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Long Circulating Micelles based on Helix Bundle-Forming Peptide-Polymer Conjugates JESSICA SHU, UC Berkeley, HE DONG, Retired, NIKHIL DUBE, UC Berkeley, JAI WOONG SEO, UC Davis, YU FEI MA, UC Berkeley, KATHERINE FERRARA, UC Davis, TING XU, UC Berkeley — Stable, multi-functional organic nanoparticles that combine long in vivo circulation, the ability to cross vessel walls to reach tumor tissues and controlled disassembly for eventual clearance will have a significant impact in nanomedicine. Although current self-assemblies of amphiphiles provide a versatile platform to generate modular organic nanoparticles, it remains a significant challenge to simultaneously control nanoparticle size in the range of 10-30 nm, enhance particle stability and tailor disassembly within suitable timescales. We have advanced this goal by designing a new family of amphiphiles based on coiled-coil 3-helix bundle forming peptide-polymer conjugates. By attaching a polymer chain to the middle of a helical peptide, the protein tertiary structures are used to position entropic forces of compressed polymer chains comprising the headgroups so as to effectively slow down the subunit desorption rate and enhance the in vivo stability. The resultant monodispersed nanoparticles are composed of subunits, < 4 nm in size, that form highly stable 15-17 nm diameter particles and demonstrate an in vivo circulation half life-time of 28 hrs, minimal accumulation in the liver and spleen and effective urinary clearance. By uniquely combining the configurational entropy of a polymer chain with a common protein structure, i.e. coiled-coil helix bundle, and a lipid core, self-assembled nanoparticles have been engineered with tunable stability and disassembly.

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