TARGETED PROTEOMICS IDENTIFIES PROTEOMIC SIGNATURES IN LIQUID-BIOPSY OF THE ENDOMETRIUM TO DIAGNOSE ENDOMETRIAL CANCER AND ASSIST IN THE PREDICTION OF THE OPTIMAL SURGICAL TREATMENT

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INTRODUCTION

Diagnosis based on uterine aspirate samples is associated to a 22% of diagnostic failure due to insufficient cells in the sample. The pathological examination of uterine aspirates should also provide information about staging. Unfortunately, a high-interobserver variability in the pathological interpretation leads up to a 50% of incorrect preoperative staging.

WE AIM TO develop a molecular tool based on the assessment of protein biomarkers in the fluid fraction of uterine aspirates. This will contribute to:

1. Diagnose 100% patients with this biopsy
2. Reduce the number of more invasive hysteroscopies
3. Improve the preoperative staging of EC cases
4. Select the optimal surgical management for each patient

GENERAL WORKFLOW

Diagnostic biomarkers

The levels of 17 proteins were found statistically higher in EC cases compared to controls (adjusted p-value < 0.05, fold change > 2) with high specificity and sensitivity (AUC > 0.8) in both cohorts of patients: verification set (n=38) and validation set (n=107). Importantly, all these proteins enabled the detection of the EC cases in the initial stage IA with AUC >0.79.

Prognostic biomarkers

The combination of two proteins achieved an AUC of 0.96 in discriminating between EC and control patients.

RESULTS

CONCLUSIONS

The first protein of the panel has been previously transferred from MS to a more available technology in hospitals (i.e., ELISA assays), showing a very high correlation (R=0.93).

For this first protein, a faster electrochemical technique has been tested. This would enable the development of a point-of-care device.

Results in 1h

Less volume of sample and reagents needed

The combination of two proteins achieved an AUC of 0.96 in discriminating between EC and control patients.

- Uterine aspirates are an excellent source of protein biomarkers for gynecological diseases such as EC.
- High resolution mass spectrometry operated in PMF mode presents striking advantages for verification and validation phases of the biomarker pipeline in complex samples.
- Following our workflows, we have obtained signatures for EC diagnosis based on a 2-protein profile, and EC staging based on a 3-protein profile. Both have a high sensitivity and specificity.

The transferability of these results to ELISA has been accomplished for the first protein of the panel. This will allow for a faster and easier implementation of these results to the clinics.

A test based on these findings is expected to 1) improve early EC diagnosis by reducing the number of invasive tests currently in use, such as hysteroscopic; and 2) improve the preoperative staging of the EC cases, which will improve life expectancy whilst reducing comorbidities. Altogether, we will impact to reduce sanitary costs.