**Accelerating MultiModal Molecular Imaging: Innovations in structural elucidation.**

Ron M.A. Heeren

State-of-the-Art molecular imaging with MS now enable high resolution tissue screening that provides direct insight into tissue metabolism. Applications have penetrated various research domains from drug metabolism to the visualization of molecular signaling pathways in cancer. In this lecture we will demonstrate how mass spectrometry based multimodal molecular imaging can be used to reveal the cellular phenotypes. We will discuss the development and application of new MS based chemical microscopes that target biomedical tissue analysis in various diseases as well as other chemically complex surfaces. There is a clear need to add analytical structural separation utilizing ion mobility of gas phase ion chemistry. We will demonstrate how to elucidate the way in which local environments can influence molecular signaling pathways on various scales. The integration of this pathway information in a surgical setting is imminent, but innovations that push the boundaries of the technology and its application are still needed. The imaging MS community is driving translational molecular imaging research and these needed developments rapidly forward.

More and more researchers realize that a single technology provides only a subset of the molecular information needed to obtain an in depth understanding of a clinical problem. Multimodal approaches enable the study of clinical samples at a variety of molecular and spatial scales. The molecular complexity on the genome, proteome and metabolome level all needs to be taken into account. The distribution of several hundreds of molecules on the surface of complex (biological) surfaces can be determined directly in complementary imaging MS experiment with different desorption and ionization strategies. High throughput, high resolution MALDI techniques offer three dimensional molecular data on the tissue level. Ambient desorption and ionization techniques complement MALDI in their capabilities to reveal different molecular signatures that can be employed for direct tissue typing in molecular pathology. State-of-the-art molecular imaging mass spectrometry has evolved to bridge the gap between different disciplines such as MRI, PET, fluorescence imaging and histology. The combination with tools from structural biology makes it possible to perform imaging experiments at length scales from cells to patients