HIGH EXPRESSION OF FAP+ CANCER-ASSOCIATED FIBROBLASTS PREDICT POOR OUTCOME IN PATIENTS WITH HIGH-GRADE SEROUS OVARIAN CANCER WITH HIGH CD8-POSITIVE T-CELL INFILTRATION

Introduction/Background Tumor biology studies have implied that fibroblasts act as negative regulators of immune cell function in cancer. We investigated the impact of FAP-positive cells in high-grade serous ovarian cancer (HGSC) in relation to CD8 expression.

Methodology A discovery cohort (N=113) of HGSC was subjected to immunohistochemistry (IHC) of FAP and CD8. Marker status was correlated with overall survival (OS) and progression-free survival (PFS). Findings were confirmed in a validation cohort (N=121) and in public available datasets (TCGA and GSE9891).

Results We confirmed previous findings that high density of CD8+ cells in HGSC is associated with longer OS compared to low density (HR=0.55; 95% CI 0.33–0.85; p=0.008). In the discovery cohort high intensity of FAP was associated with shorter median PFS in cases with high density of stromal CD8+ cells (11.4 versus 18.6 months) compared to low intensity of FAP (p=0.007). In contrast, high intensity of FAP was not associated with PFS in cases with low density of CD8+ cells. In the validation cohort, high intensity of FAP in the patients with high density of stromal CD8+ cells was associated with shorter OS compared to low intensity of FAP (p=0.01). This association was not seen in the cases with low density of CD8+ cells. The association between high FAP expression and poor outcome in the high density CD8+ group was confirmed in two independent gene-expression data sets, with a shorter PFS in the TCGA dataset and shorter PFS and OS in the GSE9891 dataset.

Conclusion The study shows a specific FAP positive fibroblast-subset of cases with poor prognosis restricted to a CD8 high density group of HGSC. Therapy targeting the immunosuppressive action of fibroblasts may be a tool to enhance the known positive prognostic effect of CD8-cells in ovarian cancer and may be explored in T-cell depended immune therapy.

Validation of self-sampling use for a multiplexed biomarker assay for HPV and dysplasia detection

Introduction/Background The use of self-sampling in cervical cancer (CxCa) screening increases the number of participants and enables the inclusion of prior underscreened women in rural areas. For PCR and DNA-based testing self-sampling is as sensitive as physician-sampling. We compared self- and physician-sampling for analysis by QuantiGene-Molecular-Profiling-Histology assay (QG-MPH) to detect and grade cervical dysplasia in a triage setting.

Methodology Women with an equivocal screening result were recruited and a cervical sample (Cervex broom) was taken into ThinPrep/PreservCyt. Participants were asked to take a self-sample (Evalyn-Brush) and fill a questionnaire. Crude lysates were used for the QG-MPH assay. This multiplexed Luminex bead-based technology platform (QuantiGene 2.0) detects and quantifies the mRNA abundance of 18 Human Papillomavirus (HPV) genotype-specific oncogenes, reference genes and cellular biomarkers characterizing dysplasia stages, simultaneously. Formerly developed biomarker-based risk scores predict CIN2+, CIN3+, or CxCa.

Results Of 699 study participants, 601 performed self-sampling (85.9%). Invalid samples in QG-MPH was comparable between self- and physician-sampling with 16.1% and 14.9%, respectively. Of 132 histologically confirmed CIN3 lesions QG-MPH determined in the physician-taken sample 61.4% (n=81) as CIN3 or higher, 25.8% (n=34) as low-grade lesions, and 12.9% (n=17) were not evaluable. Of 109 self-samplers from CIN3 positive women QG-MPH determined 17.4% (n=19) as CIN3 or higher, 59.6% (n=65) as low-grade and 22.9% (n=25) were not evaluable. PCR-based HPV testing detected 78.2% of physician- and 74.9% of self-samples positive while QG-MPH 52.5% (n=315) and 32.3% (n=194), respectively. Concordance was 82.0% by PCR and 63.8% by QG-MPH.

Conclusion While cellularity of self-taken samples is sufficient for valid measurement by QG-MPH, less high-grade lesions and HPV-infections are detected. Optimization of cutoffs for the self-taken sample may improve the sensitivity. We hypothesize that ‘missed’ CIN3 by QG-MPH biomarker profiling may be non-progressor lesions. This will be investigated further.

MESENCHYMAL PROGNOSTIC SIGNATURE IN OVARIAN CANCER

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