

SPECIFIC ONGOING PROJECTS

Dr. Erica Sneider is using *ApoE* knock out mice as a model of murine hypercholesterolemia to study the effects of “triple diet” therapy, i.e., a diet containing tetrahydrobiopterin, L-arginine alpha ketoglutarate and L-ascorbic acid, on the oxidative stress known to occur in the presence of dyslipidemia. The specific focus of the project is the effects of the independent variables (diet, genetics) on the dependent variables of post-ischemic arteriogenesis and angiogenesis, and most specifically on the effects of the independent variables on platelet function in post-ischemic neovascularization (platelet production of nitric oxide and SDF-1 α , and the interaction of these platelet functions on vessel repair.

Dr. Sebastian DiDato is studying adiponectin, an adipose derived protein, which previous studies have shown, may have a protective effect in cardiovascular disease. The project involves using a gain of effect and loss of effect model to determine if restoration of adiponectin expression in adiponectin deficient mice will restore the ability of bone marrow mesenchymal stem cells to differentiate into endothelial cells. In addition, he plans to use a mouse model of hindlimb ischemia to follow the recovery of adiponectin deficient mice in which adiponectin expression has been restored. He plans to use these results to better characterize the molecular mechanism of adiponectin on the differentiation of mesenchymal stem cells and help generate novel therapies in the treatment of cardiovascular disease.

Dr. Sujuan Guo is studying the effects of “triple diet” therapy (a diet containing tetrahydrobiopterin, L-arginine alpha ketoglutarate and L-ascorbic acid) on the evolution of atherosclerosis in *ApoE^{h/h}Ldlr^{-/-}* mice, a genetic model of profound hypercholesterolemia that yields early, severe atherosclerotic plaque. The dependent variables under study include cardiac function (per echocardiography), plaque area, measures of aortic root oxidative stress markers, eNOS expression and function, and hematopoietic stem cell quantity and quality within the bone marrow. The project is designed to test the hypothesis that the oxidative stress characteristic of hypercholesterolemia exerts an effect on hematopoietic stem cells, which in turn affect the rate of progression of atherosclerotic plaque.

Dr. Jinglian Yan is studying the effects of type 2 diabetes mellitus on the function of mesenchymal stem cells (MSC), a unique bone marrow or tissue derived stem/progenitor cell that is critical in tissue healing and repair, particularly the repair of post-ischemic vascular lesions. In this context, healthy MSC are pluripotent, i.e., they are able to differentiate into a wide range of terminal cells. The study hypothesis is that type 2 diabetes exerts a negative effect on MSC via generation of oxidative stress (both environmental and within the MSC itself, reducing its pluripotency). The project seeks to confirm that reduction of the effects of oxidative stress within the MSC improves its function, specifically restoring MSC pluripotency, and thus improves the capacity of type 2 diabetic mice to recovery from hindlimb ischemia and surface (skin) wounds.