An economical, effective and biocompatible gene therapy strategy promotes cardiac repair

July 6 2012

Dr Changfa Guo, Professor Chunsheng Wang and their co-investigators from Zhongshan hospital Fudan University, Shanghai, China have established a novel hyperbranched poly(amidoamine) (hPAMAM) nanoparticle based hypoxia regulated vascular endothelial growth factor (HRE-VEGF) gene therapy strategy which is an excellent substitute for the current expensive and uncontrollable VEGF gene delivery system. This discovery, reported in the June 2012 issue of *Experimental Biology and Medicine*, provides an economical, feasible and biocompatible gene therapy strategy for cardiac repair.

Transplantation of VEGF gene manipulated mesenchymal stem cells (MSCs) has been proposed as a promising therapeutic method for cardiac repair after myocardium infarction. However, the gene delivery system, including the VEGF gene and delivery vehicle, needs to be optimized. On one hand, long-term and uncontrollable VEGF over-expression in vivo has been observed to lead to hemangioma formation instead of functional vessels in animal models. On the other hand, though non-viral gene vector can circumvent the limitations of virus, drawbacks of the current non-viral vectors, such as complex synthesis procedure, limited transfection efficiency and high cytotoxicity, still needs to be overcome.

Co-investigators, Drs. Kai Zhu and Hao Lai, said "Hypoxia response elements were inserted into the promoter region of VEGF gene to form

HRE-VEGF, which provided a safer alternative to the conventionally available VEGF gene". "The HRE-VEGF up-regulates gene expression under hypoxic conditions caused by ischemic myocardium and turns it off under normoxia condition when the regional oxygen supply is adequate."

The hPAMAM nanoparticles, which exhibit high gene transfection efficiency and low cytotoxicity during the gene delivery process, can be synthesized by a simpler and more economical one-step/pot polymerization technique. Drs. Zhu and Lai, said "Using the hPAMAM based gene delivery approach, our published and unpublished results explicitly demonstrated that it was an economical, effective and biocompatible gene delivery vehicle".

Dr Guo concluded that "Treatment with hPAMAM-HRE-VEGF transfected MSCs after myocardium infarction improved the myocardial VEGF level, which improved graft MSC survival, increased neovascularization and ultimately improved heart function. And this novel VEGF gene delivery system may have clinical relevance for tissue repair in other ischemic diseases".

Dr. Steve Goodman, Editor-in-Chief of Experimental Biology and Medicine said "Guo and colleagues have provided an exciting new nanoparticle based gene therapy for cardiac repair. This novel approach has great promise for repair of the heart after myocardial infarction."

Provided by Society for Experimental Biology and Medicine

Citation: An economical, effective and biocompatible gene therapy strategy promotes cardiac repair (2012, July 6) retrieved 25 April 2024 from https://medicalxpress.com/news/2012-07-economical-effective-biocompatible-gene-therapy.html

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