

Myocardial protection and angiogenic synergism in acute myocardial infarction using dual growth factor with self-assembling peptide nanofiber hydrogel

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Statement of Purpose: Here we demonstrate that myocardial protection of infarcted heart using dual growth factor delivery with self-assembling peptide nanofiber hydrogel (SAP). The SAP, RADAI-16, forms fibers (5 to 10 nm) and assembles into a 3D scaffold at physiological pH and osmolarity¹⁻³. Since SAP can be easily designed and modified in a variety of ways, it is promising candidates for biomaterials in tissue engineering and regenerating medicine⁴⁻⁷.

Methods: Myocardial infarction (MI) was produced in ~150g Sprague-Dawley male rats. After left coronary artery ligation, growth factor with SAP (AcN-RARADADARADADA-CNH2, Peptron, Daejeon, Korea) was injected into infarcted border zone (n=6 in each group: Sham, MI, MI + SAP, MI + SAP/FGF-2, MI + SAP/PDGF-BB, MI + SAP/FGF-2/PDGF-BB, and MI + FGF-2/PDGF-BB). The hearts were harvested 4 weeks after surgery for functional (hemodynamics) and histological analysis.

Results: In Masson's trichrome staining for infarct size measurement, injection of SAP could prevent cardiac fibrosis and dual growth factor with SAP was significantly reduced (35.91 ± 4.91 % in MI, 28.88 ± 3.33 % in MI + SAP, and 9.25 ± 2.57 % in MI + SAP/FGF-2/PDGF-BB, figure 1).

In TUNEL staining, injection of SAP were reduced ~50 % of cardiomyocyte apoptosis in border zone compared with MI. In dual growth factor with SAP group, there was no difference with sham group.

To validate the capillary density, arterial density and maturation index, myocardial sections were examined by double staining with anti-von Willebrand factor antibody (vWF, for endothelial cells) and anti- α -smooth muscle actin antibody (α -SMA, for smooth muscle cells). Capillary and arterial density in dual growth factor with SAP group was dramatically increased and statistically no difference with the sham group (figure 1). Additionally, ~80 % of the newly formed vessels were matured in this group (no difference with the sham group).

Moreover, consistent with the results obtained in histological analysis, cardiac function of this group was almost recovered and ejection fraction was 43.7 ± 1.4 % (18.37 ± 2.9 % in MI and 51.0 ± 1.8 in sham).

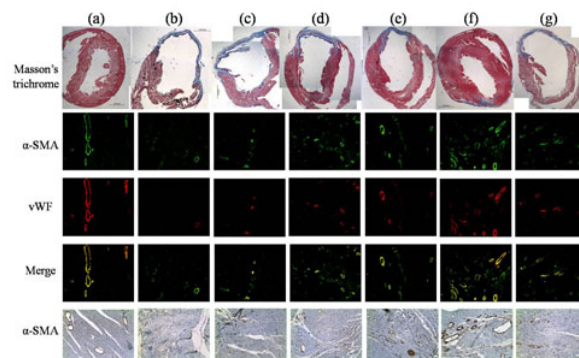


Figure 1. Histological analysis 4 weeks after surgery. Masson's trichrome staining for infarct size measurement, α -SMA staining for arterial density and vWF staining for capillary density. Sham (a), MI (b), MI + SAP (c), MI + SAP/FGF-2 (d), MI + SAP/PDGF-BB (e), MI + SAP/FGF-2/PDGF-BB (f), MI + FGF-2/PDGF-BB (g).

Conclusions: In conclusion, dual growth factor with SAP is effective to myocardial protection and angiogenesis, and leads to improvement in cardiac function.

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