Targeted Proteomic Method Development for Cancer Biomarkers Discovery

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INTRODUCTION: According the reports of World Health Organization, cancer is responsible for 13% of all deaths worldwide. The continuous populational growth and aging will affect significantly the number of cancer cases around the world mainly on the low and mid developed countries. Among all sorts of cancer, ovarian cancer correspond to the most lethal gynecological disease, representing the sixth most frequently neoplasia in women and contributing with 200,000 new cases every year. Therefore, new therapeutic and diagnostic approaches are urgent to decrease ovarian cancer mortality. **OBJECTIVES**: In order to contribute to the identification and validation of new protein-targets for ovarian cancer we aimed to develop a targeted proteomic method for analysis and validation of such targets in benign and malignant patient samples. **MATERIAL AND METHODS**: MRM (Multiple Reaction Monitoring) method was developed based on previous highthroughput proteomic data from ovarian serous carcinoma fluid pools (benign and malignant). We selected representative proteotypic standard peptides and synthesized them in isotope tagged format, which helped on MRM method development and sample quantification. A scheduled MRM method was refined based on standard peptide retention time using our UPLC system, as well as adjusting best mass transitions and their associated collision energy for our Xevo-TQs mass spectrometer. All these processes were aided by Skyline software, which also performed final data analysis and quantification. **DISCUSSION AND RESULTS**: We obtained a robust method within thirty minutes of chromatography to detect tagged and untagged peptides associated with twenty-two proteins-targets for ovarian cancer. After analysis of 20 patient samples, we identified the peptide representing SERPINF2 as statistically significant to discriminate malignant from benign patient. **CONCLUSION**: The targeted proteomic method allowed us to evaluate many protein-targets in ovarian cancer patient samples using a quick multiplex method that combines the efficiency of UPLC and sensibility of mass spectrometry.

Palavra chave: cancer, method, proteomic, MRM, mass spectrometry

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