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

Of all the brain tumors, gliomas account for 27% of the cases. A glioblastoma (GBM) prognosis signifies a survival time of 14-16 months with only 5% of patients surviving more than 5 years. A challenge in GBM therapy 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; c) monitor GBM status and therapy non-invasively. There is an unmet need for tailored materials capable of targeted therapy and diagnosis or theranosis to handle these issues.

While considerable efforts have been made in developing protein-based systems as drug-delivery carriers or as diagnostic agents, we developing a single protein-based system combining drug delivery capabilities with the ability to cross the BBB and remain at cancer site due to enhanced permeation and retention (EPR) effect. This biomaterial also incorporates tags detectable via MR spectroscopy as well as near-infrared fluorescence (NIRF) imaging.

We have engineered a protein-based theranostic agent called fluorinated thermo-responsive assembled protein, (F-TRAP) bearing fluorinated amino acids using a technique called non-canonical amino acid (NCAA) incorporation. Through dynamic light scattering (DLS) we found that F-TRAP self-assembles into micellar structures about 30nm in diameter and through CD (circular dichroism), we confirmed its alpha helical structure consisting of hydrophobic pores, that encapsulate chemotherapeutic drug molecule, doxorubicin. Importantly, our preliminary animal data suggests that F-TRAP exhibits desirable pharmacokinetic properties with a half-life of about 112 minutes and a favorable plasma retention time in vivo. Our studies also indicate successful delivery of the drug-encapsulating fluorinated nanomaterials as a trojan horse across the generally impermeable BBB, potentially making it a powerful theranostic agent.