

Dr. Sendurai Mani (2015 Award)
Targeting cancer stem cells to treat metastasis

With this project, we deepened our understanding of cancer stem cell function and the role of the FOXC2 protein in breast cancer stem cells. We previously discovered that cancer stem cells need FOXC2 protein to become and continue functioning as cancer stem cells, and that FOXC2 is critical for breast cancer metastasis. With the METAvivor grant we were able to determine that the protein level of this critical player (FOXC2) is regulated by changing the stability of the protein. In breast cancer stem cells, FOXC2 stability is regulated by the kinase PLK1. When PLK1 is active in the cell, FOXC2 protein is present and the cells are cancer stem cells. On the other hand, when PLK1 is made inactive, by using a specific drug, FOXC2 protein expression is lost and the cancer cells can no longer function as cancer stem cells. The drug that inhibits PLK1 is much more potent in cancer stem cells than in regular cancer cells. These findings are important for the future treatment of metastatic breast cancer, because if we can change cancer stem cells to regular cancer cells, these altered cells are now sensitive to chemotherapy, and this offers us an opportunity to eliminate metastasis. Owing to METAvivor support, we have published some of this work, with another manuscript in preparation. This support has also enabled us to obtain substantial extramural funding from the National Institutes of Health (R01, 2R01CA155243-06A1) for this critical project. This project is impactful in terms of future treatment design for MBC, and furthering this project will enable pioneering treatment options for this disease.