

# Instructive Nanofibrous Scaffolds for Cardiac Tissue Engineering

## Patrick C.H. Hsieh

Associate Professor & Attending Surgeon

Graduate Institute of Clinical Medicine and Center for Clinical Research,  
Department of Surgery & Graduate Institute of Biomedical Engineering,  
National Cheng Kung University & Hospital, Tainan, Taiwan

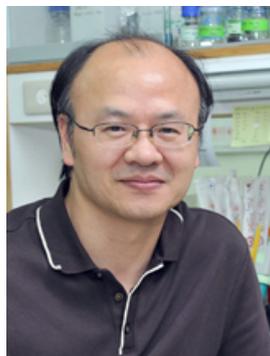
Joint Assistant Research Fellow

Taiwan Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan

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Angiogenic therapy is a promising approach for tissue repair and regeneration. However, recent clinical trials using protein delivery or gene therapy to promote angiogenesis have failed to provide therapeutic effects. A key factor for achieving effective revascularization is the durability of the microvasculature and the formation of new arterial vessels. Accordingly, we carried out experiments to test if intramyocardial injection of self-assembling peptide nanofibers (NF) combined with vascular endothelial growth factor (VEGF) may create an intramyocardial microenvironment with prolonged VEGF releasing to improve post-infarction neovascularization in rats. Our data showed that when injected with NF, VEGF delivery was sustained within the myocardium for up to 14 days, and the side effects of systemic edema and proteinuria were significantly reduced to the same level as control. We also found NF/VEGF injection significantly improved angiogenesis (2.8 folds increase in capillary density), arteriogenesis (4.9 and 4.4 folds increase in arteriole and artery densities, respectively) and cardiac performance (51% increase in left ventricular fraction shortening) 28 days after myocardial infarction. As a result, NF/VEGF injection not only allowed controlled local delivery, but also transformed the injected site to a favorable microenvironment that recruited endogenous myofibroblasts and helped achieve effective revascularization. Strikingly, the engineered vascular niche further attracted a new population of cardiomyocyte-like cells to home to the injected sites, suggesting cardiomyocyte regeneration. Furthermore, large animal study also revealed consistent benefits. In summary, this study demonstrates a new strategy for cardiovascular repair with great potential for future clinical translation.

**Organizer: GCOE Program Center for Medical System Innovation through Multidisciplinary Integration, The University of Tokyo**

**Teruyuki Nagamune, Professor,**

**Department of Bioengineering, Graduate School of Engineering, The University of Tokyo**

**Cooperation: Center for NanoBio Integration, The University of Tokyo**

**For Further Information Contact: Kiyoko Jarnes at CMSI Office**

**Phone: 03-5841-1509 / Fax: 03-5841-1510**

**E-mail: [jarnes@cnbi.t.u-tokyo.ac.jp](mailto:jarnes@cnbi.t.u-tokyo.ac.jp)**

**Registration: <http://park.itc.u-tokyo.ac.jp/CMSI/>**

