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### Developing new tissue imaging methods for 2-D metabolomics

Metabolomics is becoming a widely used and important research field in functional genomics. Wet chemistry-based metabolomics typically involves homogenizing tissue samples and then extracting the metabolites prior to the measurements using analytical techniques such as chromatography and mass spectrometry (MS). In the wet chemistry-based metabolomics, the spatial information about the analytes within tissue specimens is lost. Tissue imaging, mainly using matrix-assisted laser desorption/ionization (MALDI)-MS, provides not only the relative quantitation of but also the spatial distribution patterns of dozens to hundreds of biological molecules directly from the surface of a thinly-cut tissue section. However, when applied to small molecule tissue imaging, MALDI-MS is subjected a few shortcomings such as the high background noises in the mass region for endogenous metabolite detection.

We have screened and evaluated a series of small molecules as potential MALDI matrixes for tissue imaging of endogenous metabolites in mammalian tissues by ultrahigh-resolution Fourier transform ion cyclotron resonance (FTICR) MS. We have discovered dithranol and a family of natural hydroxyl-flavone compounds that are suitable for MALDI tissue imaging of small-molecule metabolites and these matrixes are well compatible with the high source vacuum of an FTICR MS instrument. With dithranol, over 70 different lipid molecules were imaged from a single tissue section of mouse liver, heart or kidney. The results from bovine lens tissue imaging showed that acylcarnitines were uniquely localized to young fiber cells in the outer cortex region of bovine lens. Using poly-OH flavones as the MALDI matrixes, more than 160 lipids have been successfully imaged from a single tissue section and these MALDI matrixes showed significant advantages over several commonly-used MALDI matrixes. In addition, we also focused our effort on developing new techniques for quantitative tissue imaging. Such a method is to use MALDI-multiple reaction monitoring (MRM) on triple-quadrupole mass spectrometers for localization as well as absolute quantitation of the analytes directly from a tissue section. Our proof-of-concept experiment showed the feasibility of MALDI-MRM imaging for precise and accurate quantitation of proteins directly from rat brain tissue sections with a dynamic range of over 2 orders of magnitude. Further development of this technique will be promising for quantitative tissue imaging of metabolites as well.

#### Biography

Christoph H Borchers received his B.S., M.S. and Ph.D. from the University of Konstanz, Germany. After his post-doctoral training and employment as a staff scientist at NIEHS/NIH/RTP, in North Carolina, he became the director of the UNC-Duke Proteomics Facility and held a faculty position at the UNC Medical School in Chapel Hill, NC (2001-2006). Since then, Borchers has been employed at the University of Victoria (UVic), Canada and holds the current positions of Professor in the Department of Biochemistry and Microbiology and the Don and Eleanor Rix BC Leadership Chair in Biomedical and Environmental Proteomics. He is also the Director of the UVic-Genome BC Proteomics Centre, which is one out of five Genome Canada funded Science & Technology Innovation Centers and the only one devoted to proteomics. His research is centred around the improvement, development and application of proteomics technologies with a major focus on techniques for quantitative targeted proteomics for clinical diagnostics. Multiplexed LC-MRM-MS approaches and the immuno-MALDI (iMALDI) technique are of particular interest. Another focus of his research is on technology development and application of the combined approach of protein chemistry and mass spectrometry for structural proteomics. Dr. Borchers has published over 145 peer-reviewed papers in scientific journals and is the founder and CSO of two companies, Creative Molecules Inc., and MRM Proteomics Inc. He is also involved in promoting proteomic research and education through his function as HUPO International Council Member, Scientific Director of the BC Proteomics Network and President of the Canadian National Proteomics Network.

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