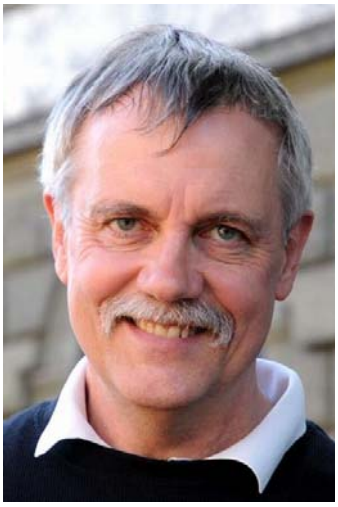
Department of Biochemistry



Fall 2014 Seminar Series
Beach Distinguished Lectures

Presented by

Ruedi Aebersold

Institute of Molecular Systems Biology
ETH Zurich

Monday and Tuesday, October 27 & 28, at 3:30

Deans Auditorium (PFEN 241)

Genotypic Variability and the Quantitative Proteotype

The question how genetic variability is translated into phenotypes is fundamental in biology and medicine. Powerful genomic technologies now determine genetic variability at a genomic level and at unprecedented speed, accuracy and (low) cost. To date, the effects of genomic variability on the expressed information of the cell has been mainly studied by transcript profiling.

In this presentation we will discuss emerging computational and quantitative proteomic technologies to relate genotypic variation to the proteome. Proteomic data to support such correlations need to be quantitatively accurate, highly reproducible across multiple measurements and samples, and generated at high throughput. Ideally, the data also would provide information about spatial arrangement of proteins in the cell. Data with these qualities can now be generated by the targeted proteomic methods selected reaction monitoring (SRM) and, at higher throughput, by SWATH-MS (1).

We will discuss the principles of these mass spectrometric methods, discuss the computational challenges they pose for data analysis, and demonstrate with selected applications, using genetic reference strain compendia, their ability to determine the effect of genetic variability on the quantitative proteome, thus functionally connecting the genome to the proteome (2,3).

Chemical Cross-Linking / Mass Spectrometry and the Structural Biology Toolbox

For various technical reasons, many molecular machines remain refractory to structural analysis by high-resolution methods. Emerging methods in structural mass spectrometry (MS), complementary structural biology techniques, particularly cryoEM, and computational data integration pose an exciting alternative to classical structural biology methods. They require relatively low sample amounts and have comparatively high measuring speed, and are generally referred to as hybrid structural methods.

In this presentation we will describe chemical cross-linking of native complexes and the mass spectrometric identification of the cross-linked residues as a mature, integrated technology to generate spatial proximity information native complexes (1). Differential analysis of two or more structural states of a complex, e.g. active or inactive conformation, also indicate subtle structural changes.

We will further describe applications of the technology to gain new insights into the organization of protein networks in the living cell (2) and to better understand the function of selected macromolecular assemblies (3). As this integrated technology is applicable to a wide range of complexes, we expect it to become an important component of the structural biology toolbox.

About the Beach Lectures:

David W. Beach was born in 1925 in London, England. Following service in the Royal Navy, he married Doris Holmes and began his career as a Chartered Accountant. Feeling the urge to expand his horizons, he moved to Canada and began a series of jobs in the aluminum industry that included General Manager of Kawneer, Canada and Vice-President of Kawneer, Inc. As Vice-President of ALUMAX Aluminum Corporation he was instrumental in making it one of the largest and most profitable aluminum companies in the world, prior to his retirement. Inspired by his son's enthusiasm for science, he has chosen to share his good fortune by supporting this biochemistry graduate program. This long-term support is intended to promote intellectual curiosity, a commitment to excellence, and an appreciation of science in all those involved.