

CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER
Pediatrics

SUMMER RESEARCH OPPORTUNITIES
FOR UNDERGRADUATE WOMEN

APPLICATION DEADLINE: MARCH 1, 2005

The Department of Pediatrics is pleased to offer the following research project for the summer of 2005. 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.

A research study of cockroach sensitization as an important cause of asthma.

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Cockroach sensitization has been recognized as an important cause of asthma for over 30 years. In addition to the potent allergens that cockroaches produce, it has recently been shown that cockroach and other aeroallergens contain protease activity. Inhalation of these proteolytically active molecules may have a direct effect on the airway epithelium. In fact, the house dust mite protease (Der p 1) has been shown disrupt intercellular tight junctions and detachment of lung epithelial cells. Our laboratory has been studying the role of German cockroach (*Blattella germanica*) proteases in modulating airway inflammatory responses. Recently we discovered that German cockroach extract increases epidermal growth factor receptor (EGFR) expression in a human bronchial epithelial cell line (16HBE14o-). EGFR is an important primary regulator of epithelial repair and mucin production. In fact, increased EGFR levels have been reported in bronchial mucosa taken from subjects at autopsy from asthma. Studying the regulation of cockroach extract-induced regulation of EGFR would be a possible project for a WISE undergraduate student. This project will consist of performing western blot analysis of dose curves and time courses of cockroach extract treatment with quantitative real time PCR performed to confirm transcriptional regulation. The involvement of the cockroach serine proteases will be investigated by abolishing the active serine proteases in cockroach extract prior to treatment of the cells. Cockroach-derived proteases have been previously shown to activate the signaling intermediate ERK (extracellular regulated kinase). To determine the mechanism of cockroach extract-induced upregulation of EGFR, we would begin by using chemical inhibitors of the ERK signaling cascade to inhibit EGFR upregulation caused by cockroach extract. In addition, confirmation that the increased EGFR is localized to the plasma membrane will be accomplished using flow cytometry. Lastly, since overexpression of EGFR is associated with increased mucin production, and since allergen exposure increases mucin synthesis (MUC 5AC) in rats, we want to investigate the role of cockroach extract on mucin production *in vitro*. This will be accomplished by quantitative real time PCR and ELISA. Completion of this

project will yield insight into the role of cockroach protease on direct modulation of the human airway epithelium.