Targeted Nanomedicines for Cancer Therapy: More than Just Crossing the BBB

Jason Thomas DUSKEY - *University of Modena and Reggio Emilia*

Nanomedicine (NMed) delivery systems are becoming major players in the novel research to treat Glioblastoma Multiforme (GBM). This is because they offer the possibility to deliver therapeutics to the brain which normally would not enter. While delivering novel pharmaceutics or genetic material (DNA, siRNA, mRNA) with NMed delivery systems has made vast improvements on drug delivery, therapeutic success of NMeds against GBM requires selective accumulation in the cancerous cells without causing toxic effects to healthy cells nearby. In this study, NMeds based on the FDA approved polymer poly(lactic-co-glycolic) acid were surface modified with 4 ligands that could potentially be upregulated in GBM cells: Adenoassociated coat peptide AAVF [1], the glycopeptide g7 [2], and two monoclonal antibodies against Cell Surface Vimentin (M08 and M08J) [3]. NMeds were optimized and fully characterized. Uptake and toxicity of the NMeds were analysed *in vitro* on GBM cells (C6). Further demonstrating the GBM specificity, co-culture assays with GBM (C6) and healthy astrocytes (DITNC1) showed not only a significantly higher uptake by GBM cells over healthy astrocytes for NMeds conjugated with M08, but also a reduction of GBM cell growth with increased growth of healthy astrocytes. Finally, MO8 conjugated NMeds were tested for their ability to selectively transport the anti-cancer drug Paclitaxel with improved effects. These results demonstrate the ability of optimized NMeds to enhance specific targeting not only to the brain but specifically to the GBM cells which will help increase the pharmaceutical effectiveness while limiting off-target effects.