BioTechMed GRAZ

FUTURE SPACE

Innovation Workshop

May 6th and 7th, 2015

FOREWORD

Univ.-Prof. Dr. Christa Neuper
Rector of the University of Graz
Chairperson of the BioTechMed-Graz Steering Committee

Working together innovatively and promoting research for health. The University of Graz, Graz University of Technology and the Medical University of Graz are expanding their collaboration step by step in BioTechMed-Graz. Setting the agenda together testifies to success: three professorships have been jointly filled, 13 postdoc places promote young scientists, and investments of more than 14 million euros chronicle the creative force at location Styria. Innovation is the slogan of the Future Space event, and benefits integration using unusual approaches.

Univ.-Prof. Dr. Horst Bischof
Vice-rector of the Graz University of Technology

Cooperation and convergence over disciplinary boundaries is one of the pillars of the whole BioTechMed-Graz program. A radical scientific breakthrough can only be expected where different disciplines meet. Future space is designed to foster projects that lie across these boundaries. Young researchers have the creative spirit to explore new territories whereas experienced researchers have the necessary overview to identify the most promising ideas.
Therefore, radically new project ideas in future space will be developed across disciplines by researchers of diverse scientific age.

Univ.-Prof. Dr.Dr.h.c. Irmgard Lippe
Vice-rector of the Medical University of Graz

The name says it all: “Future Space” is an event in which the future takes center space. By organizing the Future Space, BioTechMed-Graz provides a new format and forum for researchers eager to cooperate and to contribute to creating the future. It gives participants the opportunity to present their own innovative ideas, to learn about other people’s ideas, to make new contacts and find partners for pushing forward new developments. Join in, sketch new projects ideas – and seize your chance of winning an initial financial “boost” for getting your future project(s) started.

Contents

PROGRAM

BioTechMed-Graz Event 'Future Space'
Seifenfabrik Graz on May 6th and 7th, 2015

06.05.2015

Hours	Items of the agenda
11:00-11:30	Registration
11:30-12:30	Welcome address & introduction
12:30-13:15	Lunch snack
13:15-17:30	Interlinking & theme input
17:30-18:15	Evening snack
18:15-20:00	Screening of ideas
From 20:00	Final notes and networking

07.05.2015

Hours	Items of the agenda
09:00-09:15	Welcome and outlook
09:15-11:15	Selection of top ideas
11:15-13:30	Elaboration of top ideas & Development of project drafts
13:30-14:15	Lunch snack
14:15-17:30	Presentation of top ideas in the presence of the rectorates & Prioritization and recommendations
17:30-18:30	Concluding remarks

IPR REGULATIONS

EXPLANATION

In the framework of the "BioTechMed-Future Space" innovation workshop there are very clear regulations concerning the utilization of and acting on ideas which originated in the context of the event.

1. **The traceability** of the generation of an idea at any time during its emergence and development shall be safeguarded.

2. Those present define one **primary contact person** per project idea. Moreover, all the cooperation partners involved in or who worked on the idea must be specified.

3. Communication after the event shall take place through the executive level of BioTechMed-Graz (Rectorate, coordinators, etc.) exclusively with the respective primary contact person per project idea.

4. The primary contact person takes over responsibility for the further communication of projects and ensures that no submission of a project, utilization of an idea or any other kind of acting on any of the ideas shall take place without all those involved being contacted.

Participants are kindly asked to take note of these IPR Regulations before the event. These regulations shall be deemed as accepted by participants on active participation in Future Space; participants are obliged to adhere to them during and after the event.

PERSONAL CODE

All participants receive a personal code during registration which allows their participation in project ideas to be safeguarded and documented. We ask you to identify every idea you are involved in using this code. The code written in red means that you are the primary contact person, and the code written in black means that you are a project partner.

GENERAL INFORMATION

THE KEY IDEA BEHIND „FUTURE SPACE“

BioTechMed-Graz is the strategy and development platform of the three partner universities whose aim is to link up researchers in the medium term in different research areas and disciplines in the field of “Research for Health”. This is to be pursued in such a way as to promote top-level innovative interdisciplinary research and to develop scientific topics through which unique selling propositions can be achieved.

BioTechMed-Graz wants to create an interdisciplinary atmosphere of innovation and cooperation and aims to bring about medium-term location effects.

BioTechMed-Graz “Future Space” is one of the main formats to produce this networking and to create a shared “knowledge space” in the medium term for all the researchers involved.

BioTechMed-Graz “Future Space” is the initiative’s innovation workshop in which researchers from different research areas and disciplines come together in the framework of a one-and-a-half-day creative event to exchange information about the most important findings and trends in their research areas, and to experiment together with innovative project ideas and develop them in interdisciplinary groups.

In a new and creative event format, Future Space enables researchers to:

- Present research focuses and the challenges and trends of the next few years to a broad BioTechMed-Graz Community;
- Make new contacts to research groups in the Graz location;
- Work in interdisciplinary teams on complex problems in the “Research for Health” subject area;
- Be granted access to diverse know-how and specific methods and infrastructures that transcend the boundaries of individual disciplines;
- Present new project ideas directly to university executive management;
- Receive specific seed funding for project applications.

To supplement the usual working processes carried out at universities, in Future Space a freer format of information exchange will be created in which ideas for innovative, future-oriented projects can be experimented with and concrete cooperation projects developed without restrictions. The boundaries between individual universities, disciplines and research areas are no longer an issue, and the common research projects can stand alone at centre stage in the Research for Health field.

In addition to the abundance of project ideas which can emerge and be pursued by researchers autonomously, the most promising projects will be chosen together in the community and presented to the rectorates of the three universities.

Each of the best three projects will be awarded 10,000 euros in seed funding to enable an application to be submitted. Additionally, a further grant of 10,000 euros is planned for the first project to be developed in the framework of Future Space which secures third-party funding.

PROCEDURE

Since there will be more than 100 people at the event, we kindly ask you to adhere to the program times and to be punctual.

WLAN CODE

WLAN:”Gast Seifenfabrik”, without password.

STEP 1: INTERLINKING AND THEME INPUT

SCIENTIFIC SPEED DATING

So that people can get to know each other across disciplines in a speedy way and at sufficient depth, different researchers will encounter each other in three “scientific speed dating” rounds.

Please pay attention to the sequence of tables for the first, second and third rounds, which you received at registration. On hearing the instructions from the moderators, seek out the relevant table.

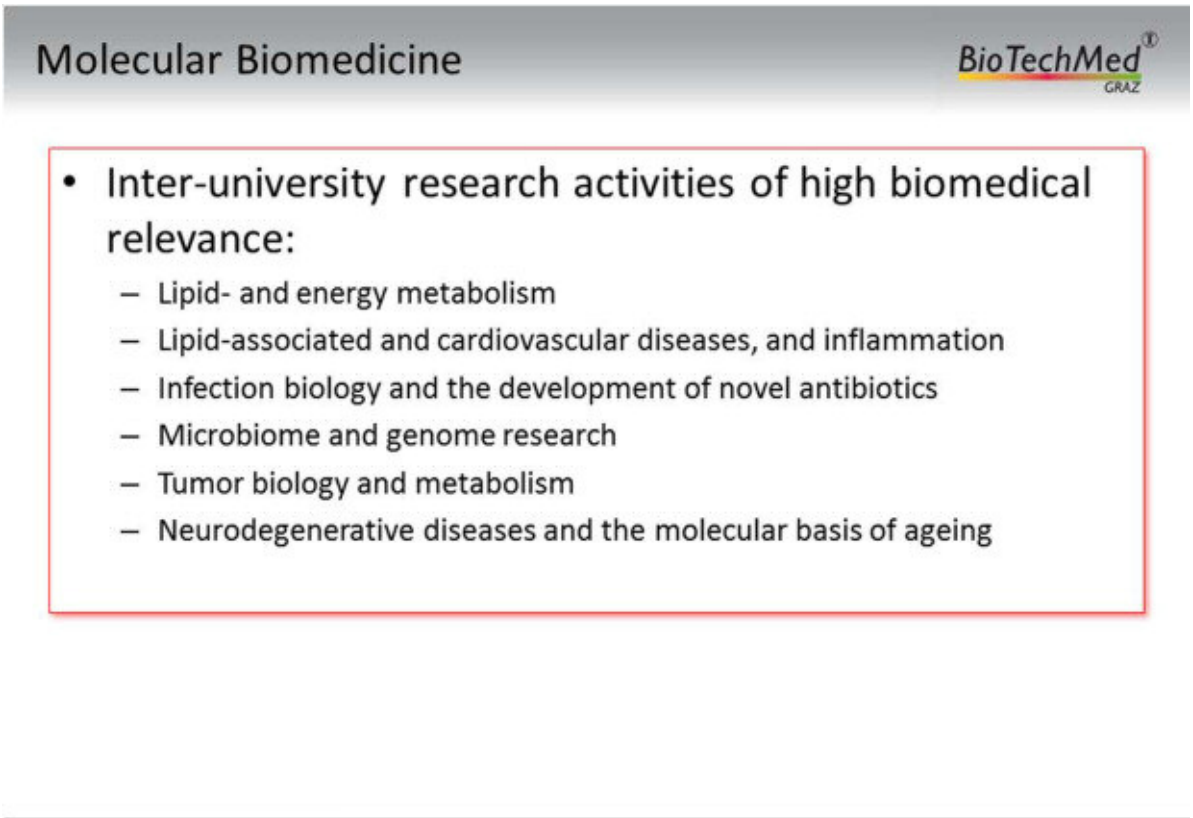
Exchange information about the following questions:

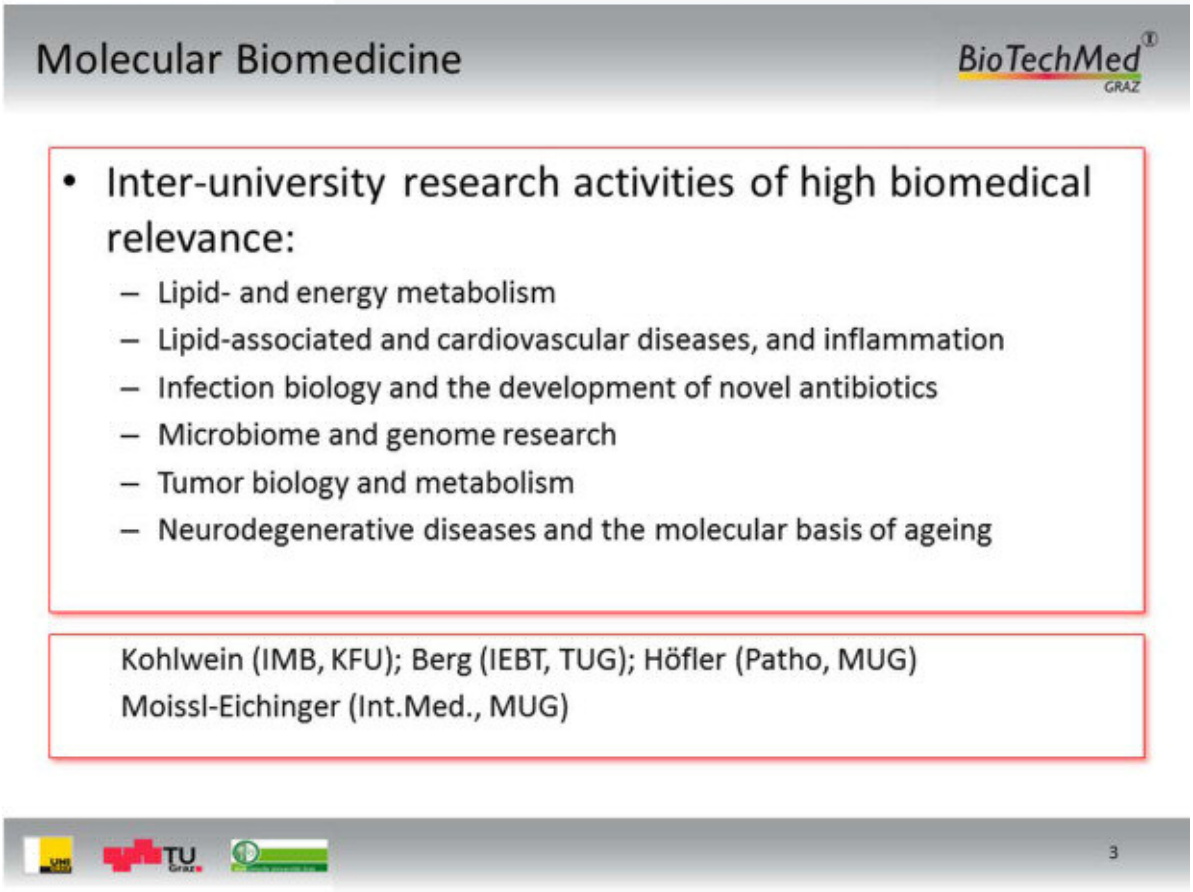
- My personal background
- My current field of activity/What am I personally working on at the moment?
- My work group/organisation: What are we working on? What are our particular strengths? What kind of challenges are wie interested in?
- Where do I see myself in 5 years?

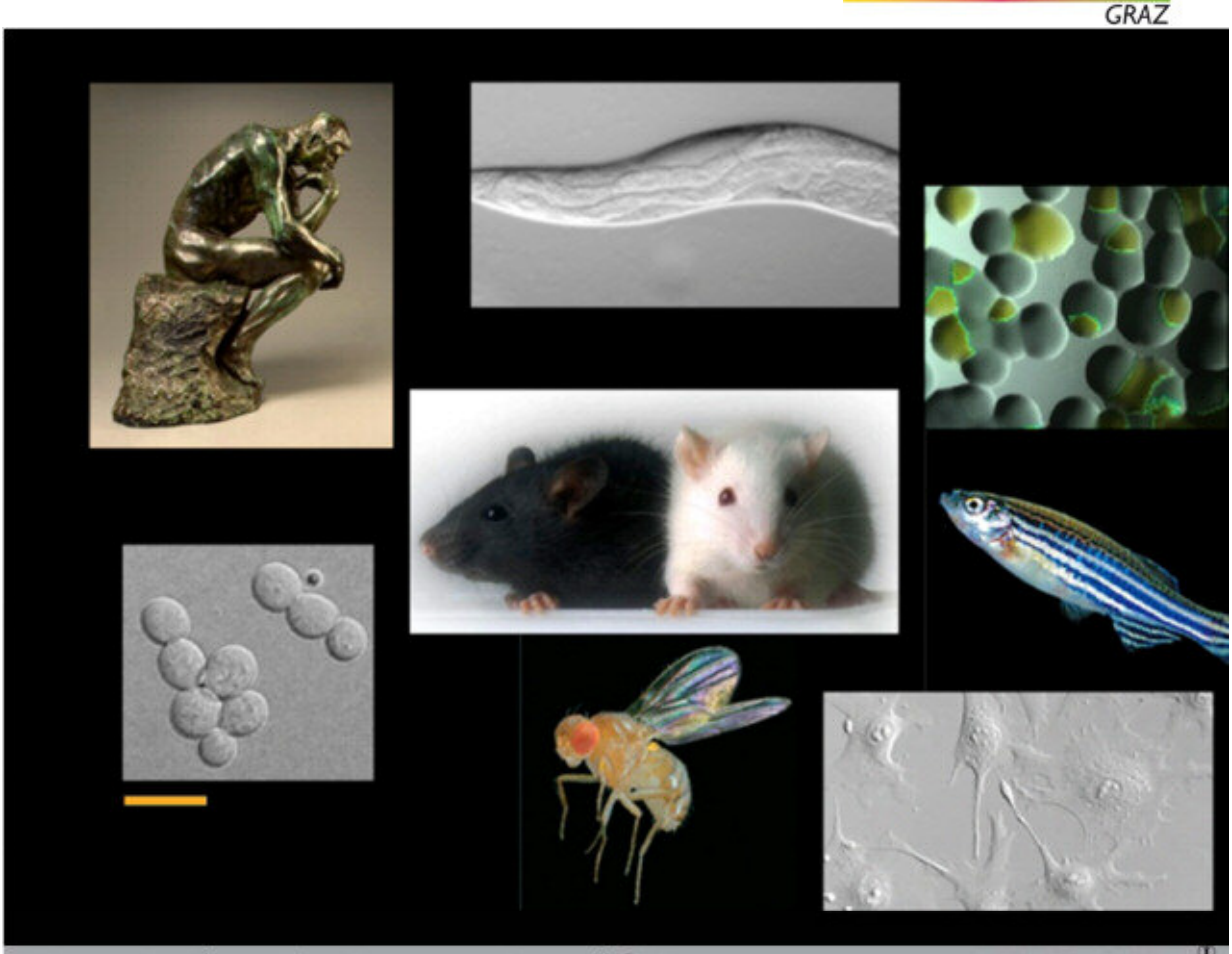
After 15 minutes, a signal will be sounded, and you then seek out the next table. The previous procedure is repeated up to round 3.

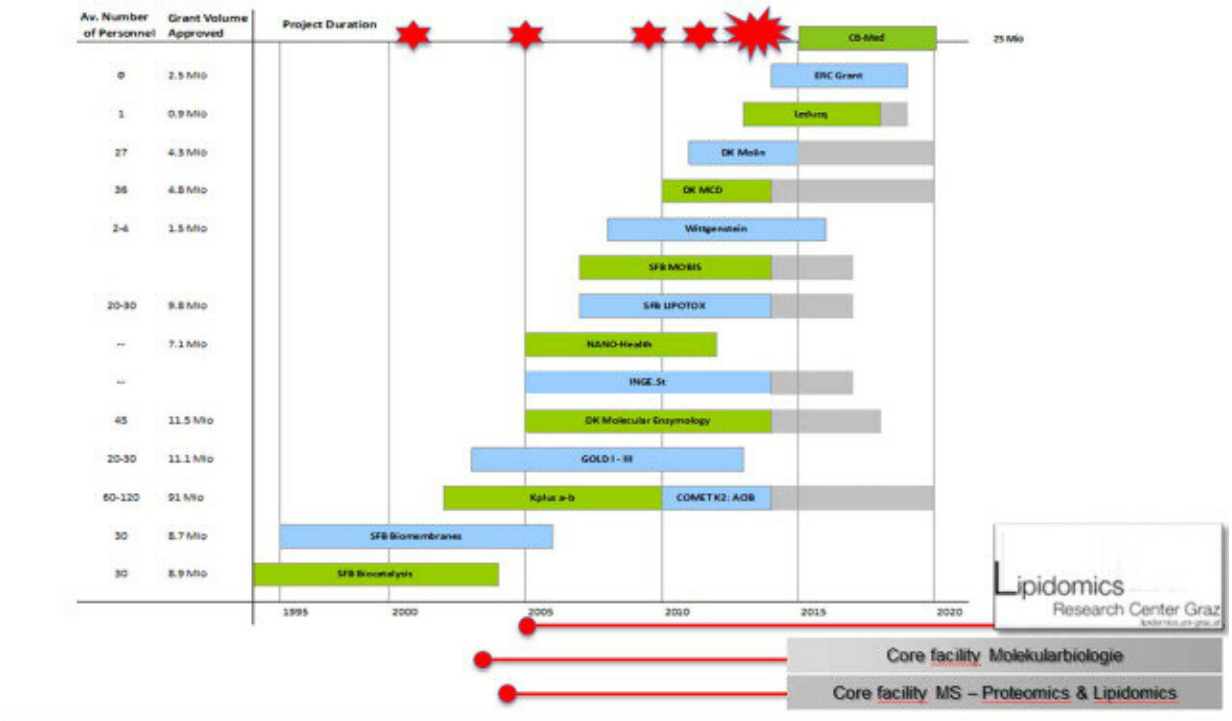
RESEARCH TOPICS

INPUT MOLECULAR BIOMEDICINE

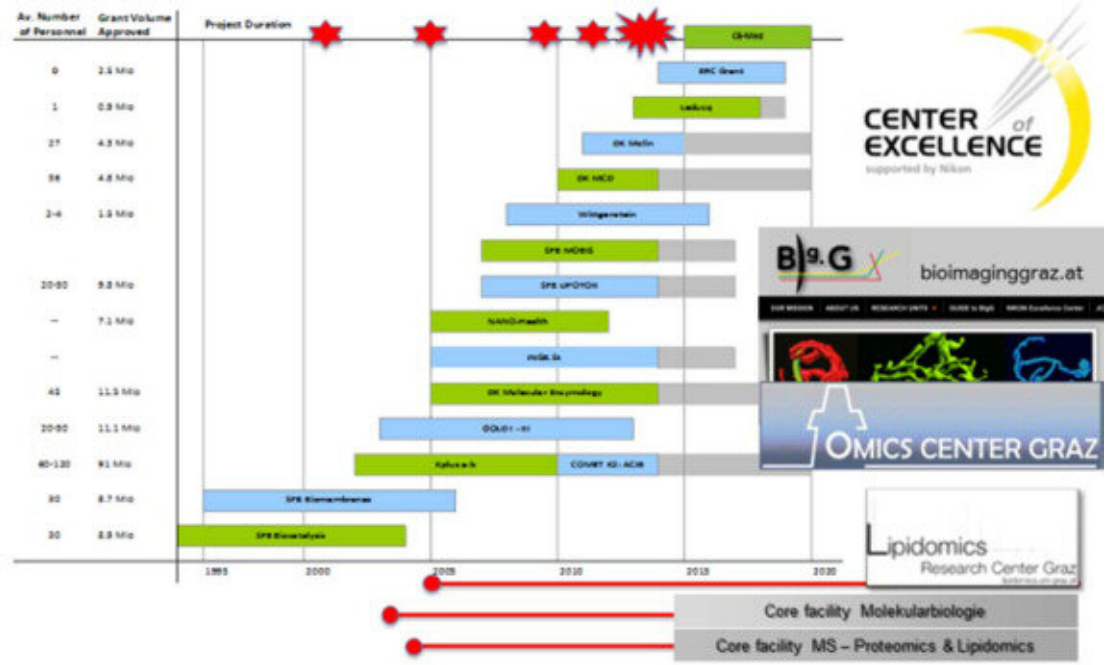





Integrated projects – past and future...
BioTechMed GRAZ


Av. Number of Personnel
Grant Volume Approved
Project Duration
CD-Med
25 Mio
ERC Grant
DK MCD
Wittgenstein
SFB MOBIS
SFB LIPOTOX
NANO-Health
INGE.St
DK Molecular Enzymology
GOLD I - III
COMET K2: AOB
SFB Biomembranes
1995
2000
2005
2010
2015
2020
Lipidomics Research Center Graz
Core facility Molekularbiologie
Core facility MS – Proteomics & Lipidomics

Integrated projects – past and future...



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Molecular Biomedicine

- Multiple national and international research programs
- Local *ongoing* research networks
  - SFB LIPOTOX (KFU, MUG, TUG; 2007-)
  - DK Molecular Enzymology
  - DK MOLIN
  - DK Metabolic and Cardiovascular Disease
  - K1 Competence Center CB-Med
  - *ACIB*
- International cooperations
  - Joint programmes w/Singapore (NUS, Duke-NUS, SBIC) *in preparation*
  - EuroBioimaging *in preparation*

Infrastructure

- ZMF, OMICS Center (MUG, KFU, TUG)
  - Imaging, ultrastructure analysis (confocal, multiphoton, electron microscopy)
  - Mass spectrometry (proteomics, lipidomics)
  - Transcriptomics, NextGen sequencing
  - Bioinformatics
  - Clinical Research Center
- NIKON Center of Excellence (MUG, KFU)
  - Super-resolution microscopy
- NAWI Graz – Central Lab Core Facilities
  - FACS Center GRACIA
- Core Facility Net

CENTER of EXCELLENCE supported by Nikon

OMICS CENTER GRAZ

Infrastructure

http://zmf.medunigraz.at/

http://omicscentergraz.at/

http://bioimaginggraz.at

http://www.nawigraz.at/de/research/infrastruktur/central-labscore-facilities/

https://corefacilitynet.org/share/page/site/core-facility-net/dashboard

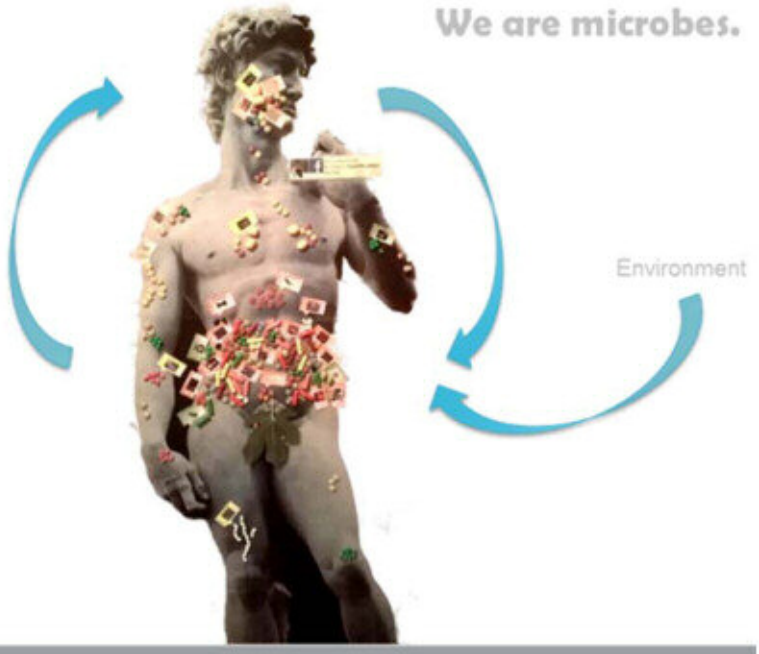
Molecular Biomedicine

- Flagship project:

  Interactive
  Microbiome research

- Why is microbiome research so important?
- Why do we need new (interdisciplinary) approaches and the view beyond?
- How can it bring different research disciplines together?

C. Moissl-Eichinger
Prof. for Interactive Microbiome research



Interactive Microbiome Research

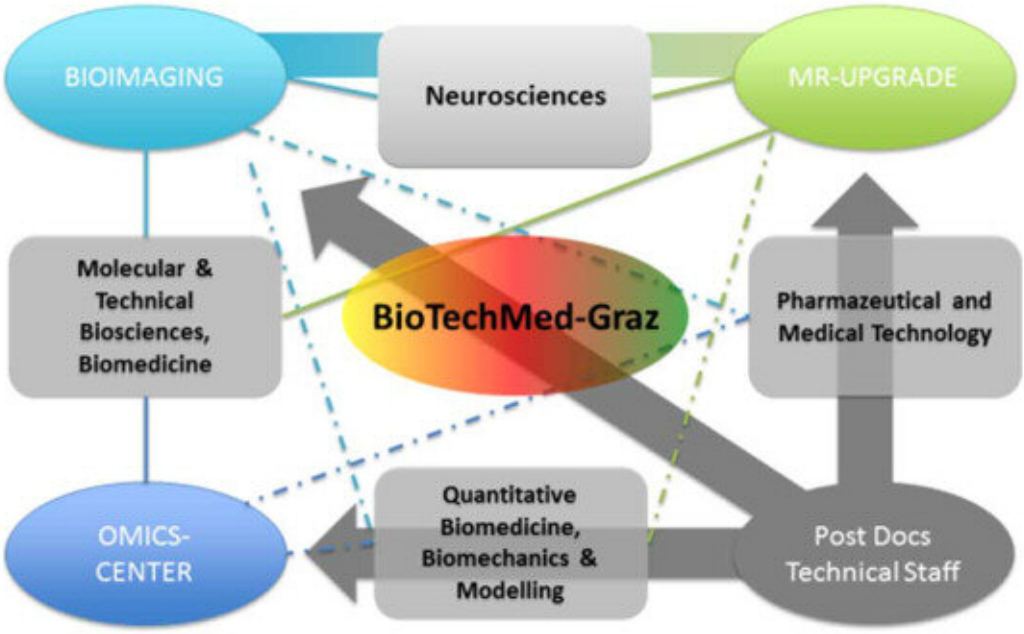
- MIGRobeZ: Mikrobiominitiative Graz
  - Collaboration of microbiome researches from all BioTechMed universities
  - Provide standards, procedures/ Infrastructures
  - Joint publications and acquisition of funding

MIGrobeZ
Microbiome Initiative Graz

- Our questions for the future:
  - Bacteria and beyond?
  - Increase the efficiency of microbial cultivation?
  - How can we „control" the microbiome? Interaction of the microbiomes?
  - How does the microbiome influence our health, behaviour, well-being?
  - How can we influence the microbiome?
  - ...
- Seeking for collaboration partners with new, interdisciplinary ideas ... and questions!

  Imaging/ modelling/ microbe tracking/ method development: quantification/ function...

Interactions



What is missing...

- Stronger involvement of the Technical Biosciences
  - Molecular Biotechnology, TUG
  - ACIB (Industry)
- Better tech support
  - Personnel (infrastructure without personnel support = waste of money)
  - Relief from administrative work
- *More Room for Research*

INPUT NEUROSCIENCES

Representative

- Prof.Dr. Franz Fazekas, MUG and team
  - stroke, small vessel diseases of the brain, multiple sclerosis, aging of the brain, neurorehabilitation

Representative

- Prof. Dr. Anja Ischebeck, KF UNI & colleagues
  - cognitive and affective neurosciences, number and language processing, learning, emotion, research using functional imaging and brain stimulation

Representative

- Prof. Dr. Gernot Müller-Putz,TUG
  - Brain-Computer Interfacing for communication (e.g., disorders of consciousness), control (neuroprosthetics), functional brain mapping, motor system, neurorehabilitation

Current Situation

- **Existing, quite successful collaboration** between the three universities in the neurosciences
  - Research on **neuronal plasticity** and **functional compensation** of the brain during development and aging and in the context of neurologic diseases
  - Research into **cognitive and affective neurosciences** with functional imaging and brain stimulation
  - Development of a new method for communication and control (**Brain-Computer Interface, BCI)** for individuals with severe motor disabilities, including neurofeedback and neurorehabilitation

Current Situation

- **Broad spectrum of methods and devices**
  - Morphological and functional magnetic resonance imaging (**two 3T MRT**)
  - Electrophysiological methods (EEG, EP)
  - Non-invasive brain stimulation (TMS, tACS, tDCS)
  - Functional near-infrared spectroscopy (fNIRS)

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Current Situation

- **High regional, national and international visibility**
  - Initiative Gehirnforschung Steiermark (INGE St)
  - Publications in high and very high ranked *peer-reviewed* journals
  - Third party funding (e.g., FP7/H2020 EU Projects, FWF Projects)

Goals

- Structural and functional MRI studies (fMRI) for **neuronal plasticity** and **functional repair/compensation** and broadening of the topics of **learning** and **competence preservation** in **aging**
- **Development** and **evaluation of new rehabilitation techniques** based on EEG, functional near-infrared spectroscopy, fMRI and non-invasive brain stimulation
- Development of a **Brain-Data-Bank** (focus: *quantitative morphometry*, *functional cerebral networks*) in healthy individuals and neurological disease

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Goals

- Clinical and epidemiological, genetic and biochemical investigations of **molecular fundamentals** of neurologic and psychiatric diseases with respect to new treatment strategies
- **Translational Research in the animal model** (genetic, neurophysiological, behavioral, imaging methods)

INPUT PHARMACEUTICAL AND MEDICAL TECHNOLOGY

The objective of the pharmaceutical and medical technologies for the BioTechMed-Graz project is in the area of drug targeting. This is understood to be the targeted application or the target transport of a drug or an active substance to the location in the body where the substance should take effect. For a drug to reach its place of effect, a series of techniques is available. In the area of pharmaceutical technology, carrier materials, polymers or particles are often used. The enrichment at the place of effect can, however, also take place using medical technologies, e.g. the targeted application through a catheter or the control of an active substance in the body through magnetic fields.

The development and research of such future-oriented drugs represents a major challenge for the scientists involved. Only internal networking of the various expiries today allows processing such complex questions. For the BioTechMed-Graz project, the added value of a cooperation between all three universities is in the fact that although a large number of the technologies required for this exists at the location of Graz at the individual institutions, they can only be used optimally in sum – for instance, for drug targeting with the use of particles, the technical expertise in the production and process technology at the TUG is in place, while the pharmaceutical expertise is available at the KFUG. In the area of application, models of the MUG and analytical and image-forming procedures at the TUG at used.

The objective as part of BioTechMed-Graz will be to create the bases for the development of such target-oriented drugs for the future. In doing so, it will also be necessary to examine methods and processes for the production of such drug targeting devices.

INPUT QUANTITATIVE BIOMEDICINE AND MODELLING

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Quantitative Biomedicine & Modelling

Computational Cardiology – MUG

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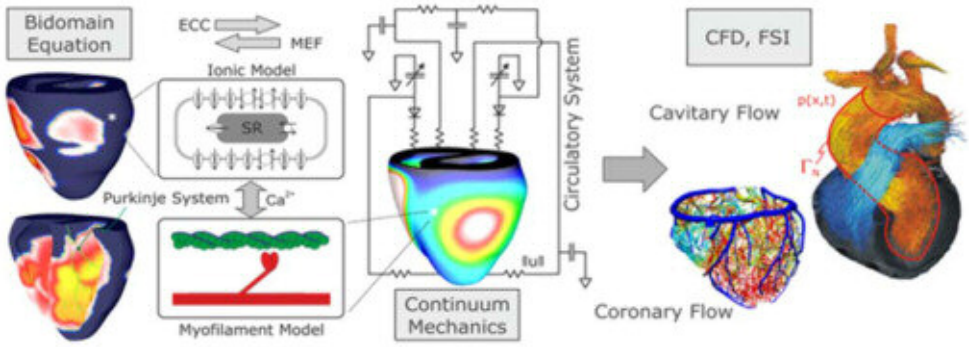
Computing a heart beat

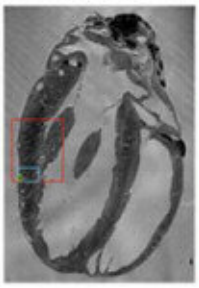


- **Modeling and Computing**
  - Electrophysiology (EP)
  - Non-linear Elasticity
  - Fluid Flow
  - Porous Media Flow
- **EP Applications**
  - Arrhythmogenesis & Defibrillation
- **Mechanics Applications**
  - Heart Failure and CRT
- Flow Applications
  - Aortic Valve Disease and Coarctations

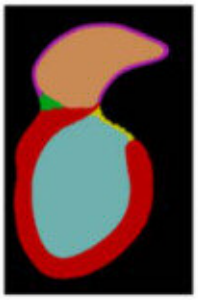
Model Building and Computing

BioTechMed GRAZ

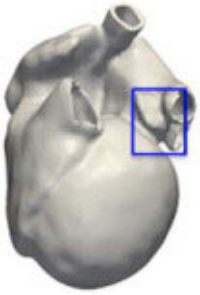
Imaging



Segmentation



FE Meshing



Mathematical Description

$$
\begin{aligned}
\nabla \cdot (\boldsymbol{\sigma}_i + \boldsymbol{\sigma}_e)\,\mathbf{C}^{-1}\nabla\phi_e &= -\nabla \cdot \boldsymbol{\sigma}_i\,\mathbf{C}^{-1}\nabla V_m - I_e \\
\nabla \cdot \boldsymbol{\sigma}_i\,\mathbf{C}^{-1}\nabla V_m &= -\nabla \cdot \boldsymbol{\sigma}_i\,\mathbf{C}^{-1}\nabla\phi_e + \beta\ I_m \\
I_m &= C_m\frac{\partial V_m}{\partial t} + I_{\text{ion}}(V_m, \boldsymbol{\eta}) \\
V_m &= \Phi_i - \Phi_e \\
\frac{\partial \boldsymbol{\eta}}{\partial t} &= f(\boldsymbol{\eta}, V_m, \sigma_a) \\
\operatorname{div}\boldsymbol{\sigma}(\boldsymbol{u}) &= \mathbf{b}, \\
\boldsymbol{\sigma} &= \boldsymbol{\sigma}_p + \boldsymbol{\sigma}_a \\
\boldsymbol{\sigma}_p &= J^{-1/3}\overline{\mathbf{F}}(2\frac{\partial \Psi}{\partial \mathbf{C}})\overline{\mathbf{F}}^{\mathrm{T}} \\
\boldsymbol{\sigma}_a &= \sigma_a(\overline{\mathbf{f}} \otimes \overline{\mathbf{f}}) \\
\sigma_a &= h(V_m, \boldsymbol{\eta}, \lambda, \dot{\lambda})
\end{aligned}
$$

EP

ECC

MEF

Deformation

EP and mechanics are bidirectionally coupled through excitation-contraction coupling (ECC) and mechano-electric feedback (MEF)

Electrical Defibrillation

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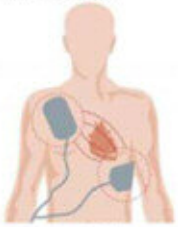
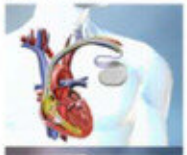
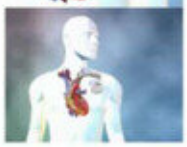
„External"

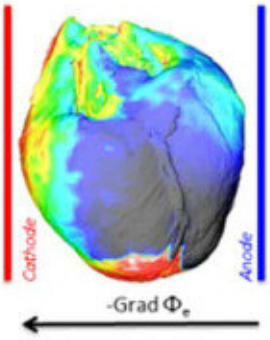


„Internal"

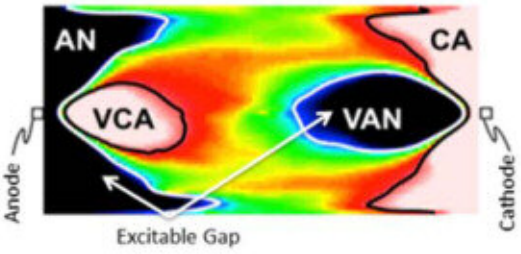




Shock Delivery



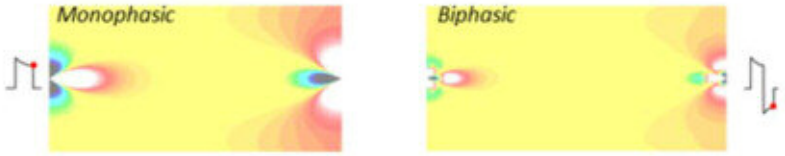
Postshock Virtual Electrode Polarization



- Only reliable therapy to prevent Sudd Cardiac Death
- Detrimental effects affect Quality of Life (Pain Perception)
- Stochastic phenomenom, success depends on strength, location, timing, polarity and pulse shape of shock

Optimal Control Approach

Tissue Response to Defibrillation Shock – Dependency on Shock Waveform

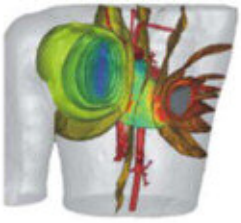


PDE Constrained Optimization

$$\mathcal{L}(V_m, w, I_e, p, q) = J(V_m, I_e) + \langle e(V_m, w, I_e), (p, q) \rangle$$

$$J(V_m, I_e) = \frac{1}{2}\int_0^T \left(\int_{\Omega_{obs}} |V_m - V_d|^2 \, d\Omega_{obs} + \alpha \int_{\Omega_{con}} |I_e|^2 \, d\Omega_{con} \right) dt$$

Optimize Lead Placement

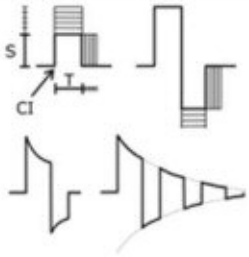


Subcutaneous ICD

Wide Area Defibrillation

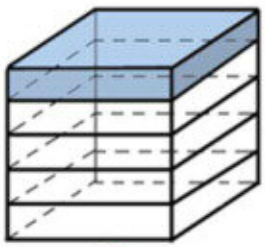
Xu et al, 5:3329, Nature Comm

Optimize Timing/Pulse Shape



Insitute of Biomechanics – TU Graz

- Image stack (z-stack)



Collagen fibers in the human adventita

- Image size (25x water objective)
  - 534 x 534µm
- Image depth
  - 300nm
- Distance between images
  - 1µm

Human abdominal aorta before and after optical clearing
Schriefl et al. [RSI], 2013

7

Insitute of Biomechanics – TU Graz

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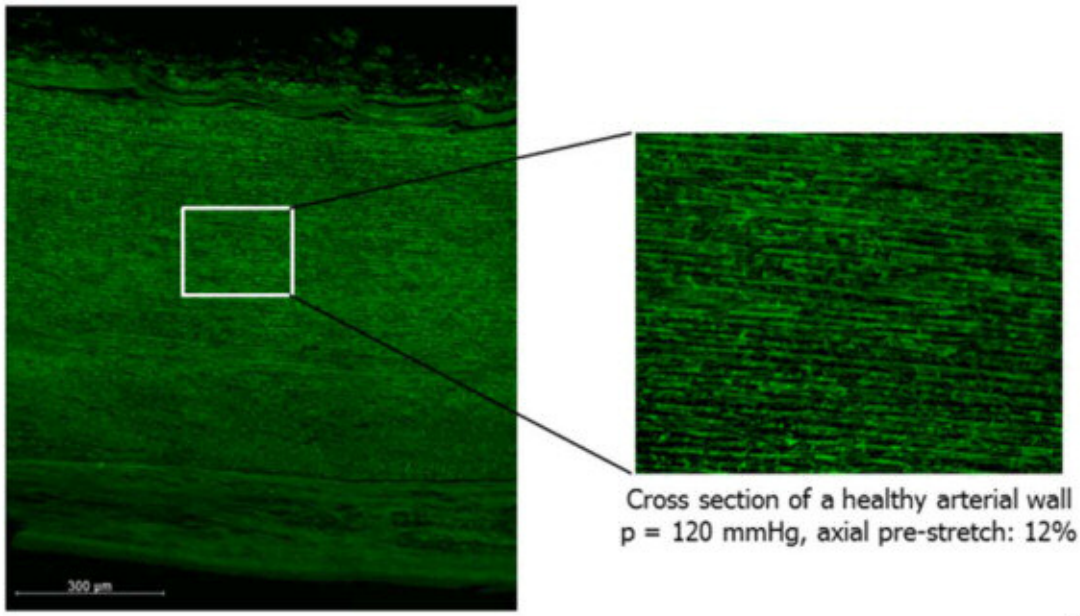
- In-plane collagen fibers in the human media



Cross section of a healthy arterial wall
p = 120 mmHg, axial pre-stretch: 12%

Insitute of Biomechanics – TU Graz

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- **Material and structural modeling**

- Strain-energy function of the artery wall

$$\Psi_{\text{iso}} = \Psi_{\text{g}}(\bar{\mathbf{C}}) + \sum_{i=4,6} \Psi_{\text{fi}}(\bar{\mathbf{C}}, \mathbf{H}_i)$$

- Energy stored in the two families of dispersed collagen fibers

$$\Psi_{\text{fi}}(\bar{\mathbf{C}}, \mathbf{H}_i) = \frac{k_1}{2k_2}[\exp(k_2\bar{E}_i^2) - 1], \quad i = 4, 6$$

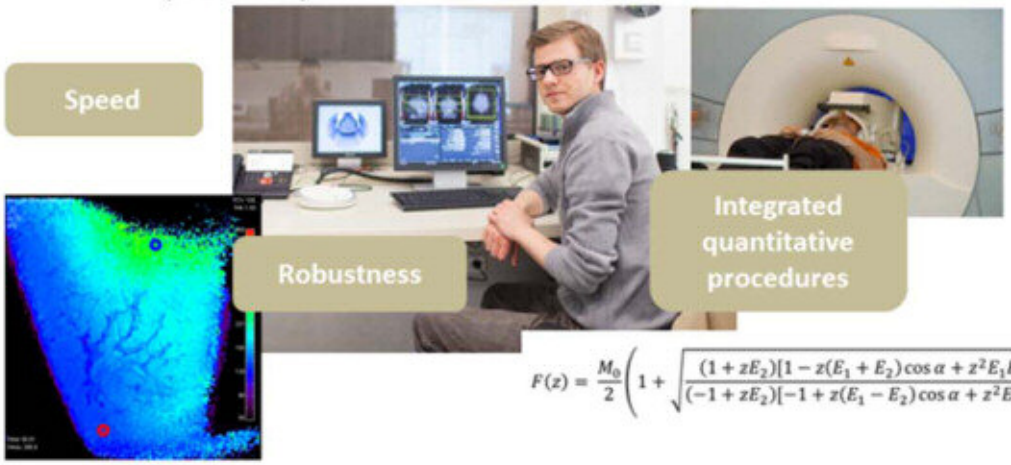
- Green–Lagrange strain-like quantity

$$\bar{E}_i = A\bar{I}_1 + B\bar{I}_i + (1 - 3A - B)\bar{I}_{\text{n}} - 1$$

A and *B* consider the measured **structure** of the collagen fibers

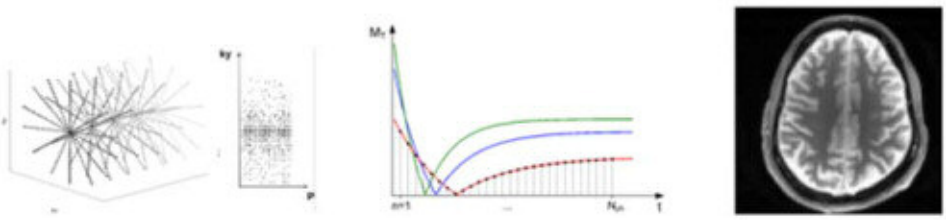
General Goal of MR Research at IME

- **The development of MRI towards a biomarker imaging technique by the application of advanced MR principles and mathematical methods.** (SFB Mobis).



$$F(z) = \frac{M_0}{2}\left(1 + \sqrt{\frac{(1+zE_2)[1-z(E_1+E_2)\cos\alpha + z^2E_1E_2]}{(-1+zE_2)[-1+z(E_1-E_2)\cos\alpha + z^2E_1E_2]}}\right)$$

Integrated Proc: Multiparameter MRI (mpMRI)



mpMRI:

1. Multiple parameter encoding

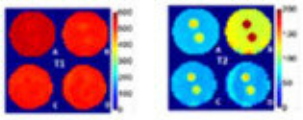
$$s_n(T) = \|\vec{M}_n(x,y)\|$$
$$\vec{M}_n = \frac{1}{K}\sum_{k=1}^{K} \mathbf{E}\mathbf{R}_z(\alpha_{n,k})\,\mathbf{R}_z(\pi)\left(\mathbf{E}\vec{M}_{n-1} + \vec{e}\right) + \vec{e}$$

2. Generating function for transient sequences

3. Model based reconstruction

$$\min_{T=\{T_1,T_2,M_0\}} \frac{1}{2}\sum_{c,n} \|\mathcal{P}_n\mathcal{F}(c_c s_n(T)) - d_{n,c}\|_2^2 + \lambda \mathrm{TGV}(T)$$

Visibility study Phantom T1,T2



Robustness: Image Sequences and Motion Correction

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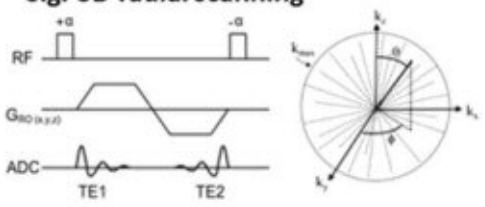
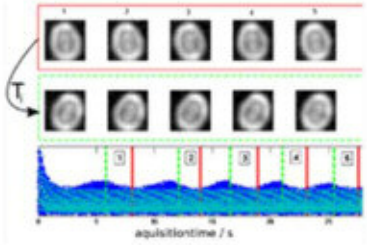
- Body motion is still a problem for MRI
- **Goal: retrospective motion correction**

e.g. 3D radial scanning



Low resolution Subsets ⇒



Forward operator model with mapping of motion dependent position to k-space data

$$K : u \mapsto \sum_{t=1}^{N} \mathcal{F}_t(b_j T_t u)$$

Challenges and research objective:

- Motion correction of time-resolved 3D radial acquisitions for free-breathing dynamic MRI
- Motion correction high resolution 3D
- Investigation new math. Approaches

Available Infrastructure

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- 3T MRI (Research System)
  Siemens Skyra, 45mT Gradient, different Array coils, Head Coils with 20 and 32 channels, Mouse & Rat coil., fMRI equipment, Elastography unit.
- Pulse programming capabilities
- Advanced signal modelling
- Fast offline reconstruction for new algorithms

Research Grup

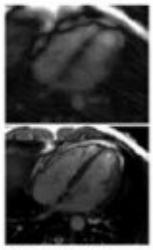
BioTechMed GRAZ

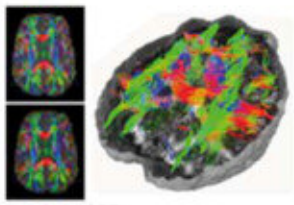
Inverse Problems & Mathematical Imaging
Institute for Mathematics and Scientific Computing

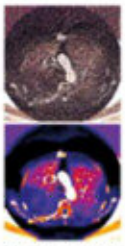
Fields of research

- Variational modelling and optimization for advanced reconstruction and quantification of image data
- Application to medical imaging (MRI/CT), microscopy, and beyond

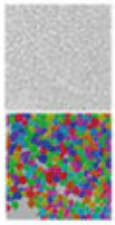
SFB Research Center Mathematical Optimization & Applications in Biomedical Sciences


Dynamic MRI


Regularized DTI


Dual-Energy CT


Binary surface smoothing


Cell segmentation

Involved Researchers

BioTechMed GRAZ

Inverse Problems & Mathematical Imaging

Univ.-Prof. Dr. Kristian Bredies
Head of group

- Advanced imaging techniques/Inverse problems
- Optimization and variational approaches

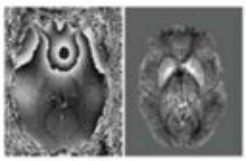
Dr. Martin Holler
Postdoctoral researcher

- Dynamic imaging and reconstruction
- Image/Video compression techniques

Dr. Kamil Kazimierski
Postdoctoral researcher

- Image data analysis and quantification
- Regularization approaches for inverse problems

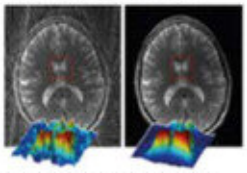
Research Question and Trends



Inverse Problem: Quantitative susceptibility mapping

$$\mathrm{TGV}^2_\alpha(u) = \min_{w \in \mathrm{BD}} \alpha_1 \|\nabla u - w\|_{\mathcal{M}} + \alpha_0 \|\mathcal{E} w\|_{\mathcal{M}}$$

Advanced regularization



Compressed sensing in MRI (10% of the data)

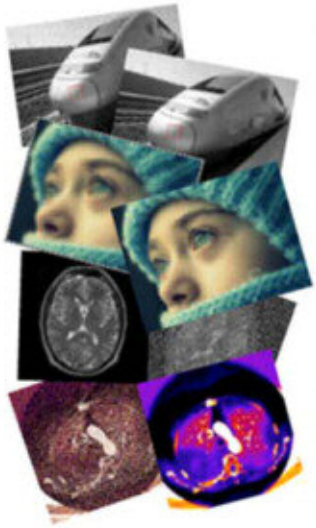
Inverse problems: How to reconstruct from measurements?

- Modelling: Describe measurements process
- Inversion: Find solution explaining given measurements
- Regularization: Make solution reasonable
- Optimization: Find best of out many solutions

Recent developments

- Inverse problem paradigm becomes established in medical imaging
- Development of advanced regularization approaches
- Compressed sensing: Reconstruction from few measurements
- Availability of powerful optimization algorithms

Cooperation Potential



Available expertise

- Image enhancement: Denoising, deblurring & beyond
- Modelling and realization of reconstruction strategies
- Reconstruction from incomplete data
- 2D/3D image data & image sequences

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- Strengthen cooperations with practitioners
- Improve mathematical models
- Enhance efficiency of numerical algorithms

Omics Center Graz, Proteomics and Metabolic pathways

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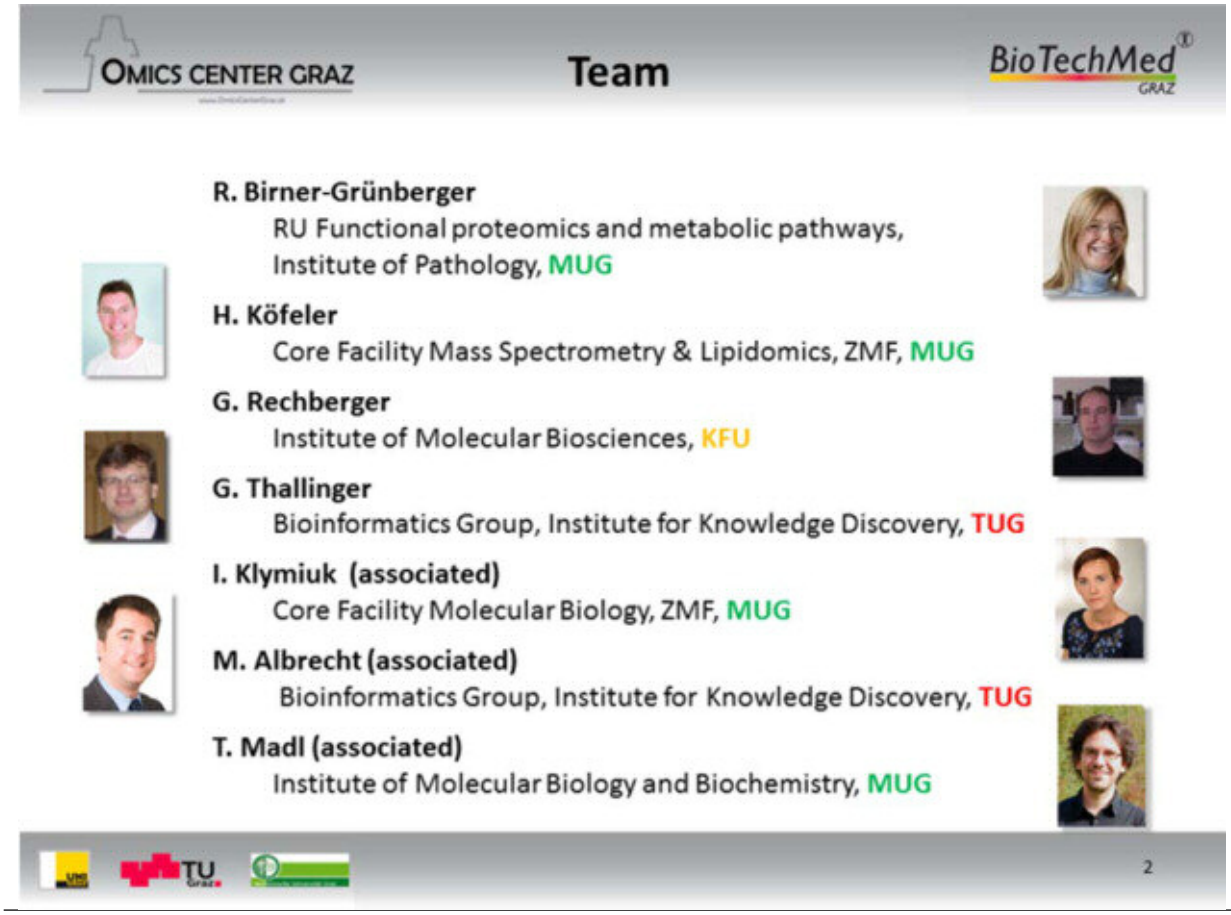

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Know How

BioTechMed GRAZ

- **Proteomics**
  Birner-Grünberger
- **Lipidomics / Metabolomics**
  Köfeler, Rechberger, Madl
- **Transcriptomics / Genomics**
  Klymiuk
- **Bioinformatics**
  Thallinger, Albrecht

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Investment

BioTechMed GRAZ

- Hochschulraumstrukturmittel Call 2013: **1.5 Mio€**
- **Infrastructure:**
  1 Q-TOF (MUG), 1 IT (MUG), 2 TQ (1 MUG, 1 KFU) (May 2015)

Bruker Center of Excellence for Mass Spectrometry in Life Science

- **Personnel:**
  3 Postdocs (Bioinformatics, Proteomics and Metabolomics) and 1,5 Technicians (Lipidomics and Metabolomics) for nearly 2 years

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Major Aims

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- One -omics technology platform in Graz
- Multi-omics, integrative systems biology
- Metabolomics and metabolic flux analysis
- Educate young scientists in cutting edge technologies
- Node for collaboration

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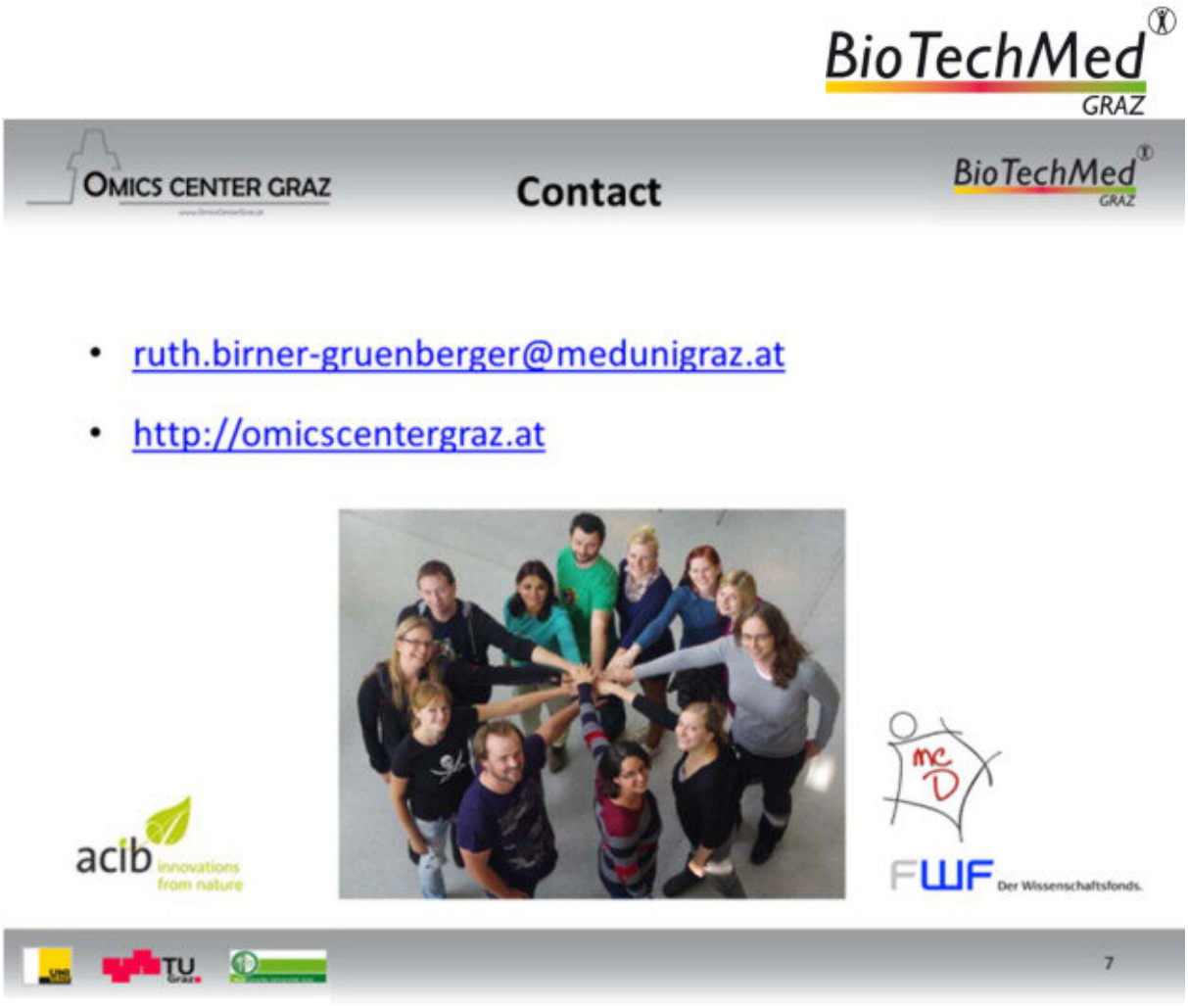
My Favorite Topics

BioTechMed GRAZ

- Lipid metabolism, lipolysis and its regulation
- Cancer metabolism
- Enzyme discovery
- Function of proteins
- All flavors of proteomics



Same mechanism ... very different disease?

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Institute of Molecular Biology and Biochemistry
Medical University of Graz

1. Scientific profile of the research group

My research focuses on structural biology of signal transduction and metabolomics. One of my major interests are the general mechanisms by which transcription factors are acting as key regulators of cell and organismal fate, and how they contribute to diseases and ageing. Transcription factors are at the heart of signaling cascades and tightly regulated by a plethora of co-factors and post-translational modifications. My focus is on transcription factors that link the regulatory Wnt pathway with insulin/growth factor signaling and oxygen metabolism. I study the involved dynamic transcription factor – co-factor complexes and the modulation of the interactions by post-translational modifications and disease mutations.

To this end I employ and develop an integrated structure determination approach in which I combine Nuclear Magnetic Resonance (NMR) spectroscopy, Small-angle X-ray/neutron scattering (SAXS/SANS) and modeling strategies which are especially suited to study the structure of large and dynamic protein complexes. Several novel innovative approaches have been developed and applied to challenging biological systems in the last few years (Cell 2014, Mol Cell 2014, Nat Struct Mol Biol 2011/2010, Nature 2011, J Struct Biol 2011, Angew Chem Int Ed Engl 2011/2010/2009).

Another research topic of my group is the molecular mechanisms of signal transfer mediated by disordered proteins. Distortions in signal transduction lead to a plethora of diseases (i.e. cancer and neurodegenerative disorders) and are linked to ageing. I aim to reveal the molecular mechanisms

underlying interactions of disordered proteins to provide insight into the intricate link between their function, regulation and human diseases. My first results on the molecular mechanisms driving the neurodegenerative disease ALS (amyotrophic lateral sclerosis; EMBO J 2012), the interaction of the Alzheimer protein tau with molecular chaperones (Cell 2014), and colorectal cancers (FOXO tumor suppressors, Mol Cell 2013; Axin-1 mutations, under review) will have a great general impact by promoting better understanding of how these diseases develop and will provide novel strategies for their diagnosis and treatment.

Ten most important and relevant publications (since 2010)

Lorenz O., Freiburger F., Rutz D., Krause M., Zierer B., Alvira A., Cuéllar J., Valpuesta J.M., **Madl T. (co-corresponding author)**, Sattler M., Buchner J., Modulation of the Hsp90 chaperone cycle by a stringent client protein (2014) **Mol Cell** 53, 941-953.

Karagöz G.E., Duarte A.M.S., Akoury E., Ippel H., Biernat J., Luengo T.M., Radli M., Didenko T., Nordhues B.A., Veprintsev D.P., Dickey C., Mandelkow E., Zweckstetter M., Boelens R., **Madl T. (co-corresponding author)**, Rüdiger S.G.D., Hsp90-Tau complex reveals molecular basis for specificity in chaperone action (2014) **Cell** 156, 963-974.

Zhang Y, **Madl T (shared first author, co-corresponding author)**, Bagdiul I, Kern T, Kang HS, Zou P, Mäusbacher N, Sieber SA, Kramer A and Sattler M, Structure, phosphorylation and U2AF65 binding of the N-terminal domain of splicing factor 1 during 3'-splice site recognition (2013) **Nucleic Acid Res** 41, 1343-1354.

Putker M., **Madl T.**, Vos H.R., de Ruiter H., Visscher M., van den Berg M.C.W., Kaplan M., Korswagen H.C., Boelens R., Vermeulen M., Burgering B.M.T., Dansen T.B., Redox-dependent control of FOXO/DAF-16 by transportin-1 (2013) **Mol Cell** 49, 730-742.

Dormann D., **Madl T.**, Valori C.F., Bentmann E., Tahirovic S., Abou-Ajram C., Kremmer E., Ansorge O., Mackenzie I.R.A., Neumann M., Haass C., Arginine methylation next to the PY-NLS modulates Transportin binding and nuclear import of FUS (2012) **EMBO J** 12, 4258-4275

Tripsianes K, **Madl T**, Machyna M, Fessas D, Englbrecht C, Fischer U, Neugebauer KM, and Sattler M, Structural basis for dimethylarginine recognition by the Tudor domains of human SMN and SPF30 proteins (2011) **Nat Struct Mol Biol** 18, 1414-20.

Mackereth CD, **Madl T**, Bonnal S, Simon B, Zanier K, Gasch A, Rybin V, Valcarcel J, and Sattler M, Multi-domain conformational selection underlies pre-mRNA splicing regulation by U2AF (2011) **Nature** 475, 408-11.

Madl T, Guttler T, Gorlich D, and Sattler M, Structural analysis of large protein complexes using solvent paramagnetic relaxation enhancements (2011) **Angew Chem Int Ed Engl** 50, 3993-7.

Güttler T., **Madl T. (shared first author)**, Neumann P., Deichsel D., Corsini L., Monecke T., Ficner R., Sattler M., Görlich D., Structural basis for the recognition of diverse nuclear export signals by the exportin CRM1 (2010) **Nat Struct Mol Biol** 17, 1367-76.

Simon B, **Madl T**, Mackereth CD, Nilges M, and Sattler M, An efficient protocol for NMR-spectroscopy-based structure determination of protein complexes in solution (2010) **Angew Chem Int Ed Engl** 49, 1967-70.

Structural Biology of Proteins in Lipid Metabolism

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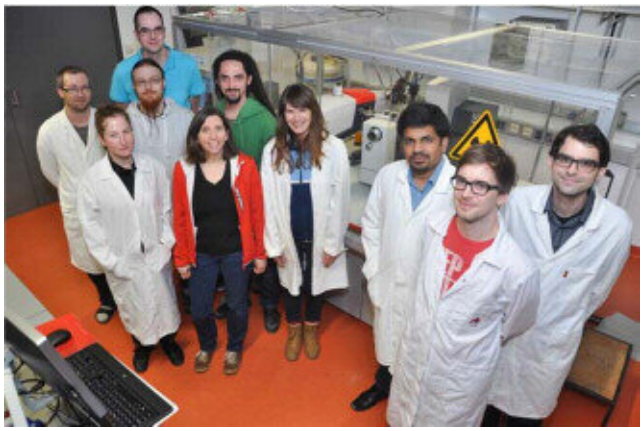
Institute of Molecular Biosciences
University of Graz

The group of Assoz. Prof. Dr. Monika Oberer was founded in 2006 after her post-doctoral training at Harvard Medical School (USA) and is now is embedded within the Structural Biology network at the Institute of Molecular Biosciences at the University of Graz. The young team (currently six Ph.D. and three diploma students) focusses on the structure-function relationship of proteins involved in lipid

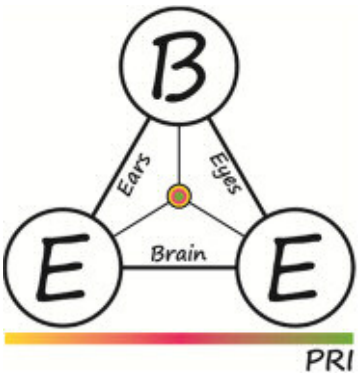
metabolism. The researchers use biochemical and biophysical methods including NMR spectroscopy and X-ray crystallography. The structural and mechanistic characterization of proteins performed in the group of Dr. Oberer have also paved the way to the development of lead molecules of high pharmacological interest. Currently M. Oberer's team is involved in high-ranking program project grants (SFB Lipotox, DK Molecular Enzymology, the Transatlantic Network of Excellence Program Leducq) and national single grant projects (FWF, NAWI Graz). Accordingly, the group has different international research partners and is intensively collaborating with other researcher groups in Graz (Graz University of Technology, Medical University of Graz, University of Graz).

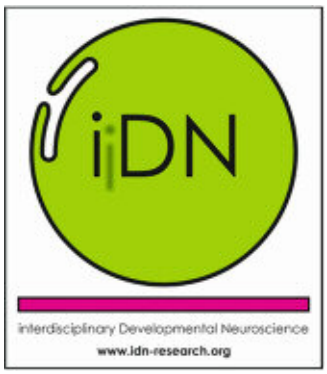
Related links:
http://unipub.uni-graz.at/oazuzt/periodical/pageview/375659
https://molekularbiologie.uni-graz.at/de/forschen/forschungsbereiche/strukturbiologie/
http://derstandard.at/1282979153325/Geistesblitz-Gaensehaut-beim-Fettstoffwechsel



BEE-PRI: Brain, Ears & Eyes – Pattern Recognition Initiative

Florian Pokorny, Univ.-Ass. Dipl.-Ing.
E-mail: florian.pokorny@medunigraz.at
Institute of Physiology
Medical University of Graz





One-stop solution for high content drug screening

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Institute of Molecular Biology and Biochemistry
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One-stop solution for HIGH CONTENT DRUG SCREENING

Emrah Eroglu, Dipl-Ing. BSc
Wolfgang F. Graier, Univ.-Prof. Mag.pharm. Dr.rer.nat.
Roland Malli, Assoz. Prof. Priv.-Doz. Mag.pharm. Dr.rer.nat

NeGeF-*I*

Next Generation Fluorescense-*Imaging*
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1

Bottlenecks of Current High Troughput Screenings (HTS)

SUPERFICIAL & SINGLE DESCRIPTIVE
Even large pharmaceutical companies cannot sustain as many HTS facilities as they need for efficient drug screening.

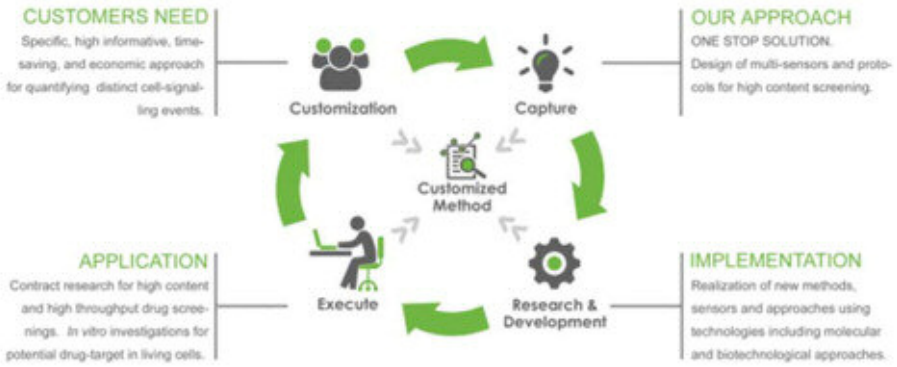
TIME WASTING
Superficial high throughput screenings can take a great deal of time and effort.

For academic labs, research institutions, spin-outs and for small start-ups it is impossible to invest in their own HTS system

COST WASTING
Superficial high throughput screenings systems are highly automated and very efficient, but very expensive to set up, very expensive to run.

LOW CONTENT
Superficial HTS does not provide in detail data that can further be analyzed for drug development.

One-stop Solution



Our Approaches and State of the Art

BIO-SENSOR DESIGN

PATENTS:
geNOp-Technology PP: GB 14 190 73.0
Kringle Domain Sensor P: WO2006077241(A2)
Stable Sensor cells

AUTOMATIC SCREENING SYSTEM

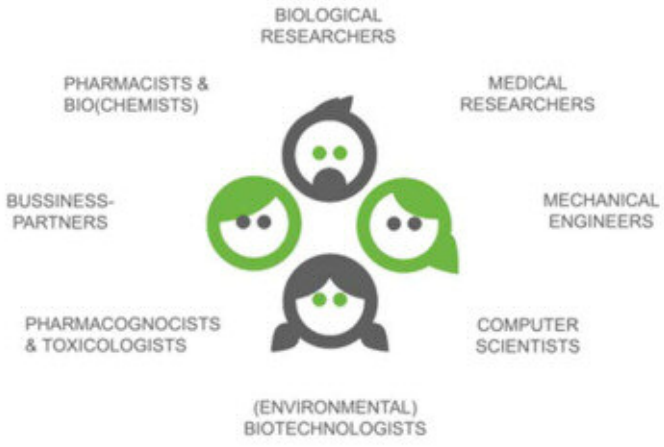
PATENT:
Perfusion Robot. Software controlled perfusion system and Imaging analysis software PP: GB 14 171 40.9

LIVE-CELL IMAGING FACILITY

Next Generation Fluorescence Imaging NeGeF-I

Concept design and implementation.
Evaluation and assesment of technical feasability.
Scheduling of innovative methods.

Potential Co-Operation Partners



Elevated AdoHcy is responsible for triacylglycerol accumulation in yeast models of hyperhomocysteinemia

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Hyperhomocysteinemia (HHcy), a common pathological condition characterized by elevated homocysteine (Hcy) levels in the blood, is linked to a number of diseases of modern society such as cardiovascular and neurological disorders, fatty liver, obesity, diabetes and cancer. Central to the pathology of HHcy is low adiposity along with an accumulation of triacylglycerol (TG) in non-adipose tissues.

Current research in HHcy is focused on a direct precursor for Hcy synthesis, *S*-adenosyl-*L*-homocysteine (AdoHcy), which is shown to be a more sensitive marker for cardiovascular afflictions than Hcy. AdoHcy is a common by-product and a strong competitive inhibitor of many *S*-adenosyl-*L*-methionine (AdoMet)-dependent methyltransferases involved in methylation of a broad spectrum of cellular compounds including nucleic acids, proteins and lipids. A ratio of AdoMet to AdoHcy serves as an indicator of methylation potential and either decrease of AdoMet levels or increase of AdoHcy level lead to methylation deficiency.

We have shown that elevation of AdoHcy levels is responsible for TG accumulation as well as for changes in membrane lipids and accumulation of palmitoleic acid in yeast models of hyperhomocysteinemia. We propose that the mechanism of TG accumulation in response to elevated AdoHcy levels may include inhibition of the synthesis of the main membrane lipid, phosphatidylcholine (PC), by the methylation pathway, changes in membrane molecular lipid species composition, membrane dysfunction, induction of unfolded protein response, activation of phospholipid remodeling and TG accumulation.

key words
methionine, choline, AdoMet, AdoHcy, methylation deficiency, hyperhomocysteinemia, lipotoxicity, deficient phospholipid methylation, ER dysfunction, TG accumulation, regulation of fatty acid metabolism

Anaerobic microorganisms with relevance for medicine and space

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Targeting therapeutic resistance in acute myeloid leukemia

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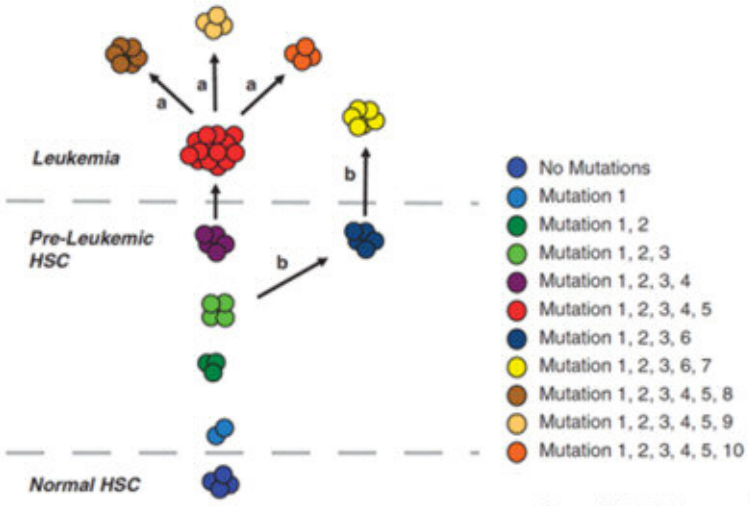
www.medunigraz.at/myeloidcellsleukemia

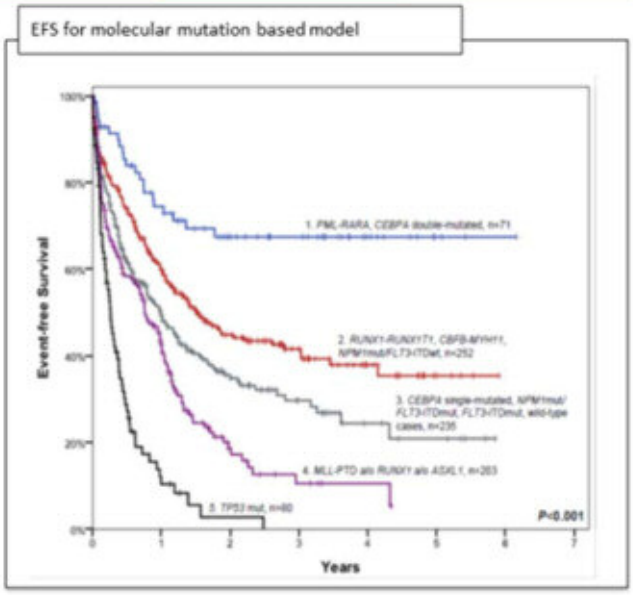
AML: Pathogenesis



Jan and Majeti, Oncogene 2013

BioTechMed GRAZ

AML: Survival



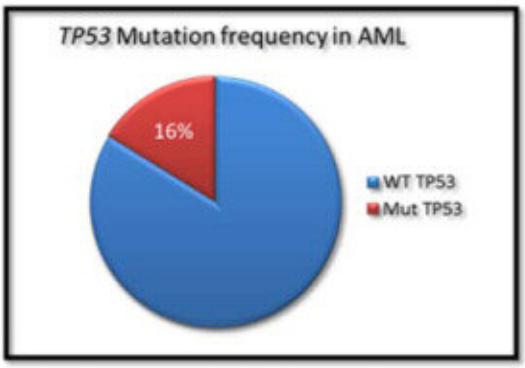
Gene	Frequency
TP53	11,5%
FLT3	15,9%
MLL	6%
NPM1	29,2%
CEBPA	7,5%
RUNX1	17,9%
ASXL1	15,4%
IDH1 *IDH2*	*7,8%* *13,7%*
TET2	*28,8%*
DNMT3A	*27,3%*

Haferlach et al. Blood 2012

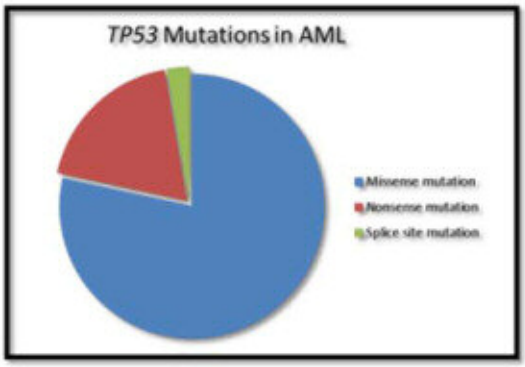
Hypothesis

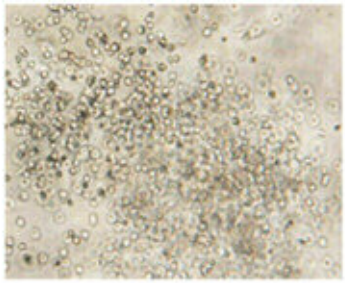
***TP53* mutations are driver events of leukemogenesis contributing substantially to resistant disease**

I: Assess the leukemogenic potential of p53

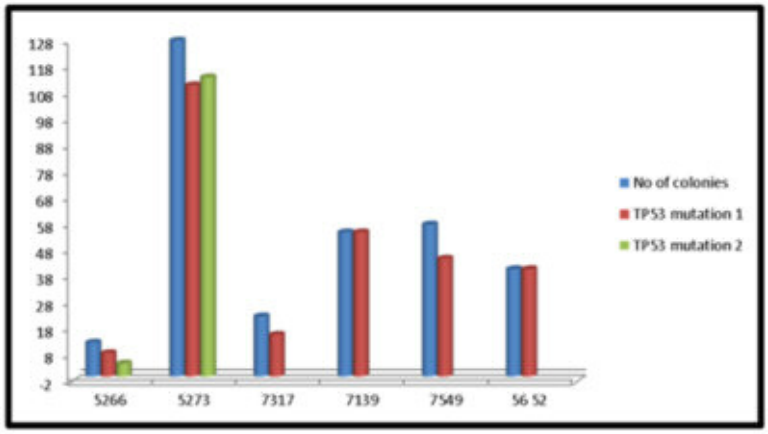


n=170, Leukemia Biobank Hematology





In vitro clonogenic assays



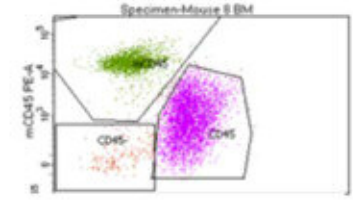
BioTechMed GRAZ

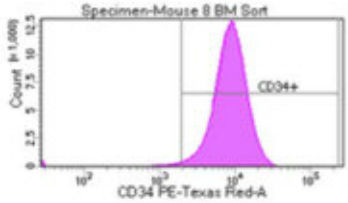
NOD/SCID IL2RY$^{-/-}$ (NSG) X NOD/SCID SGM3 (NSS)

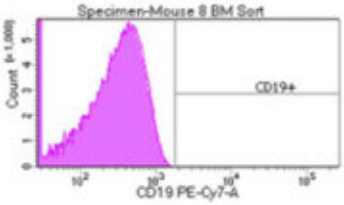
↓

NSG-SGM3 (NSGS)

Engraftment without irradiation







II: Identify drug resistant pathways

Isogenic leukemic cell lines
(+/- mut. p53)

↓ ***Cytarabine, doxorubicin***

Expression analysis

↓

Druggable targets??

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K. Kashofer, G. Höfler
ZMF, MUG
B. Rinner
Daniel-Swarovski Research Lab, MUI
J. Troppmair

Quantitative MRI Methods in Neurosciences

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Investigating the microbiomes of the International Space Station and an Intensive Care Unit in Graz

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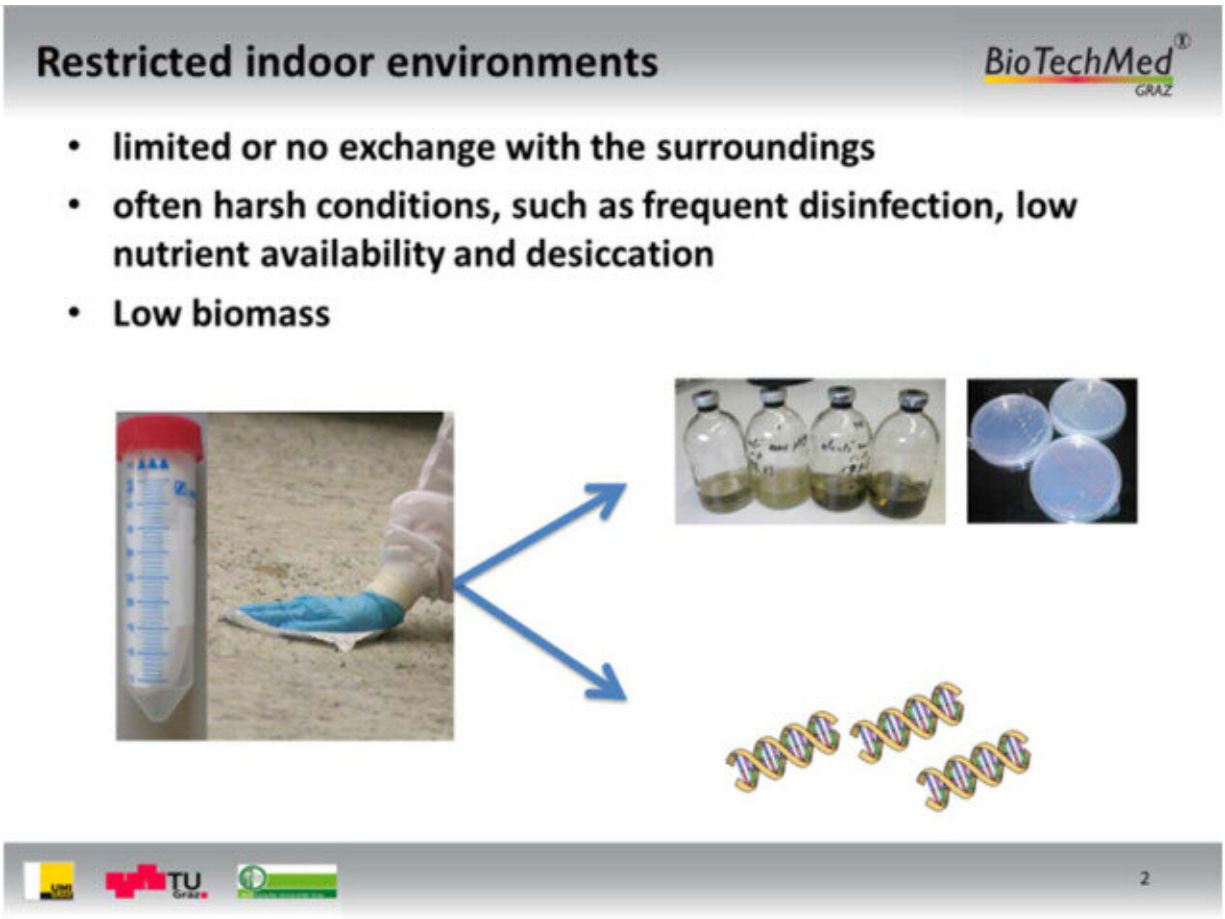
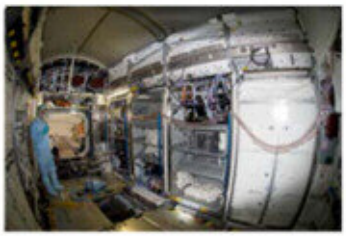


International Space Station ISS

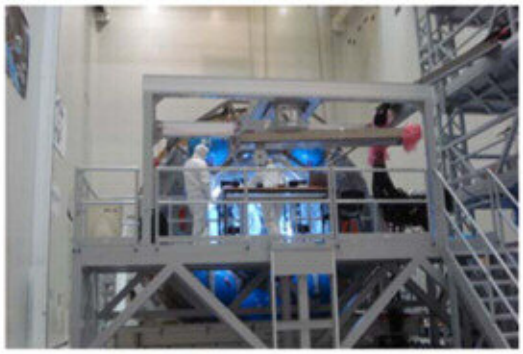
- Almost completely sealed off from the outside world
- Crew and cargo from earth as the only possible contamination sources
- Extreme conditions (e.g. irradiation and microgravity)
- Weakened immune system of crew members[1]
- Microbial monitoring to assess health risks and degradation risks of spacecraft hardware[2,3]
- Part of the ARBEX project (ARchaeal and Bacterial Extremophiles onboard the ISS)



3

Clean rooms

- Up to now focus on clean rooms for spacecraft assembly
- High efficiency particle air (HEPA) filtering and isolated by air locks
- Mandatory clean room clothing for contamination control
- Rigorous cleaning protocols
- Oligotrophic, desiccated environment



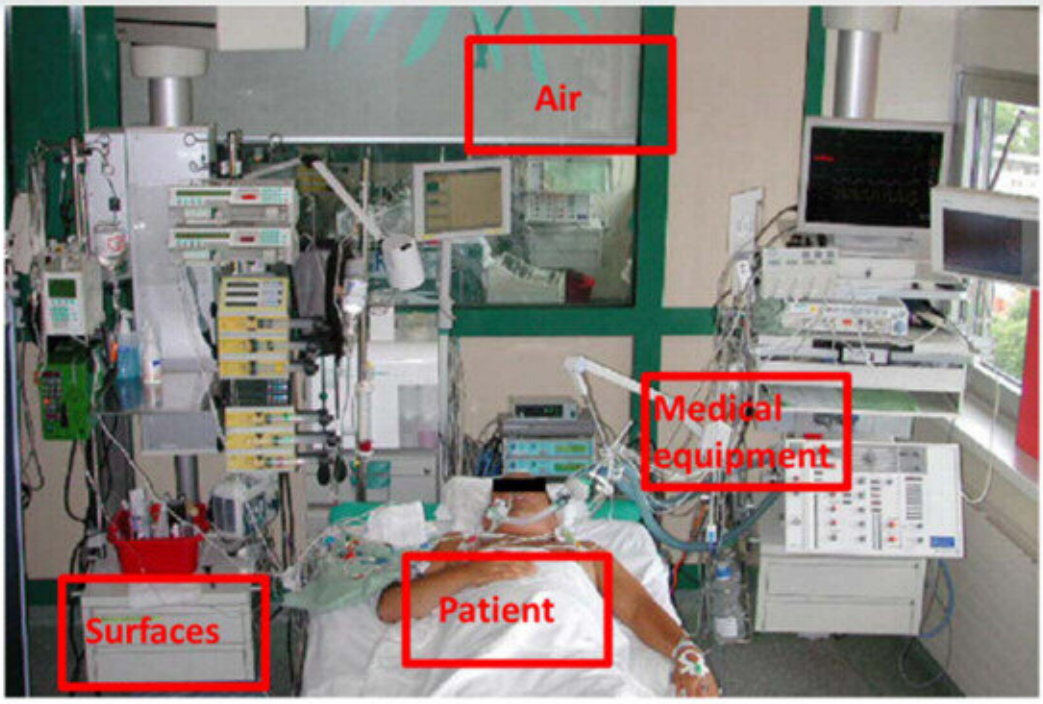
4

ICU-Project

- Limited exchange with outdoor environment
- Strict sanitation protocols
- Lower microbial diversity than in non restricted indoor environments[4]
- High proportion of genera known to include (opportunistic) pathogens[4]
- Patients are possible vectors for (opportunistic) pathogens
- Patients generally already have a weakened immune system

5

ICU-Project



6

References

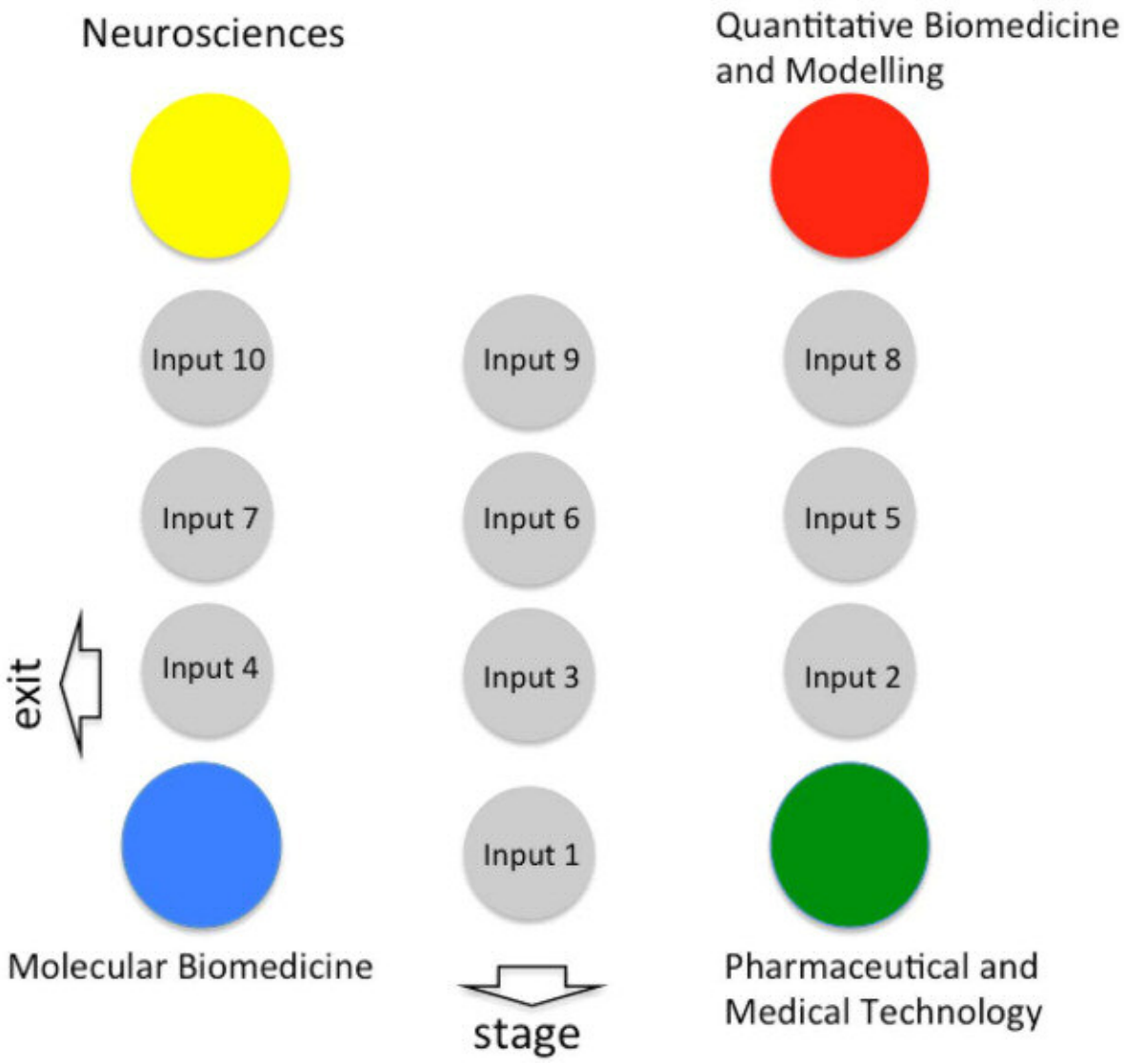
BioTechMed GRAZ

1. Aponte et al. (2006). Considerations for non-invasive in-flight monitoring of astronaut immune status with potential use of MEMS and NEMS devices; *Life Sciences 79:1317–1333*
2. Castro et al. (2004). Microbial Characterization during the Early Habitation of the International Space Station; *Microbial Ecology 47:119–126*
3. Alekhova et al. (2005). Monitoring of Microbial Degraders in Manned Space Stations; *Applied Biochemistry and Microbiology 41(4):382-389*
4. Oberauner et al. (2013). The ignored diversity: complex bacterial communities in intensive care units revealed by 16S pyrosequencing. *Scientific reports, 3.*

MARKETPLACE

After the introduction slots, you now have an opportunity to ask questions and establish contact with the speakers. Use the time to speak with several persons. To give you an idea of the time, a signal will be sounded every 20 minutes.

Below, you can see the table plan, where you can find the different speakers:



STEP 2: SCREENING OF IDEAS

You now have time to exchange information with other researchers about possible project ideas in several free-form session. Regarding project ideas in the framework of BioTechMed-Graz, researchers from at least two different universities should be involved.

NOTES:

NOTES:

NOTES:

STEP 3: SELECTION OF TOP IDEAS

3 steps to prioritize your ideas

1. Identify the TOP 7 ideas, without ranking them
2. Select the two best ideas. Each person gets three points (sticky dots) which can be allocated freely to the ideas.
3. Each pair of ideas with the most points (sticky dots) will be subsequently presented and discussed further.

IMPORTANT:

Please write each idea down on a card with a key word, and mark the card with your personal code. The code written in red means that you are the primary contact person, and the code written in black means that you are a project partner.

STEP 4: DEVELOPMENT OF PROJECT DRAFTS

One idea should be developed in detail in each of two rounds (two ideas in total).

There should be a minimum of three persons and a maximum of 15 persons in each group.

In groups, the following points should be developed and presented later:

STEP 5: PRIORITIZATION

Step 1:

Speed dating group 1

Step 2:

The ideas are discussed in the groups, and the following questions should have priority:

- Which ideas have the potential to become an international flagship project?
- Which ideas would secure real added value with regard to current research expertise?

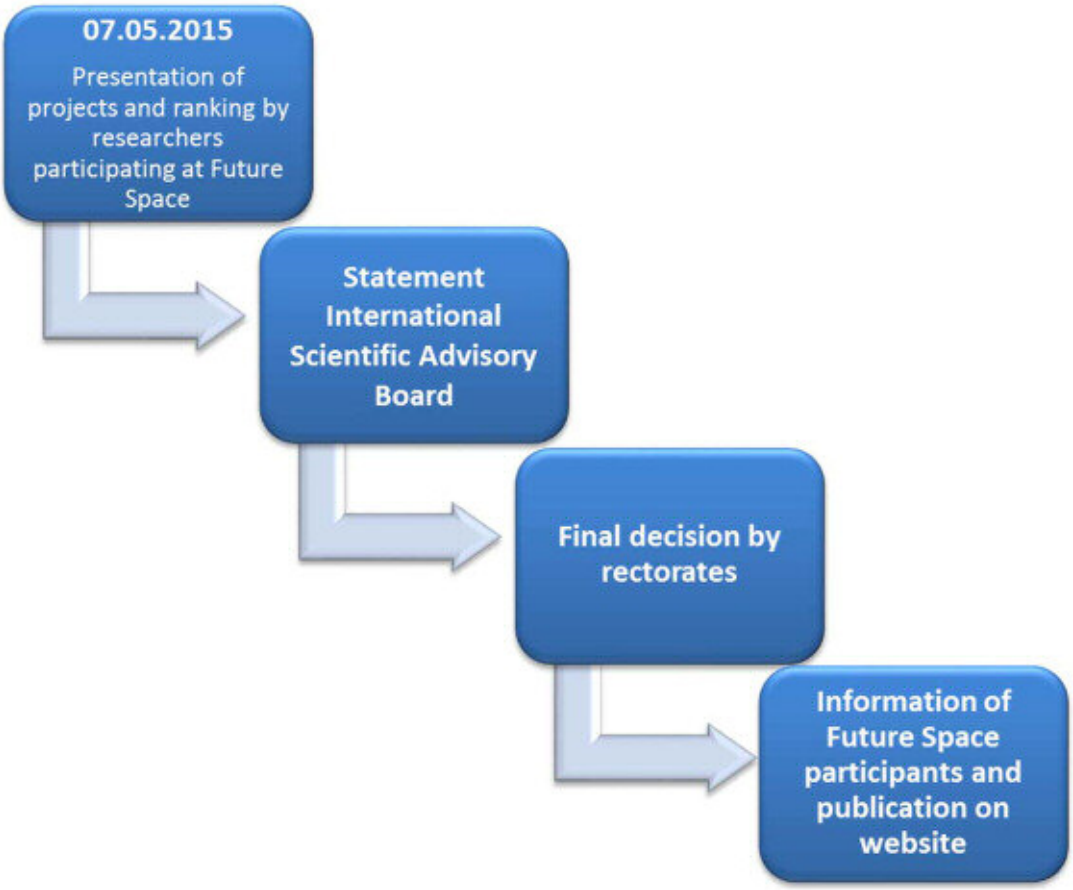
Step 3:

Individual reflection and individual valuation by allocating seven points (sticky dots) to the project ideas.

DECISION-MAKING PROCESS

The following illustration depicts the decision-making process. The ideas will first be passed on to the International Scientific Advisory Board for its opinion. Subsequently, the Rectorate shall make the final decision, and the three funded projects will be decided on and publicized.

Each of the best three projects will be awarded 10,000 euros in seed funding to enable an application to be submitted. Additionally, a further grant of 10,000 euros is planned for the first project to be developed in the framework of Future Space which secures third-party funding.



PARTICIPATING RESEARCHERS

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- **Field of Work:**
  Optimization and Modelling in Magnetic Resonance Imaging

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- **Research Interests:** Functional Near-Infrared Spectroscopy (fNIRS)

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- **Field of Work:**
  Genetics and Transcriptomics
- **Research Interests:**
  PoC Diagnostics

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- **Field of Work:**
  - Magnetic Resonance Imaging (MRI)
  - Magnetic properties of tissue
  - Temperature and Fixation Effects on MR parameters
  - Postmortem Imaging
  - MRI of neurodegenerative diseases
  - SQUID magnetometry of biological tissue

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Medical University of Graz

- **Field of Work:**
  Proteomics, Biochemistry
- **Thematic Priorities:**
  Metabolism, Lipids, Enzymes, Protein regulation, Protein function, Proteins
- **Research Interests:**
  Metabolism in health and disease

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- **Field of Work:**
  conduct of clinical studies (Clinical Research Center)

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- **Field of Work:**
  Cancer Biology of lymphoid malignancies
- **Thematic Priorities:**
  Functional and comprehensive analysis of various gene with tumro suppressive or oncogenetic propertiers

Valentina Di Biase, PhD.
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- **Field of Work:**
  My field of research is cellular neurobiology. In particular, I study the cell biology of voltage gated calcium channel in neuronal environment. My working model is primary culture of murine hippocampal neurons. The techniques of analysis are live fluorescence microscopy, immunolabeling and molecular engineering.

- **Thematic Priorities:**
  My research focuses on the modes of formation, regulation, and trafficking of the signaling complexes including calcium channels subunits and regulatory receptors. Furthermore, I am interested in the regulatory mechanisms underlying synaptic scaling and axonal elongation.
- **Research Interests:**
  I am particularly interested in molecular mechanisms of the neurodegenerative diseases in the central nervous system, calcium signaling, synaptogenesis, and neuronal development.

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Institute of Molecular Biosciences
University of Graz

- **Field of Work:**
  Ageing, Autophagy, Cell Death
- **Thematic Priorities:**
  Regulation of Autophagy during Ageing, Influence of microbiota on autophagy and ageing in model organisms
- **Research Interests:** Crosstalk of microbiota with host cell function/ Influence of microbiota and microbiota-derived metabolites on host (cell) metabolomes

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Medical University of Graz

- **Field of Work:**
  Molecular and cellular physiology, cell biology, molecular biology and biotechnology
- **Thematic Priorities:**

Development and application of genetically encoded fluorescent biosensors for high-throughput high-content screening

- **Research Interests:**
  nano biotechnology, protein isolation, purification, immobilization technologies. enzymology, development of tools and devices for high-throughput high-content screening

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- **Field of Work:**
  Pharmaceutical Engineering

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Medical University of Graz

- **Field of Work:**
  Nanotoxicology, Microscopy, FACS
- **Research Interests:**
  Biological (toxicity) testing of new products

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- **Field of Work:**
  Cancer research
- **Thematic Priorities:**
  My work is focused in understanding the molecular mechanisms of invasion of neuroendocrine tumours.
- **Research Interests:**
  Neuroendocrine tumours, metalloproteases, invasion, angiogenesis, tumour spheroid culture, chick chorioallantoic membrane assay

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- **Field of Work/ Thematic Priorities/ Research Interests:**
  microbiome research

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- **Field of Work:**
  - protein-lipid interactions
  - ion channels
  - optogenetics

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Center for Medical Research (ZMF); Core Facility Computational Bioanalytics
Medical University of Graz

- **Field of Work:**
  The Core Facility Computational Bioanalytics provides technical support and consultation to scientific and clinical investigators in the field of biostatistics and bioinformatics.
- **Thematic Priorities:**
  Application of cutting-edge methods for integrated analysis of multiple -omics datasets
- **Research Interests:**
  microbiome research, biomarker identification and variant classification studies

---

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  Microbiome and Metagenomics

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- **Field of Work:**
  Occupational Health Promotion

- **Thematic Priorities:**
  Effects of factors at the work environment and social factors of the workplace on physical and mental health of employees.
- **Research Interests:**
  Leadership and health, especially possible projects which include the application of technical solutions in the occupational health promotion (e.g. web portals, apps).

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- **Thematic Priorities:**
  tissue regeneration

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Institute of Mathematics and Scientific Computing
University of Graz

- **Field of Work:**
  modelling and optimization
- **Thematic Priorities:**
  - Mathematical modelling of biological processes
  - modelling and optimization of measurement processes in the fields of biology and medicine
- **Research Interests:**
  application of modern mathematical methods and modells in the fields of biology and medicine

---

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- **Field of Work:**
  Allergies; Bacterial Conjugation in G+ Bacteria; DNA-transfer;
- **Thematic Priorities:**
  - Allergies: The structure of allergens and structure based epitope-mapping
  - Bacterial Conjugation in G+ Bacteria:
    Structure and function of a type IV secretion system (T4SS) in G+ bacteria; in particular we are working on the T4SS of the broad host range plasmid pIP501 and the pheromone plasmid pCF10, both found in pathogenic Enterococci (e.g. E. faecalis and E. faecis)

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- **Field of Work**:

Infection Biology/Molecular Biology

- **Thematic Priorities:** My special interest is directed towards pathogens and commensals which exhibit the ability to cause disease, either in certain niches or under specific conditions, and how these pathogens interact and subsequently influence their (human) host cells. The main focus of my research in recent years has been to establish model systems and investigate the interplay of bacterial communities in complex environments and their impact on mammalian hosts. On the bacterial side, I am especially interested in Campylobacter species, Helicobacter pylori and Klebsiella oxytoca. On the host side, I am mainly using the mouse as a model system.
- **Research areas:** molecular biology, genetic engeneering, microbiota/microbiome research, and immunology

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- **Field of Work:**
  Lipidomics & Metabolomics

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- **Field of Work:**
  My background is in environmental ecology, microbiology and genetics. I am interested in the microbiome research: the membership and function of microbial communities, particularly in human body, but also in different environments, such as in our immediate surroundings like indoor air, to as far as space. I am interested in how the microbes are transferred between environment and human host, how they influence and interact with their environment, and how they survive in different habitats.
- **Thematic Priorities:**
  My major scientific interests include studying the membership and function of diverse microbial communities in human body and in our environment. It has been shown that both the environmental biodiversity and our own microbiome can have a significant effect on our health, and that there is interaction between these two, but the mechanisms are largely unknown. My main aim is to study the human microbiome and specific microbial groups (e.g. Archaea) in relation to certain diseases, and also the interaction between environmental microbes and human microbiome in different contexts (e.g. in intensive care unit environment).
- **Research Interests:**
  I am interested in finding new cross-disciplinary collaborations in microbiome research.

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Medical University of Graz

- **Field of Work:**
  Lipid and energy metabolism
- **Thematic Priorities:**
  Consequences of conditional or global lack of enzymes on tissue and systemic lipid and energy metabolism

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- **Field of Work:**
  Leukemic stem cells and drug resistance
- **Thematic Priorities:**
  The TP53 gene plays a major role in acute myeloid leukemogenesis as somatically acquired mutations in this gene confer an exceedingly adverse prognosis. We are testing the hypothesis that these events occur in (pre-) leukemic stem cells by employing in-vitro assays and in-vivo mouse models. Furthermore, we aim at identifying pathways mediating resistance to conventional therapies. These approaches may allow the development of more efficent targeted therapies - a personalized approach enabling improved survival in this patient cohort.
- **Research Interests:**
  - Cancer and leukemia stem cell
  - in-vivo mouse models
  - drug resistance
  - expression analysis
  - bioinformatics

Christian Langkammer, Dipl.-Ing. Dr.techn.
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- **Field of Work:**
  MRI
- **Thematic Priorities:**
  Neuro and postmortem MRI

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Medical University of Graz

- **Field of Work:**

ion channel research, protein purification, rekonstitution of membrane proteins in artificial lipid bilayer, lipid-protein interactions, optopharmacology

- **Thematic Priorities:**

Gating mechanisms and optical control of cation channels in heart and brain
Reasearch interests: neuronal functions and cell preparations, mouse behavioral tests (fear memory), optogenetics, cryo-electron microscopy, X-ray crystallography

---

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- **Field of Work:**
  - Cognitive Neuroscience - research focusing on neurological diseases and functional and structural MRI
  - Neuropsychology - assessment of cognitive status
- **Thematic Priorities:**
  Alzheimer's disease affects functional and cognitive performance, and consequently daily life. Emerging deficits can be assessed with various established procedures (e.g. Consortium to Establish a Registry for Alzheimer's disease (CERAD) – Plus, or the Clinical Dementia Rating (CDR)) portraying the patient's status. However, the underlying cerebral neuro-pathological substrates are insufficiently understood. Due to the impact on patients, family members and caregivers the prediction of cognitive and functional decline is desirable. Hence, we focus on the identification of biomarkers for the prediction of cognitive and clinical deterioration in Alzheimer's disease using functional (resting state networks) and structural micro- and macroscopic brain imaging.
- **Research Interests:**
  Mathematical/bio-statistical models for longitudinal data analysis

---

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Medical University of Graz

- **Field of Work:**
  My particular interest is microbiome research, which means that I am trying to understand the thousands of microbes we interact with – their function, diversity and role. We analyze the microbiome of different environments, including extraordinary natural biotopes, indoor environments, such as clean rooms, intensive care units and the International Space Station, plants and the human body. The microbiomes are tremendously influenced by biotope changes – with severe impact on human health and well-being.
- **Thematic Priorities:**
  - I am particularly interested in microorganisms which are overseen by standard methods, but might have important roles – such as Archaea, which thrive in the human gut and on our skin. We currently try to understand their distribution and their function.
  - We are also experts in the cultivation of “complicated” microorganisms. Microbial cultures are important to correlate genome information with function. However, it is currently well accepted, that only 1% of all microbes of a certain biotope can be cultivated in the laboratory. With our methods, including cultivation under anoxic conditions, we try to push the border.
  - We also want to understand, which parameters affect a microbiome- and how a microbiome affects the human body. Is it possible to “control” the human microbiome?
  - We are also interested in the microbiome transfer: how are microorganisms transported, which resistances do they need to survive, when and how do they manifest in a new biotope? Is it true, that everything (all microbes) is everywhere, but the environment selects, as Lourens Baas Becking has hypothesized about 100 years ago?
- **Research Interests:**
  - I am highly interested in all techniques and methods that might be helpful to pursue our research, which includes microbial cell sorting (single cell sorting), genomic analysis, OMICS, imaging techniques, bioinformatics…
  - Generally, we are seeking interdisciplinary collaborators, which help us to extend our perspective and raise novel questions in the field of microbiome research.

Maximilian Mora, MSc.
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Department of Internal Medicine
Medical University of Graz

- **Field of Work:**
  I am a microbiologist focusing on the investigation and comparison of different indoor microbiomes via cultivation and molecular analysis. At our laboratory at the ZMF, we are well equipped for aerobic and anaerobic cultivation of microorganisms under regular and extreme conditions and have the methods and know-how to isolate DNA also from low-biomass (e.g. environmental) samples for further applications, as e.g. (real time-)PCR or next generation sequencing.
- **Thematic Priorities:**
  With my projects, I would like to understand the impact of the indoor-microbiome on the biotope itself, and also the persons working and living in these areas. To analyse this interaction, we focus on restricted indoor environments, such as the international space station (ISS) or the intensive care unit here at the Medical University of Graz (ICU-project).
  The ISS and related clean-rooms are investigated in the frame of the ARBEX project (ARchaeal and Bacterial EXtremophiles onboard the ISS). ARBEX deals mainly with the detection and investigation of microorganisms yet unknown to exist onboard the ISS. Additionally, we will compare the ISS microbiome with clean-room ground controls to tackle the question whether the microbes have adapted to a life in space. This project is expected to deliver important information for planning and conduction of future long-term space missions as well as for space-travel related health issues of astronauts.
  The main goal of the ICU-project is to investigate the microbiomes of the indoor area and the housed patients in order to evaluate the interplay between the human and the ICU-indoor-microbiome. We aim to identify and/or exclude possible infection routes within the ICU which may result in an improved treatment of ICU patients in future.
- **Research Interests:**
  I am open towards any input/comments regarding the mentioned projects and also possible future collaborations. For the mentioned projects I would be particularly interested in ways to e.g. model or graphically display the facilities, possible airflow and/or infection routes.

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- **Field of Work:**
  - Biochemistry
  - Structural biology
- **Thematic Priorities:**
  Structure-function relationships of proteins

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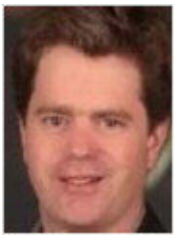

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University of Graz

- **Field of Work:**
  Membrane Biophysics
- **Thematic Priorities:**
  Research is focused on physical principles that pertain to the function of biological membranes with the aim to aid the development of specific membrane active compounds (peptides). For example we are studying the role of physical properties of membrane domains (rafts) in protein (ion channels, receptors) sorting and functioning, effects of the aqueous environment (pH, ion specificity, etc.), or the elastic response of membranes to peptide insertion. The approach involves a broad selection of biophysical techniques, such as small angle x-ray (neutron) scattering, calorimetry, or fluorescence microscopy to name but a few.
- **Research Interests:**
  - Lipid Analytics & Synthesis
  - Lipids in Disease
  - Drug / Cell Interactions

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Institute of Physiology
Medical University of Graz

- **Field of Work:**
  - machine learning
  - probabilistic modeling
  - speech/audio processing
  - signal processing
  - computer science
- **Thematic Priorities:**
  - Early recognition of cognitive disorders in infants,
  - basic research of early development of infants using pattern recognition and probabilistic modeling tools

Alexandra Perras, MSc.
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Department of Internal Medicine
Medical University of Graz

- **Field of Work:**
  To assess the habitability of foreign planets like Mars requires knowledge about life and its limit on a more accessible place- the Earth.
  In a joint activity of several institutes all over Europe, the MASE project (Mars Analogues for Space Exploration) establishes a sample collection of anaerobic (non- oxygen utilizing) microorganisms from Mars similar habitats. The isolated microbes (Archaea and Bacteria) will be subjected to environmental stresses to test their limits of growth and tolerance.
  Samples of several Mars analogues sites e.g. cold marshes and lakes, subsurface environments and

permafrost settings are currently undergoing an anoxic isolation and cultivation process. Interestingly, most obtained isolates are close relatives to pathogenic microbes (i.e. *C. botulinum, Yersinia sp.*), which can cause severe diseases in humans. Information on microbes living in extreme environments compared to information about closely related human pathogens might answer the question, how human-associated microbes evolve their capability to survive in extreme niches and establish the human body as final host. In conclusion, this knowledge will not only deliver a better understanding of pathogens but can also be the key to control their viability and pathogenicity.

- **Thematic Priorities:**
  - Anaerobic cultivation of extreme microorganisms
  - Retrieving valuable information about the evolution of pathogens via bioinformatics (e.g. genomics, metagenomics)
  - Retrieving valuable information about the limit of life via stress tests

  Not only pathogens, but high valuable microorganisms can be detected in Mars similar environments. The cell surface appendages, "hami" of a so-far uncultivated archaeon ("Candidatus *Altiarchaeon hamiconexum*") are ordered in an unseen, complex barbed-wire reminiscent filament ending in a nano-grappling hook. These structures are constructed from one major, self-assembling protein species and are considered to be highly useful in bionanotechnology. The protein is currently in progress of recombinant expression in a suitable host system.
- **Research Interests:**
  - Recombinant protein expression of archaeal cell surface appendages and their biochemical investigation
  - Assessing new tools for nanotechnology

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- **Field of Work:** Magnetic Resonance Imaging

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Daniela Pinter, Mag. Dr.rer.nat.
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Division of General Neurology
Medical University of Graz

- **Field of Work:**
  - Neuroplasticity
  - Stroke
  - Multiple sclerosis (MS)
  - Rehabilitation

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Institute of Physiology
Medical University of Graz

- **Field of Work:**
  Computational Physiology, Pattern Recognition
- **Thematic Priorities:**
  Early detection of neurodevelopmental disorders

Ruth Prassl, Assoz. Prof. Univ.-Doz. Dr. (BioTechMed-Graz Spokesperson)
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Florian Prüller, Priv.-Doz. Dr. Dr.med.univ.
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Clinical Institute of Medical and Chemical Laboratory Diagnostics
Medical University of Graz

- **Field of Work:**
  Coagulation, Platelet Function Testing
- **Thematic Priorities:**
  Improvement of coagulation assays

Gerald Rechberger, Mag. Dr.rer.nat.
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- **Field of Work:**
  - Biochemical analysis
  - Lipid analytics

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University of Graz

- **Field of Work:**
  Mathematical Optimization and Applications in Biomedical Sciences
  (SFB Mobis)

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Institute of Molecular Biology and Biochemistry
Medical University of Graz

- **Thematic Priorities:**
  Our lab studies molecular and cellular mechanisms that induce altered brain lipid homeostasis. Our current research focuses on identifying pathways that result in the generation of bioactive lipids in response to inflammation-associated oxidative and chlorinating stress. We aim to characterize downstream signaling effects on cells constituting the neurovascular unit, in particular brain microvascular endothelial cells and microglia. We integrate animal models, slice and primary cell cultures, and biochemical/analytical techniques to address these questions in biologically valid model systems. A thorough understanding of these pathways could foster the development of new pharmacotherapeutic strategies in neurological diseases where lipid homeostasis is compromised.

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Institute of Medical Engineering
Graz University of Technology

- **Field of Work:**
  Medical imaging, magnetic resonance imaging
- **Thematic Priorities:**
  development of new mechanisms for MRI contrast agents, nuclear quadrupole spectroscopy
- **Research Interests:**
  nanoparticles, material sciences, characterisation of particles and surfaces, targeting

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Anne Schienle, Univ.-Prof. Dr.rer.nat.
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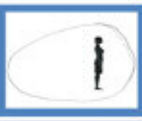
Institute of Psychology
University of Graz

- **Field of Work:**
  Affective Neuroscience (Head of the Department of Clinical Psychology & Clinical Outpatient Clinic 'PsyAmb')
- **Research Interests:**
  Investigation of altered affective processes in mental (neurological) disorders via fMRI and EEG, e.g.,
  - Enhanced reward sensitivity in eating disorders (e.g., binge eating disorder)
  - Elevated disgust proneness in anxiety disorders (e.g., spider phobia, blood phobia)
  - Neuronal correlates of successful psychological interventions (e.g., psychotherapy, placebo administration)
- **Future Research/Cooperation:**
  - Additional biological approaches/ markers
  - 'new' disorders

Representative research/ publications

	Schienle et al. (in press) Effects of personal space intrusion in affective contexts: an fMRI investigation with women suffering from borderline personality disorder. Social Cognitive and Affective Neuroscience
	Schienle et al. (2014). Disgust regulation via placebo: an fMRI study. Social, Cognitive and Affective Neuroscience, 9, 985-990.
	Schienle et al. (2013). Sex differences in the functional and structural neuroanatomy of dental phobia. Brain Structure and Function, 218, 779-787.
	Leutgeb & Schienle (2012). Successful exposure therapy leads to enhanced late frontal positivity in 8- to 13-year-old spider phobic girls. Biological Psychology, 90, 97-104.
	Schienle et al. (2009). Binge-eating disorder: reward sensitivity and brain activation to images of food. Biological Psychiatry. 65, 654-61.

Caroline Schober-Trummler, Mag.
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Institute of Molecular Biosciences
University of Graz

- **Field of Work/Thematic Priorities/Research Interests:**
  Caroline Schober-Trummler is a biochemist and molecular biologist with a track record in management. As a Marketing and Change Management Consultant she worked on industrial minerals projects in the USA and China. After almost a decade of managing large research consortia and program project grants at the University of Graz she became the Manager of the Institute of Molecular Biosciences in 2011. There she manages the institute's finances and administration and coordinates research grants and networks. Moreover, she helps coordinate the special research area Molecular Enzymology and Physiology and is active in several networks including BioTechMed-Graz and NAWI Graz.
  Her professional focus is on streamlining administration and management processes in order to create the most favorable conditions for the scientists. Additionally, she "translates" between scientists on the one side and the media, the public and companies on the other to promote both public relation work and cooperation with industry partners. Caroline Schober-Trummler acts as a bridge to funding agencies, university officials and international collaborators. A key issue is the strategic development of the molecular biosciences in Graz. She currently supports scientists in the fields of energy metabolism, aging research, infection biology, structural biology and biophysics.

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Maria Sensen, M.Sc. PhD
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Graz University of Technology

- **Field of Work:**
  The cases of Inflammatory bowel diseases are constantly increasing in the developed countries as well as other part of the world. Among the causes of the disease there are genetic mutations, environmental factors, but infection(s) cannot be excluded either. For long time the Mycobacterium paratuberculosis was a candidate, but recently MAP is regarded as more a consequence than a cause of the problem. Other possible candidate(s) should be identified.
- **Thematic Priorities:**
  Molecular Biomedicine:
  - human gut microbiome in relation to inflammatory bowel diseases
  - changes of the microbiota of Clostridium difficile patient after fecal transplant treatment
- **Research Interests:**
  Diet, medical treatments like antibiotics, travel, diseases etc. can result in changes of the microbial palette of the gut microbiome. By using next generation sequencing we can follow the changes of the composition of the microbiome on a rough scale, but we have no information what is the pathogenicity level of the actual microbiome.
  Recently it became available a method to study the methylation level of the microbiome which has a relationship to the virulence status.
  By comparing the methylation status of the microbiome before and after Fecal transplant treatment, we could gain more information of the healthy versus pathogen level of the gut.

Heinz Sill, Univ.-Prof. Dr.med.univ.
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Division of Hematology
Medical University of Graz

- **Field of Work:**
  Translational Research in Leukemia
- **Thematic Priorities:**
  Pathogenetic signalling as potential targets for innovative therapies
- **Research Interests:**
  - Acute myeloid leukemia
  - Oncogenic signaling
  - Mechanisms of drug resistance

- Development of targeted therapies

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Institute of Molecular Biosciences
University of Graz

- **Thematic Priorities:**
  Mimicking of neurodegenerative diseases in various model organisms, and unravelling of underlying molecular mechanisms thereof.
- **Research Interests:**
  Neurodegeneration, neuroscience and related novel technologies/methodologies, in order to gain a more extensive insight into complex disease biology (i.e. metabolic, proteomic or systemic approaches).

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Oksana Tehlivets, Dr.rer.nat.
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- **Field of Work:**
  We are interested in the elucidation of the pathological mechanisms triggered by S-adenosyl-L-homocysteine (AdoHcy) accumulation. AdoHcy is an inhibitor of S-adenosyl-L-methionine (AdoMet)-dependent methylation. Deficiency of AdoHcy catabolism in humans leads to severe pathological consequences. Also a common pathological condition, hyperhomocysteinemia, exhibits the accumulation of AdoHcy that has been proven to be more sensitive marker than homocysteine for cardiovascular afflictions.
  Phospholipid methylation consumes the major amount of AdoMet both in yeast as well as in mammals. Its inhibition results in the accumulation of neutral lipids, but can also interfere with the membrane function, since phosphatidylcholine synthesized via phospholipid methylation displays higher levels of unsaturated fatty acids. In order to understand this and other mechanisms induced by AdoHcy accumulation we use, under application of biochemical, genetic and molecular biological methods, yeast as an experimental model.
- **Thematic Priorities:**
  S-adenosyl-L-methionine, S-adenosyl-L-homocysteine, methylation deficiency, hyperhomocysteinemia, lipotoxicity, deficient phospholipid methylation, ER dysfunction, regulation of fatty acid metabolism

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Working Group Bioinformatics of the Institute of Knowledge Discovery
Graz University of Technology

- **Field of Work:**
  Bioinformatics and Biostatistics
- **Thematic Priorities:**
  - Analysis of Next Generation Sequencing Data (genome assembly, RNA-seq, Bisulfite-seq, Chip-seq, RAD-seq, dRNA-seq, transcriptome sequencing)
  - Analysis of Mass Spectrometry Data from Metabolomics (Lipidomics) studies
  - Integrative Analysis of OMICS Data
- **Research Interests:**
  Microbiome Modeling

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Center for Medical Research
Medical University of Graz

- **Field of Work:**
  bioinformatics
- **Thematic Priorities:**
  NGS, data analysis, microbiome, genome variant analysis
- **Research Interests:**
  NGS

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- **Field of Work:**
  - Nutritional Assessment
  - Body Composition
  - Metabolic Perturbation Tests
- **Thematic Priorities:**
  - Energy Sensing
  - Dysfunctional and Eating Disorders
  - Body Fat Topography
  - Early Nutrition Strategies
- **Research Interests:**
  - Nutrition, Lifestyle and Genes
  - Nutrigenomics of Food
  - Nutritional Systems Biology

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- **Field of Work:**
  - Human nutrition and metabolism
  - Biomarkers for health claim support
  - Bioactive food compounds
  - Healthy aging

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University of Graz

- **Field of Work:**
  Molecular and cellular biology
- **Thematic Priorities:**
  Organelle remodeling / lipid metabolism
- **Research Interests:**
  Cellular imaging

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- **Field of Work:**
  Brain-Computer-Interfaces

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Research Center Pharmaceutical Engineering (RCPE)
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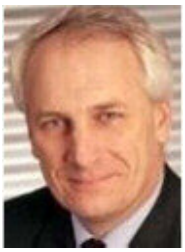
- **Field of Work:**
  In silico modelling of oral and inhalation products.
- **Thematic Priorities:**
  Biopharmaceutics
- **Research Interests:**
  Biopharmaceutics, Molecular biomedicine, in vitro bioanalysis



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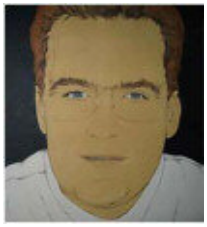

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