

Summer Externship Opportunities 2016

Clinical
&
Research
Guidebook

SUMMER EXTERNSHIP CLINICAL PROGRAM

Kaiser Permanente Medical Center (4 Positions)

Riverside Medical Clinic (2 Positions)

Riverside University Health Systems (6 Positions)

Summer Externship Clinical Program is a 6-week program consisting of one-week rotations in medicine, cardiology, general surgery, orthopedics, family medicine, neurology, pediatrics, and/or other services the student desire. This program acquaints the student with the private practice aspects of the various specialties in order to be in a better position to choose their eventual specialty.

Renuance Plastic Surgery Clinic (2 Positions)

The Renuance Cosmetic Surgery Center is located in Temecula, California. This one-site surgery center is nationally accredited through AAAASF, which is the highest level for outpatient surgery centers. They perform a broad range of cosmetic surgeries including breast augmentation, abdominoplasty, liposuction, facelifts and more. Dr. Brian Eichenberg, founder, is certified through the American Board of Plastic Surgery and specializing in areas of plastic surgery and aesthetic treatment. Facility has an on-site medical spa for multiple laser treatments.

Students will be acquainted with the clinical practice of plastic surgery and learn the basic surgery principles and practices. They will become familiar with multiple cosmetic surgery procedures as well as general operating room environment and will learn the underlying mechanisms for wound healing, flaps, suture techniques, Botox, filler and lasers.

SUMMER EXTERNSHIP RESEARCH PROGRAM

SPONSOR: Dr. Bahman Anvari

CONTACT: anvarib@ucr.edu

OPPORTUNITIES: 1 Position

Research activities in Anvari's lab are focused on the utility of biological materials as building blocks for engineering and fabrication of optically-activated nano- and micro- structured materials. For example, we have constructed such materials from erythrocytes, which can be doped with various near infrared organic chromophore, including the FDA-approved indocyanine green (ICG). We are interested in ultimate clinical translation of these materials as light-activated theranostic agents for photothermal treatment of port wine stain cutaneous lesions, and cancer imaging.



SPONSOR: Dr. Monica Carson

CONTACT: Monica.Carson@ucr.edu

OPPORTUNITIES: 2 Positions

Traumatic Brain Injury (Concussions) and Neurodevelopmental disorders

Project 1: 90% of TBIs are mild and difficult to detect with standard clinical imaging methods. As yet, there is no reliable method to predict which individuals will have poor outcome following single or repetitive injury. Here we are seeking to develop a blood panel defining risk and likelihood for poor progression in young athletes in the Inland Empire. Project involves both lab work and community outreach.

Project 2: Infancy and childhood are a time of first encounters with common infectious agents. Hence it is a time of frequent systemic immune challenges that for most of us does not lead to overt defects in cognition and/or brain function. However, infections during infancy and childhood do correlate with increased incidence of a wide spectrum of neurodevelopmental disorders ranging from autism spectrum disorders to epilepsy. Our lab uses murine models of systemic challenges to define which and how genetic, environmental and inflammatory factors interact to increase susceptibility to these neurologic disorders. Here, the project would involve the use quantitative analysis of behavior, gene expression, flow cytometry or confocal



microscopy to quantify neuronal development and brain function in murine models of epilepsy and neurodevelopmental disorders.

Publication and Presentation Opportunities:

The medical student would work with post-doctoral fellows leading ongoing projects and have the opportunity to present their research at the annual SoCal symposium on Glia-Neuronal Interactions in Health and Disease, January 2017. Potential exists to help develop a critical review on TBI or neurodevelopmental disorders for publication

SPONSOR: Dr. Iryna Ethell
CONTACT: Iryna.Ethell@ucr.edu
OPPORTUNITIES: 2 Positions



Research in my lab focuses on understanding how neuronal networks are developed and maintained in the brain, with the goal of applying this knowledge to the development of therapeutics for neurodevelopmental and neurodegenerative diseases. We utilize new molecular and imaging approaches in neuroscience and mouse genetics to conduct research on the molecular basis of neurologic diseases. In particular, we are interested in molecular and cellular mechanisms that govern the synapse formation and plasticity in the brain areas that play a critical role in learning and memory.

Two research projects are available in the lab as follows:

Project 1: To study the mechanisms underlying the pathophysiology of Fragile X Syndrome (FXS), a neurodevelopmental disorder associated with intellectual disability and autism; My lab discovered the role of MMP9 in pathophysiology of FXS and demonstrated beneficial effects of minocycline and MMP-9 deletion on synapse development and behavioral performance in an animal model of FXS (Bilousova et al., 2009; Dansie et al., 2013; Sidhu et al., 2014; Lovelace et al., 2016). These findings prompted several clinical trials that tested the effects of minocycline treatment in patients with FXS. Ongoing studies focus on the role of MMP9 and extracellular matrix in autistic behaviors associated with FXS, including the mechanisms of auditory hypersensitivity. In collaboration with Drs. Binder and Razak we are working to develop a preclinical model of auditory processing deficits in FXS. Our studies will determine the interactions between structural and functional changes in auditory circuits in Fragile X mice and will generate therapeutic ideas by targeting multiple pathways involved in the pathophysiology of FXS.

Project 2: To study glial control of synapse development and injury-induced synapse remodeling in the brain and its role in PTSD-related behaviors following traumatic brain injury (TBI). Our new studies also suggest that ephrin-B/EphB receptor signaling is involved in synapse remodeling triggered by TBI. While considerable efforts were devoted to the treatments that enhance neuron survival following brain injury, our understanding of the mechanisms that regulate injury-induced brain rewiring is limited. Brain injury can cause dramatic changes in synaptic connectivity in the brain may lead to cognitive and neuropsychological changes that persist for decades. In the ongoing studies, we investigate new mechanisms of astrocyte-mediated remodeling of synaptic connections in the brain that may aid the functional brain recovery after brain injury. The collaborative studies with Dr. Andre Obenaus's laboratory at the Loma Linda University we are investigating whether the regulation of ephrin-B levels in reactive astrocytes plays a protective or destructive role in the recovery after TBI using both genetic and pharmacologic approaches in a combination with biochemical, anatomical, electrophysiological methods and non-invasive MRI imaging.

SPONSOR: Dr. David Lo

CONTACT: David.Lo@ucr.edu

OPPORTUNITIES: 1 Position

Our lab is studying the mucosal barrier and immune surveillance at this barrier. We are focusing on one cell in the epithelial barrier called the M cell, which captures bacteria and viruses and transports them across the barrier and hands them off to cells in the immune system.



We recently found that in models of Inflammatory Bowel Disease, numerous M cells are newly generated in the colon. Since the colon has the highest concentration of microbes in the gut, we would like to know whether these M cells are helpful to immune surveillance or whether instead they enhance invasion of microbes into intestinal tissue, driving continued tissue inflammation.

In the small intestine, we also found that the toxin produced by the bacteria responsible for cholera (*Vibrio cholerae*; producing cholera toxin) also rapidly induces a different type of M cell in the distal ileum but not elsewhere in the gut. Again, we are interested in whether this phenomenon helps promote colonization by the bacteria or alternatively whether it is an attempt to boost local immune surveillance.

Projects in the lab will involve tissue imaging including Scanning Electron Microscopy to assess its potential as a novel diagnostic tool in endoscopic biopsies, as well as confocal and multiphoton imaging of immune surveillance mechanisms. Gene expression studies will also be done to identify key regulatory pathways in host epithelial responses. We will focus these studies on the question of whether M cell induction in these two models either (1) serves the host in increasing immune surveillance, or (2) serves the pathogens by enhancing their ability to invade and colonize, or (3) does something more complicated.

SPONSOR: Dr. Christian Lytle

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OPPORTUNITIES: 1 Position



The colon cultivates a vast community of beneficial microbes that generates a diverse mix of >500 small (50-1500 Da) molecules. A number of diseases (obesity, diabetes, cardiovascular disease, colorectal cancer, Crohn's disease, food allergies, asthma, autism, eczema) have been associated with disturbances in the microbiome and/or its luminal metabolome. The mechanistic links between the gut metabolome and human health remain poorly understood. A systematic effort, using a combination of approaches, is urgently needed to delineate the subset of metabolites that impact health and to understand how these bioactive molecules exert their systemic effects. We hypothesize that the intestinal epithelium selectively absorbs a limited number of luminal metabolites with bioactive potential while actively excluding potential toxins.

Work in my lab is aimed at mapping the stratification of luminal metabolites across functional segments of the rodent colon using a discovery metabolomics approach that combines the dynamic range and precise identification of ¹H NMR with the sensitivity and resolution of GC/MS. In addition, we are exploiting a novel using chamber approach to delineate the repertoire of fecal solutes that are selectively transported across the colonic epithelium, and the stratification of these transport processes across functional segments of the colon. In addition to identifying microbial metabolites that are afforded access to the systemic blood circulation, our approach enables us to follow the fate of luminal solutes that are metabolically transformed during transit through the colonic epithelial cells. Our work could suggest novel strategies for dietary supplementation of beneficial microbial metabolites in the treatment of microbiome dysbiosis (diarrhea, parenteral nutrition, inflammatory bowel disease).

SPONSOR: Dr. Declan McCole

CONTACT: Declan.McCole@ucr.edu

OPPORTUNITIES: 1 Position

Our lab is focused on understanding the mechanisms involved in regulating epithelial barrier function. When the epithelial barrier in the intestine becomes “leaky” this can allow bacterial products to stimulate inappropriate immune responses and trigger inflammation. Increased permeability of the intestine is a very early event in many diseases including Crohn’s disease, ulcerative colitis, celiac disease & diabetes. We use epithelial cell culture models, transgenic mice and intestinal biopsies from patients to study the role of a candidate gene (PTPN2) associated with all 4 of these diseases in regulating epithelial barrier function in health & disease. We also study how mutations in this gene contribute to barrier disruption in disease.



A summer research project in the McCole lab will focus on identifying signal transduction pathways that are increased in intestinal epithelial cells with deficient PTPN2 gene activity, and how these signaling pathways compromise intestinal barrier function. The project will involve learning some or all of the following approaches:

- i) Epithelial cell culture techniques.
- ii) Permeability assays to measure barrier function.
- iii) Biochemical techniques to identify signaling pathways regulating the epithelial barrier (i.e. Western blotting).
- iv) Fluorescence microscopy to identify changes in localization of key proteins in cultured cells and tissues.

SPONSOR: Dr. Ilhem Messaoudi

CONTACT: Messaoud@ucr.edu

OPPORTUNITIES: 2 Positions

Two research projects are available this summer in the Messaoudi lab:

Project 1: Impact of maternal BMI during pregnancy on neonatal immune outcomes: Obesity during pregnancy is associated with several



health complications for both mother and infant. The risks to the offspring can persist into adulthood and include increased risk of developing metabolic syndrome (including obesity, diabetes and cardiovascular disease), cancer, cognitive disabilities (ADHD, schizophrenia and autism), and asthma/wheezing. Several of these diseases have an inflammatory component, which suggests that pregravid obesity leads to a dysregulation of the offspring's immune system. To uncover the impact of maternal obesity on the neonatal immune system, we are comparing frequency and function of several key immune cells in cord blood samples collected from babies born to obese, overweight and lean mothers. To understand the molecular basis for immune dysregulation in the offspring, we are characterizing epigenetic changes in circulating immune cells. Research activities will range from recruiting/consenting patients to collecting cord blood samples and processing them for analysis using flow cytometry and next generation sequencing.

Project 2: Impact of chronic HIV infection on inflammation and response to vaccination: The development of highly active anti-retroviral therapy (HAART) for HIV infection in the 1990s transformed a disease that was once regarded as a death sentence into a manageable, chronic condition. Today, the average life expectancy after HIV diagnosis is 22.5 years with some patients living up to 50 years longer. Indeed, in 2012 nearly one quarter (24%) of the 1.2 million HIV+ Americans were 55 years of age and older. Despite highly successful viral suppression, individuals with long-standing HIV infection suffer from several HIV-Associated Non-AIDS (HANA) conditions including cardiovascular disease, lung disease, cancer, neurocognitive/neuropsychiatric disorders, osteopenia/osteoporosis, liver cirrhosis, and renal disease indicative of accelerated aging. The mechanisms underlying the increased incidence and severity of HANA conditions in older HIV+ individuals are poorly understood. Consequently, very few interventions are available to counteract these adverse outcomes. We will collaborate with CVCRI, home to Project GRACIE (Geriatric Research of AIDS Comorbidities in the Inland Empire) to establish a registry of older HIV infected and uninfected subjects. We will test the hypothesis that long-term HIV infection exacerbates age-related inflammatory changes due to increased bacterial translocation thereby accelerating the aging phenotype by measuring circulating, inflammatory factors and changes in microbiome. Research activities will range from recruiting/consenting patients to collecting blood/saliva samples and processing them for analysis using flow cytometry and next generation sequencing.

SPONSOR: Dr. Aaron Seitz
CONTACT: ASeitz@ucr.edu
OPPORTUNITIES: 1 Position

The Brain Game Center is having the mission to research, test, and disseminate game software instrumented with expert knowledge to optimize human brain processes with an aim to make scientifically principled brain games that



translate to performance in real-life activities. Projects in the brain game center include assessment and training of cognitive function in healthy and cognitive impaired individuals of a number of different demographics. Opportunities depend upon student interest but include cognitive training in seniors, children with ADHD, individuals with TBI, etc. Please contact Aaron Seitz for more information and to discuss particulars of specific studies.

SPONSOR: Dr. Frances Sladek

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OPPORTUNITIES: 2 Positions

Project 1: We have an on-going diet-induced obesity project in the lab that is focused on evaluating effects of various vegetable oils at the transcriptomic, molecular and metabolomic levels particularly in relation to development of metabolic syndrome. Interested students will be able to learn/perform procedures such as nuclear extract preparation, western blotting, frozen sectioning tissues and doing histological staining with hematoxylin-eosin as well as with Oil-Red-O and ALT assays. In addition, they will also be involved in data analysis and interpretation. This project is important as there is an increasing realization that long held dogma about certain aspects of our diet, such as potential health risks of saturated versus unsaturated fats, are actually not based in sound scientific evidence and could benefit from new analysis using the gamut of modern omics tools.



Project 2: Single nucleotide polymorphisms (SNPs) are an important genetic basis for phenotypic traits as well as disease susceptibility. We have developed a high throughput DNA binding assay called Protein Binding Microarrays (PBMs) with which we have identified 1000's of SNPs in the human genome that alter the ability of nuclear receptors, ligand-dependent transcription factors, to bind DNA. The goal of this project is to use CRISPR/Cas9 to edit the genome of a human colon cancer cell line to provide in vivo proof-of-principle that those SNPs can alter DNA binding to the chromatin and subsequently affect gene regulation. The student will use molecular cloning techniques to generate gRNA/CRISPR/Cas9 vectors and tissue culture techniques to select colonies with the appropriate genome edits. If time allows they will confirm functionality of the edits by ChIP and qPCR assays.

SPONSOR: Dr. Kate Sweeny
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OPPORTUNITIES: 1 Position



Currently, no guidelines exist as to how patients are informed of their medical test results. Of concern to an upcoming project in my lab are two broad options for the delivery of results: (1) open-ended timing, in which patients are contacted without warning when test results become available and the clinician's time allows; or (2) closed-ended timing, in which patients are provided with a specific day and time when they will learn their test results. These options differ in two key ways. First, patients are likely to receive their test results sooner on average when physicians use open-ended timing because closed-ended timing requires that the "appointment" for test result delivery (whether in person, on the phone, or online) be scheduled at a time when the clinician is reasonably certain that the results will be ready. Second, closed-ended timing allows patients to prepare themselves for the event of learning their test results rather than being surprised by a phone call or email notifying them that the results are available. Although we know of no research examining these contrasting approaches to delivering medical test results, a preliminary study found that a majority of patients who were currently awaiting medical test results would have preferred closed-ended timing. In contrast, over 90% of these patients expected to receive their results with open-ended timing.

To address this issue, we will soon be starting a project in collaboration with the Family Care Clinic at the Riverside University Health System – Medical Center (RUHS) to examine the optimal way to deliver medical test results. Our project provides the first comparison between patients' experiences with open- versus closed-ended timing. Clinic staff will identify eligible patients at their appointment and introduce the study when they check in. All patients between the ages of 18 and 90 years' old who visit the clinics for one of the following tests during the study period will be eligible to participate: X-ray, mammogram, Pap test, colorectal screening, or biopsy (all types). Consenting participants will receive either an email or a text message (whichever they choose) approximately 24 hours after their appointment with a link to the first questionnaire. They will receive a second email or text with the link to the follow-up survey within a week after the anticipated date on which test results would be delivered, as indicated by typical processing time for each test. In the initial survey, patients will indicate the type of test they underwent and whether they were provided with open- or closed-ended timing for their anticipated test results. Surveys will also assess patient satisfaction, well-being, and adherence intentions as the primary outcome measures, and test type, demographic variables, dispositional measures, and subjective health status as potential predictors of patient preferences and outcomes.

Joining this project for the summer will involve coordinating with physicians and other staff at RUHS and other potential research sites; interacting with patients to introduce the study and obtain consent; managing data collection; and collaborating with myself and graduate students in my lab to optimize study procedures and measures.