Targeted Proteomics of Regulated Proteins Identified in Ovarian Cancer Tumor Fluid

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Introduction. Despite advances in cancer research, ovarian cancer has a high mortality and remains a major challenge due to a number of particularities, especially late diagnosis caused by vague clinical symptoms, the cellular and molecular heterogeneity of tumors and the lack of effective treatment. Different body samples have been used and tumor fluid has emerged as a rich source for the identification of biomarkers in the context of proteomics studies. **Objectives.** To contribute to the elucidation of new sets of ovarian cancer tumor markers, we combined hightroughput and targeted proteomic analysis to discover and verify panels of regulated proteins in ovarian tumor fluid samples. **Material and Methods.** We performed a quantitative proteomic study consisting of albumin immunodepletion, isotope labeling with acrylamide and in-depth proteomic profiling by LC-MS/MS in a pool of 10 tumor fluid samples high-grade serous ovarian tumor (malignant) and benign serous cystadenoma tumor. Based on this profile, we developed a panel for targeted proteomic analysis using the multiple reaction monitoring (MRM) method for verification of regulated proteins in undepleted individual samples. **Results and Discussion.** 1135 proteins were identified, corresponding to 505 gene products. 223 proteins presented associated quantification and the comparative analysis of malignant and benign tumor fluid pools revealed 75 regulated proteins. We confirmed by MRM method the regulation of 27 proteins out of 33 identified in the hightroughput analysis, and APOE (Apolipoprotein E), SERPINF2 (Alpha-2-Antiplasmin) and SERPING1(Plasma Protease C1 Inhibitor) were statistically significant between benign and malignant groups. The majority of the MRM data was concordant with hightroughput data, indicating that the mean of values observed for individuals in each group was in agreement with acrylamide isotopic ratio for pooled samples. **Conclusion.** This molecular signature can contribute to improve tumor stratification and shall be investigated in combination with current biomarkers in larger cohorts to improve ovarian cancer diagnosis.

Keywords: Ovarian Cancer, Tumor Fluid, Multiple Reaction Monitoring (MRM), Biomarkers, Hightroughput Proteomics.

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