UNIVERSITÄT
SALZBURG

Research Topics in Biology and Molecular Biology

Laboratory impressions...

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Welcome address

Teaching guided by state-of-the art research: this principle represents one of the real strengths of education at academic institutions. Students can expect to be instructed in cutting-edge scientific problems and technologies. I am very proud that the Paris-Lodron University of Salzburg can offer a very broad spectrum of research topics in the areas of biology and molecular biology, giving the students a wide range of choices for getting involved in real-life biological questions and systematic approaches to address them.

This little brochure is intended to serve concerned students as a guide into the major research topics represented by the Departments of Cell Biology, Molecular Biology, and Organismic Biology of the Paris-Lodron University of Salzburg, as well as several Departments of the Johannes-Kepler University of Linz collaborating with the University of Salzburg in the Bachelor Program „Molecular Biosciences“ and the Master Program „Molecular Biology“.

Selecting an appropriate topic for Bachelor-, Master- and PhD Theses represents a very fundamental decision with regard to one‘s own personal future and professional carrer. This decision should be primarily guided by the personal interests and talents of the students. However, timeliness of the topic as well as the opportunity to get acquainted to a toolbox of modern technologies in a scientifically stimulating environment should also be considered to be crucial for this decision.

In due consequence, I am encouraging all interested students to utilize this guide as a valuable source of information, which aids in taking a wise decision with respect to specializing for an appropriate topic for elaborating bachelor-, master, and PhD theses in the areas of biology and molecular biology. Please do not hesitate to seek direct contact with the team leaders in order to obtain more detailed information about the proposed research topics, to personally meet their research groups, and to see the existing infrastructure.

Salzburg, October 2015

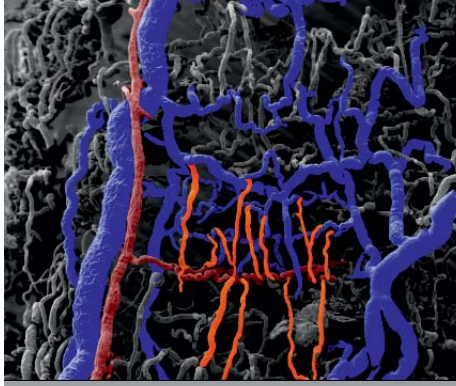
Fátima Ferreira-Briza, Vice Rector of Research

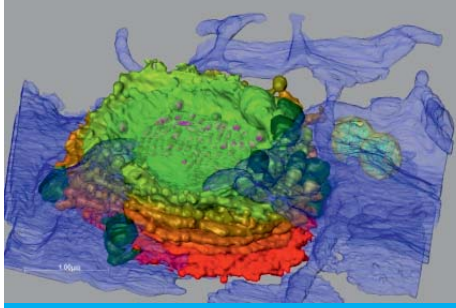
The Department of Cell Biology

Research at the Department of Cell Biology involves approximately twenty faculty members working in the areas of **cellular stress**, biosynthetic and morphogenetic **analysis of cellular substructures, cellular physiology,** and **stem call aging**. The model systems used are yeast cells, selected algae, Arabidopsis, mammalian **primary cells** and tissues. **State of the art facilities, equipment and methods** for genetic, biochemical, molecular and biological structure analysis, including light-, confocal laser scanning- and energy filtering transmission electron microscopy, instrumentation for modern biochemical and molecular methods, corrosion casting, and advanced histology techniques including immuno-transmission electron microscopy, stereology, 3D-morphometry, as well as electrophysiological (voltage/patch clamp) and imaging techniques (confocal laser microscopy) are routinely employed within the Department or are available within shared facilities within the life sciences.

The **Division of Genetics** pursues research aimed at a detailed understanding of cellular stress, its role under physiological conditions (cellular response and ageing) and during pathological developments (arteriosclerosis, cancer, neurodegeneration) as well as stem cell biology and regeneration. Of particular interest in this context are studies on **oxidative stress, apoptosis, mitochondrial function, iron metabolism** as well as their respective correlates during differential transcriptional and translational gene expression. The **Division of Plant Physiology** explores **cellular structures** and functions, and analyses molecular **biosynthetic pathways** of cell wall polymers related to growth and development.

The **Division of Cellular and Molecular Neurobiology** explores cellular physiology and molecular neurobiology. Of particular interest are studies of **ion channel modulation** and functions as well as **cellular signaling pathways** in diseased and drug altered conditions. The **Division of Animal Structure and Function** focuses on the growth, regression and **pathologies of vascular systems**, the s**tructural changes in skeletal muscle** under the influence of training, ageing, genetic variation and after death, the c**ellular patterning and stem cell behavior in vertebrate embryos**, and **mechanisms of innate immune response** in pathogen defense and inflammatory disease.





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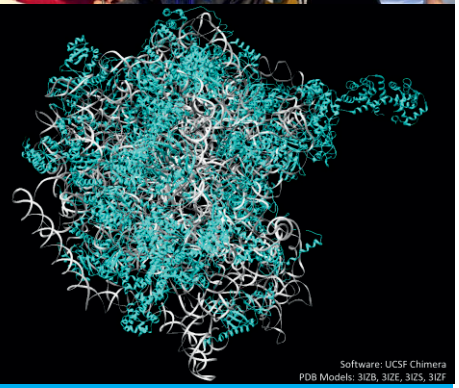

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Team Hannelore Breitenbach-Koller/Michael Breitenbach
Division of Genetics

The **research focus** of the Breitenbach Labratories, LBK and MB, is on the **genetics, biochemistry and molecular biology of adaptive cellular processes in health and disease**. In particular, we study signal transduction pathways in oxidative stress response during aging (MB) and dynamics of protein signatures induced by modulation of the protein synthesis machinery (LBK).

The **major goal** of the LBK laboratory **to understand the role of individual ribosomal proteins in generation of specialized ribosomes,** devoted to the translation of selected mRNA species. This is based on fine structure determinations of the ribosome, the molecular machine that translates mRNAs into proteins. Collectively, these studies revealed that ribosomal proteins(RPs) and ribososmal RNA (rRNAs) serve as instruments to generate **specialized ribosomes** for quantitatively and qualitatively fine tuning initiation and elongation of mRNA translation. A specialized ribosome resulting from molecular intervention to favorably alter protein expression of a particular, disease associated mRNA, without compromising bulk translation, is called a **therapeutic ribosome.**

We have developed a **specialized ribosome screen,** which identified a distinct RP as target for increasing protein expression of mutant LAMB3 mRNA , which induces the most severe and lethal form of the blistering skin disease **Epidermolysis bullosa (EB),** JEB-H. In **cooperation with the eb-Haus Austria,** we are now advancing to **small molecule screening of target RPs.** We aim to identify and characterize drugable molecules **to induce therapeutic ribosomes** for increase in mutant LAMB3 production, first in patient derived keratinocyte cell lines and ultimately, in patient skin cells.

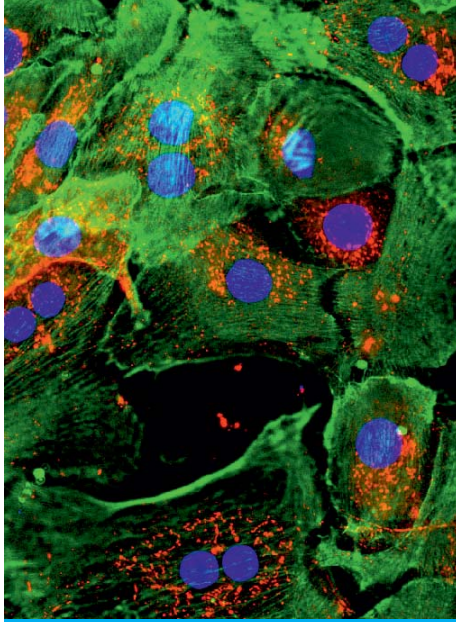
The **major goal** of the MB laboratory **is to understand the role of redox-sensitive proteins in age specific signal transductuion pathways.** Presently, we use genetics and protein biochemistry to characterize the functional interplay between NADPH oxidases and mitochondrial funtion during the cellular aging process.

Team Nikolaus Bresgen
Division of Genetics

We are studying the role of the cellular iron storage protein ferritin, in particular investigating the **cytotoxic effects of secreted ferritin isoforms**. We have shown that isoferritins released from primary hepatocytes as well as liver and brain tumor cells stimulate apoptosis by increasing intracellular oxidative stress leading to p53 and Fas dependent MOMP (mitochondrial membrane permeability). At present our research is addressing two central aspects of ferritin mediated cell death: (i) the **involvement of the endo-/lysosomal "compartment"** in ferritin mediated cell death including the participation of autophagy and (ii) the **stress signaling exerted by 4-Hydroxynonenal**, an aldehydic lipid peroxidation product the generation of which is linked to lysosomal stress initiated by ferritin endocytosis.

Employing primary **rat hepatocyte cultures** as well as several **tumor-derived cell lines**, we follow a complementary approach combining **live cell imaging** as well as **immunocytochemistry** and **cytotoxicity testing** with biochemical methods including standard techniques (**SDS-PAGE, Western blotting**), **protein purification**, and **secretome analyses**. Based on these methods, cellular stress reactions are studied by exposing the cells to distinct modifications of the cell culture conditions (e.g. addition of different supplements such as ferritin, iron, growth factors, inhibitors of proteolysis and autophagy, exposure to hypoxia /reoxygenation etc.).

Cooperations with the University of Vienna, Brescia (Italy) and Nagoya (Japan) extend our research in specialized fields. To address clinical aspects of ferritin cytotoxicity especially related to **inflammation and degenerative disease** (neurodegeneration, atherosclerosis, hepatitis) as well as **cancer** (hepatocellular carcinoma, glioma) we cooperate with the Paracelsus Medical University in joint research projects. In addition we started a cooperation with the pharmaceutical industry (Merck-Millipore) investigating the effects of iron supplementation for the optimization of mammalian cell lines for biotechnological production processes.



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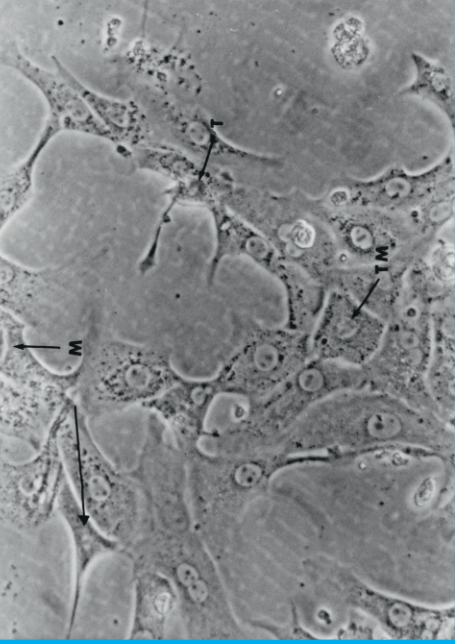

Team Peter M. Eckl
Division of Genetics

Research in our team is focused on **physiological and pathophysiological aspects of oxidative stress**. Cells of multicellular organisms are exposed physiologically to a wide range of oxygen concentrations depending on the organ, tissue and the blood supply ranging from oxygen partial pressures of 159 mm Hg (skin) to virtually zero (cartilage). Cell culture is usually carried out under ambient air oxygen. Cells will therefore in most instances face a hyperoxic environment leading to adaptation und thus experimental responses which do not reflect the physiological responses, and derived cell lines will eventually be susceptible to *in vitro* transformation and premature senescence. We therefore currently investigate **potential changes of the expression of genes involved in oxidative stress**, the **metabolism of** the lipid peroxidation product **4-hydroxynonenal** (HNE), **HNE-modified proteins** and **markers of cell proliferation and cell death** during the *in vitro* replicative aging of human skin fibroblasts at physiological and ambient air oxygen. A similar study will be carried out also with human chondrocytes as an example of very low physiological oxygen tensions.

In a second focus we are investigating **antioxidants**, in particular those contained in traditional medicinal herbs, i.e. Arab and Monglian traditional herbs, and the potential **pro-oxidative effects of antioxidants**. With respect to the latter we are investigating the **oxidative breakdown of β-carotene** to toxic aldehydic products employing rat hepatocytes and rat and human pneumocytes. Since it has been demonstrated that smokers who also consume β-carotene have a higher risk to develop lung cancer particular attention is given to the oxidative burst of alveolar macrophages and neutrophils, which may be causatively involved in the formation of β-carotene breakdown products.

Within our research focus there are **cooperations** with several domestic (Vienna, Graz, Salzburg) and international (i.e. Milano/Italy; Birmingham/England; Wageninger/The Netherlands; Madison/USA; etc.) research institutions and industry partners, i.e Merck/Darmstadt/Germany; TECAN/Salzburg; IGOR/Wels.

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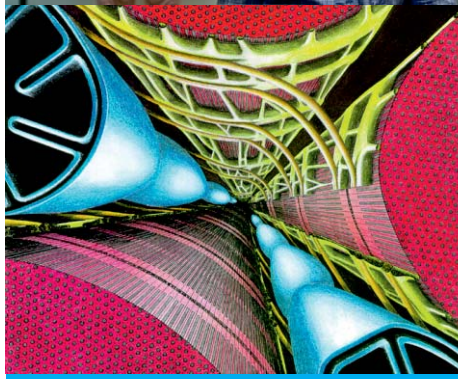
Team Stefan Galler
Division of Muscle Physiology

Many **groundbreaking discoveries** about life functions were obtained from **research on muscle**. Examples include glycolysis, the role of ATP and Ca^{2+} and the laws of thermodynamics. Despite the significant discoveries, many puzzles remained unresolved; thus muscle is still a **hot research topic** with the chance for making fundamental discoveries. The research ranges from the measurement of the forces on individual motor molecules to observation of molecular movements inside the contractile protein scaffold on a millisecond time scale with the help of X-ray diffraction in the synchrotron.

Our team measures the response of the contractile machinery of **individual muscle fibres** to instantaneous disorder for elucidating molecular processes. A disorder can be caused by a jerky movement that directs the motor molecules a few nanometers or by a sudden increase in the concentration of ATP by photolysis of an inactive precursor by a UV flash.

Thematically, we are concerned with the question of the **molecular causes of the great diversity** of the muscles. We especially investigate the function of specialized muscles of human and the animal kingdom which are still poorly understood at a molecular level. For example, what is the cause of the drastically reduced ATP consumption during the holding period in specialized muscles? Our findings showed that the underlying mechanism is not a simple slowing of the cyclic activity of motor molecules as assumed for several decades. Hence we are searching for specific holding molecules. To address these important questions, our team is collaborating with several research teams around the world, which are specialized in other techniques.

In teaching, our team is trying to convey the molecular details in a **physiological context**. Students should understand how molecules are involved in life functions like seeing, thinking and moving. Furthermore, they should understand the great complexity of research of many different disciplines in producing new knowledge applicable in medicine.



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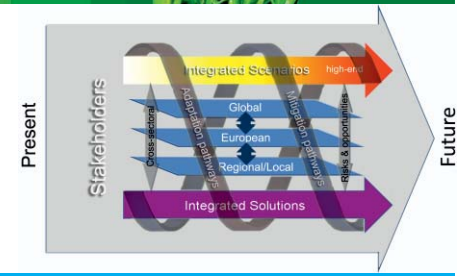

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Team John R. Haslett
Division of Animal Structure and Function

The research interests of this team are multidisciplinary, covering a spectrum of the biophysical and now also the social sciences, at local to pan-European scales. However, a general interest in classical zoology and insect biology has been maintained, primarily involving flower-visiting Diptera and Hymenoptera, but also covering other insect groups. Particularly, present research includes **taxonomy and functional biodiversity of syrphid flies** along altitudinal gradients and under different land uses in the Austrian Alps, and **occurrence of potential pollinating insects** (wild bees, syrphid flies) in a garden landscape in Salzburg. Activities in biodiversity and conservation research expand upon this to cover more general principles, such as the development and implementation of a **European Strategy for the Conservation of Invertebrates** for the Council of Europe under the Bern Convention, integrating policy and management in Protected Areas and biodiversity protection in relation to the provision of **Ecosystem Services** (everything that nature provides that is of benefit to humans) and integration into sectoral policy.

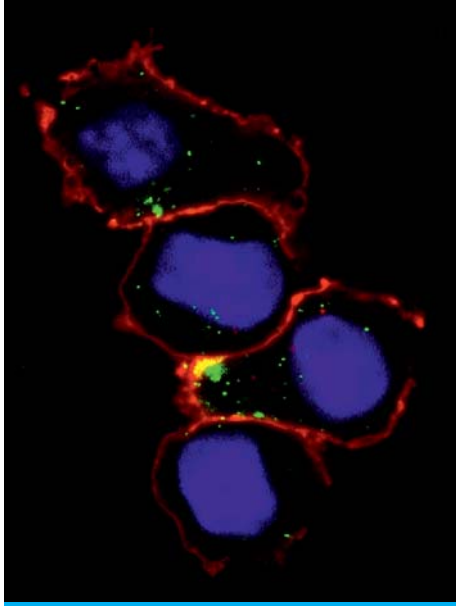
Further active research focuses on the provision of Ecosystem Services under dynamic conditions of environmental change, including climate change, and **understanding the consequences of possible extreme climate change** (greater than the present 2°C warming target) for decision-making across Europe. These are contributions to international EU research projects: The FP7 BESAFE project focuses on improving our understanding of alternative ways in which the **"value of biodiversity"** can be used to improve policy-making and governance at local to European and global scales (www.BESAFE-project.net). The FP7 Project IMPRESSIONS (www.impressions-project.eu) has the general aim to advance understanding of the **consequences of high-end climate and socio-economic scenarios** and to evaluate how such knowledge can be embedded within integrated adaptation and mitigation decision-making processes. These projects have also ensured close co-operation with a large number of high level research institutions across Europe and globally.

Team Hubert H. Kerschbaum
Divison of Cellular & Molecular Neurobiology

The main goal in our Center for Neurocognitive Research is to trace the **consequences of hormone-induced changes on ion channels and transporters** from the single cell to the entire organism. Each cell contains in its plasma membrane a diversity of ion channels, transporters and receptors. At the single cell level, ion channels and transporters are essential in gene expression, cell division, migration, phagocytosis, and cell death. With the expertise of colleagues from the Laboratory for Immunological and Molecular Cancer Research in Salzburg on leukemia, we demonstrated that selective blockade of a potassium channel suppresses proliferation in human leukemic cells. In collaboration with colleagues from the Paracelsus Medical University in Salzburg, we described that blockade of chloride channels or amino acid transporters impair phagocytosis in microglia. Furthermore, we showed that activation of adrenergic receptors modulates phagocytosis in microglia and that progesterone suppresses activation of lymphocytes. In an integrative approach with colleagues of the Department of Cell Biology we study the significance of intracellular ion homeostasis on autophagy and cell death.

In a systemic approach, we **evaluate associations between behavior, hormones, and neural activity in humans**. Specifically, we **quantify the impact of sex hormones** (progesterone, estradiol, testosterone), **hormonal contraceptives, and the stress hormone, cortisol, on attention, memory, and categorization processes**. In collaboration with colleagues from the Department of Psychology, we evaluate neural correlates of hormone associated modulation of cognitive processes using fMRI and EEG. In these studies, it is of fundamental importance to consider sex differences, menstrual cycle phases, and consequences of hormonal contraceptives.

Our technical approaches range from **cell culture, patch clamp** to characterize ion channels and transporters, **confocal laser microscopy, and electron microscopy** to analyze single cells to fMRI and EEG to evaluate the entire brain.



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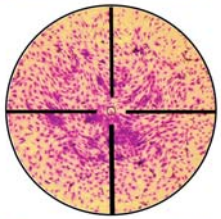

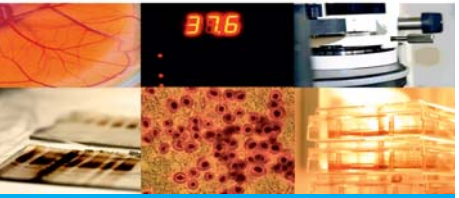

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Team Günter Lepperdinger
Division of Genetics

Stem Cell dysfunction is associated with age-related degenerative and proliferative diseases such as osteoporosis, sarkopenia, and cancer. Limiting the consequences of stem cell aging is generally believed to **promote healthy aging** by developing new therapies against age-related diseases. Also, the promise of regenerative medicine implies that mastering stem cell biology will open new avenues for truly rejuvenating therapies. For this promise to become reality, not only stem cell-intrinsic changes but also the changes in local and systemic conditions impact stem cell function and thus the **regenerative capacity** in many tissues.

We work to better understand **adult human mesenchymal stem cell** (MSC). Ubiquitously present in the body, this cell type is considered responsible for the maintenance and repair of many tissues and organs. Hence, MSC are best known for cell-based medical therapies and extra-corporal engineering of tissues and organs. Being highly resilient to stress, MSC are capable of **sensing stress levels** in order to balance quiescence, self-renewal and/or turning into progeny destined to differentiate.

We are building on a long standing expertise in the lab, which is cultivation of primary MSC isolated from human bone biopsies. We can also derive MSC-like cells from **induced pluripotent cells** (iPS). In contrast to MSC, culture expanded iPS are devoid of cellular aging and can be easily manipulated to genetically engineer human MSC for investigating the molecular network of MSC stemness, lineage decision and the formation of stromal niches for immune competent cells or tumors. Taken expertise and technologies together, we have commenced work reconstructing functional bone marrow through a combination of 3D printed bio-degradable scaffolds, growth factors and cells.

Working in close interaction with molecular biologists, biogerontologists, tissue engineers and physicians we want to translate our knowledge and established experimental technologies in stem cell biology into new therapeutic approaches in regenerative medicine. Supported by international networks in Biomedical Aging Research we are currently conceiving measures how to effectively inducing **healthy aging in humans**.

Team Ursula Lütz-Meindl
Division of Plant Physiology

Research of our team focuses on structural and **ultrastructural analysis of cellular stress** in order to obtain insight into physiological defense, tolerance and detoxification mechanisms. By means of modern **energy filtering transmission electron microscopy** (EFTEM) and integrated element analytical methods such as electron energy loss spectroscopy (EELS) and electron spectroscopic imaging (ESI), we investigate uptake and distribution of heavy metals into algae cells and impact of ionic or oxidative stress on ultrastructural alterations of organelles. We are interested in **sub-structural hallmarks of degradation processes** such as **autophagy** and **programmed cell death** and we analyze structural membrane transformation during these events.

Cultivated cells of the **freshwater green alga *Micrasterias denticulata*** serve as a model system for our studies. This alga is very well suited for cell biological investigations on stress impact as its considerable cell and organelle size and its extraordinary cell pattern allow precise definition of the single cell stages and facilitate recognition and interpretation of stress induced alterations. Additionally, studies on *Micrasterias* enable conclusions on evolutionary development of stress reactions, since algae of the group to which it belongs are regarded as closest relatives of higher plants.

It is one of the major goals of our work to combine the data on structural cellular stress reactions to **physiological stress responses** for obtaining a general comprehensive view on the capability of a plant cell to cope with stress. In parallel to our ultrastructural work we therefore measure photosynthesis, respiration, and ROS production, conduct enzyme activity assays, and employ protein biochemical and molecular biological methods. In this context we are collaborating with various national and international experts.

In order to extend conventional 2-dimensional TEM to more informative **3-D analyses** we are about to establish **electron tomography** in our lab and we are using focused ion beam scanning electron microscopy (FIB-SEM) in cooperation with the LMU Munich.

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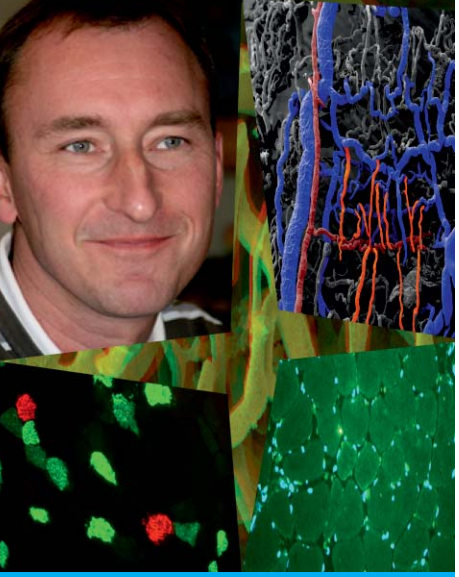

Team Bernd Minnich/Alexandra Sänger/ Alois Lametschwandtner
Division of Animal Structure & Function

The scope of our **Vascular- & Exercise Biology Unit** is to connect **modern animal biology and medical applications in the field of vascular-, muscle- and performance** research. This covers both, fundamental- and applied research. The research focus of our team which consists of 3 researchers, 2 technical assistants as well as doctoral- and master students is twofold.

The vascular focus covers basic research on **blood vessel development and regression in the African Clawed Toad**, Xenopus leavis as model organism and **biomedical research on coronary bypass surgery, tumor-vascularization and the study of cannabinoid (THC) effects on the skin and the reproductive system**. Our group is one of the worldwide leaders in the field of vascular corrosion casting. Besides in **vascular corrosion casting** we are experts in **scanning electron microscopy, 3D morphometry, histology, PCR and intravital microscopy**. Cooperations exist with industry, international research facilities and with clinics of the Paracelsus Medical University of Salzburg (PMU).

Our focus in performance biology basically concentrates on a**daptive processes of the musculo-skeletal system**, being induced by physical training, trauma, aging, death, genetic effects or extracorporal shock waves. The scope of these studies is to gain fundamental knowledge on involved molecular and cellular events, to establish training protocols in preventing aging dependent deterioration of the appropriate tissues as well as in terms of therapeutic tasks, and to provide routine methods to delimitate the time since death being applied in forensic medicine. Research projects are in co-operation with the Department of Forensic Medicine, the Department of Sport Sciences & Kinesiology, and the PMU. Methods comprise **histo- and immunocytochemistry, transmission electron microscopy, in situ-hybridization, image analyses, as well as molecular biological approaches**.

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Team Wolfgang Pfeiffer
Division of Plant Physiology

Plant growth depends on **intracellular and extracellular variables** and their linkage, mediated by the **cell membrane**. Studying various organisms, e.g. **autotroph and heterotroph cell cultures of *Chenopodium* and larvae of *Tenebrio***, our analyses involve **arthropod plant interactions, plant biochemistry, cell physiology, membrane biology, olfactometry and statistics**. Approaches realized in our group **Plant Membrane Biology and Growth** include collaborations with Anchalee Chaidee, Chulalongkorn University, Bangkok, Chatchawal Wongchai, University Phayao, and Ilse Foissner, Division of Cellular Dynamics, Universität Salzburg.

Global warming causes various environmental **stresses** reducing plant growth. Thus, we are interested in plant cell responses to **salt and hyper-osmotic stress, heat stress and insect biotic stress**. The later can be mediated by compounds of the digested insect cuticle, so-called **elicitors**, i.e. **chitosans**. Our olfactometry analysis of the negative feed-back of plant cells to chitosans revealed an interesting repellent activity. Since the very efficient synthetic repellent N,N-diethyl-meta-toluamide **(DEET)** can affect human health, the enhancement and quantification of repellent activity in Chenopodium cells may represent a promising **alternative** for general push and pull strategies.

Multivariate analysis of proton flux in plant cell suspensions after **salt stress and metabolite sensing** is a further topic. The effects of salt stress, hyper-osmotic stress, ion channel inhibitors, salt stress modulator proline, amino acids, carboxylic acids and plant growth regulators characterize five principal components of extracellular proton flux in *Chenopodium* cell cultures. A component depending on the antagonistic regulation by **ɣ-aminobutyric acid (GABA)** and salicylic acid indicates a function of acid sensing ion channels (**ASICs**) in salt stress sensing. The **extreme temperature-dependence** of proton flux and its linkage to responses of the **actin cytoskeleton** are part of this field of research.

Literature: Wongchai C, Chaidee A, Pfeiffer W (2013) Arthropod-Plant Interactions 7: 69-82.

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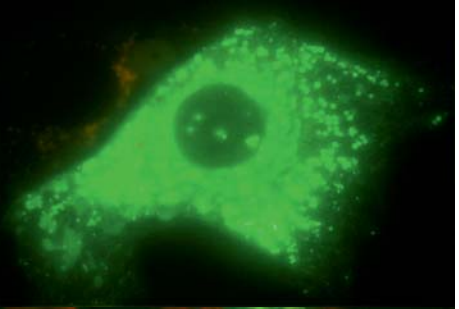

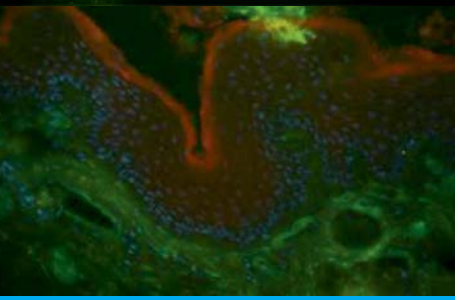

Team Klaus Richter/ Mark Rinnerthaler
Division of Genetics

The focus of our research lies in the investigation of **pathways that drive the aging process**. Life expectancy has been growing continuously during the past decades. Unfortunately not the healthy lifespan has increased dramatically, but the period of frailty. Therefore a major challenge for aging research is to find ways for aging in good health. So far we have more than 300 theories for aging but no one that is able to explain aging sufficiently well.

Generally expected is that **excessive reactive oxygen species (ROS) are inflicting damage on DNA, proteins and lipids** leading to defective mitochondria and oxidized proteins which promote aging. The cell itself is trying to get rid of damaged material by the process of autophagy which is assumed to be a major restraint for aging.

We are using **human skin for our studies to investigate changes taking place on the molecular level during the aging process**. This research is performed in close cooperation with the Paracelsus Private Medical University (PMU). With the help of **microarrays** we are able to **identify genes that are up- or down-regulated during aging**. These results have to be verified by **reverse-transcription-polymerase chain reaction and also by Western-blot** technique to see if the protein level correlates with gene expression on the mRNA level.

Using **primary keratinocytes isolated from epidermis** in cell culture gene expression can be manipulated under standard conditions. This way we have the possibility to influence gene expression by the addition of small molecules with the aim to oppose the aging process. With the help of **reporter-constructs** we are able to **describe the function of a particular gene promoter in great detail** and in this way study the interconnection of different aging pathways.

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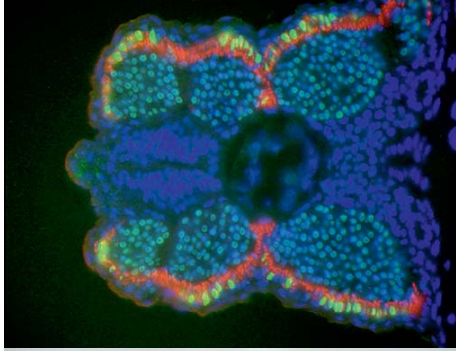
Team Peter Steinbacher
Division of Animal Structure and Function

Over the last two decades, **teleost fish** have gained a high profile as suitable model organisms for **developmental biology**, especially for study of the spatial patterns and causal mechanisms of **vertebrate organ formation** and **cell differentiation**. This research has many important implications, extending from the formation of complex structures and functions through individual ontogeny and over evolutionary time to aspects of human disease. Our specific interest is focused on the **development and growth of skeletal muscle** and its plasticity in response to external factors and interspecific variation.

We have identified the fish **dermomyotome**, a transient structure of the somite that provides most of the **muscle precursor cells** in the embryo, and have shown how such cells enter the myotome. Recent work demonstrates that the proliferation-differentiation balance of these stem cells is dependent upon **environmental factors**, with important downstream effects on fish growth in later life. A particular focus has been put on the formation of **hypaxial and fin muscles**, the fish homologues of terrestrial vertebrate limb, tongue, laryngeal and diaphragma muscles.

In a second research area, we investigate the remarkable capacity of cells to adapt to changes in activity and functional demands. In this context, the **plasticity of muscle cells** is of particular interest due to the fact that physical fitness reduces the risk of many diseases. Our research in this direction aims to understand how **exercise training** exerts influence on **fibre type composition**, **fibre type specific gene expression**, **precursor cell activation** and **muscle cell fine structure**. We are also interested in investigating the effects of **gene mutations** on these variables. In a current project, we study the effects of endurance training on the muscle of humans with single nucleotide polymorphisms in the **PGC1α** and **PPARδ** genes. Both genes are important regulators of **mitochondrial biogenesis** and master regulators of enzymes involved in oxidative phosphorylation. They also play an important role in the pathogenesis of insulin resistance and type 2 diabetes



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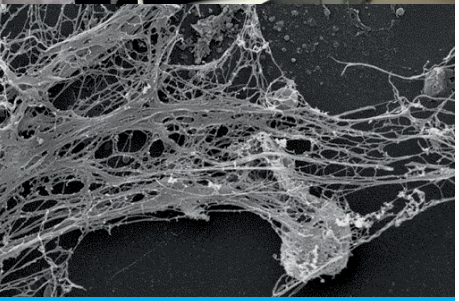

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Team Walter Stoiber/ Wolf-Dietrich Krautgartner
Division of Animal Structure & Function

The main research interest of our team is the **pathogen-host interaction**. The research is increasingly focused on **neutrophil extracellular traps** (NETs) since these webs of extruded DNA were identified as important elements of innate immune response. Being decorated with cytotoxic proteins, NETs act in a fragile balance between antimicrobial defence and fatal host tissue damage, with most important implications for the pathogenesis of chronic inflammatory disease and acute organ failure. The main pathway of NET generation (NETosis) by neutrophils is a special form of cell death mediated by molecular signals, for example by the chemokine CXCL8/IL-8. It involves the generation of reactive oxygen species (ROS) and histone protein citrullination. A second type of NETosis has been shown to leave neutrophils viable and phagocytotic active.

Our research group has over the years gained a high degree of expertise in **analysing the microstructure and pathogenic potential of NETs**. Combining **electron microscopy** (TEM, SEM) with **immunolabelling, in situ hybridisation** and other advanced histology techniques, we have made significant contributions to clarify the **maturation of NET-forming ability in neonates** and to test CXC receptor antagonists as a possible means of therapeutic intervention. Impressive evidence has been collected that **NETs decisively contribute to chronic inflammation in the periodontium and especially in the airways during cystic fibrosis** and **chronic obstructive pulmonary disease (COPD)**, and that NETosis involves chromatin decondensation to beads-on-a-string fibres.

The work has entailed fruitful collaborations with internationally renowned research groups (presently at PMU Salzburg, Saarland University, University of Tübingen). The potential benefit of this research is expanding. Entangled with respiratory burst and autoantibody induction, NETs are turning out be almost omnipresent in inflammatory response, playing important roles in rheumatoid arthritis just as for the osseointegration of titanium implants.

Team Raimund Tenhaken
Division of Plant Physiology

The research focus or our team is the analysis of pathways which **convert sun energy into usable biomass**. In order to do so, plants need to synthesize activated sugars – **nucleotide sugars** – which **are the building blocks for polymers**. Surprisingly, several of the necessary enzymes are unknown. We purify the proteins, clone the genes and characterize the recombinant enzymes functionally to provide important data to the community about the function of previously unknown genes. **A broad range of biochemical, analytical and molecular methods is used in each project** to characterize proteins and mutants. Sugar analysis including oligomeric structures is performed on specialized HPLC-systems.

In several cases the discovery of novel enzymes allowed us to use them for biotechnology. A novel strategy against soil nematodes is an actual research topic, which became evident from transcriptomic analysis of infected roots. We provide the molecular technology for knockout mutants, if necessary in multiple genes.

The cloning of a gene for alginate precursors from brown algae now allows screening for inhibitors of alginate polymers in bacteria, an alternative strategy to antibiotic treatment for several human pathogens, which hide from the immune systems by surrounding themselves with an alginate layer.

Plant molecular biology is used to test the importance of different **pathways for abiotic stress tolerance**, the presumably most important contribution to improve crops in the future during climate change and higher demands for plant biomass.

We develop new methods for sensitive analytics and metabolomics and provide this technology to collaborators. We break the barrier of sequenced model organisms by **applying next generation sequencing to challenging biological problems**. The cloning of so far unknown putative genes and assigning a function to them is an important contribution to ultimately understand the role of all genes within a genome.

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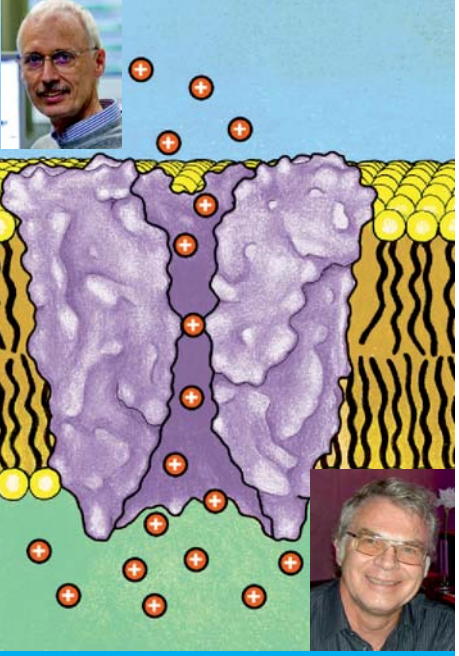

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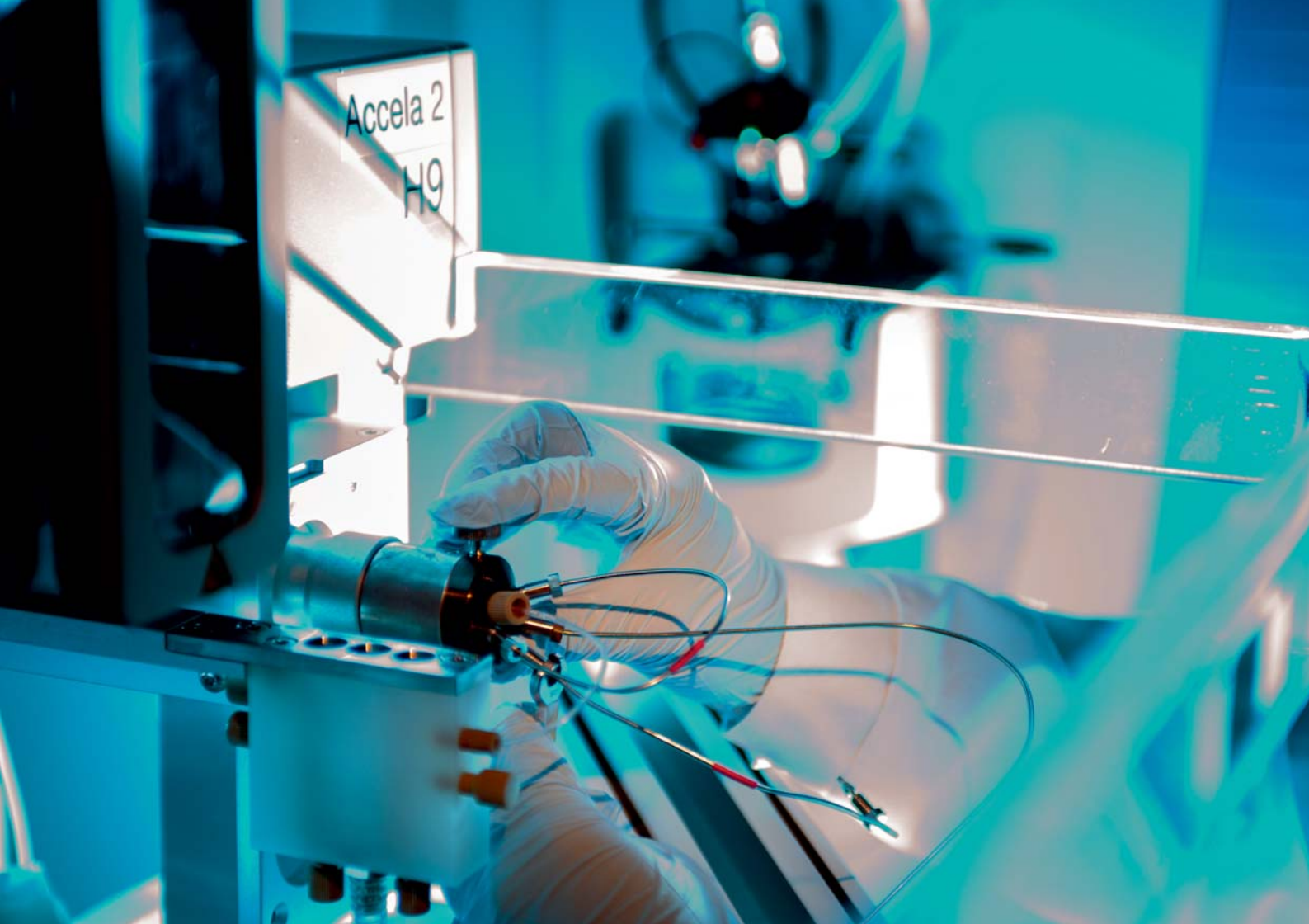
Team: Thomas Weiger/Anton Hermann
Division of Cellular & Molecular Neurobiology

The two groups of Anton Herman – "**Neurophysiology-Signaling**" and Thomas M. Weiger – **"Neurophysiology"** work closely together. Their main experimental foci are on the: **Cellular action of ethanol/acetaldehyde and gasotransmitters, in particular hydrogen sulfide (H_2S) on maxi calcium-activated potassium ion channels (BK)**. Further interests are on cellular **actions of polyamines and herbal traditional medicine** in the context of ion channel activity.

BK ion channels, the channels we mainly study in detail, **are molecular integrators of electrical events at the plasma membrane and of activation of intracellular messenger systems.** BK channels are involved in a plethora of cellular functions from bacteria to men and play an essential role in controlling electrical activity of cells, hormone secretion or vasoregulation to name a few. **They are a main target of ethanol and acetaldehyde being involved in the tolerance of organisms against alcohol.** Mutation at BK channel proteins are associated with epilepsy, paroxysmal disorder, cerebellar ataxia, hearing loss, autism, mental deficiency or chronic hypertension.

Gases, such as nitric oxide (NO), carbon monoxide (CO) or hydrogen sulfide (H_2S), termed gasotransmitters, play an increasingly important role in understanding of how electrical signaling of cells is modulated and fine-tuned. I**n our studies we found that H_2S as well as alcohol and acetaldehyde modulate BK channel activity.**

We use primarily **cell culture and electrophysiological techniques** (voltage clamp and patch clamp for measurement of whole cell and single channel currents) and apply **Ca^{2+} imaging** and/or **confocal laser scanning techniques** or measure **cell proliferation**.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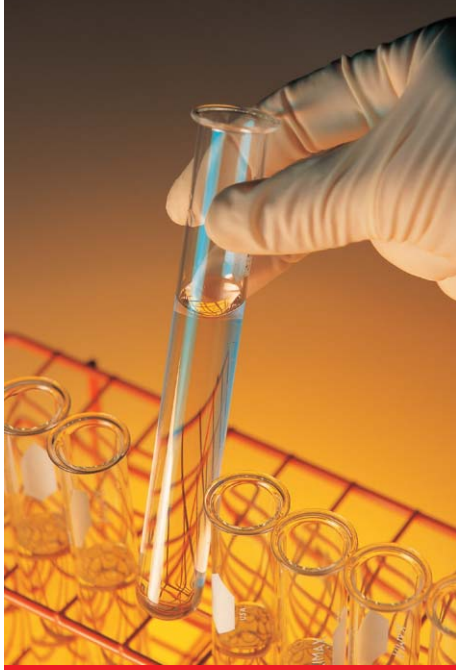
The Department of Molecular Biology

The sixteen research groups of the department cover a **broad variety of expertise**, ranging from immunology, allergology, structural biology, tumor biology, genomics, glycobiology to bioinformatics, molecular plant biophysics and biochemistry, bioanalytics, biological chemistry and microbiology. In a **highly mutidisciplinary approach** and by employing cutting-edge technologies the department addresses urgent and current topics in the fields of **allergy and immunology, tumor biology, and nanotoxicology**.

The **division of allergy and immunology** works on the development of new tools for allergy diagnosis and allergen-specific immunotherapy, prophylactic vaccination against allergies, signal transduction within cells of the immune system, the effects of environmental pollutants on immunity, and molecular mechanisms associated with allergy and asthma. In the **division of cancer research and epigenetics**, researchers try to understand the mechanisms set in motion by oncogenic signaling pathways during the initiation and growth of human malignancies. On the therapeutic side, cellular mechanisms of photodynamic tumor therapy are investigated.

The **divisions of structural biology and bioinformatics** and **chemistry and bioanalytics** are specialized on the study of molecular details and mechanistic principles of proteins central to allergy or cancer. Genomic, proteomic, and metabolomic approaches are implemented to reveal a global view on the molecular networks involved in biological processes. Interactions of host cells with microbial pathogens are studied in the **division of microbiology**. Finally, biological functions of glycans in the regulation of cell differentiation, signal transduction, control of apoptosis and in the development of malignant cancers as well as the polarity in biological systems such as pollen tubes are studied in the **departments of glycobiology** and **molecular plant biophysics and biochemistry**.

Candidates interested to join the research activities will obtain a **multidisciplinary training in state of the art techniques**. The department provides access to the necessary technological infrastructure and expertise that is necessary to conduct biological research on an internationally competitive level.



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Team Fritz Aberger
Division of Cancer Research and Epigenetics

Cancer is a leading cause of death worldwide. Despite considerable progress in the treatment of cancer patients, the incidence and death toll are globally increasing, urgently calling for intensified research to better understand the molecular basis of this disease and to identify improved strategies and drugs for personalized therapy.

As partner within national and international research consortia and active founding member of the Cancer Cluster Salzburg (CCS), the Aberger lab applies a combination of *in vivo* cancer models and state-of-the art cellular, molecular and global genomics approaches, to **unravel novel molecular targets for cancer therapy**. A central research focus is on the analysis of pathways controlling proliferation, survival and metastatic potential of **cancer stem cells**, a small subpopulation of cancer cells responsible for tumor growth, metastasis, drug resistance and disease relapse. On the clinical side, the group mainly studies the molecular processes underlying **pancreatic** and **non-melanoma skin cancer** development.

The core competence of the group is the functional analysis of oncogenic **Hedgehog signaling** in malignant cells and stem cells. By bringing together the expertise of tumor biologists and clinicians within the CCS, the Aberger group studies the molecular basis of tumor initiation, growth and metastasis. In particular, the lab investigates interactions between multiple oncogenic signals with the aim to design **rationale-based combination treatments** for better therapeutic outcome.

The Aberger lab has recently deciphered **oncogenic signals and putative drug targets** responsible for malignant disease progression. In collaboration with partners from innovative biotech and big pharmaceutical industry, the group is involved in the development of novel drugs for targeted and improved cancer therapies.

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Team Hans Brandstetter
Division of Structural Biology and Bioinformatics

The research of our team focuses on **proteolytic enzymes**, their cofactors, substrates and inhibitors. Proteolytic enzymes are master switchers in health and disease. By their highly specific recognition and modification of protein substrates, **proteases serve as signaling and decision matrices**. Of particular interest to us are proteolytic actions in the field of immunology/allergy, blood coagulation, and cancer.

We employ a broad spectrum of **biochemical, biophysical and computational techniques** to **characterize the molecular function of important target proteins**. Most importantly, we use **x-ray crystallography** to determine the three-dimensional architecture of the molecular targets. The structural information guides us to rationalize and experimentally test hypotheses about possible molecular mechanisms of action as well as their significance in the molecular, cellular and systemic context.

Questions of immunological interest are linked to the **cellular pass control** which is implemented *via* antigen processing and presentation. Each cell has to identify itself towards the immune system by presenting intracellular peptides at the cell surface. Despite its enormous efficiency, some **harmful cells escape the screening** (pass control) of the immune system, e.g., by presenting unsuspicious peptides only. On the other side, **allergens,** which are *per se* harmless proteins, **can trigger excessive immune reactions**. We investigate the complex protease machines involved in antigen processing. A detailed understanding promises treatment options against immunological and infectious diseases, and also tumors.

The (innate) immune system is multiply linked to the **blood coagulation system** which primarily serves to stop life-threatening bleeding without causing fatal vessel occlusions (thrombosis). For this purpose nature employs a **molecular proofreading principle** that requires simultaneous and concerted molecular actions. We investigate disharmonies in these molecular orchestra that lead to bleeding disorders such as hemophilia.

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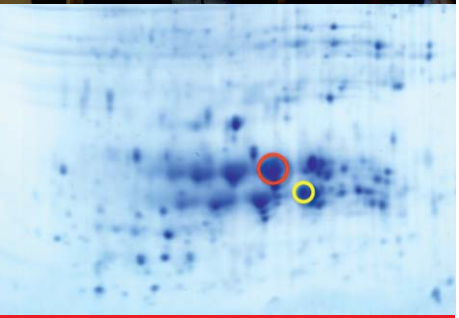

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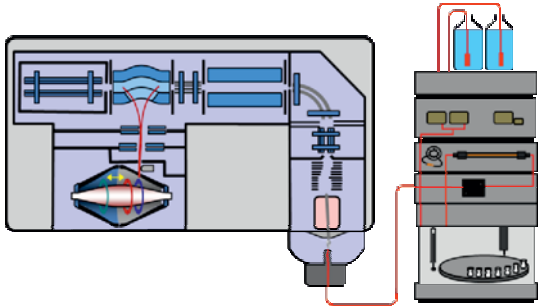
Team Peter Briza
Division of Allergy and Immunology

With the development of modern tandem mass spectrometers, **proteomic research** became an increasingly important tool to identify and characterize proteins in complex samples. Several complementary approaches are possible. Proteins are extracted from cells or organelles, digested with protease and the resulting peptides are separated by reverse phase HPLC and analyzed by a directly coupled tandem mass spectrometer. Another option is to separate the extracted proteins by **one- or two-dimensional gel electrophoresis**, digest protein spots with protease and analyze the peptides by MS. Tandem MS instruments are able to simultaneously acquire peptide masses and peptide fragmentation patterns. With this information, **proteins can be unequivocally identified in protein data bases**. Sequence information obtained for unknown proteins can be used for cloning the corresponding genes. Our group uses a state-of-the-art Quadrupole-Orbitrap mass spectrometer with electrospray ionizatiion, optionally coupled with a capillary HPLC.

Using the methodology described above, we try to **characterize and verify purified allergens**, as well as **identify unknown proteins or protein isoforms that induce type I allergies in allergic patients**. Our main focus are allergens from tree (birch and selected trees), weed (mugwort, ragweed) pollen and food (peanut). Our work is done in close cooperation with the group of Fátima Ferreira.



Team Chiara Cabrele
Division of Chemistry and Bioanalytics

Our research focuses on the investigation of the chemical, biophysical and structural properties of proteins, aiming at the deep understanding of their mode of action and with the long-term goal to exploiting the acquired knowledge to design and develop artificial molecules as positive or negative modulators of protein activity. In particular, we are interested in small regulatory proteins that play a role in cancer and vascular diseases.

Proteins are key biomolecules in many cellular processes including the activation of DNA transcription, the transport of messenger RNA from the nucleus to the cytoplasm, the biocatalysis of reactions (which otherwise would be slow and unspecific), the regulation of signaling cascades. Despite their diversity, all these processes share a fundamental mechanism, namely **protein molecular recognition**. Proteins may recognize themselves or other proteins as well as different classes of molecules (e.g. DNA, RNA, glycans) by means of specific non-covalent interactions such as hydrogen bonds, electrostatic and hydrophobic contacts. It is thus important to characterize the non-covalent network that allows biomolecules exerting their function. This implies a deep sight into the structure and dynamics of proteins by using spectroscopic techniques (circular dichroism, fluorescence, nuclear magnetic resonance), which in some cases requires the use of **chemically modified proteins.**

Organic chemistry methods applied to proteins allow reproducing, mimicking and manipulating these very interesting biomolecules. For example, the preparation of **proteins containing post-translational modifications** (e.g. phosphorylation, acetylation, methylation, glycosylation) provides the tools to evaluate the structural and functional importance of these modifications that are essential to regulate the activity of proteins in the cells. Furthermore, the mimicry of protein interfaces by means of synthetic scaffolds leads to **artificial, proteolitically stable modulators of protein-protein interactions**, which are of significance for the development of drug-like molecules.

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Team Albert Duschl / Jutta Horejs-Höck
Division of Allergy and Immunology

At the center of our interest are **effects of various factors on the human immune system**. We are constantly subjected to a multitude of natural environmental stimuli (bacteria, viruses, fungal spores, allergens, etc.), but anthropogenic factors are present as well and may be increasing (fine dust, nanoparticles, exhaust gas, etc.). The current boom in nanotechnology may create safety hazards, but also promises groundbreaking applications, including medical ones. Against this background, **investigations into nano-bio-interactions** and into **molecular mechanisms of regulations** for different immune cells have developed into our major areas of research. Some *hot topics*:

Nanosafety – nanotechnology applies extremely small materials (1-100 mm), which have novel and attractive properties based on low mass and high surface area, allowing new technical applications. Due to their small size and their high surface reactivity they are able to penetrate body barriers, like airways, lung and gastrointestinal tract, which may induce both toxic and immuno-modulating responses. Biological effects can carry risks, but may also be useful for medical applications.

Nano-Bio-Interactions – the highly reactive surface of nanomaterials causes quick and often rather stable binding of biological molecules, mainly proteins, which affects reactions of the body. This property may be used for intentional transport of proteins and other substances; however, binding to nanosurfaces can alter structure and function of proteins. Consequences for immunity are under study.

Interaction between unspecific and specific immune response – Dendritic cells recognize foreign substances via *„pattern recognition“* receptors, take up antigens and activate T-cells, which induce now an immune response that will either result in defensive actions, or in the establishment of tolerance. We focus on molecular mechanisms involved in activation of dendritic cells, since they play a key role in deciding how the immune system will react to non-self substances.

Team Fátima Ferreira-Briza / Michael Wallner
Division of Allergy and Immunology

Type I allergic reactions comprise a wide range of IgE-mediated diseases, which affect more than 20% of the population and represent a major health problem worldwide. The primary interest of our group is the development of new tools for **allergy diagnosis** and for safer and more efficient **vaccines for allergy**. Our research focuses on **allergic reactions triggered by pollen** (birch, mugwort, ragweed), **mites,** and **foodstuffs** (apple, peach, celery, nuts). One major goal of our research is to understand why some proteins are allergenic and others not.

The identification of novel allergen molecules is essential for improving molecule-based allergy diagnosis. For this purpose, we have established methods for cloning and **recombinant production** of allergens in heterologous expression systems like bacteria, yeast and plants. The identity and secondary structure elements of the purified allergens are routinely characterized using **physicochemical** (gel electrophoresis, mass spectrometry, amino acid analysis, circular dichroism, dynamic light scattering) and a wide array of **immunological methods** (ELISA, mediator release assays, simulated antigen processing assays, uptake by antigen presenting cells, immunization models).

Well-characterized allergen molecules are used for diagnostic studies including the development of **allergen microarrays**. Another goal of our group is the generation of safe and efficient tools for allergy vaccination. Using knowledge-based approaches, we have developed **hypoallergenic molecules** of important pollen and food sources (e.g. birch pollen, peach). Before clinical trials, the **efficacy of candidate vaccines** is usually tested in murine models of allergic sensitization. The **hypoallergenic birch pollen vaccine** BM4, which was developed in our lab, is currently being clinically evaluated in the framework of a project financed by the European Union. As member of the Christian Doppler Laboratory for Biosimilar Characterization, we want to generate novel structural and immunological tools for comparison of originator biopharmaceuticals and biosimilars.

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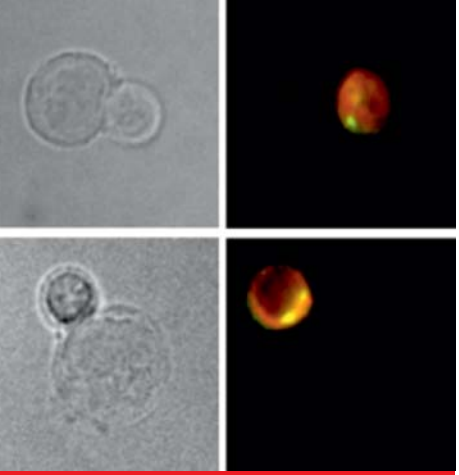

Team Iris Gratz / Gerti Achatz
Division of Allergy and Immunology

Allergy and autoimmunity are chronic and debilitating conditions for which current treatment approaches are unsatisfactory. These inflammatory diseases are caused by immune cells attacking **harmless (self-)antigens in host tissues**, which they are supposed to protect. However, further basic research is required to fully understand the disease mechanisms and immune-regulatory processes in the target tissues.

Our research aims to **elucidate the mechanisms that control the balance of immune activation versus tolerance** because this balance ultimately determines the outcome and severity of disease. Understanding these mechanisms will help to develop novel therapeutic strategies. In our studies of autoimmunity and allergy we focus on immune-regulatory processes of two major epithelial body surfaces, skin and lung.

Our main research questions are: 1. The **role of Foxp3+ regulatory T cells** (Treg) in inflammation, their generation and recruitment to the target tissues. 2. **Immune cell stability and memory formation of T and B cells** with an emphasis on apoptotic processes and their regulation by cytokines. 3. **Modulation of human immune responses** in clinical settings such as gene therapy

In our projects we study cellular processes of T and B cell differentiation, memory formation, and IgE-regulation. For these studies we use **innovative mouse models and humanized mice**, which we manipulate with genetic and biomolecular tools. We combine the use of these **transgenic and knock-out mice** with the application of biologics, antibodies and small molecules to manipulate immune cells in vivo.
In all of our approaches we focus not only on the phenotypes of selected lineages but also on the **crosstalk between immune cells of the innate and adaptive immune system**. We are particularly interested in the **interaction between T cells and antigen-presenting cells (APCs) or B cells**.

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Team Christian Huber / Hanno Stutz
Division of Chemistry and Bioanalytics

The research focus of our team regards the development and application of **analytical workflows** to address biological questions in the fields of **protein, proteome, metabolite, and metabolome** (and eventually transcriptome) **analysis.** Samples comprising **cultured cells, tissues, or biological fluids** are processed and their constituents of interest (proteins or metabolites) isolated for further determination. The analytical methods are primarily based on instrumental, bioanalytical separation methods (**liquid and gas chromatography, capillary electrophoresis**) in combination with **mass spectrometry** (time-of-flight-, triple-quadrupole-, linear ion trap-, and Orbitrap mass analysis). Because of the enormous amount of generated raw data, we collaborate with bioinformaticians and statisticians in order to properly interpret the experimental data and put them into a biological context.

The major goal of our work is the collection of information about **changes in protein or metabolite concentration** that are **caused by stimulation** of cell models (cancer stem cells, dendritic cells, monocytes, hepatocytes, lung epithelial cells) upon treatment with drugs, nanomaterials, or **by diseases such as allergy or cancer**. These changes allow us drawing conclusions on the **biochemical pathways and mechanisms** involved in disease or toxic effects of drugs and nanoparticles. In such experimental setups, we use, e. g., dendritic cells isolated from human blood to study the effects of allergens on the immune system.

In a second focus area we collaborate with the **pharmaceutical industry** (Sandoz) and the **laboratory supplier industry** (Thermo Fisher Scientific) in the **Christian Doppler Laboratory for Biosimilar Characterization**. Here, we use our expertise for the in-depth protein characterization (peptide mapping, sequencing, determination of impurities, glycosylation, oxidation, and deamidation) to aid the industry in establishing **workflows that guarantee the safety and efficacy of their biopharmaceutical drug products**. This research focus requires collaborations with groups of the department having expertise in protein production, chemical protein modification, structural biology, and biochemical protein characterization.

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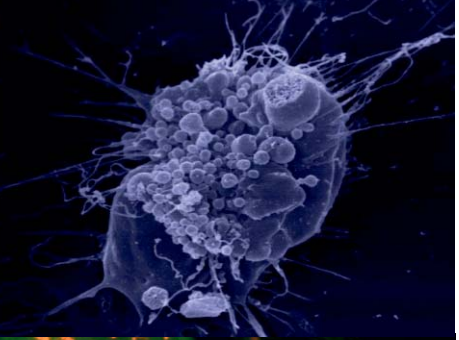

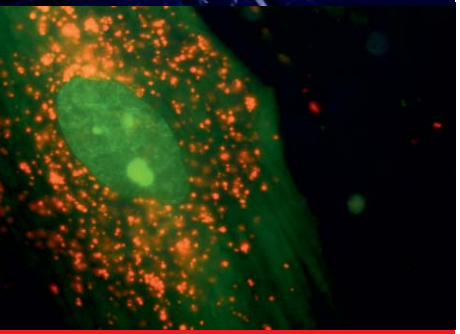

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Team Barbara Krammer
Division of Cancer Research and Epigenetics

In research we focus preferentially on **molecular and cellular mechanisms of the Photodynamic Tumor Therapy (PDT) and Diagnosis**. PDT combines a selective uptake of a photosensitizer (PS) to tumor tissue with irradiation using visible light. By this, the PS is activated followed either by fluorescence or physico-chemical reactions with other molecules, mainly molecular oxygen. The f**luorescence identifies the tumor (clinical diagnosis)**; the chemical reactions lead to **formation of reactive oxygen species** at the target sites, **leading to cell death**. This mechanism is used to eradicate tumors and vessels at inner and outer surfaces of the body. No major side effects or mutagenicity occur.

Since we are interested in investigating the mechanisms leading to the observed clinical effects and developing improved protocols, we use a large variety of in-vitro methods ranging from s**pectroscopic measurements over cell based assays to molecular techniques**. This includes equipment to measure fluorescence such as flow cytometer, microplate reader, fluorescence microscope and fluorescence spectrophotometer.

One of our aims is to test **new photosensitizers**; photosensitizer coupled with carriers such as polymers, nanoparticles and dendrimers; or photosensitizers coupled with proteins, peptides and antibodies to improve the targeting function. Another aim is to investigate **signaling pathways leading to cell death** (e.g. in apoptosis), **adaptive response or survival** following PDT. Furthermore we try to analyze the **immunogenicity,** which is commonly observed following PDT. Based on a mouse study, where we showed complete tumor eradication und immunity following low dose PDT, we currently search for factors responsible for immune stimulation, e.g. damage-associated molecular pattern molecules.

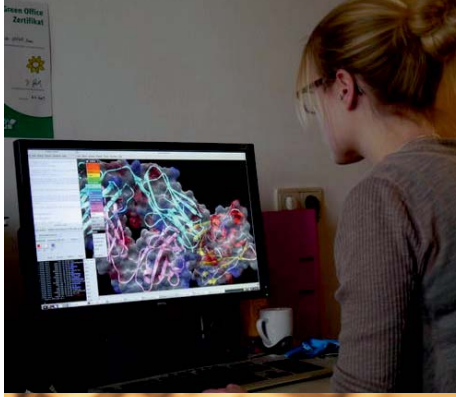
Another focus is on the cellular and molecular investigation of **effects of low-level-alpha-radiation**, which is responsible for the health effects of radon spas. We cooperate with groups from our faculty, the PMU and SALK as well as with national and international researchers and with the industry (Sanochemia, Tecan, Planta, W&H).

Team Peter Lackner
Division of Allergy and Immunology

Our team concentrates on the development and a**pplication of bioinformatics methods in the area of immunology and allergy research**. The objects of our investigations are proteins. These molecules are major players in immunological pathways but also origin of allergies. In particular we are interested in allergens. We aim to contribute to answer two central questions: **Why are some proteins allergens while closely related ones are not?** And, how can we transform natural allergens by protein engineering into drugs (hypoallergens) for allergy treatment.

To come closer to answers, we **analyze, compare and predict properties of these proteins like the 3D-structure** per se, molecular functions, interactions, stability or flexibility. Subsequently we try to modify certain properties of the allergens to deliberately change their molecular behavior and make them accessible as drugs for allergy treatment. Our **research is highly interdisciplinary** and is performed in close collaboration with experimental groups of the Division of Allergy and Immunology. In terms of computational problems we collaborate with the Universities of Applied Sciences in Salzburg and Upper Austria.

For the analysis and prediction tasks we use a panel of publicly available tools such as **molecular graphics, molecular modeling, sequence and structure comparison**, etc. Occasionally, the publicly available methods are not tailored for specific tasks or they are simply insufficient in terms of reliability or performance. Other methods are circuitous to use, especially when applied to larger data sets. In these cases we implement our **own software solutions to overcome the deficiencies using modern technical approaches like machine learning or distributed computing**. Bioinformatics methods developed in our team are often of broader interest and thus they are released to the community.



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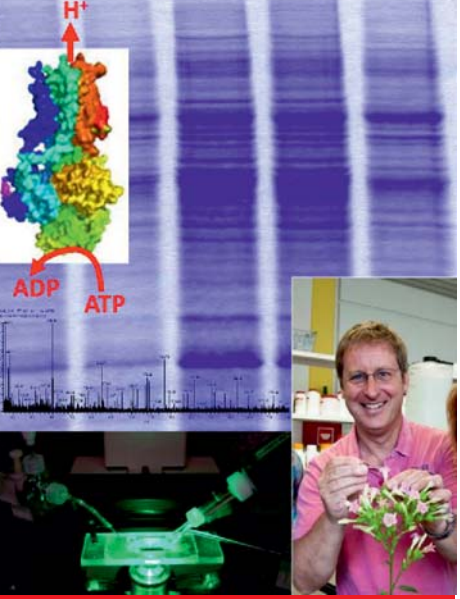

Team Gerhard Obermeyer
Division of Molecular Plant Biophysics and Biochemistry

The research focusses on the central biological question how cells develop and maintain **polarity**. An extreme example of polarity is the growth of **pollen** tubes: the growth zone is restricted to the first 20 µm of the tube tip but pollen tubes can reach a length of several centimeters while maintaining a diameter of only 10 µm. Furthermore, growth of pollen tubes through the style tissue is a prerequisite for successful fertilization which guarantees high **crop yields** for human nutrition. Future problems caused by **global warming** are already addressed in today's research and the effects of high temperature and draught on pollen fertility are studied, too.

To understand the molecular mechanisms behind pollen tube growth, the function, structure and activity of **membrane proteins** is studied using a broad panel of different methods ranging from single molecule to systems biology approaches: **biophysical techniques** like patch-clamp, turgor pressure and ion-sensitive electrodes, microscopy methods to localize membrane proteins, protein interactions or cytosolic ion concentrations in living cells by fluorescence resonance energy transfer or ratio imaging using fluorescence tagged proteins or genetically engineered **nanosensors**, respectively, and biochemical methods as well as up-to-date **omics techniques** (proteomics, metabolomics, transcriptomics) to reveal functional **protein complexes** in the plasma membrane and active **signaling pathways**. Recent publications include the characterization of a glutamate receptor-like protein in plants (Michard et al 2011, Science 332: 434) and the world-wide first study on the pollen metabolome (Obermeyer et al 2013, Plant Physiology 1822).

The group is well-established in an international and national research network: students and co-workers from all over the world (Australia, Czech Republic, Egypt, France, Germany, Greece, India, Israel, Italy, Mexico, Myanmar, Spain, Turkey, UK, USA) have already joined the group. We welcome students for Bachelor-, Master and doctoral thesis who are interested in working on innovative aspects of plant sciences in a stimulating and pleasant atmosphere.

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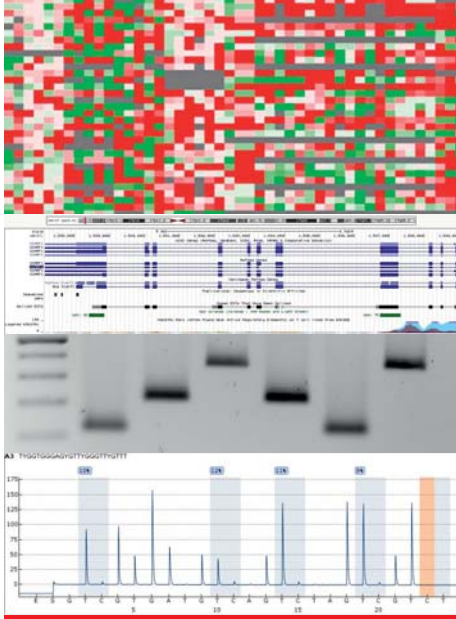
Team Angela Risch
Division of Cancer Research and Epigenetics

The research of our team focuses on **genetic and epigenetic variations and aberrations in the context of cancer**. Interindividual genetic and epigenetic variation, as well as acquired genetic and epigenetic changes can affect cancer risk, tumor development and clinical prognosis. Methylation patterns differ across tissues, but can also change as a result of age, disease or exposure, e.g. to tobacco smoke. We are interested in their potential **use as biomarkers of exposure, or as diagnostic/prognostic markers**. Epigenetic dysregulation may also point us to important new mechanisms in carcinogenesis.

We employ a broad spectrum of molecular biological techniques with appropriate bioinformatic and statistical analysis. Most importantly, we employ a range of methods for **methylome analysis**, e.g. in clinical samples, and then use sequence specific quantitative methylation analysis to validate findings and to better characterize the epigenetic dysregulation. This is further followed by in vitro analyses of target genes or miRNAs for functional characterization.

Within large international consortia we investigate **single nucleotide polymorphisms (SNP)** and their functional consequences as risk factors for disease, with a particular emphasis on lung cancer. Within **genome-wide SNP association studies**, risk regions have been defined, but the mechanisms of such associations mostly remain unclear. We are now determining methylation patterns at high resolution, and are looking to correlate SNPs with epigenetic patterns with the aim of identifying functionally relevant SNPs and mechanisms promoting carcinogenesis.

Inflammation-related epigenetic changes and alterations in epigenetic patterns as a result of tumor-microenvironment interactions hold particular promise in the context of identifying potentially **clinically useful biomarkers. Epigenetic drugs** are being used in the context of cancer treatment, but much remains to be learned about their mechanisms of action and optimal use.



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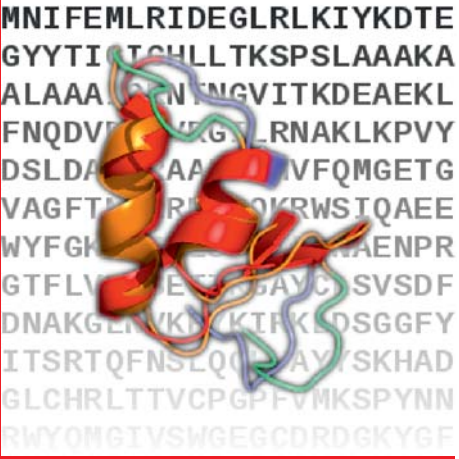
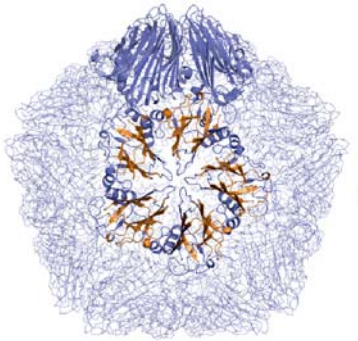
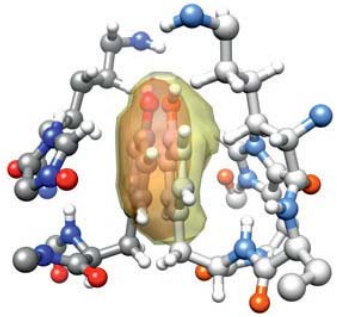


Team Manfred Sippl / Markus Wiederstein
Division of Structural Biology & Bioinformatics

Our major research programmes concern the **validation, refinement, prediction, and classification of protein structures**. We develop **computational tools** and programs for protein structure comparison, high speed structure data base searches and protein domain decomposition. We use s**tatistical thermodynamics and information theory** to derive energy functions for protein structure validation, refinement and prediction. We employ Python and C/C++ for the implementation of computer source code. We share finished programs with the scientific and commercial communities.

Current major research projects include: comparison and alignment of **three-dimensional structures of proteins**; fast and sensitive **structure data base searches**; methods for the automated decomposition of protein structures into domains; understanding the f**orces that govern protein folding and protein stability**.





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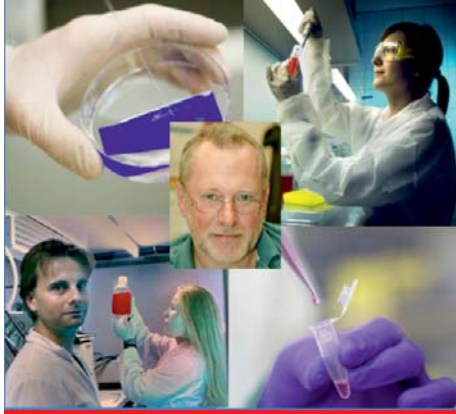
Team Josef Thalhamer / Richard Weiss
Division of Allergy and Immunology

Due to the increasing prevalence of type I allergy, there is an urgent need for novel therapeutic but also prophylactic approaches against this disease. We have long lasting experience in the field of intradermal **genetic immunization** and have demonstrated the proof of concept for tailor-made allergy vaccines based on plasmid DNA and messenger RNA. The optimal safety profile makes RNA a promising candidate for a first human prophylactic vaccine for early protection against allergic sensitization. While prophylaxis may be the most efficient intervention, the high incidence of allergic diseases calls for improved therapeutic vaccines. Allergen specific immunotherapy suffers from low patient compliance due to the need for a multitude of subcutaneous injections over several years and the risk of systemic side effects. Yet, painless alternatives such as sublingual immunotherapy lack efficacy.

The skin has been rediscovered as an effective route for vaccination, not only for gene vaccines but also for protein vaccines. It is rich in antigen presenting cells and is efficiently drained via local lymph nodes. We have recently established **transcutaneous immunotherapy** via laser-generated micropores, which displays similar efficacy compared to subcutaneous immunization. Using glycoconjugates of allergens and carbohydrates, we design **nanoparticles with decreased allergenicity** (so-called hypoallergens) and increased immunogenicity, which specifically target skin dendritic cells via different receptors.

These translational research approaches are based on studies of **cellular and molecular mechanisms of skin immunity**, with a focus on immune polarization and allergic sensitization. Currently, we use state-of-the-art transgenic mouse models to investigate **immune functions of epidermal Langerhans cells** by inducible antigen expression after genetic immunization, and the influence of **structural stability of proteins** on immunogenicity and **immune response polarization** using in silico mutation and screening approaches followed by wet lab analysis.



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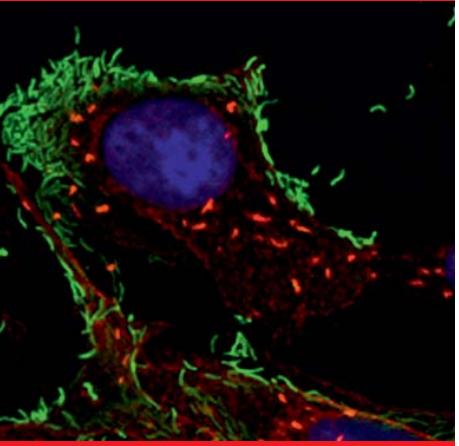

Team Silja Weßler
Division of Microbiology

Precise regulation of **signal transduction** is required to control normal biological processes. Pathogens developed fascinating strategies to deregulate cellular signaling pathways, which have been related to a number of disorders, ranging from relatively non-life-threatening disorders to extremely virulent diseases such as cancer as a consequence of growth control loss and resistance to apoptosis. Focus of our research is the investigation of the molecular mechanisms of how the bacterial **class-I carcinogen *Helicobacter pylori*** interferes with host cell functions leading to gastric carcinogenesis.

H. pylori induces depolarization and migration of epithelial cells, which is enhanced by translocation of the pathogenic factor CagA into host cells. Once injected into the cytosol CagA is rapidly phosphorylated by Src family kinases. We identified the non-receptor tyrosine kinase c-Abl as an additional crucial mediator of *H. pylori*-induced migration and novel CagA kinase, which maintains CagA phosphorylation in epithelial cells. As **Src and c-Abl kinases** are important in driving cells toward neoplastic transformation they represent a promising field in future treatments of gastric cancer progression. In current projects we investigate those derailed non-receptor tyrosine kinases in *H. pylori* associated carcinogenesis.

Depolarization of epithelial cells also implies the disruption of E-cadherin-mediated adhesion junctions (AJs). We analyze the disintegration of E-cadherin-dependent AJs and identified the **serine protease HtrA** as a new secreted virulence factor of *H. pylori* that directly cleaves the E-cadherin ectodomain leading to the disruption of the epithelial barrier functions and allow *H. pylori* to access the intercellular space. Since HtrA-mediated **E-cadherin** cleavage appears to a prevalent mechanism in bacterial infections we analyze the functional consequences of HtrA activity in the pathogenesis of a wide range of further gastrointestinal pathogens (e.g. *Campylobacter jejuni, or Listeria monocytogenses, etc*.) and develop **inhibitory compounds** to prevent HtrA-dependent pathogenesis.

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The Department of Ecology and Evolution

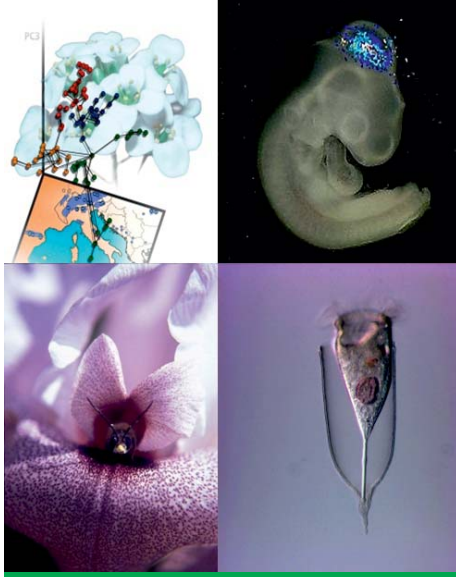
The Department comprises four organizational subunits: ***Ecology, Biodiversity, and Evolution of Animals/Plants***; ***Neurosignaling & Neuroecology***; **and the *Botanical Garden***.

The integrating rationale of our Department is to understand the **diversity of organisms**, how they live and **interact with each other and their environment**, and how **short-term (ecological) and long-term (evolutionary) processes** influence the composition, diversification and adaptive responses of populations and species within a community. In times of global climate change and biodiversity crisis, these issues are gaining increasing importance from both **basic and applied-oriented perspectives** (e.g., conservation biology, ecosystem management and service).

We apply state of the art methods, ranging from **field and lab experiments** to **molecular, developmental, neurophysiological, chemical-analytical, and statistical/computational approaches**, to address a multitude of **ecological and evolutionary questions**.

Examples include: How will aquatic and terrestrial ecosystems respond to climate change and habitat fragmentation? How do plants communicate with their pollinators? How do migrating birds find their way? What is the genetic basis of stress tolerance in plants? What abiotic and/or biotic factors trigger rapid bursts of orchid speciation in Madagascar? How many lichen species are in Antarctica – and how many protist species in a single bromeliad tank?

Our department provides students with the opportunity to conduct exciting research on plants and animals - along the disciplines of ecology and evolution. Our former graduates have pursued diverse careers in academia, government (teaching, nature/landscape conservation, natural history museums, botanical gardens), industry (pharmaceutical companies, environmental analytics) and private sectors (e.g. consultancies).



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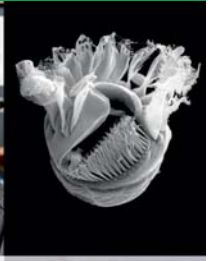

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Team Sabine Agatha
Division of Ecology, Biodiversity, and Evolution of Animals

The research of our team focuses on the **biodiversity of protists**, specifically ciliates (Alveolata, Ciliophora), by the **descriptions of new species** and redescriptions of insufficiently known species from marine, freshwater, and terrestrial habitats collected during field trips. By means of **light microscopy** (bright field, interference and phase contrast), **scanning and transmission electron microscopy**, and application of a wide spectrum of **histochemical staining methods**, we investigate the cell morphology and division, resting cysts, conjugation processes, cell ultrastructures, and the chemical composition of ciliate loricae and cysts. Our **computer-based cladistic analyses** of the yielded characters provide together with molecular studies (primarily gene sequencing) insights into the **evolution** and adaptations of these organisms as well as into the **phylogenetic relationships** among protists, that again represent the base for the **classification**.

Our research yields not only everlasting publications, but is also very important as sequencing of environmental samples clearly demonstrated that protist diversity is an order of magnitude larger than previously assumed and that the vast **majority of species are undescribed**. Since protists are **crucial components of all food webs**, species circumscriptions are essential for studies concerning the ecological role and **geographic distribution** of species, and especially when the taxa are model organisms (e.g., Nobel Prices 1989 and 2009) or used for barcoding (identification by marker genes). Accordingly, **taxonomic expertise is urgently required**, particularly as there are only a few ciliatologists worldwide. Generally, our investigations are conducted in collaboration with international scientists, e.g., from Canada, China, France, Korea, Germany, the USA, and Austria.

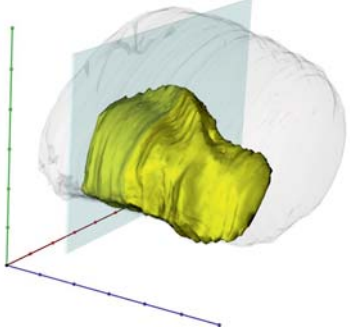
We welcome students for Bachelor-, Master-, and Doctoral Thesis who are interested in learning and applying the whole spectrum of methods for ciliate taxonomy and phylogenetics.

Team Gustav Bernroider/Hannelore Bauer/Günther Bernatzky/ Helmut Mayer; Division of Neurosignaling and Neuroecology

The dominating research projects of our time, such as the Human Brain Project are focused around the question how the brain's organization relates to the impressive and large diversity of it's functions. 'Connectomics', the study of the wiring pattern in the brain, is at the centre of many, conceptually and technically highly demanding approaches.

Our research team tries to **integrate traditional neurobiological techniques** (anatomy, tracing and reconstruction, R Fuchs) **with modelistic, mathematical methods** (patterning and network analysis**,** G Bernroider), **behavioural and molecular developmental** (H Bauer) approaches. Applications are found throughout the field of neuro-ecology (e.g. animal migration, the social brain hypothesis), behavioral neurobiology (social recognition), pain research and therapies (G Bernatzky), comparative and computational cognition (e.g. neuro-robotics, H Mayer).

The main conjecture that we pursue is that s**ocially relevant behaviours are the main driving force in brain development** towards advanced cognitive skills and the emerging organizational aspects behind neural connectoms are substantially based on convergent, unifying, single solution principles in vertebrates. Our intention is to **unravel the static and dynamical properties that characterise these principles across diverse animal models**.



Illustrations: single photon emission tomography of enzymatic activity in the mesencephalon of a chick embryo (G Bernroider).
3D computer reconstruction of the striatal avian forebrain (R Fuchs)

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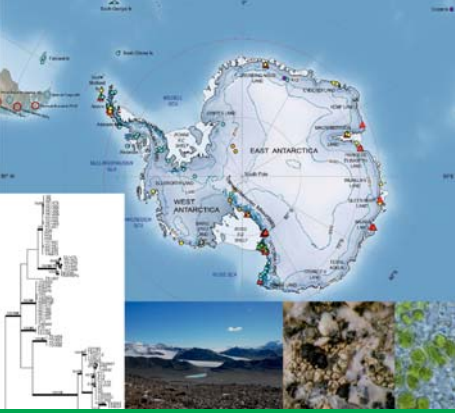

Team Georg Brunauer/Ulrike Ruprecht
Division of Lichen Ecology and Genetics

Our research team focuses on the **taxonomy, diversity, distribution and ecology of lichens in diverse habitats**. We are interested in understanding the survival strategies, physiological mechanisms, and symbiotic specifics of these underexplored fungal-algae partnerships.

Lichens as poikilohydric and less competitive organisms are colonizing areas where the growing conditions for plants are unfavourable, like cold and hot deserts, tree barks, and bare rocks. Our research objects are leading us from Austrian Red List species and lichen communities in populated areas of Europe to untouched regions in Antarctica, South America, from the sea-level to high alpine areas.

Our "methodological toolbox" comprises up-to-date **molecular genetic methods in combination with classical morphological analysis** to study phylogenetic relationships, species diversity and mycobiont-photobiont specificity (co-speciation, photobiont-switch). In addition to **phylogeographical data we use ecophysiological measurements** (gas-exchange/photosynthetic activity) to make inferences about the lichens' habitat preferences.

Our major project currently focuses on the relative **importance of ecological** (climate-related) **factors** influencing the origin and maintenance of species boundaries in lecideoid lichens from Antarctica, and the selectivity of their symbiotic partnership. Other research projects are addressing **the enzymatic pathways of lichen secondary metabolism**; and the **impacts of airborne pollutants** (e.g. pollutant-carrying nanoparticles) on lichen physiology.

Our group offers students **education in molecular genetic techniques and data analysis methods, ecophysiological measurements and microbiological culture techniques** in a team with our in-house experts and with our partners in collaborating laboratories. For further information, please see our **Master Course "Molecular Co-evolution" (PLUSonline)** in collaboration with Anja Hörger.

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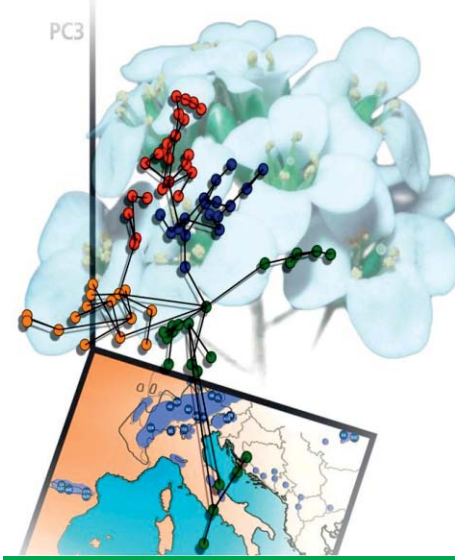
Team Hans Peter Comes/Andreas Tribsch/Ulrike Gartner
Division of Molecular Phylogenetics and Ecology of Plants

Our research is rooted within the fields of ***Molecular Phylogenetics*** & ***Molecular Ecology***, which implies addressing evolutionary and ecological questions above and below the species level and at different spatial and temporal scales.

We reconstruct evolutionary relationships among plant species by generating and analysing **DNA sequence data** for various gene regions. These molecular phylogenies are used to test hypotheses about geographical, morphological/reproductive, and ecological diversification in the plant groups of interest. One of our current research objectives is to understand how, when, and why shifts from outcrossing to selfing occurred in tropical orchids from Madagascar. This project also involves extensive crossing experiments in the glasshouse, X-ray micro-computed tomographic studies, and ecological niche modelling.

In addition, we are currently using fast evolving **molecular markers (e.g., amplified fragment polymorphisms/AFLPs; microsatellites)** for genotyping alpine plant populations. This allows us reconstructing their spatial dynamics over the last ice ages, including areas of survival (refugia) and routes of (re-)colonization. Likewise we are interested in understanding how habitat conditions (e.g., calcareous/siliceous soils) have interacted with past climate variations to influence plant adaptation and speciation in alpine regions.

Our projects involve fieldwork and/or collecting trips to obtain leaf samples for molecular analyses. We aim at integrating ideas and techniques from across biology, including evolutionary biology, gene-ecology, population genetics, molecular biology, biogeography, morphology/anatomy, taxonomy, and bioinformatics. Students in our lab thus have the opportunity to conduct fieldwork, labwork and/or computational work. For more, see our **Master Courses "*Molecular Biodiversity Research I & II*"** (PLUSonline).



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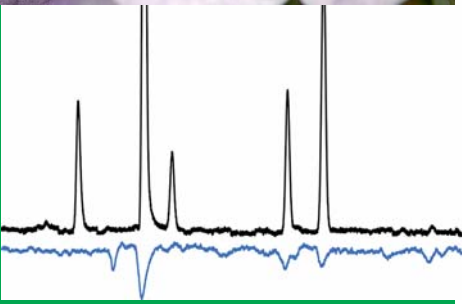

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Team Stefan Dötterl
Division of Ecology, Biodiversity, and Evolution of Plants

Plant Ecology

The research of our team focuses on the **ecology and evolution of floral signals** and **plant-pollinator interactions**. We rely on a **multidisciplinary approach** that consists of field observations, state of the art chemical-analytical and electrophysiological techniques, behavioral bioassays, and statistical approaches. We take advantage of our **well-equipped chemical-ecological lab** with tools to analyze floral phenotypes, such as colors (spectrophotometry) and the identity and pattern of olfactory floral signals (floral scents; gas chromatography combined with mass spectrometry). Furthermore, we have electro-antennographic techniques available used to study the olfactory system of insect pollinators. Studies are performed in Europe, Africa, Asia, and America.

One main interest is the **identification of floral signals used by insects to find rewarding host plants**. We typically work with non-model systems and generalized as well as specialized pollination systems. Plants included in our study are from **diverse angiosperm lineages** and the pollinator partners are mainly from the group of insects with a focus on **bees, beetles, butterflies, and flies**. Besides systems where the interaction is of benefit for the plant as well as the pollinator, we also work with **mimicry systems of deceptive plants** that signal a reward to the pollinators but do not provide it.

Most flowering plants depend on pollinators for sexual reproduction and pollination by animals is thus a **main process in terrestrial ecosystems**. As many crop plants, such as apples and cherries, are among the plants pollinated by animals, biotic pollination also has an **enormous economic value**. Pollinator attraction is the first essential step in every plant-pollinator interaction, yet very little is known about the specific signals used by plants to attract their pollinators. Our studies try to fill this gap, and knowledge of the signals used by crops to attract their pollinators might give us a tool to manipulate pollinator attraction and increase yield of economically important plants.

Team Anja Hörger
Division of Ecology, Biodiversity, and Evolution of Plants

Our research aims to understand the **genetic, evolutionary and ecological processes driving adaptation of plants to their biotic and abiotic environment**. Thereby we focus specifically on plant-pathogen coevolution, that is the evolution of the plant immune system in response to changing pathogen (viruses, bacteria, fungi) populations, and investigate the impact of various environmental conditions (salt, drought, metalliferous soils) on these processes.

Deciphering this interplay of biotic and abiotic stress responses in plants is of importance to understanding the **impact of climate change on species persistence and adaptation**, in particular for species occurring in fragmented and/or anthropogenic habitats such as industrial, polluted sites. We therefore focus on naturally occurring plant populations, which cover diverse habitat ranges and/or grow in anthropogenically influenced habitats.

Our current main project investigates **the role of heavy metals in plant disease resistance** and the interplay between adaptation to abiotic stress imposed by heavy metals in the environment and pathogen resistance in plants accumulating heavy metals. Other research projects aim to investigate **the impact of coevolution with bacterial and fungal pathogens on plant genome evolution** using as model systems wild tomato species, which occur in mesic to arid conditions in South America.

To tackle these questions, we integrate different fields of biology and employ a diverse range of **state-of-the-art experimental and bioinformatics approaches** including **population genetics/genomics, transcriptomics, experimental evolution, biochemical assays and plant-microbial bioassays.** Students thus have the opportunity to acquire skills in various molecular, biochemical, computational and ecological techniques. For further information, please see our courses Environmental Chemistry and Environmental Analysis (with Team H. Stutz), Terrestrial Ecology (with Teams S. Dötterl and J. Petermann) and Molecular Coevolution (with Team Brunauer/Ruprecht).

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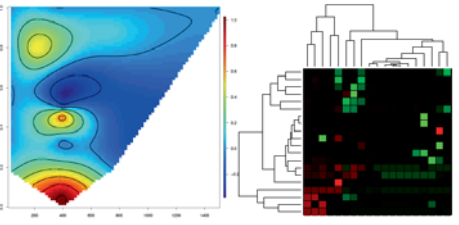

Team Robert Junker
Division of Ecology, Biodiversity, and Evolution of Plants

Functional Community Ecology

We investigate the structure and **functional composition** of diverse plant, animal and bacteria **communities** within ecosystems and along environmental gradients. We are particularly interested in how functional **plant** traits affect the behavior, distribution and diversity of **insects** and **bacteria**. Additionally, we track the **functional responses** of plant species and whole communities to global change components such as **climate warming** and the spread of **invasive species**. These approaches allow us to comprehensively evaluate the mechanisms underlying **ecosystem processes** and the vulnerability of ecosystem services.

Interactions between species naturally do not occur in isolation but are embedded in complex communities. Thus, the frequency and net effect of pair-wise interactions usually are modulated by other sympatric organisms that may alter the phenotype and/or the behavior of one or both interaction partners. To understand such **multi-trophic interactions**, we investigate how bacteria associated with plants affect ecosystem functions such as **plant–pollinator** or **plant–herbivore interactions**.

In collaborative and interdisciplinary studies in the lab and in the field (e.g. in the Austrian Alps and in Hawai'i), we analyze and manipulate the **phenotype** of plant species (e.g. scent emissions, coloration, morphology), examine **interaction networks**, reveal the composition and diversity of bacterial communities (e.g. next generation sequencing) and observe the behavior of animals as response to plant traits. In order to analyze the complex data gathered in these studies we apply and develop novel **statistical tools** to quantify the **phylogenetic and functional diversity** of communities and the **niche** size of species.

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Team Jana Petermann
Division of Ecology, Biodiversity, and Evolution of Animals

Multitrophic Biodiversity

Animal and plant species are lost from this planet at increasing rates due to habitat destruction and climate change. To understand the related processes and alleviate the effects of biodiversity loss, we need to answer two central questions: (1) How can species even coexist naturally or in other words, **how is biodiversity maintained** in healthy ecological communities? (2) And what happens to natural ecosystems when species go extinct, so what are the **consequences of biodiversity loss?** Since all ecological communities consist of species feeding on each other, our work has a special focus on **multitrophic interactions** and **food webs**.

To find general answers to the above questions, we work on a variety of **terrestrial** and **aquatic** systems in a number of exciting places, **temperate** as well as **tropical**. For example, we study **European** grassland plant and insect communities in large biodiversity experiments. In **Costa Rica and Brazil** we investigate aquatic **food webs of protists** and **insects** living in in bromeliad plants. Furthermore, we examine aquatic tree-hole insect **metacommunities** in the canopies of temperate forests, which we access using tree-climbing techniques. We also work in **agricultural landscapes**, for example studying the dispersal of **zooplankton** between kettle ponds by wind and birds. A variety of research projects are available that use a range of scientific approaches from **large-scale** observational studies in natural ecosystems to **field experiments** and **greenhouse** and lab **microcosm** experiments. We use advanced **statistics** and **modelling** to analyze and bring together the results from these various approaches.

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Team Stephanie Socher
Botanical garden

Covering an area of 1 hectare, the Botanical Garden of the University of Salzburg has several projects running to **enhance biodiversity and protect as well as propagate endangered plant species**. The garden displays a variety of themes: the rock garden with a **focus on Austrian alpine plants**, a rose garden where the history of rose-breeding is shown, and the b**og and heather areas** which show a successful natural development of these ecosystems over the past 25 years. The farmhouse garden shows a traditional Salzburger farmer's garden and the **wild crop garden** displays a diversity of 220 different ancient wild crop species. The **Salzburger Apotheker-Kräutergarten**, the herb and medical plant section in the Botanical Garden Salzburg is sponsored by the pharmacist society of Salzburg. The herb garden shows about **320 different plants for herb and medicinal purposes.**

The **orchid collection** of the Botanical Garden Salzburg comprises currently 2000 individuals of different orchid genera with a focus on the **Madagascan specie**s of the genus Bulbophyllum. The collection is not accessible to the public, and so far cultivated only for research. Research of the Division of Ecology, Biodiversity and Evolution of Plants focuses on the **mating system evolution and radiation** in Bulbophyllum. Flowering species are preserved in alcohol for further taxonomic studies and tissue samples have been taken for DNA extraction.

The Botanical garden **provides plant material** for lectures and courses, and offers the opportunity to do **experimental research in controlled glasshouse settings** as well as in **real landscape**.

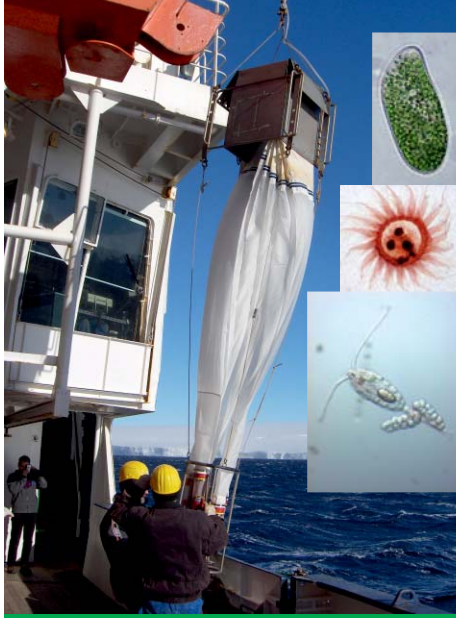
Team Stephen Wickham/Ulrike Berninger
Division of Ecology, Biodiversity, and Evolution of Animals

The research focus areas of our team (Stephen Wickham and Ulrike Berninger) is **zooplankton ecology**, primarily addressing questions about their **biodiversity** and their role in **energy fluxes** and **food web dynamics**. While we work with a broad palette of organisms, from bacteria to krill, our main focus is on ciliates, cladocerans copepods, together with their algal prey. We emphasize **experimental approaches** both in the lab and in the field. These experiments are run at the micro- and mesocosm scales, to answer questions about **aquatic population and community ecology**.

We also conduct field sampling campaigns, such as the monitoring of the Glan stream restoration, and in marine habitats, such as the Gulf of Aqaba and the Southern Ocean. We often use microzooplankton as model organisms, in order to conduct experiments posing basic ecology questions, most recently about **metacommunity** dynamics. Another area of interest concerns the occurrence and ecological role of **mixotrophic protists** in natural aquatic systems. Our ultimate aim is to **understand the drivers of biodiversity in natural habitats and the impact of biodiversity on ecosystem functioning**. This is particularly relevant in the context of **global climate change** and the threat of **biodiversity loss**. Our study sites are near Salzburg and – within individual projects - also abroad (Scandinavia, ocean-going cruises, Germany, USA, etc.).

Both for our research and in teaching we employ a broad range of methods (light and epifluorescence microscopy, molecular methods such as FISH and DGGE, rigorous statistical analyses, etc.).

Through third-party funded projects, close collaborations with other departments of the PLUS as well as partners in external research institutions and institutions from the public sector we also offer a wide range of research options including fish ecology, herpetology, topics relevant for primary and high-school education, nature conservancy, ecological restoration and functioning of stream systems. Our involvement in the National Park “Hohe Tauern” offers a platform for further basic and applied research.



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The Faculty of Engineering and Natural Sciences
Johannes Kepler University Linz

The seven research teams from four institutes of the Johannes Kepler University Linz represent a broad variety of expertise covering Soft Matter Physics, high performance analytical techniques, nuclear magnetic resonance (NMR) methodology, atomic force microscopy (AFM), various high-end fluorescence microscopy techniques, electrophysiological recording methods, and next sequencing technologies. Special focus is attained in techniques enabling single molecule resolution. The systems under study are multifaceted ranging from skin-like electronic sensors, pesticides in food, protein interactions resolved by NMR, AFM, as well as fluorescence techniques, transport through biological membranes, and recombination hotspots.

The Soft Matter Physics group of the Institute of Experimental Physics uses polymers and elastomers to develop bio-inspired devices. Their approach is multidisciplinary covering materials processing development of prototypes and device characterization. **The Institute of Analytical Chemistry** focuses on high performance separation techniques in combination with information-rich detection. The techniques are utilized for the analysis of xenobiotocs, pharmaceutical products, or food ingredients.

The Institute of Organic Chemistry uses a natural chiral pool to synthesize biologically active compounds. Recombinant DNA technology is utilized to produce soluble proteins and analyze their interactions. Biomolecular structures as well as weak intermolecular interactions are characterized by nuclear magnetic resonance spectroscopy. **The Atomic Force Microscopy Group** of the **Institute of Biophysics** has developed Molecular Recognition Force Microscopy resolving protein interaction at the single molecule level. The **Membrane Transport Group** unravels mechanism of molecular transport through biological membranes. The **Ion Channel Group** focuses on molecular key aspects of ion channels involved in Ca^{2+} signaling. Finally, the **Single Molecule Genetics Group** concentrates on meiotic recombination in recombination hotspots.

JKU
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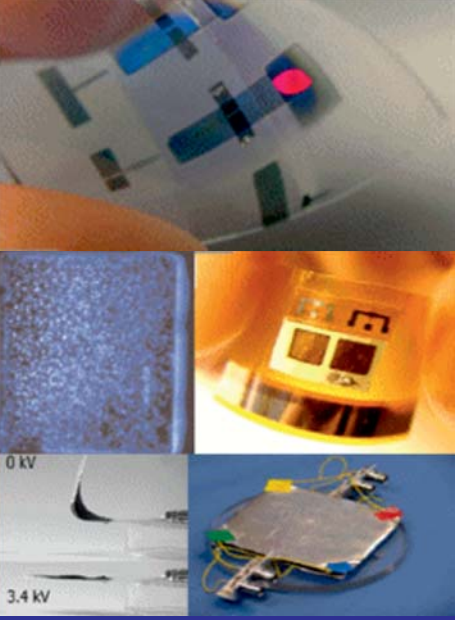

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Team Siegfried Bauer, Ingrid Graz, Reinhard Schwödiauer
Institute of Experimental Physics

Soft matter includes various materials ranging from gels, to polymers and rubbers but also biological materials such as wood or gelatin. Besides their "softness" compared to typical device materials in electronics, soft **matter exhibits a number of interesting physical properties** such as responding to external stimuli such as pressure or temperature with an electrical signal, an effect called **piezo- or pyroelectricity**, respectively. In reverse, these electroactive materials also react with a deformation upon electrical signals. Inspired by nature, we at the **Soft Matter Physics group** utilize the mechanical and physical properties of soft electroactive matter for novel devices in electronics and sensors, robotics or energy harvesting. We are pushing the limits of mechanical deformable devices by developing flexible and even stretchable electronics mimicking the human skin and robots inspired by animals like the octopus. We fabricate sensor and robot prototypes and evaluate the electroactive properties of unusual materials such as wood or gelatin for electronics.

The **Soft Matter Physics gr**oup at JKU has long standing expertise in **polymer materials** ranging from flexible sensors (piezo- and pyroelectrics), organic electronics to soft robotics. In addition to mechanical and electrical characterization, polymers and elastomers are employed in **novel sensors and actuator systems**, covering flexible pressure and temperature sensors, ultrathin electronic circuits as well as energy harvesting and stretchable electronics.

In our projects we use polymers and elastomers to develop novel **bio-inspired devices** such as **skin-like electronic circuits and sensors or mollusc-like soft robotic elements**. Our approach is multidisciplinary, covering materials processing, developing and fabrication of prototypes and device characterization. **Experimental work** includes sample preparation with **elastomer casting, 3D printing or laser cutting, fabrication of device prototypes** as well as **characterization of materials** or theoretical modelling.

Team Wolfgang Buchberger/Christian Klampfl
Institute of Analytical Chemistry

The Institute of Analytical Chemistry is involved various research activities within the fields of modern instrumental analysis of organic molecules. Thereby a primary focus is set on **high performance separation techniques** (such as gas chromatography, high performance liquid chromatography, and capillary electrophoresis) mostly in combination with **information-rich detection** (primarily high resolution mass spectrometry). As our research is mainly directed towards the development and advancement of novel methodological approaches, we deal with a wide field of different application areas.

One area of our research is analysis of **xenobiotics** in environmental matrices. Thereby we are not only interested in the detection of residues of pharmaceuticals and personal care products in water or sediment, but future research projects are also directed towards the influence of these contaminants on plants or aquatic life.

We are also involved in the development of novel analytical strategies for the characterization of **pharmaceutical products** (quality control, monitoring of production processes, elucidation of impurities)**. Food analysis** is another area of interest with ongoing research spanning from the determination of pesticides in foods (such as honey) to investigations on interactions between food and packaging materials and finally development of novel on-line capillary electrophoresis-mass spectrometry techniques for the identification of food constituents with antioxidant properties.

Finally we are involved in several large-scale projects (together with a series of other academic as well as non-university research institutions and several key-players in industry) dealing with the analysis of **industrial products,** in particular polymeric materials. In this context our research is directed towards the analysis of stabilizers in plastics with the primary goal of developing novel materials with improved endurance and performance.

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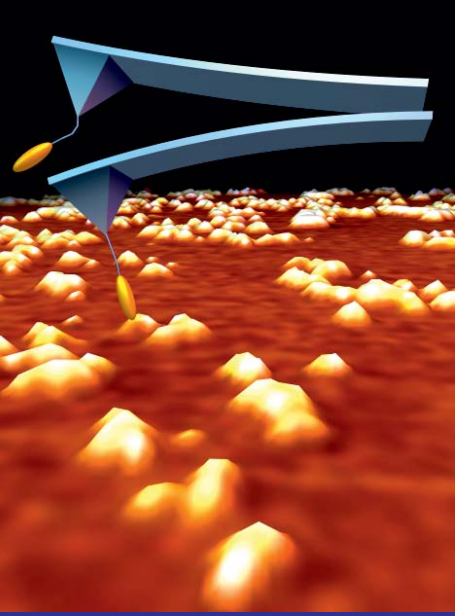

Team Peter Hinterdorfer
Institue of Biophysics

Peter Hinterdorfer and his team **Atomic Force Microscopy** at JKU have pioneered various Scanning Force Microscopy (SFM)techniques, most notably **Molecular Recognition Force Microscopy** (MRFM). They showed that the recognition experiments were greatly facilitated when a flexible linker was used to bind at least one of the receptor ligand pairs, because it relaxes constraints on their alignment as the tip is docked onto the target molecule. The group has more than 15 years of experience in single molecule force spectroscopy with diverse applications protein-protein and protein-ligand interactions, e.g. antibodies, cell adhesion molecules, molecular templates, transporters, viruses, membrane and live cells.

They also pioneered the method of **recognition imaging**, where active binding sites can be localized with nm lateral resolution. As an educated biophycisist, Hinterdorfer has 20 years of teaching experience. His lectures and practical courses include Biophysics, Characterization of Bio-Nano Structures, Methods of Biochemistry, Practicum Biophysics, Practicum Bio-Nanostructures, Biochemistry Practicum.

As core facilities, the lab is equipped with 10 atomic force microscopes (AFM), including 1 high speed AFM and 2 AFM/fluorescence microscope combinations. Furthermore available are instruments required for experiments in lipid-, protein-, and cell-biophysics, biochemistry and bioconjugate chemistry, and cell and bacterial culture.

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Team Norbert Müller/Wolfgang Schoefberger/Mario Walser
Institute of Organic Chemistry

Three main research areas are pursued at our institute. In each of these fields, we have projects ranging from fundamental research to applications of industrial relevance.

In the field of **synthetic organic chemistry**, the main focus is on stereochemistry, in particular the use of the **natural chiral pool to synthesize biologically active compounds** with high efficiency and stereo-selectivity. This area has natural links to both industrial chemistry and medicinal chemistry.

The second main research topic is **protein interactions**. We use recombinant DNA technology to produce large amounts of soluble proteins, which are involved in **biological regulation and signalling processes** and study their interactions. The results have impact on diverse fields like structural biology, natural and artificial photosynthesis as well as biomedicine.

The third field of competence is **nuclear magnetic resonance (NMR) methodology**. We provide NMR services to the regional research community through the RERI-uasb Research Centre in collaboration with the University of South Bohemia in Ceske Budejovice (CZ). This centre is equipped with three **state-of-the-art NMR spectrometers (300, 500 and 700 MHz)**. The main research focus is on the **development and application of modern NMR methodology for liquids and solids**. NMR is uniquely suited to characterize polymers and flexible biomolecular structures as well as to study weak intermolecular interactions in condensed matter, in particular solutions, under life-like conditions. Research results pertain to complementary fields of science like medicinal and biophysical chemistry, structural biology as well as generic organic and polymer chemistry.

Currently three research groups participating in international, European and regional research networks are active at the institute of organic chemistry. They are headed by the principal investigators Norbert Müller, Wolfgang Schoefberger, and Mario Waser.

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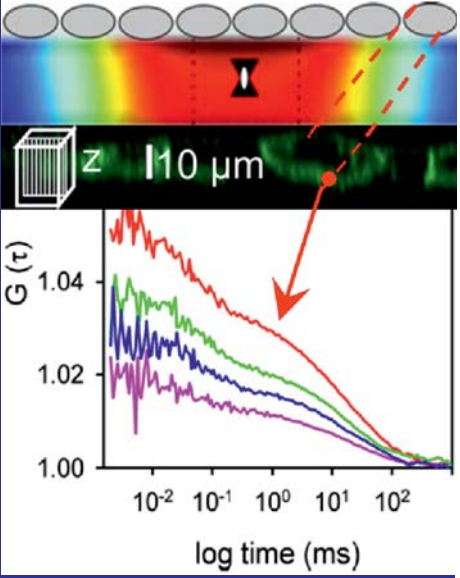

Team Peter Pohl
Institute of Biophysics

The research foci of the Membrane Transport Group include **transport of water, protons, other small molecules, and proteins through biological membranes**. We thus exploit (i) primary cells or tissues, (ii) cultured cells that are genetically modified to overexpress the protein of interest or (iii) planar lipid bilayers or lipid vesicles both reconstituted with the purified membrane transporter. Purification occurs from overexpressing *E.coli* cells or yeast cells using affinity and size-exclusion chromatography.

Our work aims to **unravel molecular transport mechanisms**. We specifically want to understand (i) the major determinants of single file water transport in potassium channels, aquaporins, artificial nanopores, (ii) the principles of water flux through secondary active transporters, (iii) the structural-functional relationship which allows the protein translocase to facilitate the passage of large molecules while maintaining the membrane barrier for small molecules, (iv) the mechanisms of lateral proton migration between two membrane proteins.

The proteins under investigation are genetically or chemically modified to test the functional importance of certain residues and to introduce fluorescent labels. We **monitor protein function** by implementing a wide variety of methods including: **recordings of current** through single channels and through channel ensembles, **streaming and boundary potential measurements**, **particle electrophoresis**, **light scattering** or **fluorescence spectroscopy** in conjunction with a stopped-flow apparatus, fluorescence correlation spectroscopy, fluorimetry, confocal fluorescence microscopy, and scanning electrochemical microscopy.

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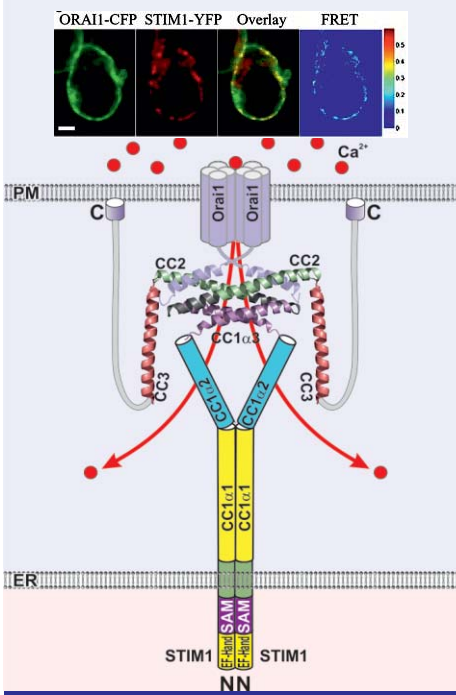
Team Christoph Romanin
Institute of Biophysics

Calcium ions are of crucial cellular importance for both short responses including secretion or metabolism as well as long term regulation of transcription, proliferation and cell growth. A main calcium entry pathway into the cell is represented by the so-called **store-operated calcium channels** (SOCs). Receptor-mediated activation of these channels is initiated via inositol-1,4,5-triphosphate (IP_3) binding to the IP_3 receptor within the endoplasmic reticulum (ER) leading to Ca^{2+} depletion of this store. Among SOCs the Ca^{2+}-release-activated Ca^{2+} (**CRAC**) **channel** is best characterized and **required for** NFAT induced gene expression, proliferation and cytokine secretion of **T-cells in the early stages of immune responses**. Function-based genetic screen by systematic RNA interference (RNAi) has identified the **STIM1 (Stromal interacting molecule)** and the **Orai** protein family as **key components of CRAC channels**.

Christoph Romanin and his group at JKU have long standing expertise in electrophysiology ranging from whole cell to single channel recordings. In addition, they pioneered dynamic protein-protein interactions in living cells by confocal FRET microscopy. Romanin covers several aspects of $Ca2^{+}$ signaling including both **voltage-gated and ligand-gated $Ca2^{+}$ channels**. With regard to the latter, major achievements were obtained and are still pursued within the **STIM/Orai** field by the characterization of the **key steps of their interaction** including the development of e.g. a STIM-derived conformational FRET sensor.

In our projects we use **molecular biology techniques** to generate various mutants or chimeras of the proteins of interest. **Biochemical work** includes protein purification, or for instance crosslinking of cysteine mutants that enables to identify movements of transmembrane segments related to channel activity. **Mammalian cell culture** devices are at hand that allow for subsequent cell transfection as well as electroporation. Ca2+ channel activity or currents are measured by **Ca2+ imaging or patch-clamp technique**. Dynamic protein-protein interactions in living cells are monitored by **confocal FRET measurements** and can be combined with electrophysiological recordings.



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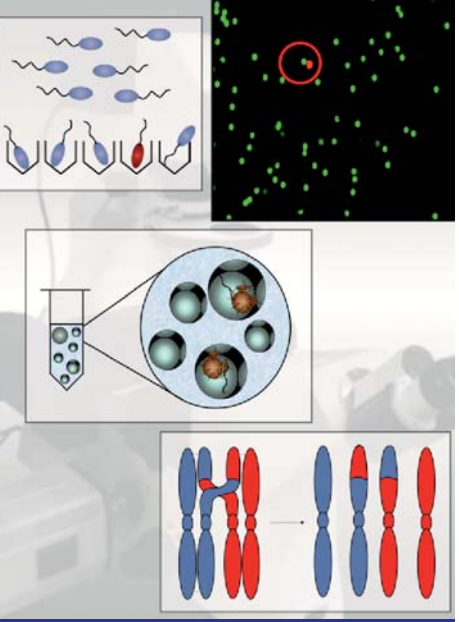

Team Irene Tiemann-Boege
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Our research group investigates **changes in the genetic material in humans especially during the reproductive process**. This research is critical for understanding how biological processes like **mutations affect our children**, and to understand the **evolution of our genome in the long term**. Specifically, our team concentrates on **meiotic recombination localized in recombination hotspots**. Meiotic recombination is a key biological process in sexual reproduction. We believe it is also an important source of new mutations, observed indirectly by the rapid change of sequences where recombination occurred, but it is still a mystery why this happens. With single molecule DNA technologies we are analyzing rare modifiers of DNA and their contribution to the evolution of recombination hotspots.

Related to this work is the understanding of why specific regions in our genome are targeted for recombination, and thus, have more mutations. Of particular interest is **what factors determine where recombination takes place in the genome**. How hotspots are activated is not fully understood, and simple models of DNA motif recognition do not explain the paradox observations of hotspot activity. We are using **highly quantitative and sensitive biophysical methods**, combined with ***in vivo* measurements of crossover activity**, to characterize binding dynamics at recombination hotspots. This allows us to understand what controls hotspots.

Our work does not only focus on rare mutations in recombination hotspots, but also tries to understand other issues such as why older men have more children with new mutations resulting in hereditary conditions like birth defects. We have developed an in-house method similar to next sequencing technologies, called **bead-emulsion amplification (BEA)** that can **count rare mutations in a large scale manner**. With this method we can study how mutations spread in the male reproductive system with age.

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