Title: The role of SOCS3 gene in the pathogenesis of Epithelial Ovarian cancer.

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Introduction: Epithelial ovarian cancer (EOC) is the most lethal disease among gynecologic cancers worldwide, often associated with drug resistance and worst survival outcomes claiming thousands of lives each year. The survival rate of patients in advanced stage is lower than 25%, with very poor outcomes. Therefore, the detection of the disease in early stages and understanding the genetic pathways involved in the EOC pathogenesis are relevant for the identification of good predictable markers. Previous studies have reported the overexpression of the transcription factor *E2F5* in early stages of EOC, suggesting its putative role as a biological marker. *SOCS3* gene, a key regulator for JAK/STAT pathway, responsible for inflammation and proliferation response, was found to be regulated by *E2F5* and its down regulation seems to have a role in the pathogenesis of different tumors including gastric and pancreatic cancers.

Objectives: in this project, we aimed to investigate the involvement of *SOCS3* gene in EOC by monitoring its expression in ovarian cancer cell lines and EOC tissue samples, then compared results to normal ovarian tissue samples. We also examined methylation status of both, ovarian cell lines and ovarian tissue specimen.

Methods: Real time qPCR was used to assess gene expression using Taq Man gene expression assay. Five cell lines (MCAS, OVSAHO, OV 2008, A2780s and A2780cp) and 19 tissue samples with different histopathology types (6 normal, 4 benign, 5 borderlines and 4 high grade serous) were examined. Methylation status analysis was performed by methylation specific PCR.

Results: OVSAHO, OV2008 and A2780s cell lines showed down regulation of *SOCS3* expression when compared to normal. Benign, borderline and high grades samples, displayed also significant down regulation of *SOCS3* expression. Analysis of methylation pattern showed no hyper-methylation in both cell lines and tissues.

Conclusions: Down regulation of *SOCS3* gene expression was detected in ovarian cancer cell lines and EOC tissue samples, suggesting a putative role of *SOCS3* in the pathogenesis of EOC. Other epigenetics mechanisms such as micro-RNAs are involved in the regulation of *SOCS3* expression in addition to hyper-methylation and therefore, further study is needed to uncover these mechanisms.

References:

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