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INTEGRATION OF PROTEOMICS WITH TRANSCRIPTOMICS AND METALLOMICS FOR THE STUDY OF ENVIRONMENTAL ISSUES

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Metal bound to biomolecules play important roles in living organisms. The identification of these metal-biomolecules in biological tissues can be performed by multidimensional methods combining orthogonal chromatographic with mass spectrometry and inductively coupled plasma mass spectrometry (ICP-MS): METALLOMICS. The integration of these analytical methods with the proteomic approach provides a powerful tool in deciphering environmental issues related to metal action. This integrated approach has an special interest when the genetic homology between model organisms and test or bioindicator organisms is demonstrated, because important conclusions can be drawn using model organisms as pattern in environmental and health studies based on non-model (non-sequenced) ones (1).

Present study is based on the use of *M. musculus* the best-known vertebrate model organism, and *M. spretus* the best characterized aboriginal species. Recently, *M. spretus* is being used as bioindicator in environmental pollution studies, through the use of different cytogenetic and biochemical biomarkers. Sequences of *Cyp* and *Gst* genes from *Mus musculus* were obtained from GenBank™. Designed primer pairs based on *M. musculus* amplified in *M. spretus* induce products exhibiting in most cases 100% nucleotide sequence identity with *M. musculus*. The application of 2-DE protein separation and high throughput MALDI-TOF-PMF analysis assess the biological effect of polluted terrestrial ecosystems on inhabitant *M. spretus* mice. Spot identification relied on peptide matching with available sequence databases from *M. musculus*. Remarkd differences are tested in the proteome of animals dwelling at different polluted environments, with specific increases and decreases in selected groups of proteins and changes that seem to be co-ordinately regulated.

For the first time the molecular size distribution patterns of elements in *Mus musculus* mice has been obtained using the SEC-UV-ICP-MS approach. The profiles of the elements obtained make possible deep insight into the interactions of elements with the different organs of *Mus musculus* as well as their possible connection with the metabolic pathways in this animal. ICP-MS allows multielement profiling in samples to be obtained in only one chromatographic run, which constitutes a reliable technique

with high throughput. A second chromatographic dimension on SEC-ICP-MS extracts using RP-HPLC-ICP-MS allows metallo-biomolecules purification and metal-species isolation for further identification by mass spectrometry techniques.

Therefore, the following conclusions can be drawn:

- A genetic homology between *Mus musculus* and *Mus spretus* has been established
- Modification of proteins expression in *Mus spretus* was defined in connection with differentially polluted ecosystems
- Metallomics allows high throughput metal-bound to proteins tracing in different tissues from *Mus musculus* and integration with proteomics and transcriptomics results can be drawn.

References: Gómez-Ariza, J.L., et al, Anal. Chim. Acta (2004) 524:15-22.

Acknowledgement: Ministerio de Educación y Ciencia. Grant: CTM2006-08960-C02-01.