



Figure: Research in Molecular Bioengineering. The diagram at the center summarizes the core interests of the research group. Molecular bioengineering refers to the targeted delivery of gene or drug therapy to a tissue or disease of interest, usually in animal models of myocardial infarction (MI) and/or heart failure (HF). Novel diagnostic methods (such as molecular imaging of targeted contrast agents by MRI or high-resolution strain imaging using echocardiography) are then used to assess therapeutic efficacy. Probing disease mechanisms with novel imaging methods often provides new insights into the pathophysiology of the disease, leading to a virtuous cycle in which the insights gleaned from biomedical and molecular imaging are used to further refine and improve the novel therapy under development.

Research interests of the Molecular Bioengineering Lab focus on developing new, more effective strategies for treating and preventing human disease. In parallel, we develop novel diagnostic imaging methods to better understand the progression/regression of disease and the impact of novel therapies on specific disease targets. A highly-collaborative, interdisciplinary approach is used to integrate recent technical advances in multiple fields with our highly translational research. In particular, cutting-edge imaging techniques such as MRI, PET and ultrasound are used to expedite research by providing accurate measures of novel therapies against cardiovascular disease and cancer. Active areas of research are described below.

Molecular Bioengineering Research Group

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“We see molecular bioengineering with targeted gene and drug delivery as a powerful tool for treating and preventing a wide variety of human diseases.”



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Interplay of Nitric Oxide with Superoxide in Health and Disease

A fundamental biological focus of our lab's research is on the physiological significance of the balance that exists between nitric oxide and superoxide in the cardiovascular system. Recent investigations indicate that this balance becomes critical in the setting of heart attack. Nitric oxide and superoxide are free radicals that react spontaneously to form peroxynitrite, a very destructive reactive oxygen species. Basic research efforts in the laboratory are focused on determining the roles played by nitric oxide, superoxide and peroxynitrite in both the acute and chronic settings of myocardial infarction.

Novel Therapies for Cardioprotection and Cardiopreservation

The more translational research focus of the laboratory is to develop novel therapies to protect the heart against myocardial infarction and heart failure. An interdisciplinary approach is used to integrate recent advances in molecular biology with cutting-edge imaging techniques such as MRI, PET and echocardiography to expedite research by accurately measuring the effect of novel therapies on cardiovascular disease. Accurate animal models of myocardial stunning, infarction and left ventricular remodeling after myocardial infarction have been implemented in rabbits, rats and mice. Using direct gene transfer techniques in these models, we have previously shown that either superoxide dismutase or nitric oxide synthase can provide the heart with substantial protection against myocardial infarction (i.e. reduce the extent of myocardial infarction by >50%). Recently, the excess production of superoxide and nitric oxide has also been implicated in the progressive loss of cardiac function that characterizes heart failure after myocardial infarction. Indeed, we recently showed that cardiac-targeted gene therapy with extracellular superoxide dismutase (EcSOD) markedly attenuates left ventricular remodeling after myocardial infarction by reducing the formation of peroxynitrite and thereby controlling oxidative damage in the heart.

RECENT RESEARCH DEVELOPMENTS

- Administering a cardiac-targeted AAV9 vector after ischemia and reperfusion provides for the preferential transduction of cardiomyocytes at risk in the infarct border zone
- Administering a single intravenous injection of cardiac-targeted AAV9 expressing EcSOD suffices to protect the heart against subsequent LV remodeling, even when injected AFTER myocardial infarction.

CURRENT GRANT SUPPORT

- US National Heart, Lung and Blood Institute – Multi-parameter CMR of post-MI Left Ventricular Remodeling in Gene Modified Mice
- US National Heart, Lung and Blood Institute – A Bioengineering Approach to Gene Therapy for Peripheral Arterial Disease
- US National Cancer Institute – Highly Specific and Efficient Vectors for Targeting Pancreatic Cancer

SEAS Research Information

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