Ovarian cancer derived exosomes: Non-coding RNA (ncRNA) signatures and therapeutic targets

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Introduction: High-grade serous ovarian cancer (HGSOC) is the most lethal gynecological cancer with most patients (75%). One reason for this high lethality rate is the lack of appropriate biomarkers for the early stages and the majority of patients are diagnosed at advanced stages. Emerging data shows that miRNAs in tumor exosomes are involved in the pathogenesis of HGSOC, and may contribute to its aggressive metastasis. In this study, we hypothesized that by profiling the microRNA expression, we could find novel biomarkers and targets for novel therapeutics in HGSOC.

Methods: Here, we isolated exosomes from three ovarian cancer (OC) cell lines and one normal ovarian cell line. These exosomes are characterized by Western blot and Nanoparticle Tracking Analysis (NTA). Then we evaluated the ncRNA cargo which was differentially expressed in exosomes versus their cells of origin using the Affymetrix Gene Chip miRNA 4.0 microarrays.

Results: A subset of five miRNAs (miR-940, miR-1281, miR-1825, miR-3921, and miR-6877-3p) showing significant up-regulation in OC-derived exosomes, than their donor cells or normal exosomes were observed. As an initial step toward understanding the function of the preferentially exported miRNAs, we employed DIANA microT-CDS to determine the genes being targeted by these miRNAs. Functional analysis of these genes revealed that the most enriched pathways targeted by at least 3 of these miRNAs were adherent junction and pathways in cancer.

Conclusion: Our results indicate that OC-derived exosomes have unique miRNA expression signatures. These results provide a starting point in future for more in-depth studies of tumor-derived OC exosomes, which will aid our understanding of tumor, tumor microenvironment and new effective therapies or non-invasive biomarkers for OC that may be translated into clinical applications.

Biography
Gouda K Helal has completed his PhD research in Neuro-Pharmacology Department at Epply Cancer Institute, The University of Nebraska Medical Center (UNMC), USA. He is currently, a Professor of Pharmacology and Toxicology and Dean of Faculty of Pharmacy at Al-Azhar University, Cairo, Egypt. He has published more than 20 papers in reputed journals. His research interests includes: Identification and isolation of RNA and DNA adducts, the roles of metallothionein in brain tumor progression, the role of natural products in protection of cerebellum against oxidative stress insults and the role of exosomal nucleic acids in cancer initiation and progression.

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