

**CHILDRENS HOSPITAL
Department of Pediatrics**

**SUMMER RESEARCH OPPORTUNITIES
FOR UNDERGRADUATE WOMEN**

APPLICATION DEADLINE: March 1, 2006

The Department of Pediatrics is pleased to offer the following research project for the summer of 2006. 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.

PATHOGENESIS OF INFLAMMATORY ARTHRITIS

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Angiogenesis plays a major role in the pathogenesis of inflammatory arthritis. Several angiogenic molecules, including vascular endothelial growth factor and angiopoietin 1, are increased during arthritis, and inhibition of angiogenesis suppresses arthritis in animal models. Angiopoietin-like 4 (Angptl4) is structurally and functionally similar to the angiopoietins. Previously, human Angptl4 was shown to inhibit endothelial cell apoptosis and induce endothelial cell tubule formation, suggesting a role for this protein in blood vessel formation and/or stabilization. We have recently reported that mouse Angptl4 mRNA and protein levels are highly upregulated in arthritic paws of collagen induced arthritis (CIA) mice, and that Angptl4 can induce endothelial cell tubule formation in vitro. These data suggest that Angptl4 may play a role in angiogenic processes during arthritis.

Angptl4 binds endothelial cells similarly to other angiopoietins, and our functional analysis demonstrates direct effects of Angptl4 on these cells. We are interested in determining which domains of Angptl4 bind EC and are responsible for its effects on endothelial cells. Similar to the angiopoietins, Angptl4 has a fibrinogen-like domain and a coiled-coiled domain, both of which will be tested for their function in endothelial cells. Molecular techniques will be used to generate deletions/mutations of the recombinant Angptl4 tagged with alkaline phosphatase and these mutations will be tested biochemically for their binding to endothelial cells and functionally for their ability to induce endothelial cell tubule formation.