Autonomously Assembling Nanomaterial Scaffolds for Treating Myocardial Infarction

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The goal of targeted therapeutics and molecular diagnostics is to accumulate drugs or probes at the site of disease in higher quantities relative to other locations in the body. To achieve this, there is tremendous interest in the development of nanomaterials capable of acting as carriers or reservoirs of therapeutics and diagnostics *in vivo*.[1] Generally, nanoscale particles are favored for this task as they can be large enough to function as carriers of multiple copies of a given small molecule, can display multiple targeting functionalities, and can be small enough to be safely injected into the blood stream. The general goal is that particles will either target passively via the enhanced permeability and retention (EPR) effect, actively by incorporation of targeting groups, or by a combination of both.[2] Nanoparticle targeting strategies have largely relied on the use of surface conjugated ligands designed to bind overexpressed cell-membrane receptors associated with a given cell-type.[3] We envisioned a targeting strategy that would lead to an active accumulation of nanoparticles by virtue of a supramolecular assembly event specific to tumor tissue, occurring in response to a specific signal. The most desirable approach to stimuli-induced targeting would be to utilize an *endogenous* signal, specific to the diseased tissue itself, capable of actively targeting materials introduced via intravenous (IV) injection. We present the development of nanoparticles capable of assembling *in vivo* in response to selective, endogenous, biomolecular signals. For this purpose, we utilize enzymes as stimuli, rather than other recognition events, because they are uniquely capable of propagating a signal via catalytic amplification. We will describe their development and utility as a multimodal imaging platform, and discuss their potential as carriers capable of targeting tissue via a new mechanism.

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