DNA as Material for Treatment of Cardiovascular Disease

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Regenerative medicine is emerging as a potential strategy for the treatment of peripheral arterial disease (PAD) and ischemic heart disease (IHD). To develop new innovative drug to stimulate angiogenesis, we identified that HGF (hepatocyte growth factor) has the potent angiogenic activity in animal studies. Preclinical studies have indicated that HGF stimulated the development of collateral arteries, a concept called "therapeutic angiogenesis". Thus, we planed a prospective open-labeled trial of gene therapy (TREAT-HGF) in 22 patients with PAD, by intramuscular injection of naked plasmid human HGF DNA. The ankle-brachial index (ABI) was significantly increased at 2 months after injection ($P<0.01$), and reduction in ulcer size (>25%) was observed in 18 of 25 ulcers. In addition, the results of The Phase II Randomized, Double-Blinded, Placebo Controlled Trial (HGF-STAT) was reported in 2006 (PI; Dr. Richard Powell, Dartmouth). Purpose of HGF-STAT was to determine the effect of intramuscular injection of HGF plasmid on limb perfusion as measured by transcutaneous oxygen tension (TcPO2) in patients with critical limb ischemia. TcPO2 in high dose group was significantly higher when compared to Placebo group ($P<0.05$). Currently, randomized placebo-control phase III trial to treat PAD is ongoing in Japan.

In addition, we employed this strategy to treat IHD. Based on these unique characters of HGF, Phase 1 clinical trial to treat IHD was finished in 2006 in USA. DNA would become a novel material for treatment of cardiovascular disease including peripheral arterial disease and myocardial infarction.