Program

2nd CABMM Symposium
Thursday, November 17th, 2011
University of Zurich Centre, K02-F-152

12:30-12:45	**Welcome** Prof. Dr. Brigitte von Rechenberg, University of Zurich, Switzerland

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Session 1: CABMM start-up grants

12:45-13:30	"Writing a research grant application and some notes on its review". Prof. em. Dr. A. Robin Poole, McGill University, Montreal, Canada
13:30-14:00	"Role of serine protease HtrA1 in spinal disc degeneration" Dr. Peter Richards, University of Zurich, Switzerland
14:00-14:15	*Coffee Break*

Session 2:

14:15-15:15	**Keynote Lecture** "From the nuclear periphery to cell adhesion by cryo-electron tomography" Prof. Dr. Ohad Medalia, University of Zurich, Switzerland
15:15-15:45	„Chromatin-Immunoprecipitation Changes Chromatin Composition by Inducing Poly(ADP-Ribosyl)ation" Dr. Sascha Beneke, University of Zurich, Switzerland
15:45-16:00	*Coffee Break*

Session 3:

16:00-16:45	**Keynote Lecture** "Osteoporosis and clinical problems" Prof. Dr. Michael Blauth, University Hospital Innsbruck, Austria
16:45-17:15	"The potential of a novel vascular target for myocardial infarction prevention" Dr. Chad Brokopp, University Hospital Zurich, Switzerland
17:15-17:45	"Intervertebral disc Regeneration – Fact or Fiction" Prof. Dr. Benjamin Gantenbein, University of Bern, Switzerland

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17:45-18:00	**Concluding Remarks** Prof. Dr. Brigitte von Rechenberg, University of Zurich, Switzerland
18:00	*Apéro*

1) „Writing a reasearch grant application and some notes on IST review“

Prof. em. Dr. A. Robin Poole
Mc Gill University, Montreal, Canada

For research to be conducted it is necessary for it to be funded. This usually results from submission of an application for research funding and its successful peer review. In this presentation I will provide some personal insights into how best to write this application and how it is reviewed.
We will discuss the topic, its relevance, importance and feasibility. The latter usually relies on preliminary data demonstrating the likelihood of the research's successful outcome based on the hypothesis, how it will be tested, preliminary data, the researcher(s) abilities and track record(s) and other resources, be they human or otherwise. Budgets must be realistic and well justified.
In peer review we will look at how an application is reviewed which is determined to a large degree by the applicant's ability to write a compelling proposal.

2) „Role of serine protease HtrA1 in spinal disc degeneration“

Dr. Peter Richards
University of Zurich, Switzerland

Degeneration of the intervertebral disc (IVD) is now regarded as being one of the major causes of low back pain (LBP), which is a highly prevalent, debilitating and costly disorder. The pathogenesis of degeneration is a highly complex and poorly understood process with many different genetic, biological and mechanical influences playing key roles in the breakdown of extracellular matrix (ECM) components. In the current study, we used tissue and cell samples from patients with varying degrees of disc degeneration in order to investigate the potential involvement of the serine protease HtrA1 in disc disease.

3) „From the nuclear periphery to cell adhesion by cryo-electron tomography”

Prof. Dr. Ohad Medalia
University of Zurich, Switzerland

Visualization of the three-dimensional (3-D) organization of a eukaryotic cell, with its dynamic organelles, cytoskeletal structures, and distinct protein complexes in their native context, requires a non-invasive imaging technique of high resolution combined with a method of arresting cellular elements in their momentary state of function. Vitrification of cells ensures close-to-life preservation of the molecular

architecture of actin networks and organelles. With the advent of automated electron tomography it has becomes possible to obtain tomographic data sets of frozen hydrated specimen. By electron tomography 3-D information from large pleomorphous structures, such as cell organelles or whole cells, can be retrieved with 'molecular resolution'. At that resolution it becomes possible to detect and identify specific macromolecular complexes on the basis of their structural signature. Here we employed cryo-electron tomography to eukaryotic cells grown directly on an EM grid. We have analyzed unlabeled cellular structures within intact eukaryotic cells by cryo-electron tomography. I will discuss our analysis of the nuclear periphery and the cell adhesion machinery.

4) „Chromatin-Immunoprecipitation Changes Chromatin Composition by Inducing Poly(ADP-Ribosyl)ation"

Dr. Sascha Beneke*
University of Zurich, Switzerland

Chromatin-immunoprecipitation (ChIP) employs a mild formaldehyde cross-linking step, which is followed by isolation of specific protein-DNA complexes and subsequent PCR testing to analyze DNA-protein interactions. Posttranslational modifications are involved in almost all cellular functions, especially in orchestrating multifactorial processes as repair, replication, transcription, and cell death regulation. These modifications also regulate chromatin composition and epigenetic events such as imprinting. In immunofluorescence experiments, we noticed formation of a specific posttranslational modification after formaldehyde-fixation of undamaged cells, which we could trace back to artificial induction of DNA damage signaling. To analyze this finding in more detail, we investigated the relationship between fixation, induction of this modification, and binding of transcription factors to their respective elements in different promoters in ChIP experiments. Compared to standard ChIP procedures, we noticed changes in promoter occupancy dependent on the transcription factor and the respective binding-element if formation of the posttranslational modification was suppressed. Our data provide evidence that the standard ChIP method itself produces changes in chromatin composition by inducing DNA damage and signaling events related to this.

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5) „Osteoporosis and clinical problems“

Prof. Dr. Michael Blauth
University Hospital Innsbruck, Austria

Osteoporosis is considered to be a serious public health concern, where 30% of all postmenopausal women have osteoporosis in the United States and in Europe. At least 40% of these women and 15-30% of men will sustain one or more fragility fractures in their remaining lifetime. An initial fracture is a major risk factor for a new fracture. An increased risk of 86% for any fracture has been demonstrated in people that have already sustained a fracture. Economic burden of osteoporotic fractures in Europe is significantly underestimated. Co-morbidities are present in every patient, therefore interdisciplinary and –professional approach is of paramount importance.
Goal: restoration of quality of life.
How to quantify local osteoporosis?
Osteoporosis deteriorates implant anchorage. DEXA is not available in acute fracture situation. In the AOTrauma Clinical Priority Program Fracture Fixation in Osteoporotic Bone several methods – image based and with the help of specific instruments – have been developed and tested. They allow for quantification of local bone quality. Clinical studies demonstrated that osteoporosis is one factor among others that may lead to failures. Each anatomical site has to be looked upon differently. In addition, based on a risk profile and local bone measurement, prophylactic surgical measures to prevent future fractures may be justified.
How to fix fragility fractures?
Implants: Angular stability, blades and augmentation increase implant-bone contact area and improve the purchase of implants significantly. Biological effects of augmentation as well as optimal material distribution are currently under evaluation.
Techniques: Functional reduction and relative stability without stress concentration with minimal invasive techniques, impaction as well as long splinting constructs address the reduced bone quality in meta- and diaphyseal fractures.
Metabolism: Correction of any metabolic issues
Prevention: Treatment of the underlying osteoporosis

6) „The potential of a novel vascular target for mycardial infarction prevention“

Dr. Chad Brokopp
University Hospital Zurich, Switzerland

Heart attacks and strokes currently kill more people every year than cancer and HIV combined. These diseases are caused by atherosclerosis; the formation of so called “plaques” in the arteries. Fibroblast Activation Protein (FAP) is a serine protease known to contribute to arthritis and inflammatory

liver disease; both of which are governed by similar inflammatory mechanis ms as atherosclerosis. Studies will be presented, which reveal that FAP is activated by inflammation in potentially life-threatening unstable atherosclerotic plaques, and also contributes to plaque destabilization and accelerated blood coagulation; the central triggers of myocardial infarction and stroke. These findings may draw attention to FAP as a novel target for myocardial infarction and stroke prevention strategies.

7) „Intervertebral disc Regeneration – Fact or Fiction“

Prof. Dr. Benjamin Gantenbein
University of Bern, Switzerland

Low back pain has been associated with intervertebral disc (IVD) degeneration and/or trauma. The IVD is the largest avascular organ of the human body and is under various mechanical loads. The etiology how epigenetic IVD pathology (e.g. herniation, collapse) evolves is still unclear. The focus of current tissue engineering is to regenerate or repair the IVD by stem cell therapy in combination with “smart” biomaterials.
However, these regenerative methods might only work if knowledge is improved on the interplay of mechano-biological and physiological factors in a healthy disc.
There is currently no ideal animal model system, which mimics the bipedality of the human spine. However, in vitro organ culture system of coccygeal large animal IVDs under controlled mechano-biological parameters is an appealing approach, where for instance complex interactions between endogenous disc cells and transplanted exogenous stem cells can be studied under clinically relevant conditions.
The main focus of the ARTORG Spine Research Center (SRC) is to understand the mechanisms of the development of disc herniation and how complex loading (e.g. 2 degree of freedom, compression and torsion) can lead to IVD failure. To achieve this, an in vitro organ culture loading device of IVD for complex loading is about to be finalized.
A second focus is the investigation into how adult bone marrow derived mesenchymal stem cells can be differentiated in vitro into disc cell precursors to achieve better outcome in terms of cell viability and remodeling for cell therapy.
A third focus is the investigation of feasibility of hydrogel-injection for nucleus pulposus repair.
Finally, new diagnostic tools need to be identified to predict patient-suitability for a biological treatment since not all stages of disc degeneration maybe suitable for biological therapies.