



## **MOLECULES TO MIND**

A Joint Annual Meeting of the  
Union of the Swiss Societies for Experimental Research  
Swiss Society for Neuroscience  
Swiss Society of Biological Psychiatry

**February 17<sup>th</sup> to 19<sup>th</sup>, ETH Zürich Hönggerberg**

### **Organizing Committee**

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Kaspar Vogt

### **Meeting Coordination**

Katrin Peter

### **IT Support**

Rolf Moser

# PROGRAM OVERVIEW

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## THURSDAY, FEBRUARY 17<sup>th</sup>, 2005

08:30 -	10:00	Registration/Coffee
10:00 -	11:00	Plenary Lecture I (Ruedi Aebersold) (HPH G1)
11:00 -	11:30	Datablitz (HPH G1)
11:30 -	13:30	Lunch / Poster Presentations/Business meetings Roche Diagnostics workshop (HPH G4)
13:30 -	15:30	Symposia S01-S05 (HPH G1-5)
15:30 -	16:00	Coffee Break
16:00 -	16:45	Friedrich Miescher Award; Best Poster Awards (HPH G1)
16:45 -	17:45	Plenary Lecture II (Thomas Jenuwein) (HPH G1)
17:45 -		Apéro (Sponsor: City and Canton of Zurich)

## FRIDAY, FEBRUARY 18<sup>th</sup>, 2005

08:30 -	10:00	Registration/Coffee
10:00 -	11:00	Plenary Lecture III (Alexander Schier) (HPH G1)
11:00 -	11:30	Datablitz (HPH G1)
11:30 -	13:30	Lunch / Poster Presentations/Business meetings
13:30 -	15:30	Symposia S06-S10 (HPH G1-G5)
15:30 -	16:00	Coffee Break
16:00 -	16:30	SSAHE Morphology Prize; Best Poster Awards (HPH G1)
16:30 -	17:30	Plenary Lecture IV (Karel Svoboda) (HPH G1)
17:30 -		Apéro

## SATURDAY, FEBRUARY 19<sup>th</sup>, 2005

08:30 -	10:00	Registration/Coffee
10:00 -	11:00	Plenary Lecture V (Pietro Pietrini) (HPH G1)
11:00 -	11:30	Datablitz (HPH G1)
11:30 -	13:30	Lunch / Poster Presentations/Business meetings
13:30 -	15:00	SSN-SSBP joint Clinical Symposium; SSBP Young Investigator Award; SSN 2004 Best Publication Award; Best Poster Awards (HPH G1)
15:00 -	15:30	Coffee Break
15:30 -	16:00	Robert Bing-Prize (HPH G1)
16:00 -	17:00	Plenary Lecture VI (Helen Mayberg) (HPH G1)
17:00 -		Apéro (Sponsor: Swiss Academy of Medical Sciences)

## Plenary Lecture I: Ruedi Aebersold

Institute for Molecular Systems Biology, ETH Zurich, Switzerland  
and Institute for Systems Biology, Seattle, USA

### WHAT CAN PROTEOMICS AND SYSTEMS BIOLOGY DO FOR YOU, NOW AND IN THE FUTURE?

The goal of systems biology is the comprehensive analysis of biological systems as dynamic networks of interacting elements. Ultimately, it is expected that a theory of the structure and dynamics of such networks will be developed that will serve as the basis for the generation mathematical models of biological processes that accurately represent and predict the behavior of a system. However, these are long term goals and it can be asked how systems biology and the high throughput technologies that support it can impact biology and medicine on a shorter time frame.

Since most biological networks involve proteins, proteomics, the global analysis of the protein complement of a cell or tissue is a central element of systems biology. In this presentation we will discuss the current status of quantitative proteomics technologies and some of the resources that have emerged from the data they produce. We will also show with selected examples how quantitative proteomics can impact common types of experiments currently carried out in many biological research projects and discuss the challenges that remain to turn proteomics into a truly genomic science.

Aebersold R, et al., Mass spectrometry-based proteomics. *Nature*: 2003: 422 (6928):198-207.

Ranish JA et al., The study of macromolecular complexes by quantitative proteomics. *Nat Genet.* 2003 Mar;33(3):349-55.

Ranish JA et al., Identification of TFB5, a new component of general transcription and DNA repair factor IIH. *Nat Genet.* 2004 Jul;36(7):707-13.

Giglia-Mari G. et al., A new, tenth subunit of TFIIH is responsible for the DNA repair syndrome trichothiodystrophy group A. *Nat Genet.* 2004 Jul;36(7):714-9.

Desiere F. et al., Integration with the human genome of peptide sequences obtained by high-throughput mass spectrometry. *Genome Biol.* 2005;6(1):R9.

MacKay VL et al., Gene expression analyzed by high-resolution state array analysis and quantitative proteomics: response of yeast to mating pheromone. *Mol Cell Proteomics.* 2004 May;3(5):478-89.

## Plenary Lecture II: Thomas Jenuwein

Research Institute of Molecular Pathology (IMP), The Vienna Biocenter, Dr. Bohrgasse 7, A-1030 Vienna, Austria, e-mail: [jenuwein@imp.univie.ac.at](mailto:jenuwein@imp.univie.ac.at)

### THE EPIGENOME IN THE CONTEXT OF THE POST-GENOMIC ERA

The last years were highlighted by the landmark description of the genomes of many model organisms, including the human genome. These 'genome projects' have shown that more complex eukaryotic organisms (e.g. mammals) have a much bigger genome than less complex eukaryotes (e.g. flies), although the increased 'biocomplexity' is not reflected by an equivalent increase in the number of protein coding genes.

Mechanisms other than DNA sequence information have been adopted during evolution to better index and regulate the various developmental programmes and key regulatory processes, such as gene expression, chromosome segregation and cell division of eukaryotic genomes.

In the nuclei of almost all eukaryotic cells, genomic DNA is highly folded and compacted with histone and non-histone proteins in a dynamic polymer called chromatin. The discoveries that nucleosome remodelling machines and histone-modifying enzymes organise chromatin into accessible ('euchromatic') and inaccessible ('heterochromatic') configurations reveal epigenetic mechanisms that considerably extend the information potential of the genetic code. Thus, one genome can generate many - epigenomes -, as the fertilised egg progresses through development and translates its information into a multitude of cell fates. These epigenetic mechanisms are crucial for the function of most, if not all, chromatin-templated processes and link alterations in the chromatin structure to gene regulation, X inactivation, chromosome organization and genome stability. The implications of epigenetic research for human biology and disease, including stem cells, cancer and aging are far-reaching and will form a modern foundation to explore the chromatin template in a 'post-genomic' era.

## Plenary Lecture III: Alexander Schier

S. Caron, M. Choy, H. Knaut, D. Prober, A. Sagasti, and A.F. Schier

Developmental Genetics Program; Skirball Institute of Biomolecular Medicine  
Dept. of Cell Biology; New York University School of Medicine, New York, NY 10016

### SENSORY GANGLIA FORMATION

To understand the formation and function of circuits that are involved in nociception, we focus on the trigeminal sensory ganglion. Trigeminal sensory neurons assemble into precisely positioned, compact clusters, arborize the skin and sense thermal, mechanical and chemical stimuli. We will discuss data that suggests that (1) chemokine signaling assembles trigeminal sensory ganglia, (2) repulsive interactions self-organize the arborization pattern of trigeminal axons, and (3) a member of the TRPA family mediates chemical sensing.

## Plenary Lecture IV: Karel Svoboda

HHMI, CSHL, Cold Spring Harbor, NY 11724, USA

### EXPERIENCE-DEPENDENT STRUCTURAL PLASTICITY IN THE ADULT NEOCORTEX *IN VIVO*

Which neural elements are plastic in the neocortex, especially in response to novel sensory experience? Answers to these questions are fundamental to the mechanisms of plasticity and the memory capacity of the brain. Our approach has been to image structural dynamics *in vivo*. A breakthrough was the development of long-term (months) time-lapse imaging at the level of individual synapses in the *adult cortex* of transgenic mice together with retrospective serial-section electron microscopy (EM).

We find that the large-scale arborization of axons and dendrites is stable, but that neurons display a rich, cell-type specific, repertoire of micrometer-level structural plasticity of dendritic spines, axonal terminals, and axonal branch tips. By combining imaging of pre- and postsynaptic elements with EM microscopy and physiological analysis we are testing if synapse formation and elimination by spine growth and retraction underlie experience-dependent rewiring of neocortical circuits.

## Plenary Lecture V: Pietro Pietrini

Laboratory of Clinical Biochemistry and Molecular Biology, Pisa University, Italy

### TOWARDS AN IN VIVO BIOCHEMISTRY OF THE MIND AND... SOUL?

Until not so long ago psychiatric disorders were grossly subdivided into  $\text{\textcircled{O}}$ organic, and  $\text{\textcircled{O}}$ functional, according to whether there was a known brain structural alteration (e.g., dementia) or not (e.g., depression or schizophrenia). This simply reflected our inability to go beyond what could be visible to the naked eye in the brain (Pietrini, *Am J Psychiatry*, 160: 1907-8, 2003). Over the last thirty years, the constant growth of non-invasive methodologies for the in vivo functional exploration of the brain, including positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), has enabled scientists to examine biochemical correlates of neuronal/synaptic activity -- the basis of whatever action, perception, thought or feeling our brain may be capable of experiencing. While studies initially focused on the investigation of the neural correlates of relatively elementary perceptual or motor tasks, more elusive aspects of mental function, including emotions and their regulation, social behavior, moral discernment and even spirituality lately have begun to attract more and more attention. In our laboratory we have developed a series of studies aimed at understanding brain correlates of perception and processing of emotional and hurtful stimuli. When individuals are physically or morally hurt they enact behavioral responses finalized to overcome the painful condition. Such responses may include aggressive behavior and desire of revenge or, alternatively, forgiveness. Forgiveness occurs when a person, hurt by another person resulting in resentment, excuses the offender. We hypothesized that forgiving enables an individual to overcome more effectively a situation that would otherwise represent a major bio-psychological stress. Adapting a previously validated experimental set-up (Pietrini et al., *Am J Psychiatry*, 157:1772-1781, 2000), we designed an fMRI study to examine emotional and behavioral responses and brain activity associated with the imaginal process of giving or withholding forgiving in relation to the experience of hurtful events in healthy young individuals with no psychiatric morbidity. Overall activations were observed in extrastriate and striate visual cortex, intraparietal sulci, motor cortex, superior and middle temporal gyri, anterior cingulate, limbic areas, ventromedial prefrontal cortex, and orbitofrontal cortex. Specifically, the hurtful conditions showed increases in anterior middle frontal and ventral temporal cortices compared to the baseline control condition. The enactment of forgiving versus unforgiving was associated with different neural activity in the right medial, middle and superior frontal cortices, right amygdala, bilateral striatum, left anterior cingulate, bilateral posterior parietal cortices and cerebellum. Thus, imaginal evocation of emotionally relevant hurtful events followed by forgiving or not forgiving was associated with modulation of brain areas implicated in visual/semantic representation and imagery, and more anterior areas, such as frontal cortex, amygdala, anterior cingulate and striatum, that regulates emotional response, moral judgment, perception of physical and moral pain, mood and decision making processes. (Supported by Grant CFR-5103-John Templeton Foundation and, in part, by a Grant from Gio.I.A. Foundation, Italy).

## **Plenary Lecture VI: Helen S. Mayberg**

Emory University School of Medicine, Department of Psychiatry, Atlanta GA USA

### **TOWARDS A NEURAL SYSTEMS MODEL OF DEPRESSION: STRATEGIES USING FUNCTIONAL NEUROIMAGING**

Converging clinical, biochemical, post-mortem and neuroimaging evidence suggests that depression is unlikely a disease of a single brain region or neurotransmitter system. Rather, it is now generally viewed as a multidimensional, systems-level disorder affecting discrete but integrated pathways involving select cortical, subcortical and limbic sites and their related neurotransmitter and molecular mediators. From a neuroimaging perspective, foci of such 'network' dysfunction identified in the baseline depressed state are considered potential etiological abnormalities as well as sites of adaptive and maladaptive intrinsic compensatory processes, accommodating both the reported variations in pretreatment scan patterns and the well-recognized heterogeneity of depressive symptoms and pre-morbid functioning (i.e., mood, motor, cognitive, vegetative-circadian; neuroticism, early trauma). Treatments for depression can be similarly viewed within this limbic-cortical system framework, where different modes of treatment modulate specific regional targets result in a variety of complementary, adaptive chemical and molecular changes. The synchronized modulation of these dysfunctional cortical-limbic pathways is thus considered critical for illness remission, regardless of treatment modality, accommodating pharmacotherapy as well as cognitive and somatic interventions. Findings from converging studies of different depressed patient cohorts using a variety of functional neuroimaging methods (blood flow/glucose metabolism PET, BOLD fMRI) will be discussed in this context, emphasizing syndromal subtypes, illness and relapse risk markers, and treatment-specific response effects. Strategies to further characterize scan-pattern variability will be highlighted as a critical next step towards the eventual development of imaging-based clinical algorithms to optimize treatment selection in individual patients.