

# FUNCTIONAL RECOVERY OF INFARCTED HEART USING VASCULAR ENDOTHELIAL GROWTH FACTOR LOADED INJECTABLE HYALURONIC ACID BASED HYDROGEL

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**Statement of Purpose:** Myocardial infarction is one of the important causes in heart failure disease. Regeneration of infarction has been tried using stem cells, growth factors. However, treating cells and growth factors to the infarction has limitations for the functional recovery because of low engraftment rate and active concentrations. In this study, we used injectable and biodegradable hyaluronic acid based hydrogel for delivering VEGF for regeneration of myocardial infarction.

**Methods:** Hyaluronic acid was derivatized using acrylating agents by two stem modification processes (Fig. 1). Hydrogel was prepared by incubating acrylated hyaluronic acid and poly(ethylene) glycol tetrathiol. Vascular endothelial growth factor (VEGF) was loaded in the hydrogel to a final concentration of 5ug in 45ul hydrogel. Myocardial infarction was induced in six week old male rats using coronary artery ligation. After 2 weeks, animals were assigned to 4 treatment group; sham operation (group I), myocardial infarction (group II), hydrogel (50ul) (group III), and hydrogel (45ul) with VEGF(5ug) (group IV). Left ventricular function was measured using Millar catheter 4 weeks after injection of hydrogel. Heart samples were collected. Infarcted area was examined using immunohistochemistry (Fig. 2).

### Hyaluronic acid MW.50,000

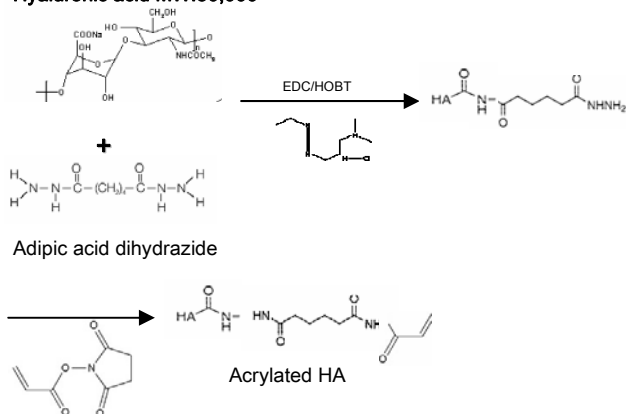


Figure 1. Acrylation reaction of hyaluronic acid

**Results/Discussion:** Rats myocardial infarction model without hydrogel was set as control showed the reduced heart function and wider infarction area. Animals injected with VEGF loaded hydrogel showed the small infarcted areas compared to the hydrogel treated animals. Left ventricular systolic pressure and end-diastolic pressure dimensions increased in the VEGF+hydrogel group than

in the hydrogel group.(Fig. 3) Immunohistochemistry show that live cells are spread in the infarcted area treated with VEGF loaded hydrogel compare to myocardial infarcted samples and hydrogel treated samples. VEGF loaded hydrogel could release the active VEGF to the surrounding infarcted tissue and VEGF induced the vasculogenesis, which could recover the heart function in the infarcted animals (Fig. 4).

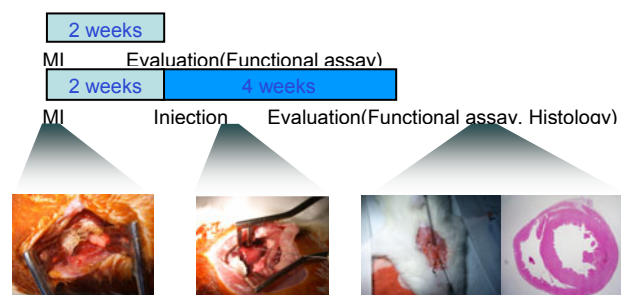


Figure 2. Experimental Scheme of animal experiments

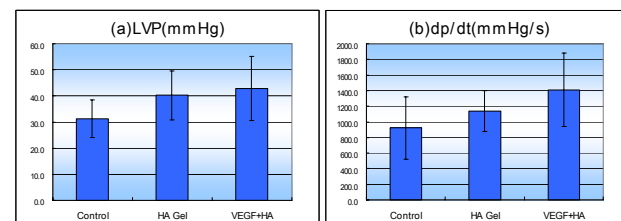


Figure 3. Functional analysis of hydrogel injected heart. (a)LVP and (b)dP/dt.

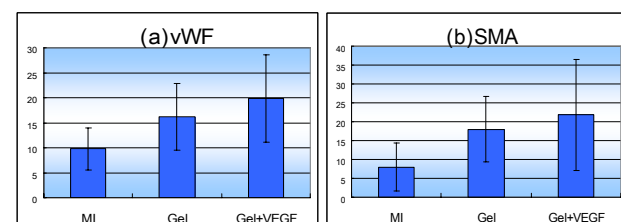


Figure 4. Histological analysis of hydrogel injected samples. (a) von Willebrand Factor and (b)  $\alpha$ -smooth muscle actin

**Conclusions:** Hydrogels with VEGF showed the significant functional recovery compared to the myocardial infarcted samples. Injectable hydrogel with biomolecules such as VEGF is one of the promising methods for recovery of myocardial infarction

### References:

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3. M. Fujita *et al.*, *J Surg Res.* 2005; **126**: 27- 33