Simultaneous Imaging of Lipids and Proteins in Alzheimer's Disease using Time-Of-Light Secondary Ion Mass Spectrometry

Louise Carlred

Biological Physic, Dept. of Applied Physic, Chalmers University of Technology
Email: louise.carlred@chalmers.se

One method that can be used for molecular imaging of biological samples is Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS). With ToF-SIMS, specific fragments of the sample are created and collected in a mass spectrum, enabling for detection of hundreds of different molecules at the same time. By repeatedly collecting information from different pixels all over the sample, images showing the distribution of molecules of interest can be created with high spatial resolution (at submicrometer scale). This method has previously been proven to successfully visualize lipid distributions in mouse brain [1]. Proteins however, have been difficult to detect intact since they generally generate small nonspecific fragments. To extend this method to include lipids and proteins, this project is aiming to use specific antibody-conjugated liposomes to target proteins of interest. By using liposomes made of different kinds of deuterated lipids, the method will potentially be able to map many proteins in parallel at a sensitivity down to the single molecular level, while simultaneously mapping the lipid distribution. Similar liposomes have been used previously to detect single DNA molecules by ToF-SIMS [2].

The method will be applied to study the correlation between lipids and specific proteins involved in Alzheimer's disease (AD). AD is a neurodegenerative disease and the most common form of dementia in elderly people [3]. Two specific features associated with AD are the formation of amyloid beta (Aβ)-plaques and neurofibrillary tangles (NFT), respectively. The Aβ-plaques are extracellular aggregations consisting of a small peptide (Aβ), while the NFT are found inside the neurons and consist of aggregations of a protein called Tau. The generation of these features is not completely understood, although different risk factors have been identified. One of the main genetic risk factors is the gene encoding for apolipoprotein E ε4, which is involved in cholesterol transport in the brain. Additionally, high levels of cholesterol have been found to be involved in the generation and accumulation of Aβ-plaques [4]. To understand this complex interplay of biomolecules in the brain, new methods are needed. By using ToF-SIMS to simultaneously map lipids and proteins of interest, such as Aβ and Tau, our method opens up for new opportunities to investigate the biochemical processes involved in the generation of AD.

References

1. Sjövall, P., J. Lausmaa, and B. Johansson, Mass Spectrometric Imaging of Lipids in Brain Tissue. Analytical Chemistry, 2004. 76: p. 4271.
2. Gunnarsson, A., P. Sjo□vall, and F. Ho□o□k, Liposome-Based Chemical Barcodes for Single Molecule DNA Detection Using Imaging Mass Spectrometry. Nano Letters, 2010. 10(2): p. 732-737.
3. St.George-Hyslop, P., Piecing together Alzheimer´s. Scientific American, 2000.
4. Puglielli, L., R. Tanzi, and D. Kovacs, Alzheimer's disease: the cholesterol connection. Nature Reviews Neuroscience, 2003.