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MEETING REPORT

Protein analysis of tissues—current views and clinical perspectives

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Abstract Proteomics raises high expectations in finding novel and reliable biomarkers for diagnosis, prognosis and therapy prediction. The goal of the 2-day workshop "Protein analysis of tissues—current views and clinical perspectives" was to bring together scientists from multiple areas of protein research interested in tissue analysis.

Keywords Proteomics · Molecular pathology · Meeting report

Much progress in tissue proteomics has been made for applications in basic sciences; translation of these methods for treatment of patients, however, is slow because the realities in the clinic are rarely taken into account and proteomic changes in cultured cell lines might not fully reflect human diseases due to the lack of the tissue (micro) environment. The goal of the 2-day workshop "Protein analysis of tissues" was to bring together scientists from multiple areas of protein research. The workshop was conceived by molecular and cell biologists, pathologists and protein scientists, supported by industry, the German Society of Protein Research and a Coordination Action funded by the European Union. A key strength of the meeting was that it combined lectures and practical aspects (wet lab courses).

Researchers from 12 European countries participated in the meeting. The fact that about 80% of the participants described themselves as primarily involved in protein analysis and only 20% were involved in histology indicated that pathologists may not be aware that there has been recent progress in protein studies—other than immunohistochemistry—in human tissues, including the use of samples stored for decades in huge archives in pathology departments.

Proteomics raises high expectations in finding novel and reliable biomarkers for diagnosis, prognosis and therapy prediction. H. Meyer (Bochum, Germany) presented data for the identification of biomarkers for liver cirrhosis using tissue microdissection, differential gel electrophoresis (DIGE) technology and mass spectrometry. Applications of laser microdissection, 2D-DIGE and matrix-assisted laser desorption/ionisation (MALDI) time-of-flight from heterogenous prostate carcinoma tissues in biomarker discovery were presented by S. Skvortsov (Innsbruck, Austria). F. Lottspeich (Martinried, Germany) presented results for the comparison of 2D-DIGE, Sypro-2D, and isotope-coded protein labelling for quantitative proteome analysis of brain tissues. H. Langen (Basel, Switzerland) explained in his talk why biomarker tests should be developed as "companion diagnostics" and escort the drug development at all stages (pharmacodiagnostic tests). This is crucial for the effective development and successful commercialisation of medicines and innovative drugs.

G. Schmidt (München, Germany) introduced an image analysis software platform for robust and fully automated means to extract quantitative information from tissues slide scans.

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Clinical tissues are typically formalin-fixed and paraffin-embedded (FFPE) for histopathological diagnosis. In order to shift diagnosis to prediction, novel tools are needed for precise protein measurements of FFPE tissues. The alternatives include the use of frozen tissues and the development of novel tissue fixatives. It is estimated that more than one billion FFPE tissue blocks exist worldwide. Many of those samples are connected to clinical data. Some lively debate at the conference focused on the use of FFPE tissues for protein analysis. KF Becker (Munich, Germany) and T. Geoui (Hilden, Germany) gave overviews about recently established methodologies for the suitability of FFPE tissue samples for protein studies. They focused on the extraction of full-length proteins from FFPE samples and the quantitative analysis of the extracted proteins using protein microarray technology. Other applications for FFPE tissues include mass spectrometry and 2D polyacrylamide gel electrophoresis.

T. Joos (Reutlingen, Germany) described applications and future challenges for protein microarrays. This technology is likely to evolve into a key technology for the characterisation of complex samples.

The almost complete absence of protein synthesis of platelets makes them ideal systems for protein studies. A. Sickmann (Dortmund, Germany) presented data on the identification of more than 2,500 proteins, more than 1,000 phosphorylation sites and more than 350 glycosylation sites. Using these data, the knowledge about platelet function will certainly benefit.

MALDI mass spectrometry has become a powerful tool in biological research, especially in proteomics. Recently, MALDI techniques were developed for direct tissue analysis and molecular imaging, allowing the detection and localisation of a large number of compounds directly from tissue sections in one acquisition. Unlike other visualisation techniques such as immunohistochemistry or fluorescence microscopy, so-called MALDI-IMAGING does not require a target-specific reagent (e.g. antibody) and, therefore, is a valuable discovery tool, since it can survey a broad range of proteins simultaneously. The advantage of maintaining the spatial location of proteins is critical in achieving a comprehensive analysis of heterogeneous tissue samples, such as cancers. S.O. Deininger (Bremen, Germany) and A. Walch (München, Germany) presented exciting novel data about the use of MALDI-IMAGING for tumour proteomics.

M. Ueffing presented data for the interactome of lebercilin, which is genetically linked to a severe form of blindness, Leber congenital amaulrosis. The interactome links this protein to the transport of vesicular cargo to the outer segment along ciliar structures.

One of the major health challenges of the twenty-first century is type 2 diabetes. H. Sarioglu (München, Germany) used liquid chromatography tandem mass spectrometry to identify 4,000 quantitative profiles of protein markers in a type 2 diabetes mouse model.

The second day of the workshop focussed on practical aspects of protein analysis from tissues. Protocols were provided and explained in detail for protein extraction from FFPE tissue samples and subsequent protein microarray analysis, MALDI-IMAGING, quantitative immunohistochemistry and quantitative approaches for mass spectrometry-based and gel-based proteomics. After a short theoretical introduction to each of the topics, participants were allowed to try some of the assays by themselves.

Because of the great success of the workshop, the organisers plan to repeat the meeting in 2011, hoping to attract more histology-oriented researchers.