

# Novel Peptide-modified Thermo-reversible Methylcellulose for Treatment of Chronic Myocardial Ischemic Damage

Tech ID: 23821 / UC Case 2011-133-0

## INVENTION NOVELTY

This invention consists of a novel peptide-modified thermo-reversible methylcellulose (MC) that has the therapeutic potential to repair chronic ischemic cardiomyopathy.

## VALUE PROPOSITION

Damage incurred by myocardial infarction (MI) includes negative structural remodeling that leads to left ventricular (LV) dilation and heart failure. For patients that have suffered an ischemic episode, treatment goals focus on preventing, limiting, and eventually reversing this structural remodeling. Clinical studies have demonstrated the safety and feasibility of administering alginate-based polymers into the LV wall to restore LV geometry and improve LV function. However, these approaches have lacked the ability to induce tissue regeneration. Recent studies have demonstrated that extracellular matrix (ECM) protein-derived functional groups can promote angiogenesis and arteriogenesis, thereby achieving the desired tissue regeneration. The novel technology described here combines polymer therapy with ECM-derived peptide therapy, and is potentially capable of delivering restoration of LV geometry and function, as well as induction of tissue regeneration. New therapies that reverse the natural progression of the disease are highly sought after since there is a 5-year mortality rate of 50% in patients with advanced heart failure.

This technology has the following advantages:

- **Novel blend of CMC polymer and ECM-derived peptides** leads to synergistic therapeutic effects (improved LV function and tissue repair)
- **Thermo-reversible** polymer eliminates need for additional mixing to achieve gelation and increases ease-of-administration
- Demonstrated utility in **cardiomyopathy**, with potential application in other types of **tissue injury**

## TECHNOLOGY DESCRIPTION

Researchers at UCSF have demonstrated that immobilization of ECM-derived peptides onto a thermo-reversible carboxymethylcellulose (CMC) polymer greatly enhanced the repair process in a chronic rodent model of ischemic cardiomyopathy. In order to generate these polymers, CMC was modified with either RGD or HepIII peptides via a previously described conjugation technique utilizing carbodiimide chemistry. The optimal polymer-peptide composition was then identified

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## OTHER INFORMATION

### KEYWORDS

myocardial infarction,  
  
methycellulose, thermo-  
  
reversible, chronic ischemic  
  
cardiomyopathy, cardiac  
  
disease, polymer

### CATEGORIZED AS

- **Biotechnology**
- **Health**
- **Medical**
- **Disease:**  
**Cardiovascular and**  
**Circulatory System**
- **Therapeutics**

### RELATED CASES

2011-133-0

using a human umbilical vein endothelial cell (HUVEC)-based cell attachment assay, followed by detailed rheological analysis to determine the gelling temperature of the polymer blend.

Effects on LV function were then determined in a rat model of myocardial ischemia/reperfusion injury. Animals were allowed to recover for 5 weeks, and then given a single echo-guided injection of polymer, followed by an additional five weeks of post-treatment time (10 weeks post-MI). At the termination of the study, the researchers observed statistically significant improvements in wall thickness, LV function, angiogenesis, and a decrease in MI size compared to controls. Furthermore, they also observed a higher concentration of cardiomyocytes in the infarct zone, indicating that not only are there beneficial effects on function, but that the treatment is facilitating myocardial tissue repair as well.

STAGE OF DEVELOPMENT

Preclinical

RELATED MATERIALS

► [Mihardja SS et al. The effect of a peptide-modified thermo-reversible methylcellulose on wound healing and LV function in a chronic myocardial infarction rodent model. Biomaterials. 2013 Nov;34\(35\):8869-77](#)

DATA AVAILABILITY

Under CDA/NDA

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	<a href="#">9,907,856</a>	03/06/2018	2011-133

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