EVALUATION OF SUNITINIB AND ONCOLYTIC RHABDOVIROTHERAPY IN A MOUSE TRIPLE NEGATIVE BREAST CANCER MODEL

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Oncolytic rhabdovirotherapy (ORV) efficacy is limited due to two factors—host anti-viral immunity and an immunosuppressive tumor microenvironment. Jha *et al*, 2013 showed that combining Su with ORV therapy improves viral productivity by inhibiting protein kinase R (PKR) activity. Literature also shows that Su has off target immune-modulatory effects on the host such as reducing the number of immunosuppressive myeloid derived suppressor cells (MDSCs) and improving anti-tumor CD8 T cell response. This led us to hypothesize that pre-treatment with Su will allow for better ORV efficacy in a ORV infection resistant model of breast cancer, 4T1. Indeed, pretreatment with Su followed by ORV therapy improved survival compared to ORV or Su monotherapy in the 4T1 model ($p<0.001$). Mechanistically, Su improves ORV productivity (1-3 logs) in the tumor and reduces IFN-β in the tumor and serum *in vivo* but not *in vitro.* Based on this data, we hypothesized that Su improves viral productivity in the tumor in a tumor cell independent manner. To start investigating this, I enumerated professional IFN producing cells such as plasmacytoid dendritic cells (pDC) and macrophages (MΦ) in the tumor and spleen. Thus far I have demonstrated that Su treatment reduces the number of splenic plasmacytoid dendritic cells ($CD11c^{lo/int}$ Gr1+ B220+), MDSCs and increases the number of lymphocytes (CD8+, CD4+ T cells and B cells) in both the spleen and the tumor of 4T1 bearing animals. Future experiments will investigate the mechanism by which Su alters pDC number, function and characterize the effect of Su treatment on anti-tumor T cell function.