Progress Report

Mechanical Ablation of Tumour Cells Using Rotating Magnetic Field

Dr. Xian Wang
DUNN with Cancer Brain Tumour Research Fellow
The Hospital for Sick Children, Toronto, Ontario

I. Summary

With the support from Dunn with Cancer Brain Tumour Research Fellowship, I was able to make progress in exploring the mechanical ablation of glioblastoma at the Hospital for Sick Children. In the past year, I have successfully established an animal model with chemotherapy-resistant glioblastoma. Applying the novel mechanical ablation treatment approach, I proved the treatment efficacy in the petri dish for both genetic and drug-selected TMZ-resistant GBM cells. Using the developed chemotherapy-resistant animal model, the treatment results showed significantly prolonged survival in mice after the mechanical ablation treatment.

I'm also happy to share the news that I have submitted a research paper to the journal Science Advances, covering the mechanical ablation method for the treatment of glioblastoma. The journal Science Advances is one of the best interdisciplinary journals, and the journal is open-access to everyone. I hope this would benefit the brain tumour community when it is published after peer review. In addition to the research journal, my colleagues and I have written a detailed technical patent application for disclosure, and hope the mechanical ablation method will be commercialized and beneficial to brain tumour patients on a larger scale.

II. Technical contributions

TMZ is a DNA alkylating agent that causes single and double-stranded DNA breaks. TMZ has become part of the standard-of-care chemotherapy for GBM patients worldwide. However, primary or treatment-induced TMZ resistance lead to treatment failure, disease relapse, and patient mortality. My colleagues and I have investigated whether the mechanical ablation treatment is effective against TMZ-resistant GBM. To model primary TMZ resistance, my colleagues have generated GBM cell lines with CRISPR-induced knockout of MSH6, which encodes a DNA mismatch repair (MMR) gene frequently mutated in TMZ-resistant glioma.

To model treatment-induced TMZ resistance, we cultured GBM cells in increasing dosages of TMZ, followed by selecting and establishing resistant cell lines.

We first studied two GBM stem cell lines (G361 and G440) and their MSH6 CRISPR knockout counterparts. As expected, parental, but not MSH6-/-, G361 cells displayed reduced cell viability upon TMZ treatment. Notably, the mechanical treatment significantly increased cell death rate, with or without TMZ treatment, in both parental and MSH6-/- G361 cells. Similarly, mechanical ablation, but not TMZ chemotherapy, displayed robust efficacy in inducing cell death in both parental and MSH6-/- G440 cells. I have orthotopically implanted G361 MSH6-/- cells to generate TMZ-resistant GBM. Seven days post tumor cell implantation, mechanical ablation treatment reagents carbon nanotubes were injected into tumor, followed by TMZ, magnetic, or combination treatment. No survival difference was observed between the control group and the group that received just TMZ treatment, demonstrating the TMZ resistance of these tumors. We found that mice with mechanical ablation treatment, with or without TMZ chemotherapy, displayed significantly extended survival compared to control.

We next studied the therapeutic efficacy of mechanical ablation against GBM with treatment-induced TMZ resistance. TMZ-resistant G411 and G532 GBM cells, which were established by culturing their parental cells with escalating dosages of TMZ, showed higher cell viability than parental cell lines upon TMZ treatment. It was found that mechanical ablation treatment increased cell death in both parental and TMZ-resistant cell lines. TMZ-resistant G411 cells were orthotopically implanted to generate GBM. Seven days post tumor cell implantation, mechanical ablation reagents were injected, followed by TMZ chemotherapy, magnetic field treatment, or both. Mechanical ablation treatment, but not TMZ chemotherapy, significantly extended mouse survival.

III. Thank you for the support

I would like to thank the foundation and donors for their generous support to me and to this research project. I will continue my work Together, we will work towards the same mission, making brain tumour treatable and eventually curable.