Matrisome Deregulation in Ovarian Cancer Metastasis

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Background and Hypothesis: Over 75% of ovarian cancer (OC) patients present with metastasis upon initial diagnosis. Since most are treated for metastatic disease, it is crucial that developing therapies target metastasis. Our analysis of OC transcriptomic changes revealed key changes in the matrisome. Matrisome genes are associated with tissue modulus and disease progression, yet comprehensive understanding of many of their contributions to OC is lacking. We hypothesize that matrisomal OC genes will have clear impacts on clinical outcomes.

Project Methods: Differentially expressed genes (DEG) in 11 paired OC primary tumors and metastases were identified using RNA-seq analysis. The DEG were compared with data from high-grade serous ovarian cancer (HGSOC) cells seeded on an organotypic 3D culture model of omentum. The overlapping genes are deregulated during early metastasis and remain relevant in advanced metastasis in OC patients. Kaplan-Meier Plots were generated to identify gene relationships with progression-free survival (PFS) and overall survival (OS).

Results: 845 genes between metastases and primary tumors and 1,182 genes between early and advanced metastatic colonization were differentially expressed; 144 genes were shared. These 144 genes were compared with matrisome proteins differentially expressed between malignant and non-malignant HGSOC cell populations. 28 genes correlated with tissue modulus, 19 with disease score, and 17 with both. Of the 30 matrisome genes correlating with either, 21 decreased PFS and 24 decreased OS.

Conclusion and Potential Impact: We have identified a matrisome signature sustained throughout metastatic tumor development. Many of these genes' mechanisms contributing to OC metastasis and therapeutic relevance have yet to be determined. In addition to influencing cell-cell communications, mechanotransduction, and metastasis progression, the altered matrisome can affect drug delivery to tumors. Further studies may guide understanding of

pathways in matrisome alteration during cancer progression and reveal future targets for chemotherapy or combination immunotherapies.