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Tubal origination of ovarian low-grade serous carcinoma: A gene expression profile study

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Background & Aim: Ovarian low-Grade Serous Carcinomas (LGSC) are thought to evolve in a step-wise fashion from Ovarian Epithelial Inclusions (OEI), Serous Cystadenomas (SC) and Serous Borderline Tumors (SBT). Our previous study showed that the majority OEIs are derived from the Fallopian Tubal Epithelia (FTE) rather than from Ovarian Surface Epithelia (OSE). This study was designed to gain further insight into the cellular origin of LGSC by differential gene expression profiling studies.

Methods: Gene expression profiles were studied in 44 samples including 11 LGSCs, 7 SBTs, 6 SCs, 6 OEIs, 7 FTEs and 6 OSEs. Correlation analyses of ovarian serous tumors including its precursor OEIs with FTE and OSE samples were performed by unsupervised hierarchical clustering. Rank-sum analyses and Pearson correlation tests were then applied to determine the likelihood of cellular origin of LGSC and its precursors. Final validation was done on selected genes and corresponding proteins.

Results: Gene expression profiles distinguish LGSC from OSE, but not from FTE cells. Furthermore, dendrograms produced by unsupervised hierarchical clustering showed ovarian serous tumors and OEIs were clustered closely in a branch, but separated from OSEs. After ascertaining the reliability of sequencing data, we found that OVGP1, WT-1 and FOM3 highly expressed in fallopian tube and OEI and ovarian serous tumors, but not in OSE. In contrast, ARX and FNC1 were mainly expressed in OSE, but not in other studied samples.

Conclusions: This study provides genetic profiling evidence that ovarian LGSC most likely originates from the fallopian tube rather than from ovarian surface epithelia. Similar gene expression profiles among fallopian tube and OEI and serous tumors further support that the majority of LGSC develops in a step-wise fashion. Such findings may have significant implications for "ovarian" cancer-prevention strategies.

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