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Novel Surface Factors on Stroma-Derived Exosomes in Pancreatic Cancer

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Pancreatic Ductal Adenocarcinoma (PDAC) is a devastating disease which is driven and supported by changes in its microenvironment, or stroma. This project dissects the intercellular communication that exists between the primary stromal component, Cancer-associated fibroblasts (CAFs) and PDAC. Specifically we focus on how CAF-secreted vesicles promote PDAC progression, with an additional goal to identify biomarkers suitable to generate a future “liquid biopsy” test for early PDAC detection. PDAC communicates with its microenvironment, in part through the exchange of specific types of extracellular vesicles (EVs), which include exosomes.

We observe distinct types of CAF-derived EVs containing unique surface receptors. One EV subpopulation of interest contains a novel surface protein, NetrinG1 (NG1), which is expressed on the plasma membrane of pancreatic CAFs, but not their normal/healthy counterparts. Further, PDAC cells, but not healthy pancreatic epithelial cells, upregulate NG1's lone binding partner, NGL1, suggesting a role for these binding partners in PDAC-selective EV uptake. Functional assays designed to test PDAC viability suggest these NG1⁽⁺⁾-EVs protect PDAC cells from programmed cell death as a result of physiological stress. Pursuing our biomarker goal, we confirm stromal NG1 expression prior to tumor development and are currently seeking to validate NG1-positive EVs in blood of PDAC patients. Altogether, this research identifies a novel mechanism of tumor-stroma communication and introduces EV biomarkers capable of identifying both early PDAC occurrences and predicted efficacy of certain adjuvant interventions.

Biography:

Kris Raghavan is currently 4th year PhD student, conducting research on pancreatic cancer in the lab of Dr. Edna Cukierman at Fox Chase Cancer Center. He completed his MSc at Georgetown University with a degree in Tumor Biology, conducting breast cancer research in the lab of Dr. Robert Clarke. Kris is the primary author for two publications: a review article on caveolin's role in breast cancer and Springer textbook chapter on stress response pathways in mammalian cells. As he approaches the completion of his PhD, Kris seeks to make professional connections in both the academic and private biotechnology sectors.