Endoplasmic Reticulum-Mitochondria tethering and alterations in lung cancer biology/pathology

Summary report for EM core funding (2018-2019)

Communication between cell organelles plays a key role in cell biology. 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 Ca2+ overloading from ER including changes in the plasticity of MERCs. One of our objectives is to understand the nature and characteristics of MERCs in lung cancer biology.

Using the preliminary funding from EM core, we have previously established a cryo-protocol for preparation of lung carcinoma cells to study MERCs in these cells. In the present studies we further refined the protocol for better visualization of these organelles upon cryo-freezing and preservation of the cell integrity. We have done experiments to identify differences in the MERCs between normal and lung tumor cells using TEM. An example of variation in MERCs between a normal and lung tumor cells are shown in Figure 1. Lung tumor cells exhibit more MERC structures in comparison with normal epithelial cells.

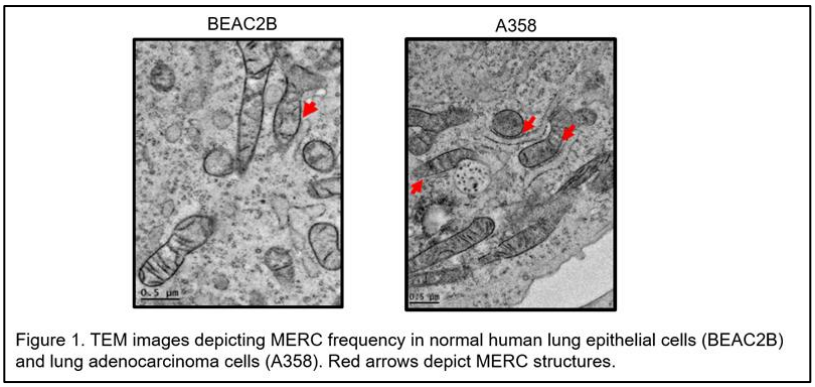

Figure 1. TEM images depicting MERC frequency in normal human lung epithelial cells (BEAC2B) and lung adenocarcinoma cells (A358). Red arrows depict MERC structures.

The preliminary studies obtained using EM core grant will aid to pursue specific grants applications from funding agencies. We anticipate to pursue our studies further to understand in depth how the MERCs contributes to cancer biology, and the EM core is a valuable partner in this pursuit.