Identification of a functional role for TOM40 and NP in ovarian cancer

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Purpose: The purpose of this study was to identify genes and proteins that are highly differentially expressed in epithelial ovarian cancer (EOC) cell lines, and to use this knowledge for the development of novel diagnostic and therapeutic markers for ovarian cancer.

Materials and Methods: We used Illumina microarray platforms to identify genes that were significantly differentially expressed between 6 EOC cell lines and 4 human ovarian surface epithelial cells (HOSEs). Using two-dimensional gel electrophoresis (2-DE) and MALDI-TOF/PMF protein profiling, we compared protein expression profiles between 3 EOC cell lines and HOSE cell. SYBR green real-time polymerase chain reaction (PCR) and immunohistochemistry (IHC) was used to validate TOM40 and NP, which had been identified as significantly overexpressed by both cDNA microarray and protein profiling data. For functional study, the effects of TOM40 and NP on cell proliferation, invasion, migration, and apoptosis were assessed with either silenced TOM40 or NP by small interference RNA (siRNA).

Results: Comparison of gene expression patterns using microarray analyses enabled us to identify 859 genes that were commonly up-regulated and 1116 genes that were down-regulated in the cancer cell lines (>2-fold, $P < 0.05$). In 2-DE and MALDI-TOF/PMF, 31 up-regulated spots were observed that had at least two-fold differences between the 3 EOC cell lines and HOSE cells used as controls. The relative mRNA expression of TOM40 and NP was significantly increased in EOC cell lines ($P = 0.004$ and $P=0.022$, respectively). IHC revealed that TOM40 and NP proteins were significantly elevated in EOC tissues ($P = 0.032$ and $P = 0.008$, respectively). Silencing of TOM40 or NP expression by siRNA tranfection into EOC cells resulted in a decrease in cell proliferation and migration.

Conclusions: These results highlighted the relevance of using primary cultures of EOC cells as a model system for gene profiling and proteomic study and showed the potential role of TOM40 and NP in the pathogenesis of ovarian cancer.