

## Identification of leptomeningeal metastasis-related proteins in cerebrospinal fluid of patients with breast cancer by a combination of MALDI-TOF, MALDI-FTICR and nanoLC-FTICR mass spectrometry

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Leptomeningeal metastasis (LM) is a devastating complication occurring in 5% of breast cancer patients. However, the current gold standard of diagnosis, namely microscopic examination of the cerebrospinal fluid (CSF), is false-negative in 25% of patients at the first lumbar puncture. In a previous study, we analyzed a set of 151 CSF samples (tryptic digests) by MALDI-TOF and detected peptide masses that were differentially expressed in breast cancer patients with LM. In the present study, we obtain for a limited number of samples exact masses for these peptides by MALDI-FTICR MS measurements. Identification of these peptides was performed by electrospray FTICR MS after separation by nano-scale LC. The database results were confirmed by targeted high mass accuracy measurements of the fragment ions in the FTICR cell. The combination of automated high-throughput MALDI-TOF measurements and analysis by FTICR MS leads to the identification of 17 peptides corresponding to 9 proteins. These include proteins that are operative in host-disease interaction, inflammation and immune defense (serotransferrin, alpha 1-antichymotrypsin, hemopexin, haptoglobin and transthyretin). Several of these proteins have been mentioned in the literature in relation to cancer. The identified proteins alpha1-antichymotrypsin and apolipoprotein E have been described in relation to Alzheimer's disease and brain cancer.

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