

IDENTIFICATION OF PROTEIN BIOMARKERS FOR STROKE IN HUMAN MICRODIALYSATES: MS/MS-BASED PROTEIN QUANTITATION IN INFARCT CORE, PENUMBRA AND CONTROLATERAL BRAIN REGIONS USING ISOBARIC TAGGING

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Human cerebral microdialysis fluid of stroke patients *in vivo* provides a tremendous valuable sample source for the discovery of protein biomarkers associated to cerebrovascular diseases[1]. Quantitative analysis of microdialysates from the infarct core *versus* the penumbra or the controlateral brain region was carried out to identify such markers by shotgun proteomic methods.

The isobaric Tandem Mass Tag (TMT[®]) technology [2] was used in its duplex version to label digested extracts from two brain regions of four patients suffering from stroke. Following the labelling, the four pooled samples were fractionated either by strong-cationic exchange chromatography (SCX) or OFFGEL electrophoresis (OGE). The obtained fractions were analysed by liquid chromatography (LC) and matrix-assisted laser desorption tandem time-of-flight chromatography (MALDI TOF/TOF) mass spectrometry (MS). The identification and quantitation of proteins were assessed with stringent criteria.

The comparison of the microdialysates from the infarct core with those from the controlateral brain region provided the quantitation of 91 proteins and the comparison of the microdialysates from the infarct core with those from the penumbra brain region allowed the quantitation of 163 proteins. Respectively, 18 and 59 of these proteins were significantly increased (with a ration superior to 3) in the infarct core microdialysates compared to the controlateral and penumbra counterparts.

Proteins such as glial fibrillary acidic protein (GFAP), cystatin-C, heart and brain fatty acid-binding protein (H- and B-FABP) and protein S100-B have been reported for the diagnosis of stroke. In this study, they were shown to be increased in the infarct core microdialysate samples, showing the relevance of the achieved quantitative proteome map, prior further validation of protein marker candidates.

References:

1. Proteomics Clin. Appl. 2008, 2, 437-443
2. Anal. Chem. 2008, 80, 2921-2931