SUMMER EXTERNSHIP OPPORTUNITIES 2018

On Campus Research Opportunities

Off Campus Research Opportunities

Sponsor: Dr. Bahman Anvari

Email: anvarib@ucr.edu

Description of Research Project:

A key focus of our lab is directed towards engineering and clinical translation of optical materials for light-based imaging and therapeutic applications. In particular, we have engineered materials derived from erythrocytes that can be doped with imaging probes and therapeutic agents. A key feature of these particles is that their diameters can be tuned to different diameters; hence; enabling them as versatile platform for various potential clinical applications ranging from vascular to tumor imaging and therapy. Activities in our lab include characterization of biochemical, mechanical, and material properties of these particles, and evaluating their efficacy in appropriate animal models.

Sponsor: Dr. Monica Carson

Email: Monica. Carson@ucr.edu

Description of the Project:

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 a 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.

Sponsor: Dr. Monica Carson

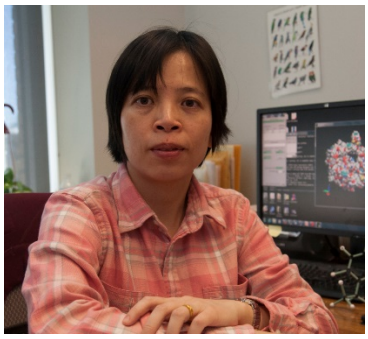
Email: Monica. Carson@ucr.edu

Description of the project

Infancy and childhood are a times of first encounters with common infectious agents. Hence it is a times of frequent systemic immune challenges that for most of us does not lead to overt defects on 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 neurological disorders. Here, the project would involve the use of quantitative behavior, gene expression, flow cytometry or confocal microscopy to quantify neuronal development and brain function in murine models of epilepsy and neurodevelopmental disorders.

Sponsor: Dr. Chia-en Chang

Email: chiaenc@ucr.edu



Description of the Project:

Amyloid-β (Aβ) is a protein produced by the cleavage of the amyloid precursor protein (APP). Aβ protein has 39−42 residues. Aβ42, the protein with 42 residues, can easily aggregate to form cross-β amyloid fibrils that are a hallmark of Alzheimer's disease (AD), and is more neurotoxic and essential to the etiology of AD. Recent advances in structural techniques brought atomic resolution structures of a monomorphic form of Aβ42 using solid state NMR, solution state NMR and cryo-EM. The aggregated fibrils all have β-strands; however, the structures are not identical. It is unclear if the difference is due to an artifact during experimental processes or the nature of the amyloid fibrils. We therefore will use molecular modeling methods to investigate protein dynamics and their inter- and intra- molecular interaction energy to reveal the driving forces of a certain structure and to examine which one(s) may be the most likely structure in cell environment.

The student will get familiar with Aβ42, learn how to get structures from the PDB webpage, and learn some molecular modeling tools. The basic tools include VMD for visualizing proteins and the AMBER packages to run molecular dynamics (MD) simulations. The student needs to learn some very basic Linux commands in order to run MD simulations. The results about the energy and dynamics information will deepen our understanding in formation of the fibril and providing strategies to prevent or destroy the aggregation for treating AD.

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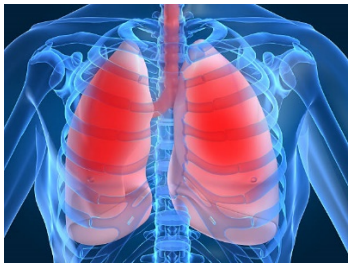

Sponsor: Dr. Amrita Dosanjh

Email: pulmd1@gmail.com

Description of the Project:

This project will study the physiologic, molecular and clinical aspects of environmental lead exposure. This is an area of scientific and clinical importance which may alter lung development and lung health. The project focus is on inflammatory pathways and epithelial airway cells in culture, and may be designed with possible space in the Breathe Center, a multidisciplinary core laboratory on campus, focusing on lung health, or database analysis using existing public databases and Pb levels to determine incidence.

Sponsor: Dr. Iryna Ethell

Email: Iryna.Ethell@ucr.edu

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. 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. Students will have an opportunity to learn or enhance their skills in cellular and molecular neuroscience using several techniques that are necessary for completion of the projects, such as mouse genotyping, preparation of brain slices, immunohistochemistry, primary cell cultures, various biochemical techniques, EEG recordings, mouse behaviors and confocal microscopy.

Students will also participate in bi-weekly Journal Club meetings where we discuss recent journal articles and research-in-progress. During this time we discuss the merits and faults of the paper and how information from the paper can apply to the project. Journal Clubs will help in developing skills at reading literature on recent advancements in brain research and clinical neuroscience.

This internship will also provide an opportunity to participate in neuroscience translational research. As a critical element for career development is environment, students' interactions with other researchers within our multi-institutional Center on FXS Research, who are participating in clinical work, will greatly enhance their training in the translational research.

Description of the project

The mechanisms underlying the pathophysiology of Fragile X Syndrome (FXS) My lab discovered the role of MMP9 in pathophysiology of FXS and demonstrated beneficial effects of minocycline on synapse development and behavioral performance in an animal model of FXS (Bilousova et al., 2009; Rotschafer et al., 2012; Dansie et al., 2013; Sidhu et al., 2014). These findings prompted several clinical trials that tested the effects of minocycline treatment in patients with FXS (Paribello et al., 2010; Utari et al., 2010; Leigh et al., 2013). Ongoing studies focus on the role of MMP9 and extracellular matrix in autistic behaviors associated with FXS, including the mechanisms of auditory hypersensitivity (Lovelace et al., 2016; Wen et al., 2017). In collaboration with Drs. Binder and Razak we are working to develop a preclinical model of auditory processing deficits in FXS. Our ongoing 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.

Sponsor: Dr. Iryna Ethell

Email: Iryna.Ethell@ucr.edu

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Description of the project

Glial control of normal synapse development/plasticity and learning. Our new studies also suggest that ephrin-B/Eph receptor signaling is involved in synapse development and their remodeling triggered by TBI (Nikolakopoulou et al., 2016) and ALS (Wu et al., 2017). In the ongoing studies, we investigate new mechanisms of astrocyte-mediated remodeling of synaptic connections in the hippocampus that may underlie new memory formation and consolidation. Our preliminary studies suggest that astrocytic ephrin-B1 may negatively influence synapse growth by mediating pruning of existing synapses or suppressing new synapse formation through its interaction with neuronal EphB receptors (Koeppen et al., 2018). These studies will provide a significant advances by unveiling a new role for ephrin-B1 in astrocytes and elucidating new mechanisms by which astrocytes regulate learning. Furthermore, these findings will establish a foundation for future studies of astrocyte-mediated synaptogenesis in clinically relevant conditions as recent work linked EphB receptors to neurologic disorders. Given widespread and growing interest in the astrocyte-mediated mechanisms that regulate learning and memory, and EphB receptor role in neurodevelopmental disorders and neurodegenerative diseases, we suspect this project has potential for future clinical applications.

Sponsor: Dr. Adam Godzik

Email: adam@godziklab.org

The student would perform database and statistical analyses of endometrial and ovarian cancer patients using the SEER database. All work would be performed on a computer, in Dr. Godzik's "dry" lab in the SOM Medical Research Building. It would provide the student with an introduction to data driven medicine, something that the new generation of MD will surely practice be the time they graduate.

Description of the Project

Cancer and autoimmune diseases seem to be the two sides of the same coin, one involved with under- and other with over- performance of the host immune system. However, strong correlation of some cancers incidence with inflammation and common mechanisms of many autoimmune diseases with blood cancer lead to contradictory results. Most studies claim positive correlation between overall incidence of cancer and autoimmune diseases, while others claim opposite effects for specific cancers. This project would utilize the Surveillance, Epidemiology, and End Results (SEER) database, which is a premier source for cancer statistics in the US. SEER project is an NIH initiative that collect incidence, prevalence and survival data and many clinical information on all cancer incidence in US. Student would be expected to familiarize him/herself with the SEER database, collect appropriate statistics and under the guidance of Dr. Godzik and staff scientists in his group, perform large scale epidemiological analysis of several type of solid tumors in patients with different types of autoimmune diseases.

Sponsor: Dr. Vagelis Hristidis

Email: vagelis@cs.ucr.edu

Description of the Project

Working with two computer science Ph.D. students and a Professor of Medicine form UCSD, this project aims to predict medical events in electronic medical records of a patient using machine learning techniques. Medicine 2.0 creates the need for applications that find similar patients based on a patient's electronic health record. (EHR). We evaluate the hypothesis that we can leverage similar HER's to predict possible future medical concepts (e.g. disorders) in a patient's EHR. Using prefixes or suffixes representing set of medical concepts from medical ontology. These are then compared with other patients using various inter-patient distance measures. *The selected medical student will help with the evaluation methods, and is expected to become a co-author to the publication when submitted.*

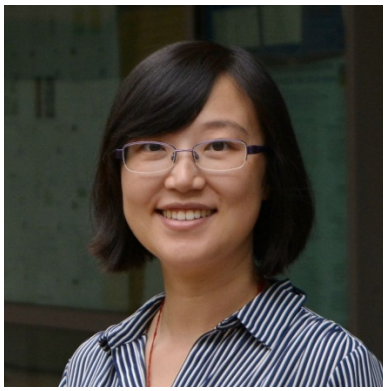
Sponsor: Dr. Ted Karginov

Email: karginov@.ucr.edu

This project would expose interested students to hypothesis-driven and exploratory research in molecular and cell biology and provide an excellent opportunity to learn a number of corresponding techniques, including mouse dissection, FACS analysis, cell culture, and basic RNA biology methods.

Description of the Project:

Our lab studies the function and mechanism of RNA-binding proteins in gene regulation. Previously, we have identified a novel RNA-binding protein and endonuclease enzyme, EndoU, to be specifically expressed in developing thymocytes, squamous cell epithelia, and placental tissues, with a hypothesized role in apoptosis. The enzyme has been characterized to possess a potent calcium-activated cleavage activity and to impact gene expression in a cell line knockout model. However, the *in vivo* role of EndoU is currently unknown, and a mouse knockout model has been obtained to investigate the cellular function of EndoU. Students will perform cellular characterization of thymocyte populations, carry out cell-based apoptosis assays, investigate the subcellular localization of EndoU and assay the molecular cleavage activity of the endogenous protein.



Sponsor: Dr. Yanran Li

Email: liyanran@engr.ucr.edu

Description of the Project

We are interested in finding the enzyme involved in the biosynthesis of brassinolide. Currently we are establishing the pathway in yeast and propose to test the candidate enzymes on the yeast platform. This 2-month project aims to establish the well-defined tobacco heterologous expression platform in our lab, and verify by heterologously express the candidate enzymes and functional analysis of the enzymes through LC/MS of the trans-infected plant materials.

Sponsor: Dr. Huinan Liu

Email: huinanliu@engr.ucr.edu

Description of the Project

Dr. Liu's Biomaterials and Nano medicine Lab research involves design, fabrication and evaluation of novel biomaterials for tissue regeneration, controlled drug delivery, and medical implant/device applications. Medical applications of nanomaterials and nanotechnology are actively explored through both fundamental studies and applied research. Materials studied in the lab include, polymer, ceramic nanoparticles, polymer/ceramic nanocomposites and biodegradable metals. Students may acquire lab skills and gain experience in material synthesis, characterization, electron microscopy, x-ray spectroscopy, optical emission spectrometry, fluorescence microscopy, bacterial culture, mammalian cell culture studies, and performing surgeries for assessing novel orthopedic or neural implants in rat models. Previous outstanding student researchers in Liu lab have co-authored publications in scientific journals, an/or presented their work at national/international scientific conferences. Specifically, medical students will assist our collaborating surgeons in implanting bioresorbable metallic implants into rat models and assessing the implant performance in vivo.

Sponsor: Dr. David Lo

Email: david.lo@ucr.edu

Description of the Project

We are working on models of inflammation in the intestine and lung. In both cases we are interested in the recruitment of mononuclear cells (e.g., lymphocytes, dendritic cells) in tissue infiltrates, and the conditions that trigger spontaneous organization of the infiltrates into organized lymphoid tissues.

The work is ongoing, and the student be part of a team of researchers already working in one or more projects. The student will have a chance to learn histology, confocal microscopy, and will begin to learn how to interpret histology images. The basic science from the first year curriculum will be very helpful background that the student can work from. In the intestine, we are working in a model of inflammatory bowel disease, and in the lung we are looking at inflammation triggered by inhaled particles and allergens.

Sponsor: Dr. Declan McCole

Email: Declan.mccole@ucr.edu

Description of the Project:

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 investigating application of a clinically approved drug to target signal transduction pathways that are overactive in intestinal epithelial cells with deficient PTPN2 gene activity, in order to correct intestinal barrier defects in PTPN2-deficient cells. 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 tissue.

Sponsor: Dr. Meera Nair

Email: meera.nair@ucr.edu

This project is a highly translational project, allowing students to profile human immune cells and investigate the immunoregulatory potential of resistin-based compounds generated in the Nair lab.

Description of the Project

Dr. Nair's lab's research focus is the identification of new regulatory pathways that can be harnessed to treat inflammatory diseases such as sepsis, a devastating often fatal disease resulting from a systemic inflammatory response to severe microbial infection. Dr. Nair's lab recently identified a critical function for the human protein resistin (hRetn) in blocking lipopolysaccharide (LPS)-induced inflammation and death in a mouse model of sepsis[1]. Based on these results, we have generated resistin-based compounds (a resistin-peptide and a resistin fusion protein) that will be tested for their anti-inflammatory potential in human peripheral blood cells. Two main aims are proposed for this externship.

Aim 1. Perform purification and quality control experiments on the resistin-based compounds. Techniques include ELISA, Western blot, protein quantification and cell viability assays.

Aim 2. Test the anti-inflammatory effect and dosing of these compounds in peripheral blood cells from healthy human donors treated with control saline or activated with LPS. Techniques include ELISA, flow cytometry, Western blot.

Based on the success of Aims 1 and 2, and dependent on sample availability, the techniques optimized above will be used to profile immune cells and resistin expression in patients with moderate and severe sepsis (n=4/group) as part of a collaboration with the Riverside University Health Systems (IRB pending). RUHS collaborators: Dr. Walter Klein, Dr. Bonenfant and Dr. Firek.

Sponsor: Dr. Khaleel Razak

Email: khaleel@ucr.edu

Description of the Project

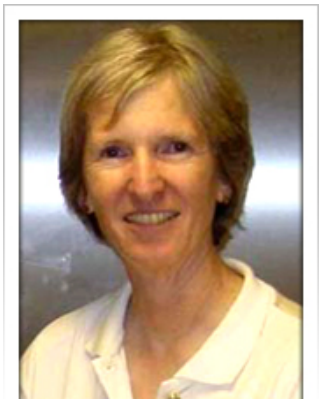
Fragile X Syndrome (FXS) is a developmental disorder that leads to intellectual disability, sensory hypersensitivity, anxiety and social/cognitive issues. FXS is the leading known genetic cause of autism. The Fmr1 knockout mouse is a well-studied model of FXS and presents several sensory and electrocortical phenotypes seen in humans with FXS. In particular, the Fmr1 KO mouse shows auditory hypersensitivity, reduced habituation to sounds and EEG/ERP phenotypes that are remarkably similar to those seen in humans. We have identified (Wen et al. Cerebral Cortex, 2017) potential mechanisms of hypersensitivity in the auditory cortex of the Fmr1 KO mice that relates to the abnormal development of an extracellular matrix component known as perineuronal net (PNN).

In the proposed experiments, I am looking for a motivated student to perform immunohistochemistry and Western blot in developing mouse auditory cortex to examine expression of an immediate early gene, Neuronal activity driven pentraxin (Narp). Narp is closely associated with PNN in sensory cortex. Narp KO mice exhibit some of the same phenotypes as Fmr1 KO mice. So we would like to compare the WT and Fmr1 KO mice for Narp expression during development.

The student we would consider should have wet lab experience and expertise with mouse handling, histological methods including immunohistochemistry. It is expected that the student achieves independent proficiency early in the training timeframe. All resources to accomplish this goal will be provided.

Sponsor: Dr. Prue Talbot

Email: talbot@ucr.edu



Description of the Project

Even though electronic cigarettes (EC) have been used worldwide for about 10 years, we know very little about how they affect human health. There is considerable debate about their safety and whether they are beneficial or harmful. The flavor chemicals used in EC are approved for ingestion but not for inhalation, and studies from our lab have shown that some flavor chemicals are likely to be toxic at the concentrations used in EC. A student working with us during the summer would be able to contribute to our project on flavor chemicals in EC. This summer we will be working with products that have been reported to make users sick. Specifically, the student would work with gas-chromatography- mass spectrometry (GC/MS) data to identify and quantify flavor chemicals in refill fluids and aerosols collected using various EC and puffing conditions. Authentic standards of the identified chemicals would be tested in vitro with 2 and 3 dimensional models of human lung. We will also be working with samples from human participants who are using these products and comparing data from human subjects to data collected with the in vitro cell models.

Sponsor: Dr. Nitin Dhamija

Email: Nitin.Dhamija@kp.org

Description of the Project

This retrospective study aims to determine the efficacy and safety of successive one-hour sub-anesthetic ketamine infusions for chronic pain patients who have unsuccessfully attempted multiple non-invasive and invasive modalities, such as medications, physical therapy, chiropractic therapy, acupuncture, steroid-based injections, or surgical interventions. Specific measures of efficacy include reduction in numeric rating scores, decreased intake (type, dose, frequency, duration) of opioid and non-opioid analgesics, and analgesic adjuncts. A specific indicator of safety would be low incidence of adverse drug effects as described above. The results/data analysis will likely guide improvement of the current program in place and positively impact patient care, in addition to guiding future prospective research work.

The medical student will gain experience in research methodologies, including writing an IRB proposal, data collection through patient chart review, statistical analysis, as well as devising an abstract, formulating a presentation, and if appropriate, submitting an article for consideration of publication. The medical student will be mentored with each step of the project.

Sponsor: Dr. Nelly Tan

Email: netan@llu.edu

Objective: To evaluate 2017 American College of Radiology thyroid nodule structured guidelines (TI-TADS) and impact on provider decision making for follow up of thyroid nodules compared to traditional thyroid reporting.

Description of the Project:

Extract 50 thyroid ultrasound reports from Montage

Collect historical data on consistency of radiologist recommendations for thyroid nodule follow up.

Have 1-2 radiologists issue new report based on 2017ACR TIRADS guidelines

Compare primary provider physician decision for follow up of thyroid nodule and provider's preference between traditional and new ACR TIRADS reports using statistical analysis.