# Improved GBM Targeting: Nanomedicines Approaches from Conception to Testing

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Glioblastoma Multiforme (GBM) is the most common adult malignant brain tumour affecting 5 in 100,000 people. Often discovered at a late stage, the life expectancy is 12-15 months with 3% of patients living 3 years or more (1-3). Current treatments (i.e. chemotherapy, radiation, surgery) cost ~$50k-$100k (2015), are extremely aggressive but only extend the life expectancy by little more than a year(4). Currently, only 4 FDA chemotherapeutics are approved for GBM treatment due to toxic effects and the lack of improved life expectancies (5,6). However, it is becoming increasingly difficult to find new compound candidates due to cost and difficulty of testing. This is often due to the fact that even though many small molecule drugs show promise and great therapeutic results in the literature they are not efficient alone to cure most diseases (even less so with CNS diseases) as they have low bioavailability, high first pass clearance, and low BBB crossing rates. Nanomedicines (NMeds) can overcome these disadvantages by encapsulating and protecting small molecule drugs increasing biodistribution, circulation, while lowering toxicity and immune response. More impressive is that they are easily modifiable with targeting ligands (abs, peptides, small molecules, aptamers etc.) that can afford selectivity in site of accumulation, increasing therapeutic efficiency.
Although Nanomedicine has the potential to offer these benefits, they are very complex systems that require advanced interactions of numerous variables. In this work we focus on designing and optimizing a complete NMed system that will better treat GBM by focusing on: 1) Optimized Polymeric (PLGA) and hybrid nanosystems for improved stability and drug loading; 2) Surface modification with BBB and GBM specific peptide and antibody based targeting ligands; 3) Analysis of the protein corona for improved biocompatibility; 4) Microfluidic scale-up validation and 5) Improved imaging methods for increased early stage detection and diagnostics. By combining this information, we want to create a pool of already optimized nanosystems that can be quickly and easily adapted to various therapeutic molecules or diagnostic tools, in order to speed up the design and production of novel and effective NMeds for the treatment and early stage diagnostics of GBM.

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