Beutenberg Campus /LGSA Workshop

Method and Concept Transfer

10th June 2010 13:00 – onwards

Lecture Hall, Abbe Center Beutenberg

The aim of this workshop is to inspire interdisciplinary cooperation and networking. The presentations can either have a **methodological** or a **conceptual approach**. The idea is to establish contacts between scientists with complementary skills and needs.

Organisers: Dr. Susanne Erland, Beutenberg Campus & Dr. Claudia Müller, LGSA

PROGRAM :

13:00 **Prof. Dr. Hartmut Bartelt** (Chairman of Beutenberg Campus Jena e.V.)
WELCOME ADDRESS and Chair of sessions

Session 1:

13:10 **Prof. Dr. Thorsten Heinzel** (CMB)
Lysine acetylation as a molecular switch

13:35 **PD Dr. Roland Zell** (IVAT)
Evolution of swine influenza viruses

14:00 **Sven Dahms** (FLI)
Subdomains of the Amyloid Precursor Protein (APP) fall into place - Crystal structure and biochemical analysis of its E1-domain.

14:25 *Coffee Break*

Session 2:

14:45 **Dr. Robert Möller** (IPHT) *Campus Award Winner 2010*
Metallic nanoparticles and nanostructures for bioanalytics

15:10 **Dr. Aleš Svatoš** (MPI-CE)
Mass spectrometric imaging of small molecules

Session 3:

15.35 **POSTERS** *with Refreshments*

Evolution of swine influenza viruses

Roland Zell

Institute of Virology and Antiviral Therapy, Jena University Hospital – Friedrich Schiller University Jena. e-mail: Roland.Zell[at]med.uni-jena.de

Influenza A virus (FLUAV) is an important human and animal pathogen. The FLUAV host spectrum includes birds, pigs, humans and some other mammalian species. Sixteen hemagglutinin (HA) and nine neuraminidase (NA) genes allow the formation of up to 144 different subtypes, of which at least 110 have already been described in aquatic birds, the main reservoir hosts. FLUAVs circulating in humans comprise the H1N1 and H3N2 subtypes and are the causative agents of seasonal influenza.
Swine FLUAVs belong to different genetic lineages. *Classical swine* H1N1 influenza viruses were first observed during the great influenza pandemic of 1918. Since then, these viruses circulate in North American pigs but were also isolated sporadically in Europe and Asia. After 1997, novel triple reassortants of the H3N2, H1N2, H2N3, H3N1, and H1N1 subtypes emerged in the USA and Canada with gene segments of *classical swine*, avian and human viruses.
Eurasian swine FLUAVs belong to genetic lineages different from the American viruses. In Europe, porcine H1N1 strains isolated since 1979 are *avian-like* as all segments derived from an avian virus. In 1984, reassortment of an *avian-like* H1N1 FLUAV and a human A/Port Chalmers/1/73-like virus yielded a *human-like* swine H3N2 strain with the HA and NA genes originating from the human virus and all segments encoding the internal proteins still being *avian-like*. Furthermore, a *human-like* swine H1N2 triple reassortant emerged in 1994 after reassortment of an European swine FLUAV with human H1N1 and H3N2 strains. Although European swine FLUAVs and reassortant progeny strains also emerged in Hong Kong and other Asian countries, they became prevalent only in the European pig population. Sequencing of numerous German isolates revealed the mechanisms driving the evolution of swine influenza viruses. Due to their ability to cause zoonotic infections, swine influenza viruses have a pandemic potential. The virus of the 2009 H1N1 pandemic was derived from gene segments of an Eurasian swine FLUAV and a North American triple reassortant. Prior to the pandemic, other novel genotypes of zoonotic FLUAVs emerged in 2004 and 2005 in Thailand and the Philippines.

Subdomains of the Amyloid Precursor Protein (APP) fall into place - Crystal structure and biochemical analysis of its E1-domain.

Sven O. Dahms, Sandra Hoefgen, Dirk Roeser, Bernhard Schlott, Karl-Heinz Gührs, and Manuel E. Than

Leibniz Institute for Age Research – Fritz Lipmann Institute (FLI), Jena
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Alzheimer's disease (AD) is the most frequent dementia worldwide occurring predominantly in the elderly population. The amyloid precursor protein (APP) is the key player in AD pathology caused by its abnormal proteolytic processing by the α-, β- and γ-secretases leading to excessive overproduction of neurotoxic Aβ peptide species. On the other hand transmembrane APP and its analogues are essential for neuronal development and cell homeostasis in mammals. We have extensively investigated structural and biochemical properties of a recombinant protein corresponding to the N-terminal 190 amino acids of APP. Using protein crystallography, the central method employed in our laboratory, we solved its structure at 2.7 Å resolution. These data show for the first time how the growth-factor like and the copper binding domains of APP interact together forming one closed conformational and functional entity, the heparin binding domain E1. The rigidity of the inter-domain association proves to be pH dependent in limited proteolysis and the resulting interaction interface includes evolutionary highly conserved residues. In addition, heparin derived dodecasaccharides induced in an endothermic and pH dependent process heparin-bridged APP-E1-dimers characterized by low micromolar binding constants. Limited proteolysis experiments in presence and absence of heparin enabled us to model the heparin $[APP\ E1]_2$ complex based on a dimer contact observed in our crystals. These results shed new light on the function of APP in cell signalling and cell-surface interactions, arguing that APP might fulfil different functions depending on its (sub)cellular localization and its oligomerization state.

Blennow et al. (2006) Alzheimer's disease. Lancet 368:387–403
Dahms et al. (2010) Structure and biochemical analysis of the heparin-induced E1 dimer of the amyloid precursor protein. Proc Natl Acad Sci U S A 107 (12): 5381-6

Metallic nanoparticles and nanostructures for bioanalytics

Robert Möller

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The need for simple and efficient detection of DNA or protein molecules with a high sensitivity has been motivating the development of detection techniques especially in the last decade. Methods based on nanoparticle labeling are one promising candidate offering a plethora of readout principles. Through the use of specific metal enhancement techniques impressive signal amplifications can be achieved, allowing the highly sensitive detection of biomolecules. Although often aimed at point-of-care application, these technical developments are also promising for routine applications in many fields in life sciences, because the requirements such as robust assays, ease of use and cost-efficient readout devices are important factors for their widespread application.

Metal nanoparticles combine the compatibility with the molecular world as demonstrated in decades of experiences in the use as labels for light and electron microscopy with the potential for different detection principles that often require not more than quite simple technical equipment compared e.g. to the optical setup in the case of fluorescence. The use of metal nanoparticles is also supported by a highly established biofunctionalization strategy. On the detection side, optical or other effects can be used for the realization of readout schemes.

For the construction of a robust and cost efficient detection scheme a detection system has been developed that relies on a simple measurement of the electrical conductivity on a chip. Through the low equipment cost and the robustness of the system it is well suited for the on site detection of biomolecules. Currently the system is adapted for the detection of plant pathogens and epizootic diseases.

To realize high multiplexing metallic nanoparticles can also be used. When using surface enhanced Raman spectroscopy metallic nanoparticles or nanostructures enhance the intrinsically weak but highly specific Raman signal, allowing the application of the detection scheme in a variety of different applications.

1) Moller et al., Nano Letters, 2005, 5(7), 1475-1482

2) Schüler et al., Biosensors and Bioelectronics, 2009, 24 (7), 2077-2084.

3) Hering et al., Analytical and Bioanalytical Chemistry, 2008, 390(1), 113-124.

Mass spectrometric imaging of small molecules

Aleš Svatoš

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Small molecules are defined as low molecular weight organic compounds (with a typical MW < 1000 Da) which could be both natural and artificial. Natural small molecules (such as secondary metabolites) are produced during genetically controlled biochemical reactions, and they are crucial to organisms' survival.

The ability to visualize biological materials or tissue samples has long helped scientists to map the distribution of organs, organelles, and cells and thus better understand the principles of life. Most methods to date have relied on microscopy and different staining/labeling techniques. However, the imaged elements are observed indirectly and lack molecular specificity. To see a metabolite directly in tissue, scientists have recently developed alternative ways to visualize or image tissues or cells; these include observing the compound-specific vibration (spectroscopy, such as NMR, CARS) or directly measuring their mass by mass spectrometry (MSI). Together with the staining/labeling approach, these direct methods are forming a new dimension in imaging studies, but their implementation is still in its infancy.

Very recent advances in MSI technology have created a vast array of molecular imaging tools, and this paper is intended to disseminate those new possibilities to the wider scientific community. The advances will be portrayed using recent example of imaging small molecules from bacteria, plants and insects. Practical utility of MSI will be critically summarized and anticipated future development will be discussed.

Shroff *et. al.* (2008): *PNAS* 105, 6196-6201; Hölscher et al. (2009) *Plant J.* 60, 907-918; Kroiß *et al.* (2010) *Nat. Chem. Biol* 6, 261-263; Svatos (2010) *Trends in Biotech.* (In press).

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Posters

No	Titel	Main Presenter (bold)	Insitute	Contact
1	Characterization of mice with cell type-specific defects in the NF-kB transcription factors RelA and RelB	**Nico Andreas,** Marc Riemann, Falk Weih	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	andreas@fli-leibniz.de
2	High Resolution MicroComputer tomography for determination of bone architecture in transgenic mouse models for osteoporosis	**Susanne Ostermay**, Alexander Rauch, Ulrike Baschant, Jan Tuckermann	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	ostermay@fli-leibniz.de
3	Functional consequences of increased adult hippocampal neurogenesis after spreading depression and hippocampus dependent learning.	**Eileen Baum**	Jena School of Medicine, Department of Neurology	ebaum@fli-leibniz.de
4	Towards the Structure of Aprataxin	**Peter Bellstedt,** Henriette Kutscha, Marcus Heier, Thomas Seiboth, Oliver Ohlenschläger, Matthias Görlach	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	pbell@fli-leibniz.de
5	miR-155 stimulates translation of C/EBPbeta-LIP	**Anna Bremer**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	abremer@fli-leibniz.de
6	Human DHX9 forms and resolves G-quadruplexes	**Prasun Chakraborty**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	prasun@fli-leibniz.de
7	Structure and Biochemistry of the APP-E2 Domain	**Sven Dahms**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	sdahms@fli-leibniz.de
8	The human kinetochore and mitotic checkpoint: structure and function of the MCC	**Volker Döring,** Christian Hoischen, Stephan Diekmann	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	vdoering@fli-leibniz.de
9	Ezrin - gatekeeper in the activation of SOS and Ras	**Katja Geißler,** Tobias Sperka, Helen Morrison	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	kgeissler@fli-leibniz.de
10	Oxidation of FLT3 antagonist PTP, PTPRJ/DEP-1 facilitates FLT3-ITD mediated transformation in AML: A novel redox circuit in cancer cells	**Rinesh Godfrey**	Institute of Molecular Cell Biology, Friedrich Schiller University	rgodfreyz@yahoo.com
11	Fish in a dish - Analysis of markers for cellular senescence in the newly established primary cell culture model of *Nothobranchius furzeri*	**Michael Graf**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	mgraf@fli-leibniz.de
12	Alterations in leptin signaling in the central hypothyroid TRH-R1 knockout mouse	**Claudia Groba**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	cgroba@fli-leibniz.de
13	Expression, Purification and Refolding of the gamma-Secretase Component Nicastrin	**Sandra Höfgen,** Yvonne Schaub, Anja Hackbart, Manuel Than	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	shoefgen@fli-leibniz.de
14	The Phenotype of Aorta T cells from Aged ApoE-/- Mice Reveals Local Rather than Systemic Autoimmunity in Atherosclerosis	**Desheng Hu,** Sarajo Mohanta, Prasad Srikakulapu	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	dhu@fli-leibniz.de
15	Unscheduled expression of Cdc45 leads to replicative stress and DNA damage	**Carsten Köhler,** Helmut Pospiech and Frank Große	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	ckoehler@fli-leibniz.de
16	Development of an HTS compatible cell based assay to visualize gamma-secretase activity and NICD trafficking	**Andreas Krämer**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	akraemer@fli-leibniz.de
17	Modulation of adhesion signalling by HPV E6	**Yu-Chieh Lin**, Georg Schwanitz, Corinne Schlosser, Michaela Pes, Aspasia Ploubidou	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	yclin@fli-leibniz.de

18	Role of PI3-kinase isoforms in ischemic neuronal injury	**Beatrix Lippert**	Jena School of Medicine, Department of Neurology	beatrix.lippert@med.uni-jena.de
19	From Proteins to Cancer: the E6 Piece of the HPV Oncogenicity Puzzle	**Andre Mischo**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	amischo@fli-leibniz.de
20	Fine mapping of the color locus in F2 intercross between the short and long living Nothobranchius species	**Enoch Ng'oma,** Alessandro Cellerino	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	enoch@fli-leibniz.de
21	Do cancer cells mimic stem cells to be immortal?	**Laura Perucho Aznar**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	laura@fli-leibniz.de
22	Transcript catalog of Nothobranchius furzeri	**Andreas Petzold**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	
23	Cytokines in glucocorticoid induced osteoporosis	**Alexander Rauch**, Susanne Ostermay, Ulrike Baschant, Jan Tuckermann	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	arauch@fli-leibniz.de
24	Increasing *C.elegans* Stress Resistance and Extending Life Span by Mitochondrial Inhibitors	**Sebastian Schmeißer**	Institute of Nutritional Sciences, Friedrich Schiller University	schmeisser@fli-leibniz.de
25	Chromodomain helicases cooperate with HPV E7 to induce centrosome dysfunction	**David Schmid**t, Michaela Pes, Aspasia Ploubidou	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	dschmidt@fli-leibniz.de
26	High Content Screening & Analysis Unit	**Simone Tänzer**, Jana Hamann, David Schmidt, Aspasia Ploubidou	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	dschmidt@fli-leibniz.de
27	C/EBPb$^{\Delta uORF}$ mice mimic caloric restriction induced metabolic reprogramming	**Laura Zidek**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	lzidek@fli-leibniz.de
28	Searching for contact sensing pathways	**Ansgar Zoch**	Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)	azoch@fli-leibniz.de