Enzyme-Responsive Nanoparticles for Targeted Accumulation and Prolonged Retention in Heart Tissue after Myocardial Infarction

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Injectable biomaterials have gained attention for use as inhibitors of negative left ventricular (LV) remodeling post-myocardial infarction (MI). However, current strategies such as preformed scaffolds and nanoparticles, are not feasible for clinical application as they utilize invasive delivery methods or suffer rapid tissue clearance, respectively. **A method for targeting to and retaining intravenously injected nanoparticles at the site of acute myocardial infarction in a rat model is described.** Enzyme-responsive peptide-polymer amphiphiles are assembled as spherical micellar nanoparticles, and undergo a morphological transition from spherical-shaped, discrete materials to network-like assemblies when acted upon by matrix metalloproteinases (MMP-2 and MMP-9), which are up-regulated in heart tissue post-myocardial infarction. We show by fluorescence that the resulting micro-scale assemblies accumulate specifically at areas of infarct, bypassing healthy heart tissue, and remain up to 28 days. Furthermore, histopathology of satellite organs at various time points post-injection (1, 7, 14, and 28 days) revealed healthy tissue, providing evidence of non-toxicity. These initial studies set the stage for the development of targeting systems for therapeutic delivery to an acute MI. Critically, with this development, injection of materials is possible via the non-invasive IV route, resulting in targeted accumulation and long term retention at the site of MI.

Figure Option 1: Nanoparticles delivered via systemic injection circulate freely in the blood system until acted upon by inflammatory enzymes at the site of damaged heart tissue.