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Engineering Fluorinated Thermo-Responsive Assembled Protein (F-TRAP) for theranostic applications in glioblastoma multiforme.

Gliomas account for roughly 27% of all brain tumors and there is an urgent need to develop new therapeutic modalities. A glioblastoma multiforme (GBM) prognosis signifies a survival time of 14-16 months with only 5% of patients surviving more than 5 years. A significant challenge for GBM is the inability to: a) treat tumor cells with cytotoxic drugs due to poor solubility and their lack of blood brain barrier (BBB) permeation; b) specifically target tumor cells while avoiding normal tissue with such cytotoxic agents; and c) monitor GBM status and therapy non-invasively. Theranostic agents which can both deliver drugs and monitor disease progression can address these requirements but treatments specific to GBM do not currently exist. While considerable efforts have been made in developing protein-based systems as drug-delivery carriers or as diagnostic agents, we are investigating a fundamental new insight that is helping us develop a single protein-based system combining drug delivery capabilities with the ability to cross the BBB and remain at cancer site due to the enhanced permeation and retention (EPR) effect. This biomaterial also incorporates functional groups detectable via magnetic resonance (MR) spectroscopy and imaging as well as near-infrared fluorescence (NIR) to enable visualization during treatment. Recently, we have engineered a protein-based theranostic agent called fluorinated thermo-responsive assembled protein (F-TRAP) bearing a non-canonical fluorinated (specific amino acid here) that can self-assemble into a micellar structure and encapsulate hydrophobic drugs. Circular dichroism and dynamic light scattering were performed to observe F-TRAP secondary structure and micelle formation, as well as 19F magnetic resonance imaging (MRI) to visualize F-TRAP and determine pharmacokinetic properties in a GBM mouse model. Results indicate that F-TRAP has an alpha-helical secondary structure and forms micelles 30 nm in size. F-TRAP showed favorable pharmacokinetic data with a half-life of 112 minutes and high plasma retention. Data also revealed the ability of F-TRAP to cross the BBB to be imaged inside the brain.