



## THE QUEST OF BIOMARKERS IN ENDOMETRIAL CANCER RESEARCH

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**Objectives:** Endometrial cancer (EC) diagnosis relies on the observation of tumor cells in endometrial biopsies obtained by aspiration (i.e., uterine aspirates), but it is associated with 22% undiagnosed patients and up to 50% of incorrectly assigned EC histotype and grade. We aimed to identify biomarker signatures in the fluid uterine aspirates to overcome these limitations.

**Methods/Patients/Interventions:** A deep literature review and an in-house developed workflow permitted us to identify 52 proteins with potential for EC diagnosis. The levels of those proteins were measured in the fluid fraction of uterine aspirates from two independent cohorts of patients of 38 and 116 patients by LC-PRM, the latest generation of targeted mass-spectrometry acquisition. A logistic regression model was used to assess the power of protein panels to differentiate between EC and non-EC patients and between EC histological subtypes. The robustness of the panels was assessed by the "leave-one-out" cross-validation procedure performed in the cohort of 116 patients and 38 patients.

**Results:** The levels of 28 proteins were significantly higher in EC patients (n=69) compared to controls (n=47). The combination of a 2-protein panel exhibited 94% sensitivity and 87% specificity for detecting EC cases. This panel perfectly complemented the standard diagnosis, achieving 100% of correct diagnosis in this dataset. Nine proteins were significantly increased in endometrioid EC (n=49) compared to serous EC (n=20). The combination of a 3 protein-panel achieved 95% sensitivity and 96% specificity for the discrimination of these subtypes.

**Conclusions:** We developed uterine aspirate-based signatures to diagnose EC and classify tumors in the most prevalent histological subtypes. This will improve diagnosis and assist in the prediction of the optimal surgical treatment.

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