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Research Interests and Objectives

The research theme in Dr. He' lab includes two major areas: Cardiovascular Injury and Biomedical Imaging

(1) The first major area focuses on mechanistic studies of the effects of obesity, exercise as well as well reactive oxygen/nitrogen species on cardiac function and injury. Currently, there are four active research projects in the lab:

- The effect of high fat diet-induced obesity and endurance exercise on myocardial ischemia reperfusion injury and cardiac remodeling. My lab has demonstrated that Western diet-induced obesity dramatically elevates myocardial tissue oxygenation and exacerbates myocardial ischemia and reperfusion injury. With endurance exercise, the detrimental effect of high fat diet-induced obesity is attenuated. In addition, we have demonstrated that endurance exercise shortens reperfusion recovery time and provides a cure for the reperfusion injury occurred in the post-ischemic heart. This project is currently supported by a grant from Diabetes Action Research and Education Foundation.

- The role of CARD9 and low grade inflammation on obesity-induced myocardial dysfunction. Obesity or diet-induced nutrient stress is associated with low grade inflammation and macrophage accumulation in adipose tissue. Caspase recruitment domain-containing protein (CARD9) plays a central role in the innate and adaptive inflammatory responses. We hypothesize that CARD9-mediated p38 mitogen-activated protein kinase (MAPK) and nuclear factor κB (NFκB) are involved in the regulation of peroxisome proliferator activator receptor γ coactivator-1α (PGC1α), nuclear respiratory factor-1 (NRF-1), and transcriptional factor of activated mitochondria (Tfam) in myocardium. We are actively engaged in an effort to dissect the relational mechanisms between diet-induced obesity, CARD9 activated signaling, and myocardial dysfunction using a novel CARD9$^{-/-}$ mouse model bred in the lab.

- Nitric oxide (NO) and reactive oxygen species and their regulatory roles in the patho/physiology of cardiovascular diseases. My lab has demonstrated that endothelium-derived NO and its derivatives critically regulate post-ischemic heart function and mitochondrial metabolism through suppression of mitochondrial enzymes. In order to determine the *in vivo* regulatory role of NO on mitochondrial respiration, we utilized our novel oximetry and redox imaging techniques to assess real-time myocardial tissue oxygen consumption and real-time tissue injury. We will continue to employ those advanced techniques and *in vivo* regional ischemia reperfusion mouse heart models to determine NO-related regulatory mechanisms in the post-ischemic myocardium. These projects have been supported by NIH R01 and related grants.

- The effects of hyperoxia and NO on post-ischemic myocardial infarct healing and repair. My lab has demonstrated that tissue hyperoxia up-regulates TGF-β signaling, trans-differentiates cardiac fibroblasts to myofibroblasts, and improves post-ischemic cardiac function. As a counteractive control, we have also demonstrated that NO down-regulates the fibrosis process in the healing myocardial infarct as a protective mechanism. These projects allow us to develop molecular and pharmacological interventions aiming at improving the post-ischemic myocardial healing and repair.

(2) The second area involves the development of novel magnetic resonance spectroscopy and imaging techniques and oximetry and redoximetry probes.

- My lab has led or participated in the development of a number of low frequency magnetic resonance spectroscopy and imaging techniques covering frequency range from 300 MHz, 750 MHz, L-band, S-band, to X-band. We have developed and characterized a number of oxygen- and redox-sensitive probes for *in vivo* and *in vitro* detection of tissue oxygenation and redox status. We have also developed a number of low frequency microwave resonators to accommodate subjects from biological tissue, isolated organs, to mouse, rat, and man. With the development of these techniques and chemical probes, we are studying the patho/physiological parameters in cardiovascular systems in normal or disease state including obesity, diabetes, and myocardial dysfunction. These projects have been supported by a number of NIH and Association grants.