PEDIATRICS/IMMUNOBIOLOGY
COLLEGE OF MEDICINE

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PROJECT TITLE: **Staphylococcal biofilms in allergic disease**

Andrew Herr
College of Medicine
Cincinnati Children's Hospital
3333 Burnet Ave, MLC 7038
Cincinnati, OH 45229
andrew.herr@cchmc.org
Phone: 513-803-7490

**Project Description**

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder that affects 15-20% of children worldwide. In addition to the characteristic lesions accompanied by intense itching, AD increases the risk of microbial colonization and allergic responses including food allergy, allergic rhinitis, and asthma, in a process referred to as the atopic march. It was noted over 40 years ago that AD lesions were frequently colonized by *Staphylococcus aureus*. Recently, lesions from AD patients were discovered to be colonized by both *S. aureus* and *S. epidermidis* strains that formed biofilms, which are adhesive surface-attached colonies that become highly resistant to antibiotics and immune responses. *S. epidermidis* is a normal skin commensal that in some contexts can antagonize *S. aureus* biofilm growth. However, we have found that *S. aureus* and *S. epidermidis* are capable of forming synergistic mixed biofilms when co-cultured, which is consistent with recent skin microbiome surveys showing increased prevalence of both *S. aureus* and *S. epidermidis* on AD lesional skin. Data from our lab and others has shown that staphylococcal biofilm growth is dependent on intercellular adhesion events mediated by the Aap and SasG proteins expressed on the surfaces of *S. epidermidis* and *S. aureus*, respectively. It has recently been shown that Aap and SasG can mediate heterophilic adhesion events between *S. epidermidis* and *S. aureus* cells. Our central hypothesis is that such heterophilic protein adhesion events facilitate the growth of strong mixed-species staphylococcal biofilms on AD lesional skin, which promote inflammation, compromise skin barrier function, and result in more severe AD and progression to asthma. Through the proposed aims, we will 1) test whether heterophilic protein interactions between Aap and SasG allow synergistic growth of mixed-species biofilms between *Staphylococcus* spp colonizing AD but not normal skin; 2) delineate the mechanistic basis by which mixed biofilms promote disease; and 3) test whether synergistic staphylococcal strains that
make the strongest mixed biofilms are associated with AD severity, barrier dysfunction, and progression to asthma in M-PAACH children.

In this project, students will learn microbiological culture techniques and biofilm growth assays applied to clinical isolates sampled from a pediatric cohort of AD patients. This would be a great project for someone interested in basic research or clinically-relevant research related to microbiology, immunology, or infectious disease.