The effects of NK cells and drug combination therapy on glioblastoma tumor growth

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Background and Hypothesis: Glioblastoma (GB) is an aggressive primary brain malignancy with a mean survival time of 15-16 months. Initial therapy is limited to surgery, radiation and temozolamide (TMZ) chemotherapy with up to seventy percent of GBs recurring in the first year and only five percent of patients still alive after five years. A reason these tumors are difficult to treat is the effect that the GB tumor microenvironment has on recurrence. One major cell type in this microenvironment is GB cancer stem cells and these cells play a major role in recurrence of the GB tumor. Our approach is that if we reduced tumor volume with the standard of care and treat with NK-cell based treatment and combination drug therapy we can improve the remission and prognosis of GB tumors.

Experimental Design or Project Methods:

To explore the killing potential of NK cells as well as combination drug treatment we set up a caspase assay that would indicate DNA damage and cell health. We set up in a 96-well plate with GB43 or Cancer stem cells with increasing consideration of either drug over 72 hours or NK cells over 48 hours. After we create, dose curves to find LD50 of both Cell based and drug based treatment.

Results:

We are still assessing the cell-based therapy and calculating LD50 for both treatments. However, we have found that in the drug based combination therapy we were able to show that paclitaxel and RG3788 both alone and in combination with the standard of care,TMZ, showed significantly reduced GB43 cell viability as concentration increased at the 72 hour time point. However, cancer stem cell remain at around 80% viability across all drug combinations and concentrations.

Conclusion and Potential Impact:

In conclusion at this point these data indicate that GB43 with the standard of care TMZ in combination with paclitaxel and RG3788 have the ability to kill cells in vitro. Moving forward we plan to package paclitaxel and RG3788 in nanoparticles

for more efficient targeting of cells to target tumors. In addition, we plan to create lethal dose curves for NK cells and control neuronal cell tissue to better assess drug toxicity and efficacy.