Role of GRM1 Expression in the Transfer of Metastatic Phenotypes via Melanoma Exosomes

Kryzysztof Zembrzuski, Kevin Eddy, Allison Isola, Suzie Chen
Rutgers, The State University of New Jersey

Melanoma has the highest mortality rate amongst skin cancers due to its high metastatic potential. When melanocytes, the pigment forming cells of the skin, ectopically express Metabotropic Glutamate Receptor 1(GRM1), the cells undergo cellular transformation in vitro and spontaneous melanoma formation in vivo. Our lab has shown treatment of GRM1+ melanoma cells with an inhibitor to GRM1 or silencing RNA to GRM1to reduce its expression results in cell cycle arrest and subsequent apoptosis. Exosomes have been shown by others to play a role in the establishment of the "pre-matastatic niche", a microenvironment which supports the outgrowth and colonization of disseminated tumor cells in forming a secondary tumor.

In vitro cultured cell studies showed that exosomes released by GRM1+ melanoma cells induce the migratory, invasive and anchorage-independent colony-forming abilities of non-tumorigenic GRM1- melanoma cells. In order to determine if in vivo exosomes release by GRM1+ cells may have the ability to induce tumor formation in non-tumorigenic, GRM1- melanoma cells, a xenograft model was used. Fluorescently tagged exosome protein markers (ptdTomato-CD81 and CD63-GFP) were stably transfected into GRM1+ (C8161) and GRM1- (C81-61) melanoma cells (respectively). One million cells were inoculated into two separate flanks of each mouse and the mice are being monitored for tumor growth. Blood was collected at several time points and exosomes were purified from the blood plasma, western immunoblots were performed to examine for the presence of fluorescence-tagged exosomes. It has been one and half to two months since we inoculated tagged cells into the mice, so far we do not detect any tumor formation on the flank with GRM1- melanoma cells.