

## **Linking Proteomics to Signalling Pathways and Diseases**

### **Speaker Bio**

Dr. Markus Ehrat is the managing director of Zeptosens, a division of Bayer (Schweiz) AG. Before Zeptosens was acquired by Bayer in February 2005, Dr. Ehrat was Chief Executive Officer and member of the board of Zeptosens AG, formed in March 1999. Dr. Ehrat organized the spin-off of Zeptosens from Novartis and founded Zeptosens together with seven other scientists. Zeptosens' focus is on research and development of high performance protein and gene microarrays and reader systems. For ultra-sensitive detection of binding events on microarrays, Zeptosens applies fluorescence excitation in evanescent fields, a project which Dr. Ehrat initiated while still employed at the BioAnalytical Research Department of Ciba-Geigy and later at Novartis Pharma AG in Basel, Switzerland. As head of this department, Dr. Ehrat was involved in the research and development of advanced analytical technologies such as MALDI-TOF MS, miniaturized analysis systems and optical sensor systems for life science and diagnostic applications. Dr. Ehrat has published numerous articles in peer-reviewed journals and has contributed to seventeen patent applications and patents.

### **Abstract**

Molecular signalling pathways are frequently triggered by extra-cellular molecules binding to receptors and activating relay systems inside cells, leading to processes that affect cellular behaviour and fate. For many genetic disorders a link between disease and signalling pathways has been established; consequently a systematic analysis of dynamic cellular networks provides an opportunity for pharmaceutical discovery, taking into consideration the complex biological context of drug targets, rather than observing the targets in isolation. Such analyses are, perhaps, ideally suited for a systems biology approach that integrates experimental data with computational modelling with the aims of discovering and validating new drug targets and biomarkers, as well as predicting potential “off target” effects of drug candidates.

A proteomics platform based on “reverse” protein arrays (RPA) is particularly suitable to monitoring cell-signalling events. These arrays are based on the principle that complex protein mixtures or proteomes (such as cell or tissue lysates) are spotted in an array format and probed with selected fluorescent antibodies in a multiplexed manner. To ensure high levels of sensitivity

and signal to noise ratio of these RPAs, we are using planar waveguide technology. The advantage of the evanescent field fluorescence detection ensures that only analyte-bound fluorescent antibodies contribute to the signal. Due to the high sensitivity and high throughput capability of the reverse protein array approach it will be feasible to obtain protein expression profiles and signalling pathway information on a wide variety of cell lines and tissue samples.

We will address selected applications including the elucidation of the dynamic aspects of pathway events and the profiling of compounds to reveal signalling and cross-pathway effects of drug candidates. In addition, analysis of healthy versus diseased tissue (including animal models) will provide insights into the pathways' underlying pathologies and provide a platform for molecular diagnostics.