

OCHSNER-UNO COLLABORATIVE UNDERGRADUATE RESEARCH EXPERIENCE (CURE) – 2023 PROJECTS

1) ITR Nephrology Lab – 1 UNO student

Juan C. Velez, MD and Doan Nguyen, PhD

Project title: Identification and validation of novel protein biomarkers in urinary casts to assess kidney function and disease

Description:

Diagnosis of the cause of acute kidney injury has significant clinical implications. As kidney tubules are vulnerable to ischemic and toxic injury, we hypothesize that urinary sediment from patients with acute tubular injury (ATI) contain cast proteins that can be used to establish the diagnosis. Using proteomic approaches, we have analyzed the protein composition of “muddy brown” granular casts and identified surrogate biomarker of ATI.

The student will assist with granular cast purification and microscopy imaging and documentation of patients with ATI. Immunofluorescent analysis will be carried out to validate and localize the identified protein biomarkers.

2) ITR Neuroscience Lab – 1 UNO student

Jignesh Patel, MD and Doan Nguyen, PhD

Project title: MicroRNA Biomarkers of Seizure Post Intracerebral Hemorrhagic Stroke

Description:

Intracerebral hemorrhage (ICH) accounts for 15-20% of all patients with ‘acute stroke’ and carried a significant morbidity and mortality of greater than 60%. Approximately 15% of patients experience seizure after spontaneous ICH. The pathogenesis of seizures post-ICH is not well-known. Neuroinflammation is believed to be an important pathophysiological process in secondary brain injury and a consequence of ICH. There are no consistent and reproducible biomarkers that predict such complications of intracranial injury. We have identified several microRNA that may serve as biomarkers f post-ICH seizure.

The student will assist with RNA extraction from plasma and peripheral blood mononuclear cells and carry out real time PCR quantification of the miRNA biomarkers. In addition, functional analysis of these microRNA will be carried out using microRNA mimics and inhibitors.

3) ITR Infectious Disease Lab – 1 UNO student

George Pankey, MD, Director and Debbie Ashcraft, MT(ASCP)SM, Supervisor

Project title: *In vitro* Interaction of Omadacycline and Other Tetracyclines in Combination with Sulbactam against Carbapenem-resistant *Acinetobacter baumannii*

Description:

Acinetobacter is a Gram-negative bacillus that can survive for a long time on skin and surfaces and is resistant to a variety of disinfectants-- making it easily spread in a hospital setting. Carbapenem-resistant Acinetobacter (CRA) is considered an urgent threat by the CDC. Nearly all CRA infections occur in patients who received care in a healthcare facility. CRA is especially prevalent in intensive care units- causing pneumonia, wound, bloodstream, and urinary tract infections. CRA carry mobile genetic elements that can be easily shared between bacteria. Since some CRA are resistant to nearly all antibiotics, combination antibiotic therapy is often needed.

Tetracyclines have good activity against Acinetobacter and are often used in combination with other antibiotics to achieve better killing of the organism. Omadacycline is a novel aminomethylcycline approved by the FDA for intravenous and oral treatment of acute skin and skin structure infections and community acquired pneumonia. It is a derivative of another tetracycline, minocycline, and has a broad spectrum of antibacterial activity against Gram-positive and Gram-negative bacteria.

Sulbactam is a beta-lactamase inhibitor that is given in combination with antibiotics. FDA-approved combination drugs that contain sulbactam include ampicillin-sulbactam and cefoperazone-sulbactam.

The objectives of this study are: 1) to determine the minimum inhibitory concentration (MIC) of omadacycline, sulbactam, and other tetracyclines for CRA isolates. Antimicrobial susceptibility testing will be performed using gradient diffusion MIC test strips and broth microdilution methods 2) to perform combination testing with omadacycline (and other tetracyclines) and sulbactam against CRA isolates using a rapid Etest method to determine if any combination shows a synergistic interaction. If synergy is detected, then time-kill studies will be performed. Results from the two methods will be compared. Data will be reviewed to see if any of the combinations may be beneficial against CRA.

The student will be introduced to sterile techniques – including subcultures, freezer banking, and processing of multidrug-resistant *Acinetobacter* isolates. The student will also learn broth microdilution MICs, gradient diffusion MICs, and synergy testing methods.

4) ITR Cancer Lab – 1 UNO student

Li Li, MD, PhD and Grace A. Maresh, PhD

Project title: Testing combinations of chemotherapies on kidney cancer in mice with human immune systems.

Description:

Project work may include immunohistochemistry (cutting paraffin blocks and staining the samples with antibodies), or RT-PCR (isolating RNA from tissues and amplifying genes to study expression), or western blots (lysing proteins, separating on gels and labeling with antibodies).

5) ITR Rheumatology Lab – 1 UNO student

Xin Zhang, MD, PhD

Project title: The Role of Tfh Population in a Collagen-Induced Arthritis Mouse Model

Description:

Rheumatoid Arthritis (RA) is a common inflammatory autoimmune disease characterized by the infiltration of inflammatory cells into hyperplastic synovial tissue and autoantibody production that results in the subsequent destruction of cartilage and bone, and ultimately lead to functional impairment and decreased quality of life. Currently the pathogenesis of RA is not fully understood and there is no cure for RA. The collagen-induced arthritis (CIA) mouse model is the most widely studied model of RA, sharing significant pathological features with human RA.

Follicular helper T (Tfh) cells are a CD4⁺ T cell subset which regulates B cell differentiation and antibody production. Dysregulation of Tfh activity contributes to autoantibody production and can play an important role in the promotion of autoimmune diseases. Our preliminary data have demonstrated that circulating Tfh were significantly increased in RA patients and CIA mouse model. Recently we found that a novel small molecule inhibitor SMI-Tfh which selectively targeting Tfh cells reduced the severity of inflammatory arthritis in CIA model. We

will further investigate the role of immune cells in the spleen of the CIA mice and confirm our results using immunofluorescent staining.

The student in CURE program will learn to examine many pathological skills such as tissue embedding, slides cutting, hematoxylin and eosin staining, immunofluorescent staining, and microscopic skills. The student will apply these skills on the spleens collected from the CIA mice and quantify the immune cells (Tfh cells) using ImageScope software. The student will discuss his/her results regularly with staff scientist and attend Rheumatology Research Meeting. The student will read literatures related to our project, make presentation at the end of the program and will be one of the authors in our abstract and/or manuscripts if the student's results are used.