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Engineering Fluorinated Thermo-Responsive Assembled Protein (F-TRAP) for Theranostic Applications in Glioblastoma Multiforme

Speaker: **Aparajita Bhattacharyal, M.Res.**
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Date: **Wednesday, November 10, 2021**
Time: 7:00 PM
Place: Zoom Meeting

Abstract:
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.[1] A significant challenge for traditional GBM drug delivery is the inability to: a) treat tumor cells with cytotoxic drugs due to their poor solubility and lack of blood brain barrier (BBB) permeation; b) specifically target tumor cells while avoiding normal tissue with such cytotoxic agents, c) stimulate drug release; and d) monitor GBM status and therapy non-invasively[2] Theranostic agents are being developed for their ability to diagnose disease and improve therapeutic delivery and can address these requirements because treatments specific to GBM do not currently exist[3] While considerable efforts have been made in developing protein-based systems as drug-delivery carriers or as diagnostic agents[4], 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 chemotherapy. The protein-based theranostic agent we have engineered is called fluorinated thermo-responsive assembled protein (F-TRAP) that bears a non-canonical fluorinated amino acid (trifluoroleucine or TFL), can self-assemble into micellar structures, and encapsulate hydrophobic drugs.

Circular dichroism and dynamic light scattering have been performed to observe F-TRAP's secondary structure and micelle formation respectively. Additionally, ^{19}F magnetic resonance imaging (MRI) has been carried out to visualize F-TRAP[5] and near infra-red fluorescence imaging (NIRF) has been utilized to determine its pharmacokinetic properties in a glioblastoma (GBM) mouse model. Results indicate that F-TRAP has an α-helical secondary structure and forms micelles 30 nm in size. F-TRAP shows favorable pharmacokinetic data with a half-life of 123 minutes and high plasma retention. Importantly, animal data also reveals the ability of F-TRAP to cross the BBB and to be imaged inside the brain.

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Appy Bhattacharya, M.Res. is a doctoral candidate in the Department of Chemical and Biomolecular Engineering at NYU Tandon School of Engineering. Appy received her Bachelor's degree in Molecular and Cellular Biology at University of Wisconsin-Green Bay, Wisconsin and her Master of Research (MRes) at University of Birmingham, UK. She is currently a graduate student at SUNY Downstate Health Sciences University and is pursuing her doctoral thesis work in Dr. Jin Kim Montclare's lab.

Ms. Bhattacharya is currently a graduate student at SUNY Downstate Health Sciences University and is pursuing her doctoral thesis work at Dr. Jin Kim Montclare's lab at NYU Tandon School of Engineering. She is working on developing and characterization of nanobiomaterials for applications in cancer drug delivery and magnetic resonance imaging (MRI) in glioblastoma multiforme. Broadly , the Montclare lab focuses on engineering of proteins for biocatalytic, therapeutic drug and gene delivery and biomaterial applications.

In addition, Appy is a member of the New York Academy of Sciences (NYAS) and through its Scientist in Residence (SiR) program, she does outreach work at local high schools. Appy actively mentors high school and undergraduate students in her current lab and enjoys it thoroughly. She is also a member of AAAS (American Association for Advancement of Science). Besides, she was selected as a Science Alliance Leadership Training (SALT) fellow through NYAS for 2020-21, which trained her further in her leadership skills. Lastly, through the pandemic, she has virtually presented posters and given talks on her thesis work at multiple conferences as well.

REFERENCES

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