Innovative Combination Therapy for Treating Brain Tumors

Using an Avatar Model to Improve Patient Outcomes

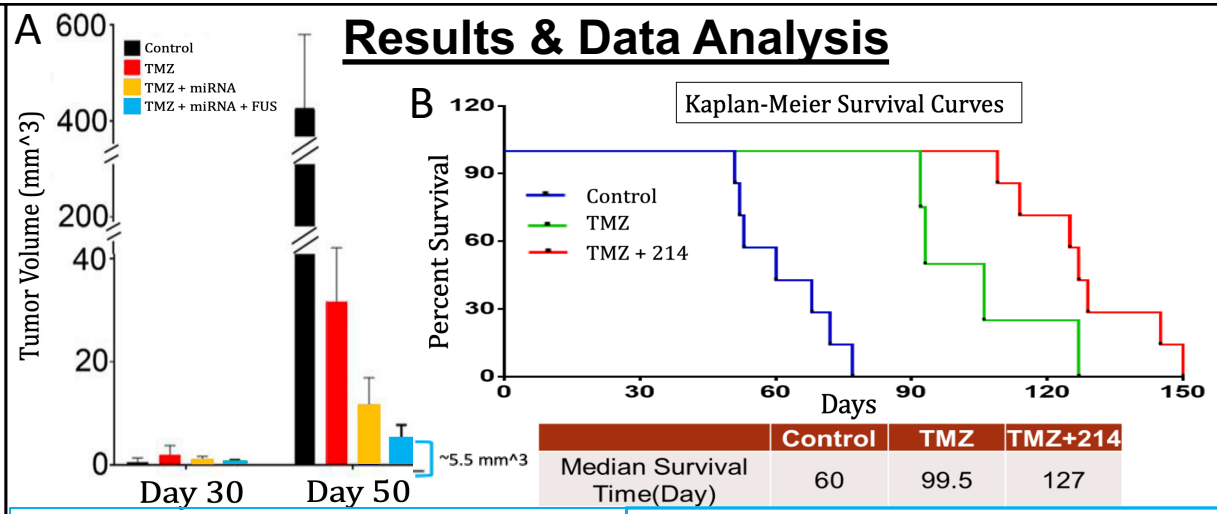
#2075, Biomedical & Health Sciences, Senior Division, Science Type Project

Problem & Research Focus

- Glioblastoma multiforme (GBM), the most malignant form of brain cancer, has no cure despite decades of research
- Surgical resection, radiation therapy, and chemotherapy are currently used to treat the disease
- Temozolomide (TMZ), the typical chemo drug for GBM, rapidly loses efficacy due to the tumor's acquired chemoresistance, which allows the tumor to grow back
- I genetically engineered micro-RNA enclosed in exosomes (CEC-m214-exos), which aims to prevent this acquired chemoresistance
- Focused ultrasound (FUS) can open the blood-brain barrier, allowing for a higher volume of TMZ and exosomes to reach the tumor target directly

Research Question: ***Can a combination therapy of TMZ, CEC-m214-exos, and FUS better treat GBM by disabling the tumor's ability to develop resistance to the chemotherapeutic agent?***

Results & Data Analysis



	Control	TMZ	TMZ+214
Median Survival Time(Day)	60	99.5	127

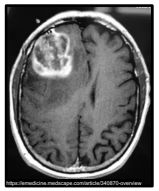
Figure A: ***~77x* volume reduction** vs. control, ***~6x* volume reduction** vs. TMZ monotherapy

Figure B: **2.12x the lifespan** vs. control, ***27.6%* longer lifespan** vs. TMZ monotherapy

Methodology

Establishing Animal Avatar Model*

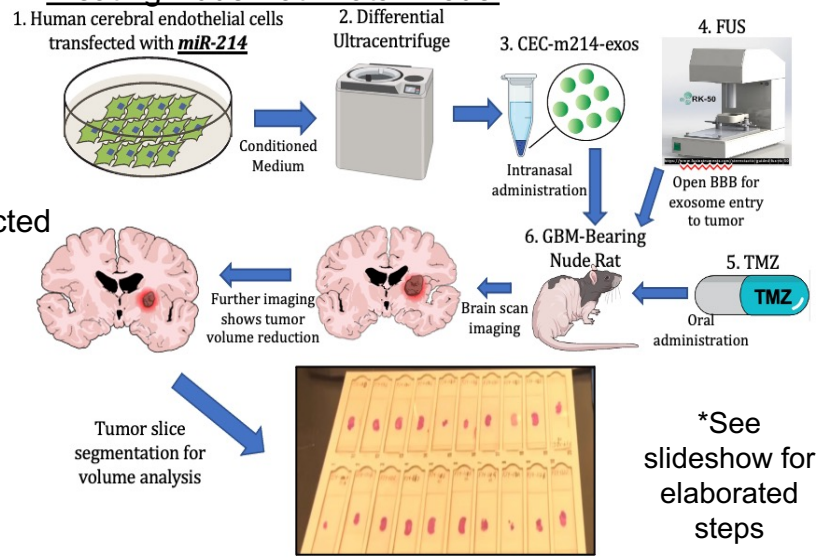
1. Patient has GBM, tumor is resected during surgery



2. I enzymatically dissociate resected tumor tissue, and neurosurgically implant in *nude rats*

3. After a cultivation period, the GBM-bearing *nude rat* becomes a completed avatar for that patient. Avatar's treatment can then be applied to actual human GBM patients

Treating Nude Rat Avatar Model



*See slideshow for elaborated steps

Conclusion & Translating Results

- Combination therapy of TMZ + CEC-m214-exos + FUS drastically reduced tumor volume & extended survival
- Successful treatment of these animal avatars provides the scientific underpinning to support innovations in translational oncology
  - Enables understanding of how a given patient's tumor responds to treatment, which then informs more precise therapies for actual patients
- Next steps and goals: This 3-part treatment could potentially advance into future clinical trials, and establish a new way to fight GBM for patients battling this devastating disease