PAP-SMEARS ALLOW THE IDENTIFICATION OF PROTEIN BIOMARKERS TO DIAGNOSE ENDOMETRIAL CANCER

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Introduction/Background* Endometrial cancer (EC) is the most common gynecological cancer in developed countries. There are no screening tools for its early diagnosis, and the diagnostic process starts with the appearance of related symptoms, mainly, abnormal vaginal bleeding (AVB). It is estimated that ~7M women with AVB will undergo the diagnostic process every year in Europe, and from those, 9% will have EC. Importantly, the current diagnostic process relies on the pathological examination of an endometrial biopsy that is always obtained by minimally-invasive to invasive methods. This overdiagnosis creates a big burden to the healthcare systems, so the development of non-invasive tools for EC diagnosis would revolutionize this scenario. Our aim is to approach a non-invasive diagnosis by the identification of protein biomarkers to accurately diagnose EC in liquid cervical cytologies.

Methodology The discovery phase consisted of a shotgun label-free proteomic approach. It included 60 patients (20 EC, 20 controls suffering AVB without endometrial or cervical pathology, and 20 controls without endometrial pathology but cervical pathology). The levels of a statistically significant set of 75 proteins (110 peptides) from the discovery phase were measured in a verification phase including 234 (107 non-EC; 127 EC) patients by LC-MSMS/PRM. Analysis was performed using MaxQuant, Skyline, SPSS and R software.

Results* The discovery study permitted to determine a total number of 2,888 proteins in our samples. Statistical analysis identified 75 potential proteins differently expressed between EC and non-EC patients to be further assessed and verified. Verification phase revealed the potential of 58 proteins measured in cervical cytologies to reach a non-invasive diagnosis of EC. Specifically, 16 proteins achieved an AUC > 0.75, and 3 proteins an AUC > 0.8. Additionally, an ELISA assay of the best performing protein was tested reproducing the results obtained by mass-spectrometry and reaching an AUC=0.927 in this dataset.

Conclusion* We identified protein biomarkers in liquid cervical cytologies to diagnose EC patients with a diagnostic power up to 92%. These results are promising for a subsequent development of an early and non-invasive screening tool for EC. This tool is expected to change the standard of care in EC diagnosis.