DOI: 10.1002/adhm.201801391

Article type: Essay

Designing Next-Generation Local Drug Delivery Vehicles for Glioblastoma Adjuvant Chemotherapy: Lessons from the Clinic

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Acknowledgements

A.T. and M.J. contributed equally to this work. This essay was supported by the Winston Churchill Foundation of the United States.

Figures and captions

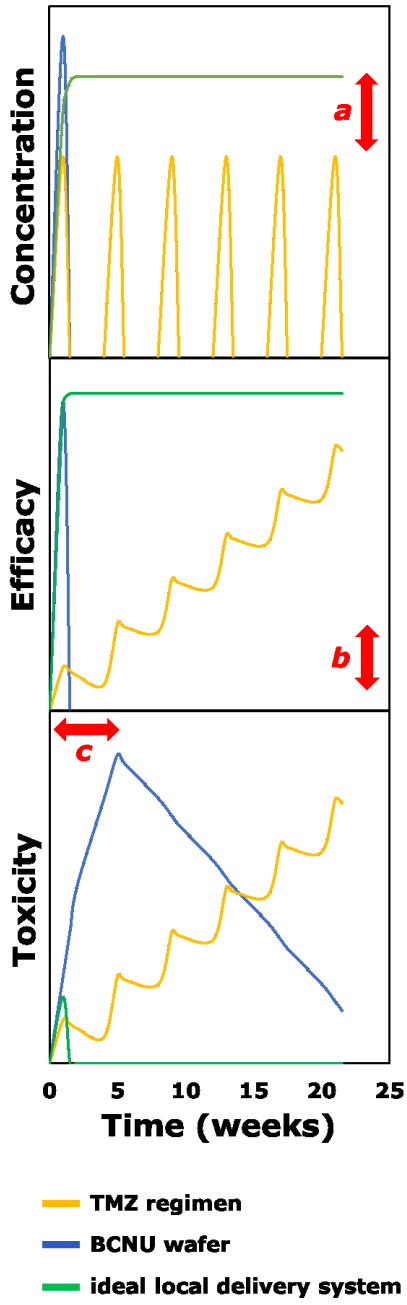

Figure 1. Graphical illustration of concentration, efficacy, and toxicity profiles of an idealized drug delivery system against systemic TMZ adjuvant therapy (Stupp protocol) and stiff FDA-approved BCNU wafers. a) Limitations in systemic toxicity of TMZ are overcome with local delivery. An ideal delivery system will possess a mitigated bolus and 0th or 1st order release kinetics. b) Achievement of a high local concentration of TMZ in local delivery systems

sustained over many weeks produces a reduction in tumor burden and increase in efficacy in the idealized local delivery systems. c) BCNU wafers' stiffness mismatch with tissue contribute to toxicity and negative side-effects after >80% of drug release. A soft idealized local drug delivery system will have minimal acute toxicity and no negative chronic immune response.

ToC

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There is an unmet medical need in glioblastoma adjuvant chemotherapy for drug delivery carriers that provide sustained and local release of small molecules and combination drugs. Herein, quantitative pharmacokinetic lessons from the clinic that can inform the next generation of materials development for local treatment of glioblastoma are summarized.