# Cardiac Remodeling Research Laboratory

Director
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## Major Research Goals:

With the use of genetically engineered animals, human heart samples, and primary culture vascular smooth muscle cells/cardiomyocyte models, this study aims to discover pathophysiologic mechanisms and therapeutic targets in heart diseases. These works will focus on polyubiquitination-mediated vascular calcification, cytokine-associated cardiac fibrosis, cardiomyocyte remodeling, and the application of microRNA in cardiomyocyte differentiation and regeneration.

## Major Research Topics

The cardiac remodeling and signaling laboratory will study the heart remodeling process of heart failure, fibrosis, and vascular calcification associated with coronary stenosis, which will provide the fundamental bases for addressing therapeutic targets for heart diseases. The study will utilize diverse animal experimental models including genetically engineered mice and will be focused into the following four projects.

- Project 1: Posttranslational modifications of vascular function-regulating proteins that are associated with coronary artery calcification: We will use coronary stenosis-associated calcification models to study posttranslational modifications such as polyubiquitination and sumoylation of epigenetics-related proteins.
- Project 2: MicroRNA-mediated regulation of cardiomyocyte differentiation and cardiac rhythm: Using engineered heart tissue(EHT) analysis, we will investigate the functional role of microRNA in cardiomyocyte differentiation. We will also study the role of microRNA in the conduction system and will delineate the functional roles of microRNA in the development of arrhythmia.
- Project 3: Roles of Akt1/2 in cardiac remodeling and rhythm: We will determine the contribution of Akt1/2 isoforms to the regulation of junctional complex-associated microstructure, fibrosis, and endothelial-mesenchymal transition in the hearts.
- Project 4: Cytokine-mediated cardiac fibrosis: We will study Cytl1, cytokine-like 1, which was first described as a pro-fibrotic cytokine by our team, and its possible therapeutic application.

## Major Achievements

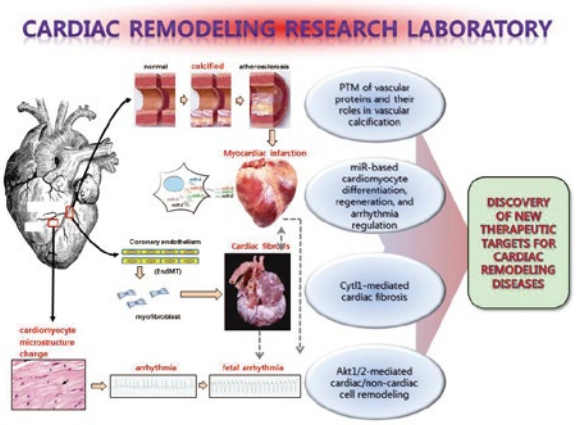
Provide mechanistic evidence of the involvement of polyubiquitination and sumoylation of major vascular proteins in coronary calcification in association with atherosclerosis.

Provide possible therapeutic targets of cardiac regeneration/remodeling and arrhythmia by investigation of microRNA and Akt isoforms.

Provide mechanistic insights and targets against cardiac fibrosis by targeting Cytl1.

Cardiac remodeling is a deleterious event that develops in association with many cardiac diseases including heart failure. In the present study, the mechanisms of cardiac remodeling in many cellular types in the heart will be investigated. This investigation will enable us to suggest novel therapeutics that directly target the heart itself rather than targeting blood vessels secondarily.

## Representative Figure of Major Achievements




## Major Relevant Publications

1. Kwon and Eom et al., MDM2 E3 ligase-mediated ubiquitination and degradation of HDAC1 in vascular calcification. Nat Commun, 7: 10491, 2016.
2. Choe et al., The microRNA miR-34c inhibits vascular smooth muscle cell proliferation and neointimal hyperplasia by targeting stem cell factor. Cell Signal. 27: 1056-1065, 2015.
3. Nam et al., Small heterodimer partner blocks cardiac hypertrophy by interfering with GATA6 signaling. Circ Res. 115: 493-503, 2014.
4. Eom et al., Regulation of acetylation of histone deacetylase 2 by p300/CBP-associated factor/histone deacetylase 5 in the development of cardiac hypertrophy. Circ Res. 114: 1133-1143, 2014.
5. Eom and Kook, Posttranslational modifications of histone deacetylases: implications for cardiovascular diseases. Pharmacol Therapeut. 143: 168-180, 2014.
6. Eom et al., Casein kinase-2α1 induces hypertrophic response by phosphorylation of histone deacetylase 2 S394 and its activation in the heart. Circulation 123: 2392-2403, 2011.

## Research Networks

1. Prof. Young-Kuk Kim, Department of Biochemistry, Chonnam National University Medical School
2. Prof. Jaetaek Kim, Department of Internal Medicine, Chung-Ang University Hospital
3. Prof. Woo Jin Park, Department of Life Sciences, Gwangju Institute of Science and Technology