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INTEGRATED PATHWAY ANALYSIS OF MICRORNA EXPRESSION IN PLASMA OF OVARIAN CANCER (OVCA) PATIENTS SHOWS LACK OF BH3 PROTEIN DEPENDENT SIGNALING

I Shapira,¹ A Naboush,¹ A Banavali,¹ E Neculiseanu,¹ K Guddati,¹ M Kopf,¹ C Mason,² A Lee². ¹Medicine, SUNY Downstate Medical Center, Brooklyn, NY, United States; ²The Feinstein Institute for Medical Research, Manhasset, NY, United States

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Purpose of Study More than 100,000 pelvic surgeries to remove ovarian masses (BOM) are performed yearly in the USA only 8% of those remove ovarian cancer. Circulating microRNA are biomarkers for disease detection. Purpose of study:

1. To analyze patterns of microRNAs in women with BOM vs. OvCa
2. Discover pathway involved malignant transformation.

Methods Used Plasma from 32 women OvCa, 24 controls 32 (BOM) was analyzed using ABI Taqman OpenArray MicroRNA pools A and B to measure the expression of 754 known miRNAs .Real-time PCR was performed on the Taqman Open Array MicroRNA arrays using the Applied Biosystem Open Array Real-Time PCR system. Data were

processed using the OpenArray Real-Time qPCR Analysis software and exported for analysis using the Applied Biosystems DataAssist Software. Data analysis was done with the R programming language. A cutoff for Ct values at 30 was used. MiRNAs with Ct values higher than 30 were considered not detected. Data was normalized using a mean-centering restricted (MCR), a modification of the traditional delta Ct method and uses miRNAs which are expressed in all samples for data normalization. Statistical analysis was performed via custom scripts based on the R/Bioconductor package LIMMA (Linear Models for Microarray).

Summary of Results BOM had higher expression (2–14 fold higher) of miRs -195, -126, -139-5p, -27b, -127, -152, -28, -106b, -17, -363, -181a, -192 relative to OvCa ($p < 0.0006$). OvCa over-expressed of miRs -1274a, -720 and -625-3p ($p < 0.0007$). Reactome pathway analysis detected involvement of miRs into pathways of activation of BAD, PI3/AKT signaling in CD28 and activation of BH3 in BOM these pathways were not detected in OvCa ($p < 0.000596$).

Conclusions BOM patients have immune recognition and pro-apoptotic protective circulating microRNAs. It is unknown whether miRs originate in ovary or another tissue. Recent work shows that BH3 mimetics are very effective in inducing cancer cell death.