Branched Amphipathic Peptide Capsules: A Singularly Versatile Drug Delivery Platform

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We have developed peptide bilayer delimited nano-capsules through the facile and rapid co-assembly of two branched amphiphilic peptides: bis(FLIVIGSII)-K-K_4 and bis(FLIVI)-K-K_4. The **B**ranched **A**mphiphilic **P**eptides (BAPs) assemble into **C**apsules (BAPCs) that possess unusual but highly desirable properties that suggest transformative applications in medicine and industry. They are resistant to heat, detergents, proteases, chaotropes and the cell's degradative machinery. This stability currently limits use for the delivery and release of encapsulated cargo. However they are ideally suited for entrapping, delivering and retaining radioactive molecules for radiotherapy as well as delivering DNA/RNA that bind to the cationic outer-surface of these structures. The surface of the structures is easily modified to mask charge, add targeting ligands or both. Optimizing their size and surface structure will give researchers and clinicians a valuable tool for safely delivering curative reagents.

As molecular medicine advances there is a need for delivering designer molecules to specific sites in the body. CRISPR/Cas9 gene editing methods, DNA vaccines and RNAi based therapies, require efficient and non-cytotoxic intracellular deliver vehicles. Many current DNA delivery methodologies function well in vitro but are too toxic for in vivo applications. Recent experiments revealed that dsDNA interacts strongly with the surface of the pre-assembled BAPCs through electrostatic interactions. The DNA-histone like complexes yield transfection rates in mammalian cells of up to 75% with minimal cytotoxicity. An in vivo DNA vaccine study was performed using a 4.7 kb plasmid encoding the E7 oncoprotein of HPV-16. It stimulated both immune and inflammatory responses, again with minimal organ toxicity. More recently this same system was able to deliver to primate cells in culture a 20 kb plasmid containing a cDNA that coded for an attenuated corona virus. The delivery of this vector (10% efficiency) resulted in the shedding of live virus.