Background: In prostate cancer (PCa), the surrounding stromal cells are activated to a disease phenotype termed cancer-associated fibroblasts (CAFs). While stromal cells are not mutated in PCa, their secretome changes to enhance prostate cancer survival and progression. Extracellular vesicles (EVs) released from the cells of the tumor microenvironment have been implicated in various aspects of prostate cancer progression and metastasis. Proteins, mRNAs, and small noncoding RNAs within these EVs communicate with surrounding cells. Our goal is to study EV microRNAs (miRs) secreted from patient-derived prostate epithelial and stromal cells and determine their effects on prostate biology and cancer.

Methods: Patient radical prostatectomy tissue was dissociated to single cells followed by selection for epithelial and stromal cells using cell type-specific media. Patient-derived prostate cells were fully characterized using prostate epithelial and stromal markers by qPCR. Prostate epithelial and stromal cell EVs were isolated from culture media via differential ultracentrifugation. Small RNAs from patient prostate cells and cell EVs were sequenced by next generation sequencing (NGS) and were validated by microRNA in situ hybridization (ISH) of prostate tissue (miRScope) and qPCR. NGS data was analyzed with edgeR.

Results: There were 190 differentially expressed miRs between epithelial and stromal cells and 278 differentially expressed miRs between EVs released from epithelial and stromal cells ($Q<0.05$). Of these miRs, 79 were differentially expressed in both comparisons. Of interest, miR-199a-5p and miR-199a-3p were specific to the stromal cells and stromal cell EVs. The localization of miR-199a in the stromal compartment was confirmed by miR ISH staining of patient radical prostatectomy tissue. Both miR-199a-5p and miR-199a-3p were robustly expressed in patient serum EVs as quantified by NGS.

Conclusions: We demonstrate that miR-199a is specific to the prostate stroma and circulates in serum EVs. We are currently working to determine the role of miR-199a in the prostate stroma and the effects it may have on prostate cancer via EV communication in the tumor microenvironment. Future experiments include overexpressing and knocking down miR-199a in prostate stroma cells and quantifying levels of target genes in both prostate cell types. A prostate cancer patient tissue microarray will be used to quantify miR-199a levels in patient-matched cancer and benign tissues. We hope to determine the role of miR-199a in promoting the CAF phenotype and CAF-mediated effects via extracellular vesicle signaling.