

**CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER**  
**Pediatrics**

**SUMMER RESEARCH OPPORTUNITIES  
FOR UNDERGRADUATE WOMEN**

**APPLICATION DEADLINE: MARCH 3, 2008**

*The Department of Pediatrics is pleased to offer the following research project for the summer of 2008. 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.*

**ROLE OF ANGIOPOIETIN-LIKE 4 IN ARTHRITIS**

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**Project Description**

Mechanisms controlling the pathogenesis of rheumatoid arthritis (RA) are still poorly understood. Within the joint tissue several processes govern the balance of anti- and pro-inflammatory factors that can greatly affect the progression of disease. To discover genes that may play a role in the pathogenesis of arthritis, ***whether anti- or pro-inflammatory***, we have analyzed gene expression during the course of disease using a mouse model of arthritis, collagen-induced arthritis (CIA). Angiopoietin-like 4 (Angptl4) was one of only five genes, out of 8734 tested, whose expression was differentially increased at least nine-fold in early CIA paws as compared to normal mouse paws and was novel to arthritis. Previous functional and structural analyses suggested Angptl4 has the potential to be anti-inflammatory. Functionally, Angptl4 has been shown to inhibit lipoprotein lipase, which can induce TNF- $\alpha$ , one of the major pro-inflammatory cytokines involved in arthritis. Structurally, Angptl4 is highly similar to Angiopoietin-1, which is involved in vascular stabilization and exhibits anti-inflammatory properties.

Our preliminary data indicate that Angptl4 is expressed in fibroblast-like synoviocytes in human and mouse arthritic tissues. *In vitro* cultures of RA or juvenile idiopathic arthritis (JIA) synovial fibroblasts show an increase in Angptl4 mRNA levels in

response to synovial fluid from systemic JIA arthritic joints. Preliminary functional analysis demonstrates that Angptl4 deficiency results in an *earlier onset* and *marked increase in incidence and severity of CIA* in C57Bl/6 female mice as compared to controls, suggesting that Angptl4 has **protective**, or **anti-inflammatory** effects on the development of arthritis. Thus our working hypothesis is that *Angptl4 is protective against the development of inflammatory arthritis*.

Projects available for WISE program students would include either (1) the analysis of histological parameters in joint tissues between Angptl4 deficient and wildtype mice, or (2) the analysis of specific cytokine inhibitors on Angptl4 mRNA expression in human synovial fibroblasts.