DEPARTMENT OF PEDIATRICS
Medical Center

SUMMER RESEARCH OPPORTUNITIES
FOR UNDERGRADUATE WOMEN

APPLICATION DEADLINE: MARCH 1, 2004

The Department of Pediatrics is pleased to offer the following research project(s) for the summer of 2004. Interested students are urged to contact the faculty member(s) directing the project that most interests them. By contacting the faculty member, you can discover more about the project, learn what your responsibilities will be, and if possible, develop a timetable for the twelve-week research period.

Congenital Heart Disease Research

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My clinical practice involves the care of patients suffering from congenital heart disease, from newborns to adults, and entails corrective and palliative cardiac surgery, heart transplantation and implementation of cardiac assist devices. In addition, I have a strong interest in both basic and translational research as it applies to congenital heart disease.

The primary goal of my laboratory is to understand and improve the outcome of the fetus with congenital heart disease. To this end, our research has two different areas of focus: (1) understanding the role of oxygen as a master regulator of fetal cardiac development; and (2) developing the principles of fetal cardiac surgery/intervention in an animal model of congenital heart disease. To accomplish our studies, we are using (1) the technology of transgenesis to express "oxygen-sensitive" genes in fetal and neonatal cardiac myocytes; and (2) operating on mid-gestation sheep fetuses to create and subsequently repair a model of hypoplastic left heart.

The molecular aspects of this project entail creating transgenic mice that express a variant of HIF (hypoxia-inducible factor 1 alpha), a transcription factor that regulates the expression of many genes involved in oxygen delivery or metabolism, such as Epo, VEGF, Transferrin, the glycolysis pathway enzymes and a few others. Normally, the expression of this protein is regulated at the translational level, such that in the presence of certain oxygen concentrations, particular proline residues of the HIF1a are hydroxylated by specific prolyl hydroxyases. The hydroxylated protein is then tagged by the pVHL/ubiquitin complex and degraded. The variant HIF1a that I am studying in the laboratory is no longer degraded in the presence of oxygen. This protein will be expressed under the control of cardiac specific promoters during different stages of heart development. This research is directed towards understanding the role of oxygen in cardiac development. Ultimately, we will also be studying the changes in tissue expression of HIF and HIF-pathway genes secondary to changes in oxygen distribution to the myocardium and the lungs from altered fetal circulation in our fetal sheep models (see below).

The alternative research project entails creating models of left heart obstruction in mid-gestation fetal sheep. In the process, we evaluate the echocardiographic, anatomic and physiologic changes of the fetal heart to abnormal blood flow patterns through the heart. Having defined the natural history of these lesions, we ultimately plant to test a trial of fetal intervention in our animal models. In addition, we are studying the response of natriuretic peptides BNP and ANP as makers of cardiovascular wellbeing in these fetuses. Our goal is to identify markers of fetal heart disease that can be implemented for prognostication and decision making in fetal intervention. Finally, as part of our collaborative effort focused toward fetal cardiac intervention and surgery, we have started preliminary studies looking at fetal cardiopulmonary bypass (CPB), using novel CPB circuitry and approach.

A variety of potential projects could be of interest to students during their summer research tenure.