**INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI**
**SHORT ABSTRACT OF THESIS**

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Thesis Title: Peptide-Based Molecular Constructs for Cellular Targeting and Small Molecule Delivery

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**SHORT ABSTRACT**

Advancement in synthesis and characterization protocols and demand of new chemical entities (NCE) have contributed to the development of peptide-based therapeutics. The introduction of cell penetrating and tumor homing peptides has opened up new avenues for drug delivery applications using peptides. In the present thesis, we rationally designed sixteen peptides for targeted drug delivery, broadly classified into three different peptide series. The conceptual advancement of Series-1 to Series-3 peptides presents the evolution of a design tree, whose roots originate from the Ramachandran plot. The restriction of geometry through structural engineering is a common trait in all the peptide series. The progressive addition of syndiotactic penetrating domains in Series-2 and Series-3 molecules have remarkably shown the effect of the geometry encoded design. All designed molecules were synthesized, characterized, and tested on various cell lines, including breast cancer (MDA-MB-231), cervical cancer (HeLa), osteosarcoma (U2-OS), non-cancerous mammary epithelial cells (MCF-10A) and human embryonic kidney cells (HEK-293). 5(6)-carboxyfluorescein and methotrexate conjugated peptides were prepared to verify their potential to target cancer cells preferentially. Flow cytometry, fluorescence microscopy, spectroscopy, and cytotoxicity assays confirm their preferential cellular uptake, cytotoxicity, and cargo delivery potential in cancer cells. Each peptide molecule is imbibed with distinct electrostatics, evident from the electrostatic fingerprints and associated functional changes.