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Protein Delivery to Cells Using Degradable Polymer Nanocapsules

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Proteins are the engines of life that perform essential functions inside cells, such as enzyme catalysis, signal transduction, gene regulation and maintaining a fine balance between cell survival and programmed death. Many diseases arise from the alterations in the functions of intracellular proteins. Therefore, a general method of delivering active forms of proteins to specific cells and organs in living organisms is an important goal in many medical applications. However, proteins have poor membrane permeability and low serum stability, and therefore require suitable transporters for their efficient delivery. A nanoscale approach to cytosolic protein delivery is the reverse encapsulation of protein cargo in a degradable polymeric layer. The polymer shell can serve as a protective layer that shields the protein from proteases and denaturants; as well as presenting a positively charged vehicle for cellular internalization. Our lab recently developed a strategy to synthesize biodegradable nanocapsules that can be used to deliver a variety of protein targets. The single-protein nanocapsules were prepared through interfacial polymerization around the native proteins with monomers and biodegradable crosslinkers. The deposit of monomers and crosslinkers is facilitated by electrostatic interactions and is therefore noncovalent in nature. Degradation of the crosslinker upon entry into the cell leads to disassembly of the nanocapsule layer and release of the protein cargo. Nanocapsules formed using this method are uniform in size (~20 nm) with overall positive surface charge, and are internalized by different cells through endocytosis. We demonstrate the utility of the nanocapsule approach in triggering apoptosis in various human cancer cell lines, including HeLa, MCF-7 and U87MG, by using caspase-3 as the protein cargo.

Dr. Yi Tang is a Professor of Chemical and Biomolecular Engineering and of Chemistry and Biochemistry at UCLA (since 2004). Yi Tang received his B.S in Chemical Engineering and Material Science from Pennsylvania State University in 1997, his Ph.D. in Chemical Engineering from Caltech in 2002 under the mentoring of Prof. David Tirrell. As a postdoctoral fellow, he worked with Prof. Chaitan Khosla at Stanford University. His research lab is focused on natural product biosynthesis, biocatalysis and nanobiotechnology. He has received numerous awards for his research, including the NSF CAREER Award (2005), Presidential Early Career Award in Science and Engineering (PECASE, 2007), David and Lucile Packard Foundation Fellowship in Science and Engineering (2007), Sloan Research Fellowship (2008), Dreyfus Teacher-Scholar (2008), the American Institute of Chemical Engineers (AIChE) Allan P. Colburn Award (2009), the Young Investigator Award from the Society of Industrial Microbiology (2010), and recently the American Chemical Society (ACS) Biochemical Technology Division (BIOT) Young Investigator Award (2011).

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