Laboratory of	Topic	Annotation
Pain Research	**Mechanisms and treatment of pain: Modulation of nociceptive signaling at spinal cord level**	The main research interest of our department is to study mechanisms of pain and to explore new possibilities of pain treatment, especially in chronic states. Our experimental work is concentrated on the modulation of nociceptive information at the spinal cord level that is the first relay center between the periphery and higher brain areas. Our goal is to study these modulatory mechanisms in order to improve therapy for pain conditions such as neuropathic and cancer related pain. This project will be focused on the role of neuroinflammation in modulation of synaptic transmission and chronic pain development. Lately we are interested in the role of TRPV1 receptors, cannabinoids, endogenous lipids, opioids and inflammatory cytokines in this process. In our research we use mainly electrophysiological, optogenetic, OMICS analysis, functional imaging, immunohistochemical, molecular and behavioral methods. In collaboration with clinics we aim to study human pathology in pain patients. Our research is supported by several ongoing grant projects.
Neurochemistry	**Mechanisms of selective modulation of individual subtypes of muscarinic receptors.**	Altered muscarinic signalling is frequently involved in neurological and psychiatric diseases as well as diseases of internal organs. To target a particular condition, selective modulation of individual muscarinic subtypes is necessary to avoid side effects. High homology of the orthosteric binding site among all muscarinic subtypes makes a finding of orthosteric ligands that bind selectively to individual muscarinic subtypes virtually unattainable. Allosteric ligands modulate binding of orthosteric ligands and functional response to agonists from less-conserved sites on the receptor. Dualsteric ligands employ both orthosteric and allosteric sites. The aim of this project is structure-guided development of novel selective allosteric and dualsteric ligands.
Cholinergic Signaling	**Acetylcholine receptors inside out as a fine tool to control neural circuits**	Acetylcholine receptors play a role in many brain diseases. It is challenging, though, to use them as a therapeutic target due to their widespread distribution. We address this issue by investigating their expression and function in specific neuronal types, and we develop tools that allow us to target them in those neuronal types. For that, we turn the receptors inside out: instead of targeting them extracellularly, we modify their functioning by ligands that are delivered inside the neurons.

Biomaterials and Tissue Engineering	**Bone tissue engineering: Enhancement of vascularized bone tissue formation using functionalized diamond scaffolds and electric stimulation**	The aim is to create an innovative 3D scaffold covered with a functionalized diamond layer that will stimulate the differentiation of stem cells and the formation of vascularized bone tissue in vitro by electrical stimulation of cells. It will include the study of the adhesion, proliferation and osteogenic differentiation of stem cells and the formation of capillary structures by endothelial cells; the material part will include the deposition, functionalization and characterization of diamond layers.
Biomaterials and Tissue Engineering	**Skin tissue engineering: Biomimetic nanofibers supporting chronic wound healing**	The aim is to study the effect of bioactive nanofibers on various skin cell types such as keratinocytes, fibroblasts, endothelial cells and stem cells in mono- and co-cultures in vitro. The study will include the evaluation of cell proliferation, differentiation/maturation, migration and extracellular matrix production in 2D and 3D environments, as well as the development and practical use of an in vitro chronic wound model.
Cellular Neurophysiology	**Rare neurodevelopmental disorders associated with variants in NMDA receptor genes**	Rare variants in genes encoding synaptic NMDA-type glutamate receptors have been associated with neurodevelopmental disorders, but the underlying disease mechanisms and therapy options remain poorly understood. We use molecular biology, biochemistry, patch-clamp electrophysiology, live-cell Ca2+ imaging, and high-resolution immunofluorescence microscopy to study the functional impact of individual patient variants of NMDA receptor genes and explore possible personalized therapeutic approaches.
Adipose Tissue Biology	**Non-shivering thermogenesis in protection against cold and obesity**	The excess of energy intake over energy expenditure leads to the development of obesity and its associated health complications. Important component of energy expenditure are various thermogenic mechanisms primarily designed to maintain a stable body temperature, but possibly also useful in ensuring balanced energy homeostasis. New PhD and pregradual projects focused on regulation and mechanisms of thermogenesis in BAT and skeletal muscle will be presented.

Molecular Physiology of Bone	**Deciphering the role of bone marrow adipocytes in mouse models of obesity: impact of sex dimorphism**	Increased bone marrow adiposity is associated with bone fragility in metabolic diseases such as obesity. Bone marrow adipose tissue (BMAT) originates from bone marrow mesenchymal stem cells (BMSCs), which can differentiate into adipocytes,osteoblasts or chondrocytes. With obesity, the function of key building blocks, bone marrow stromal cells (BMSCs) changes towards higher accumulation of BMAT, which is affected by diet and sex dimorphism. However, the precise molecular mechanism underlying sex-specific differences in the molecular properties of BMSCs and the pathophysiology of bone loss is not well understood. Our research is focused on identifying metabolic pathways contributing to obesity-induced phenotype in BMSCs and modulate their function to improve bone and fat metabolism in animal models of metabolic diseases with respect to sex dimorphism.
Metabolism of Bioactive Lipids	**Integrated approaches for metabolomics, lipidomics, and fluxomics**	By bridging computational biology, biochemistry, and experimental research, these interdisciplinary projects aim to enhance our understanding of lipid metabolism, identify potential therapeutic targets, and contribute to personalized medicine and metabolic engineering. The outcomes are expected to provide novel methodologies and software frameworks for the scientific community, advancing the field of systems biology.
Membrane Transport	**Cations - key elements for life of eukaryotic cells**	Monovalent cations H+, K+, and Na+ are key elements of life required for all cellular functions. Their intracellular concentrations are determined via the activity of membrane proteins - transporters and channels mediating the continuous flux of cations and protons into and from cells with various transport mechanisms. Using the yeast Saccharomyces cerevisiae as a eukaryotic model organism, the project will study new regulatory mechanisms maintaining monovalent-cation homeostasis in cells. The results will provide new insights into the regulation of cation homeostasis on the level of (i) particular cation transporters' proteostasis (expression, biogenesis, function, and degradation) and (ii) their distribution/organization in the plasma membrane. Obtained results will significantly advance our knowledge of molecular mechanisms required to maintain cation homeostasis and their physiological importance in healthy organisms.

Molecular Neurobiology	**Will be published later**	
Experimental Hypertension	**New therapeutic approaches for the treatment of cardiovascular diseases: the heart-kidney relationship.**	Developing new approaches to treating cardiovascular diseases (CVDs) is at the forefront of current experimental and clinical research. Many CVDs are multi-organ diseases affecting the heart, vasculature, and other organs, such as the kidneys. Therefore, chronic kidney disease and other CVD-associated diseases (hypertension, metabolic syndrome, etc.) also play a crucial role in the progression of CVD. Our laboratory of Experimental Hypertension studies the biological mechanisms of CVD and new therapeutic approaches using methodologically complex scientific work (echocardiography, telemetry, catheterization, electrophysiology, histology, modern molecular-biological methods, and omics) in unique transgenic rodent models.