Poster 33: A comparison of stemness and epithelial-mesenchymal transition factors in Mullerian carcinosarcoma based on organ of origin

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Topic
Translational Research

Objectives
Carcinosarcoma (CS) is an inherently heterogeneous biphasic tumor that can arise from different Mullerian structures. This project aims to evaluate differences in stemness and epithelial-mesenchymal transition (EMT) factors based on organ of origin.

Methods
Mullerian CS tissue samples were collected through an institutional biobank and analyzed prior to in vitro culture. De-identified clinical information was abstracted. EMT factors, stemness genes, and their corresponding proteins were evaluated via flow cytometry, reverse transcriptase quantitative polymerase chain reaction (RT-qPCR), and Western blot. Associations were identified by Student's t-tests with significance set at $p \leq 0.05$.

Results
We identified three ovarian (O1, O2, O3) and two uterine CS samples (U1, U2). O1 was collected post neoadjuvant chemotherapy; all other samples were chemotherapy naïve (O2, O3, U1, U2). Using RT-qPCR, all original samples were analyzed for expression of the stemness genes HMGA2, NANOG, LIN28A, and POU5F1 (OCT4), the epithelial markers OCLN and TJP1 (ZO1), and the mesenchymal markers SNAI1 and VIM. The uterine CS samples demonstrated a trend to higher expression of stemness genes, though this was not statistically significant ($p=0.06$), and EMT marker expression was varied. Western blot showed that, in agreement with gene expression data, uterine CS expressed higher amounts of the stemness protein LIN28A. EPCAM, an epithelial marker, expression did not follow a distinct trend amongst the samples. On flow cytometry, sample O1 showed lower levels of stemness markers ALDH1A1 (1.25% vs 6.08%) and CD44/CD117 double positive (5.06% vs 26.23%), as well as cells positive for both EMT markers CD324/CD325 (0.4% vs 3.80%) compared with chemotherapy naive sample O2.

Conclusions
Our study aimed to characterize the stemness and EMT factors displayed by uterine and ovarian CS samples. Significant tumor heterogeneity was detected amongst the samples regardless of organ of origin, and while this was not statistically significant with $p=0.06$, there seemed to be a greater trend to increased stemness in uterine CS compared to ovarian CS based on RT-qPCR and Western blot. Further research focused on incorporating EMT/stemness tumor heterogeneity in therapeutic strategies is needed.

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Abstract Table or Graph

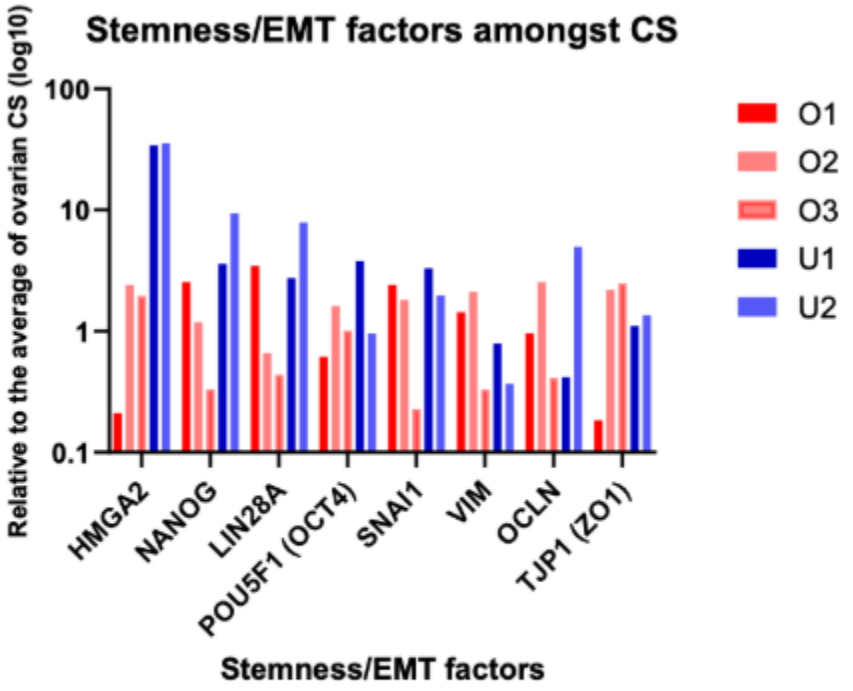

Fig. 1. RNA expression of stemness and EMT factors amongst ovarian and uterine carcinosarcoma samples via reverse transcriptase quantitative polymerase chain reaction (RT-qPCR).