Imaging of metals in biological and clinical samples by use of LA-ICP-MS: challenges and limitations

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Cellular heterogeneity that arises from stochastic expression of genes, proteins and metabolites is a fundamental principle of cell biology, but metal analysis in cells and in particular in single cells has been beyond the capability of the quickly growing metallomic technology, and even the outstanding sensitivity of ICP-MS was not yet applied for single cell analysis.

In our research we want to measure and image the metal heterogeneity of essential elements (metals and hetero-elements) in single diseased or healthy cells together with a distribution of biomarkers (proteins) measured by use of LA-ICP-MS. Three different applications will be presented.

In the first example we have grown fibroblast cells on microscopic slides and after fixation we have ablated them by a scanning 213 nm laser ablation system with the smallest laser spot size of 4 (8) µm only. Interactions of nanoparticles (Au, Ag) with cells using different incubation concentrations and times together with natural element distributions in single cells were measured. First results will be presented, which demonstrate that we can image metal distributions with a single cell resolution capability. The discussion will focus on an unsolved problems related to the calibration of the results.

The next two examples are related to immunoassays, for which we also use LA-ICP-MS for imaging. For this purpose we have applied metal tagging of antibodies (medical biomarker) to measure protein expression in tissues and protein arrays and detection of tags by LA-ICP-MS.

This new method has been applied in our lab for detection of metal tags from these cancer biomarkers (HER 2, CK7, MUC 1) in medical thin cuts of breast cancer tissue samples and the local distribution of the tagging elements clearly demonstrate the multiplex capability of LA-ICP-MS. The results will be compared with conventional immunohistochemical staining techniques and an assessment will be given.

In the third example we have developed a multi element labelling strategy of antibodies for simultaneous detection by LA-ICP-MS of many different proteins (8) in a single immunoassay. For this purpose we have spotted protein extracts from rat liver on a nitrocellulose membrane. Rats have been treated with different chemicals and drugs to investigate the expression of CYP P450 enzymes, which are used by the body for detoxification. Hundreds of such protein spots on the array from various rat experiments were incubated with 8 differently labelled antibodies and all label metals were detected simultaneously by LA-ICP-MS. Using an internal standard allowed us to measure protein expression profiles of 8 different CYP P450 enzymes.

Quantification of trace metals in human hair samples by LA-ICP-MS will ultimately require analysis of individual strands or strand bundles collected from the human subject, or in the case of forensic applications, from a crime scene. Although Legrand et al. (2004) reported the potential use of single shot LA-ICP-MS for the detection of Hg in a single strand the method was not fully developed and no quantification was possible.Â The use of an Inductively Coupled Plasma Mass Spectrometer with a Laser Ablation system gives scientists versatility in application usage and biological sampling analysis. The method discussed above provides both accurate and precise concentration data.