Enzyme-Responsive Nanoparticles For Targeted Accumulation And Prolonged Retention In Myocardial Infarction

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BACKGROUND

Heart failure following a myocardial infarction (MI) continues to be one of the leading causes of death. Immediately after MI, there is an initial inflammatory response with cardiomyocyte death and degradation of the extracellular matrix. This results in negative left ventricular (LV) remodeling leading to wall thinning, LV dilation, and depressed cardiac function. Several experimental approaches have been examined to inhibit this negative remodeling process. One promising direction is the use of injectable biomaterials, which can be used as stand-alone scaffolds to encourage endogenous repair or for delivering therapeutics such as cells, growth factors, or small molecules.

Early intervention of MI has the potential to slow or inhibit the progression of negative LV remodeling. To date, most therapeutic delivery strategies have involved intramyocardial biomaterial injections, although translation to acute MI patients is unlikely given the increased risk of ventricular rupture immediately post-MI. One promising, minimally invasive strategy is the systemic injection of nanoparticles. However, many of the investigated systems lack long-term retention within the MI.

TECHNOLOGY DESCRIPTION

Researchers from UC San Diego have developed a method for targeting and retaining intravenously injected nanoparticles at the site of acute myocardial infarction. 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. These enzyme-responsive nanoparticles provide an efficient template for targeting the acute MI and remain in the infarct for up to 28 d post-injection.

This unique approach constitutes a minimally invasive method for the delivery of a material scaffold to acutely infarcted myocardium, providing a promising approach for prolonged therapeutic delivery *(e.g.* peptide, small molecules, *etc.*) to treat an acute myocardial infarction.

STATE OF DEVELOPMENT

Demonstrated proof-of-concept that the enzyme-responsive nanoparticles target, assemble, and are retained in an acute MI, thereby providing a promising approach for delivery of therapeutics immediately post-MI and obviating the need for risky intramyocardial injections. The inventors have demonstrated through study that the responsive nanoparticles are enzyme-responsive, accumulate due to upregulation of MMPs after MI, and are deliverable through both intramyocardial and IV injection.

RELATED MATERIALS

▶ Nguyen MM, Carlini AS, Chien MP, Sonnenberg S, Luo C, Braden RL, Osborn KG, Li Y, Gianneschi NC, Christman KL. Enzyme-Responsive Nanoparticles for Targeted Accumulation and Prolonged Retention in Heart Tissue after Myocardial Infarction. Adv Mater. 2015 Oct 7;27(37):5547-52.

PATENT STATUS

Country	Type	Number	Dated	Case

CONTACT
University of California, San Diego
Office of Innovation and Commercialization
innovation@ucsd.edu
tel: 858.534.5815.

OTHER INFORMATION

KEYWORDS
MMPs; enzyme-responsive; intravenous injection; myocardial infarction; nanoparticles

CATEGORIZED AS
- ▶ **Medical**
  - ▶ Disease: Cardiovascular and Circulatory System
- ▶ **Nanotechnology**
  - ▶ Materials

RELATED CASES
2015-256-0

United States Of America	Published Application	20180092845	04/05/2018	2015-256
Patent Cooperation Treaty	Published Application	2016172386	10/27/2016	2015-256

University of California, San Diego
Office of Innovation and Commercialization
9500 Gilman Drive, MC 0910, ,
La Jolla,CA 92093-0910

Tel: 858.534.5815
innovation@ucsd.edu
https://innovation.ucsd.edu
Fax: 858.534.7345