Summer Undergraduate Research Program 2017

Faculty Project Proposal Submission

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THERE ARE 4 PROJECTS AVAILABLE TO STUDENTS

1.) Project Name(s): Unraveling the genomics, recombination and evolution of *Chlamydia trachomatis* to develop a gene transfer system

General Topic (Keywords): *Chlamydia trachomatis*, genomics, recombination, transposon, gene transfer system, tetracycline resistance

Project Description(s): Prevention of *Chlamydia trachomatis* (*Ct*) infection represents a critical unmet medical need. *Ct* causes blinding trachoma and sexually transmitted diseases that can result in infertility, ectopic pregnancy. *Ct* is also an important cofactor in cervical cancer and HIV transmission. It is the leading bacterial sexually transmitted infection (STI) worldwide with over 110 million cases worldwide according to the World Health Organization. *Ct* is also the leading cause of preventable blindness (referred to as trachoma) worldwide with an estimated 600 million cases with 9 million blind and over 150 million at risk for visual impairment or blindness. Because *Ct* is an obligate intracellular pathogen, developing a gene transfer system to study the effect of different genes has been difficult. Understanding gene function can lead to the development of potential targeted treatment and a vaccine. Our lab was the first to recognize that *Ct* undergoes recombination as an evolutionary strategy, and to perform comparative genomes on multiple different strains of the species, both of which have provided clues to developing a gene transfer system. In addition, a closely related species of *Ct* called *Chlamydia suis* has acquired a tetracycline transposon. We will evaluate the mechanisms used by *C. suis* to acquire this transposon through genetic mating studies of tetracycline and tetracycline resistant strains, determination of the mechanisms the organism uses for transfer of the transposon (e.g., enzymes, insertion sequence elements, chi sites, etc.), and genomic sequencing to identify the insertion location in the genome and genetic factors that allow for or create a barrier for integration into the chromosome. From these data, we will develop a shuttle
vector system containing a synthetic, tetracycline-free genomic island or scaffold with the gene(s) of interest for transformation into Ct as stable gene transfer system.

**Desired Skills or Experience:** Undergrad interested in a multidimensional and fulfilling lab experience – no prior experience required although some courses in molecular biology and/or genetics would be helpful.

**Time Commitment:** Full time in summer and then part time during the academic year for those students interested in continuing; the project could become a senior thesis.

**Preferred Starting Date:** Late May

2) **Project Name(s):** The ocular microbiome in heath and disease

**General Topic (Keywords):** *Chlamydia trachomatis*, other *Chlamydiaceae* species, functional genomics, microbiota, metabolomics

**Project Description(s):** *Chlamydia trachomatis* (*Ct*) is the leading cause of preventable blindness worldwide with an estimated 600 million cases with 9 million blind and over 150 million at risk for visual impairment or blindness. This blinding eye disease is called trachoma and is found in developing countries worldwide. While we know that *Ct* is a cause of trachoma, other *Chlamydiaceae* species have been implicated in disease pathogenesis, namely *C. pneumonia*, *C. psittaci*, *C. pecorum* and *C. suis*. But we lack appropriate knowledge about other microbes that many contribute to ocular disease in trachoma endemic areas. Therefore, we will be studying the microbiota among patients with and without trachoma, and with and without *Chlamydia* infection, in samples from populations in trachoma endemic regions of Nepal, Ethiopia and Vietnam. We will employ genomics to identify all organisms present at the species level, metabolomics to identify metabolic profiles, and transcriptomics to identify gene expression profiles that will enhance our understanding of what constitutes a healthy conjunctiva and what contributes to the trachomatous conjunctiva. This research will aid in the development of tests to detect ocular pathogens and provide invaluable data for drug targets and chlamydial vaccine development.

**Desired Skills or Experience:** Undergrad interested in a multidimensional and fulfilling lab experience – no prior experience required although some courses in molecular biology and/or genetics would be helpful.

**Time Commitment:** Full time in summer and then part time during the academic year for those students interested in continuing; the project could become a senior thesis.

**Preferred Starting Date:** Late May

3) **Project Name(s):** Investigation of intracellular trafficking and secretory pathways involved in regulating inflammatory proteins by *Chlamydia trachomatis* to detect drug targets and develop a rational vaccine.
General Topic (keywords): Chlamydia trachomatis, ex vivo tissue, primary human tissue, pathogenesis, tissue engineering, metabolism, protein trafficking

Project Description(s): Chlamydia trachomatis (Ct) is an obligate intracellular human pathogen that multiplies within a parasitophorous vacuole called an inclusion. Ct is the leading bacterial cause of STDs worldwide with over 110 million cases occur annually according to the World Health Organization. Our research identified the first host proteins that are translocated from the cytoplasm into the inclusion. These proteins likely support remodeling and scavenging of host lipids into bacterial-specific moieties essential to Ct growth. We are in the process of further investigating the intracellular Ct infections and trafficking of various enzymes and proteins into the inclusion using established and primary human conjunctival, cervical and endometrial cells. Primary cells more closely mirror what happens in vivo compared to knowledge that has been gained using only established cell lines or the mouse model of Ct genital tract infections. We are also exploring RNAseq and host immune responses of clinical Ct strains isolated from conjunctival swabs from trachoma patients. By identifying Ct virulence factors and elicited pro-inflammatory proteins in clinical samples, we can then examine secretory pathways involved in regulating the identified pro-inflammatory proteins in the primary human tissues. Our studies may lead to novel data to develop new drug targets and a rational vaccine to prevent Ct infections.

Desired Skills or Experience: Undergrad interested in a multidimensional and fulfilling lab experience – no prior experience required although some courses in molecular biology and/or genetics would be helpful.

Time Commitment: Full time in summer and then part time during the academic year for those students interested in continuing; the project could become a senior thesis.

Preferred Starting Date: Late May

4) PROJECT NAME: Genomics and pathogenesis of Chlamydia trachomatis sexually transmitted and ocular infections.

General Topic (keywords): Chlamydia trachomatis, pathogenesis, CRISPR, genomics, host genetic susceptibility/HLA, mucosal immunity, ex vivo tissue, primary human tissue, global patient populations

Project Description(s): Chlamydia trachomatis (Ct) is the leading cause of bacterial sexually transmitted infections (STIs) and preventable blindness worldwide. Over 18 million people develop chlamydia STIs each year in the US with untold numbers among ocular trachoma patients in developing countries. Trachoma is a chronic ocular infection caused by Ct. The majority of infections are asymptomatic in both men and women and can result in the severe complications of pelvic inflammatory disease, infertility, ectopic pregnancy and chronic pelvic pain or blindness. Disease progression is likely immune based, and may be related to host genetic factors. Very little is known about the genomic diversity of Ct strains, host immune responses to different strains or host genetic susceptibility to inflammation and disease related to Ct infections. We will evaluate: 1) mucosal immunity, including the inflammasome; 2) single nucleotide polymorphisms (SNP) in inflammatory genes and globally in the genome; 3) HLA types among patients with and without disease; and 4) genomic/genetic factors in Ct that may play a role in disease outcome using the CRISPR system to target various Ct genes and learn about their function. In this way, we will develop a better understanding of the host-pathogen interrelationship and disease pathogenesis for Ct infections to further drug target and vaccine development.
**Desired Skills or Experience:** Undergrad interested in a multidimensional and fulfilling lab experience – no prior experience required although some courses in molecular biology and/or genetics would be helpful.

**Time Commitment:** Full time in summer and then part time during the academic year for those students interested in continuing; the project could become a senior thesis.

**Preferred Starting Date:** Late May