Report on the conference:

7th SIENA MEETING

FROM GENOME TO PROTEOME: BACK TO THE FUTURE

September 3-7, 2006, Siena, Italy

The seventh annual Siena Meeting, From Genome to Proteome, once again took place in Siena, one of Italy' s most beautiful cities, situated in the center of Tuscany between the Chianti area and Maremma, rich in history, fine food, art and popular traditions. Clearly, the participants of the conference not only enjoyed the interesting talks presented, but also the impressive city.

The talks were divided in plenary sessions presented in the mornings and the parallel sessions in the afternoon. I will present some of my personnel highlights of the meeting.

Ruedi Aebersold from the Institute of Molecular Systems Biology, Zurich, Switzerland, presented in the first plenary session entitled *Systems Biology* his view on Quantitative Proteomics and Systems Biology. In his talk he nicely illustrated the concept and goals of Systems Biology. He then discussed the attempts to comprehensively analyze the proteome of eukaryotic cells, the challenges such projects face and he also outlined strategies to overcome them. Thereby he presented the PeptideAtlas, a project that has the long-term goal of full annotation of eukaryotic genomes through a thorough validation of expressed proteins.

In the second plenary session, entitled *Data Flow or Flood*, the speakers focused on the difficulty how to handle and validate large datasets. Friedrich Lottspeich from the MPI of Biochemistry, Martinsried, Germany, stated that one should not ignore the protein information. For quantitative proteomics, he presented a strategy that introduces a stable isotopic label named ICPL on the protein level. This has the advantage that proteins remain intact, all modifications still can be correlated with the proteins and the protein species can be separated by all well-established techniques whereas the correct quantification after cleaving the proteome into peptides becomes rather error prone.

The talk of R. G. Cooks from the Department of Chemistry, Purdue University, USA, in the *Imaging: From Organs to Proteins* session concerned ambient ionization using desorption electrospray ionization (DESI). It combines features of electrospray ionization (ESI) with those of the family of desorption ionization (DI). The sample is sprayed with charged microdroplets of water or a simple organic solvent and therefore the sample remains fully accessible to observation as well additional physical and chemical processing during the application. The technique should be suitable for the characterization of both large and small molecules. He presented data on ambient mass spectrometry for biomarker detection and tissue imaging where he analyzed biological samples, including proteins and lipids, on surfaces or in tissue without sample preparation. Among possible applications he demonstrated

tissue imaging with lipids as biomarkers to search for disease and in-vivo sampling of living tissue surfaces.

Among other speakers in the *From Single to Multiplexed Biomarkers* session Leigh Anderson from the Plasma Proteome Institute, Washington DC, USA, emphasized that as the study of protein biomarkers increases in importance, technical limitations in the detection of low abundance proteins and high precision quantitation remain to be overcome. To accomplish this, he is exploring the use of triple quadrupole mass spectrometry and synthetic stable isotope-labeled internal standards to quantitate signature peptides from panels of candidate plasma biomarkers, both directly in plasma digests and after enrichment using anti-peptide antibodies. He showed nice data from quantitative multiple reaction monitoring (MRM) assays for 47 medium-to-high abundance proteins directly in digests of plasma depleted of 6 major proteins with CV's ranging from 2-22% within run and reasonable sensitivity of <1µg/ml.

There were several interesting talks of the parallel sessions held in the afternoons. Definitively a highlight was the talk of P. G. Righetti from the Polytechnic of Milano, Italy, with the amusing title: Sherlock Holmes and the Proteome: A Detective story. He presented in a very entertaining way his revolutionary approach that consists in the "Protein Equalizer Technology", a method enabling the capture of all species present in proteome, but at much reduced protein concentration differences. This allows for the depletion of high abundant species and thereby bringing the "unseen proteome" within detection capabilities or it can be used vice versa to remove impurities.

Two other talks that I would like to mention are the ones of Bernd Wollscheid and Paola Picotti, both from the Institute of Molecular Systems Biology, Zurich, Switzerland. Bernd Wollscheid presented a method he recently developed named Cell Surface Capturing that allows for the mass spectrometry based identification and quantification of cell surface antigens. Using this technique, he identified more than 300 glycoproteins and glycosylation sites from cultured B and T cells. This method is in particular interesting to me since I am also using it for the detection and quantification of membrane bound glycoproteins. Paola Picotti touched a rather critical topic for people using proteomics. In her talk she reported her findings about proteolytic background, which seems to be an underestimated issue in shotgun proteomics. Her results showed an unexpected complexity of proteolytic digests, mainly due to the presence of numerous partly tryptic peptides. This issue becomes especially important if one increases the dynamic range and looks at low abundance species because the signals diminish in the proteolytic background.