LC-MS serum proteomics reveals a panel of proteins prognostic of positive responsiveness to bevacizumab therapy in late-stages ovarian cancer patients

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Topic: *Prognostic and predictive biomarkers*

Associating changes in protein levels with the outcome of a specific chemotherapy has been a widely investigated strategy to identify clinically relevant diagnostic biomarkers of a therapy progression. For this purpose, the most powerful and straightforward tool is nowadays LC-HRMS (Liquid chromatography tandem High resolution Mass Spectrometry) based proteomics, that allows the identification and quantification of over thousands of proteins per sample without the need for labelling [1].

In particular, in our translational study we aimed to identity, quantify and cluster the circulating serum proteins from of a group of ovarian cancer patients at III/IV FIGO stage, after a cycle of traditional chemotherapy (175 mg/m^2 paclitaxel and AUC 5 carboplatin, IV) combined with the administration of a 15 mg/kg dose of Bevacizumab until tumour progression or 22 completed cycles (MITO16A/MaNGO-OV2 phase IV trial) [2].

We have analysed 31 patients' serum after therapy administration with LC-MS divided in therapy responders and non-responders, with a bottom up, label free proteomics protocol. Each serum aliquot was immunodepleted with affinity chromatography and digested into tryptic peptides, which were desalted and separated on a nano-LC online coupled to an Impact HD TM UHR-QqToF (Bruker Daltonics). Spectrometric data were processed with PEAKS Studio (Bioinformatic Solutions) to identify each peptide and reconstruct the proteomes, and an ANOVA one way test was applied for group comparison. Multimerin-1, Lactate dehydrogenase A, Flavin Reductase, Extracellular matrix protein 1, WD repeat-containing protein and Fibronectin 1 resulted differently expressed between the responder and the non-responder groups (FC> 1.5, p-value < 0.05). We have performed metadata analysis and network enrichment with STRING to evidence the whole metabolic pathways modulated by the above-mentioned proteins.

Next step will include data integration with data from previous clinical studies to enlarge the sample size, and a statistical analysis of the results of the ELISA assay performed to validate the levels of the above-mentioned proteins.

References:

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