. A central cellular process in which methylation plays an important role is ribosome biogenesis; as both the ribosomal RNA and many ribosomal proteins, as well as several ribosome biogenesis factors are methylated. Aging is associated with altered cellular methylation patterns. However, it is unclear if these changes result from competition between polyamine synthesis and methylation and how the altered methylation patterns affects ribosome biogenesis.

Hypothesis and Objectives: We hypothesize that polyamine synthesis, methylation and ribosome biogenesis are interconnected in the aging process. The objectives of this project are to (i) assess changes in the methylation patterns of ribosomes (rRNA and proteins) during aging and their dependence on polyamines and (ii) determine the role of polyamine synthesis in ribosome biosynthesis and its impact in aging.

Methodology:In this MetAGE project, you will genetically and chemically manipulate polyamine synthesis and methylation in yeast (primary model organism), *C. elegans* and mammalian cells, but also analyse samples from a human clinical study. You will investigate phenotypes related to ribosome biogenesis, methylation and aging, including growth and survival assays, detection of rRNA intermediates by qRT PCR, rRNA methylation tests, affinity purification of ribosome biogenesis intermediates and immunoblotting to detect methylated ribosome biogenesis factors.

References:

1. Liu R et al. (2023). Methylation across the central dogma in health and diseases: new therapeutic strategies. Signal Transduc Target Ther. 8(1):310. doi: 10.1038/s41392-023-01528-y.
2. Dörner K et al. (2022). Genome-wide RNAi screen identifies novel players in human 60S subunit biogenesis including key enzymes of polyamine metabolism. Nucleic Acids Res. 50(5): 2872-2888. doi: 10.1093/nar/gkac072.
3. Jaafar M et al. (2021). 2'O-Ribose Methylation of Ribosomal RNAs: Natural Diversity in Living Organisms, Biological Processes, and Diseases. Cells. 10(8): 1948. doi: 10.3390/cells10081948.
4. Pang CN et al. (2010): Identification of arginine- and lysine-methylation in the proteome of Saccharomyces cerevisiae and its functional implications. BMC Genomics. 11:92. doi: 10.1186/1471-2164-11-92.

SCHERER Thomas (MetAGE Key Researcher & Deputy Director of Research); Co-PI: **KRŠŠÁK Martin**

Medical University of Vienna

Magnetic Resonance Imaging and Spectroscopy based MetAGE deep phenotyping

Background: MRI and MRS methods can access adipose tissue compartmentation, ectopic fat accumulation, ventricular function and myocardial morphology which are associated with metabolic detoriation, insulin resistance and aging. Morphologic and functional changes in the brain which are associated with cognitive aging are also accessible by ^{1}H MRI examination.

Hypothesis and Objectives: To observe and analyze aging related changes in whole body fat compartmentation, ventricular function, myocardial morphology, brain structure and functional connectivity in healthy and obese population. To analyze the relationship between these changes and metabolic aging phenotype.

Methodology: Implement, coordinate and supervise comprehensive whole body fat compartmentation (^{1}H MRI/S @ 3T), cardiometabolic phenotyping (^{1}H Cine MRI@ 3T) and brain MRI (^{1}H MRI @ 3T) data acquisition, processing and analysis pipeline. To develop and implement multinuclear MRS/I studies of organ specific glucose and fatty acid metabolism at 3T and 7T MR systems. Management of the MR Measurements of clinical cohort at the Medical Univ. of Vienna.

Specific position requirements: PhD Degree in Medical Physics, Medical Imaging, (Bio)Physics or (Bio)Medical Engineering or related subjects, Experience with MR Data Acquisition, MR Data Processing; experience with (i) MR method development and validation, (ii) Matlab and/or Python, (iii) clinical research, and interest in multidisciplinary applications of MR.

References:

Tissue specific fat accumulation and cardiovascular phenotyping

1. Harreiter J, … Scherer T, … Krššák M, Kautzky-Willer A. Sex differences in hepatic and cardiac lipid accumulation and cardiac function across a cohort with wide range of glycemia: A secondary, cross-sectional analysis. In revision for Obesity July 2024. Preprint https://doi.org/10.21203/rs.3.rs-4213314/v1
2. M. Krššák, et al. Insulin resistance is not associated with myocardial steatosis in women. Diabetologia 54(7): 1871-1878, 2011.

Comprehensive multinuclear studies of organ specific metabolism

3. M. Metz, … M. Krššák, … T. Scherer. Leptin increases hepatic triglyceride export via a vagal mechanism in humans. Cell Metab. 2022 Oct 6:S1550-4131(22)00410-7. doi: 10.1016/j.cmet.2022.09.020.
4. P. Fellinger, … M. Krššák, … Y. Winhofer. Inadequate high mitochondrial ATP-synthesis explains “non-fatty-liver” in patients with GH-excess – a model for anti-steatotic pathways. JCI Insight. 2020 Mar 12;5(5). pii: 134638. doi: 10.1172/jci.insight.134638

MetAGE Cluster of Excellence Postdoc Program

SCHERER Thomas, KAUTZKY-WILLER Alexandra, TRAUNER Michael

(MetAGE Key Researchers)

Medical University of Vienna

Metabolic control of aging and disease - MetAGE deep phenotyping cohort (Pro-Metage)

Background: The continuous increase in human life expectancy is leading more elderly people with multiple health conditions, posing significant socioeconomic challenges for our society. Aging is the primary risk factor for chronic disabilities and diseases like cardiovascular diseases, dementia, type 2 diabetes, and obesity. Therefore, promoting healthy aging has become a pressing societal challenge, emphasizing the need for validated strategies to extend the disease-free phase of life, known as health span. In this collaborative clinical project together with the Medical University of Graz and the University of Graz we are planning to build a comprehensivly phenotyped cohort with 400+ participants in eastern Austria with the aim to better understand the interplay between aging and metabolism.

Hypothesis and Objectives: We aim to prospectively identify and validate blood-based aging biomarkers in relation to cardiometabolic phenotypes of young and old,
female and male subjects with or without obesity in this clinical cohort.

Methodology: We will holistically phenotype aging lean and obsese subjects and follow these subjects longitudinally with cutting edge techniques such as cardiac, brain and whole-body MRI combined with magnetic resonance spectroscopy, actigraphy, continuous glucose monitoring, optical coherence tomography, vibration controlled transient elastography and a broad battery of patient reported outcomes to assess psychosocial factors. You will manage this clinical cohort at the Medical University of Viennan and develop own ideas for break out trials. Breakout trials with smaller subgroups are planned to mechanistically understand the process of aging and how this is correlated with metabolic control and flexibility. Furthermore, sex-specific and gender-sensitive analyses and substudies are also planned.

Specific position requirements: MD Degree + PhD; Fluent English & German

References:

1. López-Otín, C., Galluzzi, L., Freije, J.M.P., Madeo, F., Kroemer, G., 2016. Metabolic Control of Longevity. Cell 166(4):802-821.
2. Kabacik, S., Lowe, D., Fransen, L., Leonard, M., Ang, S.L., Whiteman, C., et al., 2022. The relationship between epigenetic age and the hallmarks of aging in human cells. Nat Aging 2(6):484-493.
3. Kopp, W., 2019. How Western Diet And Lifestyle Drive The Pandemic Of Obesity And Civilization Diseases. Diabetes Metab Syndr Obes 12:2221-2236.
4. Odegaard, J.I., Chawla, A., 2013. The immune system as a sensor of the metabolic state. Immunity 38(4):644-654.
5. Andersen, C.J., Murphy, K.E., Fernandez, M.L., 2016. Impact of Obesity and Metabolic Syndrome on Immunity. Adv Nutr 7(1):66-75.

SCHWEIGER Martina (MetAGE Key Researcher)

University of Graz

Immune cell dynamics re-shaping adipose tissue function with age

Background: Metabolic flexibility, the body's capacity to adapt fuel oxidation to fuel availability, ensures survival amid varying nutrient supply and is lost with age[1]. Adipose tissue (AT) is the body's largest energy store, as such controlling systemic energy homeostasis. AT displays species-conserved changes with aging, including redistribution from peripheral to visceral depots and chronic low-grade inflammation that is also characterized by an altered AT macrophage (ATM) profile[2]. Caloric restriction not only decreases total AT mass but also reduces AT inflammation, which is associated with restored metabolic flexibility and healthspan extension in various species[3]. However, the impact of nutritional interventions on age-related immune changes and metabolic flexibility is unclear.

Hypothesis and Objectives: We propose that changes in AT lipid distribution and immune cell dynamics contributes to reduced metabolic flexibility and disease upon aging. We aim to **map the subcutaneous and visceral AT immune cell composition** and correlate the occurrence of specific ATM subsets with the metabolic phenotype of the tissue, with age and with sex. Specifically, we want to delineate **which ATM subpopulations** are key to mediate the detrimental effects of aging and the beneficial effects of caloric restriction on AT function and **how they are activated by microenvironmental cues.**

Methodology: Studies in genetically modified (*e.g.,* IL4 receptor- and TLR4 receptor deficient) young/old/caloric restricted mice followed by flow cytometry analyses, whole mount immunofluorescence, immunohistochemistry, RNA-sequencing, metabolomic-, lipidomic-, proteomic-analyses of murine and human AT, will be combined with 2D- or spheroid mono- and co-cultures of primary cells or cell lines followed by secretome- and functional analyses to investigate metabolic flexibility (*e.g.,* lipolysis, lipid/glucose/glutamine uptake and -oxidation).

References:

1. Bret H. Goodpaster and Lauren M. Sparks, 'Metabolic Flexibility in Health and Disease', Cell Metabolism, 25.5 (2017), 1027–36 <https://doi.org/10.1016/j.cmet.2017.04.015>.
2. Tammy T. Nguyen and Silvia Corvera, 'Adipose Tissue as a Linchpin of Organismal Ageing', Nature Metabolism, 6.5 (2024), 793–807 <https://doi.org/10.1038/s42255-024-01046-3>.
3. Min-Yi Ou and others, 'Adipose Tissue Aging: Mechanisms and Therapeutic Implications', Cell Death & Disease, 13.4 (2022), 300 <https://doi.org/10.1038/s41419-022-04752-6>.

MetAGE Cluster of Excellence Postdoc Program

SEDEJ Simon (MetAGE Key Researcher)

Medical University Graz

Tweaking cardiac aging with caloric restriction mimetics

Background: Aging and metabolic disorders are leading risk factors that contribute to the increasing prevalence of chronic cardiovascular disease. Aging-induced cardiac decline is strongly associated with reduced autophagic activity and mitochondrial dysfunction. By contrast, caloric restriction mimetics (CRMs) improve mitochondrial quality control, which may in turn improve cellular energy supply and cardiac metabolism. Yet, the molecular details behind the effects of CRMs on promoting healthy cardiac aging remain largely unexplored.

Hypothesis and Objectives: We will study the effects of CRMs on aging- and disease-induced mitochondrial dysfunction and the associated imbalance of energy metabolism, with a focus on autophagy/mitophagy in the heart. We speculate that reinstating metabolic control through CRMs attenuates metabolic imbalance and promote healthy cardiac aging.

Methodology: Our laboratory is seeking to recruit a full-time postdoctoral researcher to perform independent and innovative research using CRMs to restore mitochondrial metabolic flexibility of aged experimental models. The candidate is expected to perform state-of-the-art cardiometabolic phenotyping (e.g., echocardiography, hemodynamics) combined with cellular and subcellular studies (confocal microscopy, high resolution oxygraphy) to explore physiological and pathological mechanisms focusing on energy metabolism and mitophagy. The translatability of preclinical studies will be evaluated by testing the efficacy of CRMs in inducing autophagy in patients at risk to develop cardiometabolic complications.
The post-doc will interact with the teams within the Cluster of Excellence “Metabolic control of aging and disease – from models to humans”, and will receive career development training.

Specific position requirements: MD or Ph.D. in cardiovascular physiology, cell biology, or a closely related field; Research experience; Publication record and demonstrated success/potential to obtain extramural funding support, Ability to work collaboratively in interdisciplinary teams, Potential to develop new areas of expertise and research.

TRAUNER Michael (MetAGE Key Researcher)

Medical University of Vienna

Role of bile acids in lipostasis and aging-associated decline of metabolic control

Background: In addition to their digestive functions, bile acids (BAs) act as signaling molecules efficiently regulating their own metabolism and transport as well as key aspects of lipid and glucose homeostasis in mutual interaction with gut microbiota (1). Changes in BA homeostasis contribute to the pathogenesis of a metabolic disorders including metabolic dysfunction-associated steatotic liver disease (MASLD) (2,3). During overnutrition, adipose tissue (AT) buffers excess energy in form of triacylglycerols. In times of increased energy need, these stores are mobilized by hydrolases (in a process termed lipolysis) to supply the body with fatty acids (FA) as both fuel and signaling molecules and building blocks for cellular membranes. Deregulated lipolysis causes FA spillover, leading to ectopic lipid deposition with so-called lipotoxic effects and subsequent tissue dysfunction in MASLD (2). The latter is also a driver of cardiometabolic morbidity, highlighting the vicious cycle induced by impaired AT function.

Hypothesis and Objectives: We aim to explore the dynamics of host and microbial BA metabolism and its impact on lipostasis during dietary, BA-targeted pharmacological interventions and aging. Given the critical (patho)physiological potential of AT, we need to better understand its function during aging to address lipolytic flexibility in a time-resolved manner (i.e., examine the ability of cells to turn on/off lipolysis under changing nutrient conditions) and how it impacts the liver, skeletal muscle and the heart (lipostasis).

Methodology: We will combine biochemical assays with lipid flux studies and whole-body metabolic holistic phenotyping, including advanced metabolic imaging to better understand the impact of aging and dietary interventions on AT and liver function. Genetic and pharmacological approaches to alter BA signaling, AT lipolysis as well as their intercations with immune cell function will give mechanistic insights into if and how these processes promote metabolic reprogramming and healthy aging. Mouse/cell culture data will be corssvalidated and integrated with findings obtained in human/clinical samples.

Specific position requirements: Experience with molecular and cell biology, cell culture and organoids, mouse studies. Interest in big data integration for a holistic approach to explore inter-organ crosstalk in metabolic disorders and aging.

References:

1. Fuchs CD, Trauner M. (2022). Role of bile acids and their receptors in gastrointestinal and hepatic pathophysiology. Nat Rev Gastroenterol Hepatol. 19(7):432-450. doi: 10.1038/s41575-021-00566-7.
2. Loomba R et al. (2021). Mechanisms and disease consequences of nonalcoholic fatty liver disease. Cell. 184(10): 2537–2564. doi: 10.1016/j.cell.2021.04.015.
3. Tincopa MA et al. (2024). New and emerging treatments for metabolic dysfunction-associated steatohepatitis. Cell Metab. 36(5):912-926. doi: 10.1016/j.cmet.2024.03.011.