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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 pelvic inflammatory disease (PID), infertility, ectopic pregnancy, and chronic pelvic pain. *Ct* is also an important cofactor in cervical cancer and HIV transmission. It is the leading bacterial sexually transmitted infection (STI) worldwide with over 131 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

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2) **Project Name(s):** The interplay of the ocular microbiome, chlamydial species, and host immune responses in the healthy versus diseased eye

**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 may 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. We will also evaluate the host immune response including eucosinoids. 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

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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 131 million cases occurring 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 intracellular *Ct* infections, effects of mutations in the tryptophan synthase operon (tryptophan is an essential amino acid for *Ct*) 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 patients with chlamydial sexually transmitted diseases and trachoma, a blinding eye disease cause by *Ct*. 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

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4) PROJECT NAME: Role of *C. trachomatis*, microbiota and host immune and signaling pathways in cervicitis.

General Topic (keywords): *Chlamydia trachomatis*, pathogenesis, microbiota, CRISPR, genomics, 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 diseases (STD) with estimates of 2.8 million cases in the U.S. and over 130 million global cases occurring each year. This is due in part to unchecked transmission because ~50% of male and ~80% of female infections are asymptomatic and remain untreated. The endocervix is a primary site of *Ct* infection, which can progress to pelvic inflammatory disease, tubal-factor infertility and ectopic pregnancy. Recent studies have shown that bacterial vaginosis (BV) is correlated with cervicitis and is also a risk factor for *Ct* infection. In contrast, the microbiota of a healthy vagina has been shown *in vitro* to protect against endocervical *Ct* infection. These data derive from a small number of publications, and the true interaction between the vaginal and endocervical microbiomes, host immune responses, cervicitis and *Ct* endocervical infection remain unknown. We propose to: 1) evaluate the vaginal and endocervical microbiota community state types (CST) and how they (and specific microbiota spp.) influence each other, and correlate with cervicitis and *Ct* infection among a large cohort of women at risk for STDs. We will control for other STIs and the secretory phase of the menstrual cycle, which is a known risk factor for *Ct* cervicitis; 2) use vaginal and endocervical samples from the same female cohort, and quantitate host cytokines/chemokines and metabolites to better define *Ct* mechanisms of adaptation to the endocervix or lack thereof within the context of vaginal/endocervical
microbiomes, including CSTs and specific microbiota spp.; 3) test findings from our female cohort in 1) and 2) in human primary endocervical cells, using Ct strains and microbiota isolated from our cohort, and perform dual (d)RNA-Seq during time points of Ct development to elucidate simultaneous host-Ct interactions associated with up- or down-regulation of immunopathogenic Ct genes and host inflammatory pathways. We will also quantitate cytokines/chemokines at the same time points and correlate these with host dRNA-seq results. Our findings will hopefully lead to a greater understanding of host-pathogen interactions and novel targets and/or treatment strategies to prevent Ct infection and decrease the incidence and prevalence of upper genital tract sequelae.

**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