Progress report for EM core funding (2017-2018)

The intracellular mobility of biological macromolecules and organelles is highly restricted by the high viscosity of the cytosol and crowding of intracellular components. The physical linkage between mitochondria and endoplasmic reticulum (ER) interface and its relevance to cancer biology remains elusive. The mitochondria-ER contacts (MERCs), in normal conditions are necessary and sufficient for propagation of ER-derived calcium signals to the mitochondria. However, this can change in conditions such as ER stress and cancer pathologies where mitochondria are prone to Ca^{2+} overloading from ER including changes in the plasticity of MERCs. One our objectives is to understand the nature of tethering between mitochondria and ER and how the heterogeneity in MERCs contribute to cancer biology.

Using the preliminary funding from EM core, we have successfully established a cryo-protocol for preparation of normal pancreatic epithelial cells and pancreatic carcinoma cells to study the ultrastructure of ER- mitochondria tethering in these cells. We have done several experiments to identify differences in the MERCs between normal and tumor cells using TEM (Figure 1).

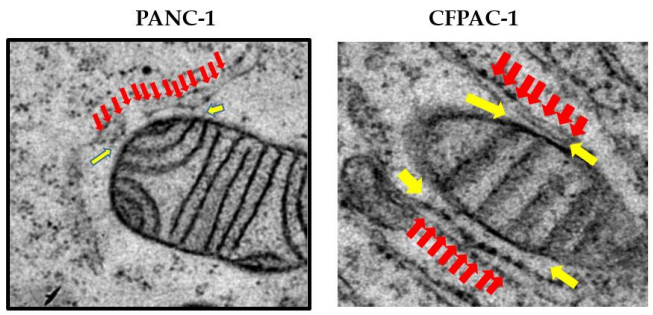

Figure 1. TEM showing the MERCs (yellow arrows) in two different pancreatic carcinoma cells. The red arrows points to ER membrane facing cytoplasm.

The grant from the EM core helped us to get started with these preliminary studies which we plan to use it for an R01 RFP. We anticipate to pursue our studies further to understand in depth how the ER-mitochondria tethering contributes to cancer biology, and the EM core is a valuable partner in this pursuit. Our goals are to expand our cancer cell studies to cancer tissues utilizing FIB-SEM microscopy.