Cell Regeneration Research Center(CRRC)

CRRC

Director
Prof. Youngkeun Ahn, M.D., Ph.D.

Major research goals

Cardiovascular injury involves the loss of cardiomyocytes, pathological fibrosis, and excessive inflammation which result in cardiac remodeling and dysfunction. Although we have hundreds of clinical therapies that include the standard drugs right now, the prevalence rate of cardiovascular disease shows a striking increase. Regeneration therapy is the hottest topic in medical field and has shown remarkable responses but those responses are quite variable, and can take a long time to occur. Mesenchymal stem cells(MSC) are regarded as safe and feasible for cardiovascular therapy in clinical applications. Cardiac function is significantly improved after stem cell therapy, mainly in association with the induction of angiogenesis, the paracrine effect, or stimulation of endogenous cardiac progenitor cells. Despite intense efforts, however, recent multiple meta-analyses have debated whether the therapeutic efficacy of MSC treatment is significant. For cardiac regeneration, we have established a Cell Regeneration Research Center(CRRC) and cooperated in basic science, medical research, bioengineering to carry out the highly effective and safe regeneration therapy.

Our research center approaches to bridge between the basic scientific evidences and clinical issues, with a goal towards identifying novel therapeutic targets for rapid translation into clinical medicine. Our lab focuses elucidates the basic mechanisms underlying cardiovascular disease with the aim to develop new cellular and pharmacological therapies to restore and promote cardiac regeneration in vivo.

Major research topics

1. Currently, our laboratory focuses on cardiac regeneration-related cellular events in cardiovascular disease. Of particular interest are the development cell optimally effective stem cell products for clinical application, the trans-differentiation of stem cell to cardiac cells by using chemical compounds, and the regenerative recovery of pathological cardiac niche.
2. We found that the phenotype modulation of inflammatory macrophages recruited in cardiovascular lesions dramatically contributed to cardiac recovery. We proved this concept by

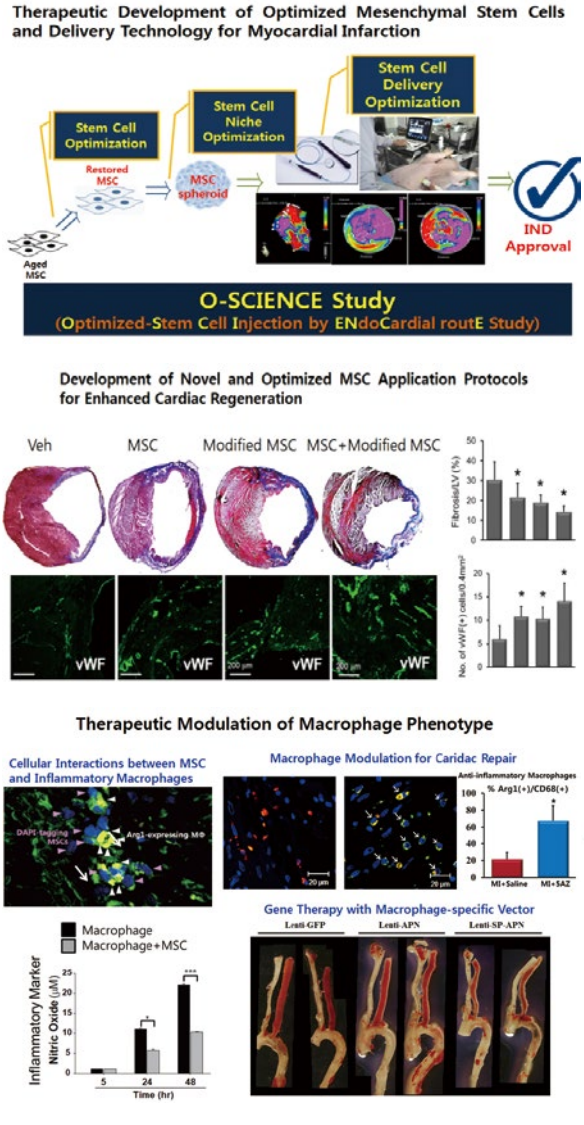
using macrophage-specific vectors and chemical compounds with research articles and patents. More powerful vector for targeting macrophages is developed and tested in animal models.

3. MSC is well known to be hardly differentiated to cardiomyocytes. We screened various compounds, and selected highly effective cardiac inducers. Several candidates are under intensive investigation to verify their safety and efficacy for further clinical application.
4. Besides stem cells, somatic cells are good and sound sources for regeneration therapy. We have already found a effective cardiac inducer for fibroblasts and myoblasts from adult human, and their action mechanisms are under investigation.

Major achievements

1. Development of reliable animal models for cardiovascular disease and equipped stable facilities for preclinical studies including mice, rats, and pigs.
2. Complete equipments of the NOGA XP System, NogaStar Catheter, and MyoStar Injection Catheter to deliver stem cells or drugs to the heart through endocardial route in pig models. This is the first and only NOGA System and trial in Korea.
3. Identification of oxytocin and apicidin as novel inducers for MSC to cardiac lineage cells.
4. Successful modification of macrophage phenotype in the atherosclerosis lesion with macrophage-specific gene delivery to exert therapeutic effect.
5. Integrated amelioration of damaged cardiac niche including cardiomyocytes, vessels, and infiltrated macrophages by using chemical compounds such as 5-azacytidine, and 6-bromoindirubin-3-oxime(BIO).
6. Of seven national research projects chosen by Korea government in our lab, five projects are strongly associated with cell regeneration.

Representative figures of major achievements



Major relevant publications

1. Mesenchymal stem cells reciprocally regulate M1/M2 balance in mouse bone marrow-derived macrophages. Cho DI, Kim MR, Jeong H, Jong HC, KimYS, AhnY. *Exp Mol Med.* 2014;46:e70
2. A macrophage-specific synthetic promoter for therapeutic application of adiponectin. Kang WS, Kwon JS, Kim HB, Jeong H-y, Kang HJ, Jeong MH, Cho JG, Park JC, KimYS, AhnY. *Gene Ther.* 2014; 21(4):353-362
3. Graphene Potentiates the Myocardial Repair

Efficacy of Mesenchymal Stem Cells by Stimulating the Expression of Angiogenic Growth Factors and Gap Junction Protein. Park J, Kim YS, Ryu S, Kang WS, Park S, Han J, Jeong HC, Hong BH, Ahn Y, Kim BS. *Adv Funct Mater.* 2015;25:2590-2600

4. 5-Azacytidine modulates interferon regulatory factor 1 in macrophages to exert a cardioprotective effect. Jeong H, Kang WS, Hong MH, Jeong HC, Shin MG, Jeong MH, Kim YS,Ahn Y. *Sci Rep.* 2015; 5:15768
5. Natural product derivative BIO promotes recovery after myocardial infarction via unique modulation of the cardiac microenvironment. Kim YS, Jeong HY, Kim AR, Kim WH, Cho H, Um J, Seo Y, Kang WS, Jin SW, Kim MC, Kim YC, Jung DW, Williams DR, Ahn Y. *Sci Rep* 2016;11;6:30726

Research networks

We have organized the Gwangju-Boston Cardiology Research group with outstanding faculties from Korea, USA, Germany, etc. and are having a regular International Gwangju-Boston Joint Cardiology Symposium since 2007. By virtue of active participations, we closely collaborate with leading researchers in the field of regeneration medicine.