CURE 2019 Projects

1) CURE student proposal from Dr. Grace Maresh in the laboratory of Dr. Li Li

Institute of Translational Research, Ochsner Health System
(1 student)

Title: Investigate the impact of Rab13 on colon cancer progression using immunohistochemistry methods

We have found that a molecule called Rab13 is expressed in normal lymph node cells, can be transferred to cancer cells and can help these tumors grow and metastasize. We now need to look closely at the expression of this molecule and several related ones in the tissues we have collected in a model system where Rab13 has been inhibited and the cancer cells grew more slowly. This would involve cutting paraffin blocks of tissues into 5µm slices, applying them to microscope slides, probing them with antibodies against several molecules, visualizing the antibodies and analyzing the results by high power microscopy (immunohistochemistry or IHC). These experiments require time and practice to learn but will result in very useful data when done properly. It would make an excellent summer project for a motivated undergraduate student. This work will help us elucidate what is happening at the molecular level in our model of the involvement of lymph nodes in cancer growth and metastasis.

2) CURE student proposal from Dr. Xin Zhang in the laboratory of Dr. Li Li

Rheumatoid Research Project (SLE and Rheumatoid Arthritis)
(1 student)

Title: The role of T cell subsets in obesity-associated lupus pathogenesis

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of autoantibodies, binding with self-antigens to form immune complexes which deposits in various organs potentially causing life-threatening renal, cardiac, or brain damage.

In a prospective cohort study among 238,130 women in the Nurses' Health Studies, the investigators found an 85% significantly increased risk of SLE among obese compared to normal body mass index (BMI) women in the more recent NHSII cohort, but no association was observed in the earlier NHS cohort. Obesity has been considered as a major factor contributing to the onset and progression of autoimmune diseases including SLE. However, the underlying mechanisms are not clear.
Accumulative evidence has shown that T cell subsets play an important role in SLE and other autoimmune diseases. Under physiological conditions, T follicular helper (Tfh) cell, a $CD4^+$ T cell subset, predominantly located in lymphoid follicles, produces cytokine IL-21 to regulate B cell survival and antibody production in germinal centers. Th17 cell, another T cell subset producing IL-17, acts through a heterodimer of IL-17 receptor A (IL-17RA) and IL-17 receptor C (IL-17RC) and downstream signaling cascades to induce inflammation that protects humans against a variety of fungal and bacterial infections such as Klebsiella pneumoniae. T regulatory (Treg) cell is an inhibitory T cell subset secreting IL-10 and TGF-β. Thus, the balance among these T cell subsets is very crucial in maintaining proper immune status by developing a robust humoral immune response to foreign antigens and self-tolerance by preventing antibody against self-antigens. Uncontrolled generation of these T cell subsets could lead to autoimmunity by increasing

autoantibody production and inflammation. Understanding the molecular mechanisms of their regulation is of critical significance in T cells-associated host defense, autoimmune diseases, and cancers.

Our preliminary data have demonstrated compelling evidence that circulating Tfh and Th17 cells were significantly increased in active SLE patients, correlated with their autoantibody titer and inflammation respectively. Based on our findings, we have formulated a novel hypothesis that the high level insulin in obesity regulated the downstream signals regulating T cell subsets development and mediating higher level of autoantibodies and stronger inflammatory responses, thereby promoting lupus initiation and progression. To test this hypothesis, we propose to achieve the following specific aims:

Aim 1. To establish a diet-induced obesity animal model and determine if obesity enhances SLE development.
Aim 2. To reveal the mechanisms underlying the link between obesity and SLE development.

Under the collaboration with Tulane University and overlooked by Dr. Robert Quinet from Rheumatology Department, we have successfully established a reliable diet-induced obesity SLE mouse model in 2018.

The student in CURE program will learn to examine serological levels of autoantibodies and many pathological skills such as tissue embedding, slides cutting, hematoxylin and eosin staining, immunohistochemical staining, and microscopic skills. The student will apply these skills on the tissues collected from the diet-induced obesity mice and control mice. This study will help us on determine the autoantibody levels and inflammation score of the obesity mouse, frequencies of T cell subsets, immune complex deposit in the kidneys, inflammation and SLE status. We will discuss the results regularly with staff scientist and physicians/fellows.

3) CURE student proposal from Paul Thevenot & Lyndsay Buckner Baiamonte in the lab of Dr. Ari Cohen

Ochsner Biobank and Institute of Translational Research – transplant laboratory
(1 student)

Title: Liver Transplant Donor and Recipient Factors Causing Preservation Injury in Transplant Recipients
[clinical and laboratory study]

During the last thirty years, orthotopic liver transplantation (OLT) has become the treatment of choice for end stage liver disease. The 16,000 potential recipients on the national waiting list far surpass the 6,000 organs available per year for transplantation. Approximately 17% of potential OLT recipients die while waiting on the transplant list. Marginal livers are a potential donor source which can help address shortages in the donor pool. Marginal status includes livers from donors that are older, have steatosis (fatty liver disease), and those with anticipated long times during which the organ is ischemic (deprived of blood flow). Marginal livers are at risk of developing primary non-function after liver transplantation. Primary non-function is a common cause for re-transplantation and death early after OLT. Optimization of "marginal" liver donors – by means of preserving healthy liver tissue that would ordinarily die over the course of an operation – would expand safe use for liver transplantation.

Beginning in 2012, the Ochsner Transplant Laboratory and BioBank have been compiling a large data set of liver transplant patients with matching specimens obtained during the transplant procedure. This dataset

includes a mix of optimal and marginal donors, ideal for identifying factors leading to primary non-function, particularly in marginal donor liver transplantation.

In this project, the student will learn how to export data from the electronic medical record into an organized database used by clinicians and scientists to study how certain variables and outcomes are linked. From this database, the student will learn how to build a study cohort and then use archival specimens and perform assays to determine inflammatory mediators in specimens obtained before and after the transplant surgery. These immune biomarkers can then be investigated with patient outcomes gleaned from the patient database and correlations/associations can be made to determine the relationships between marginal status and primary non-function as well as implicate specific inflammatory mediators in marginal liver primary non-function.

4) **CURE student proposal from Dr. Edmond Kabagambe**
   Population studies in epidemiology
   (1 student)

Title: Race and gender differences in the distribution of type 2 diabetes mellitus (T2DM) in the United States.

In this project we will use secondary data sources including NHANES to determine factors associated with prevalence of T2DM. The student will be introduced to the topic (T2DM) and available data sources and asked to formulate a research question. In a step-wise fashion the mentor will present analyzed data and work with the student to interpret the findings. The student and mentor will then examine the data to determine whether the observed associations could have been confounded by other variables such as age or tobacco use. After going through various scenarios the student will be asked to create an abstract summarizing the nature of the relationship between race, gender and T2DM in the United states. If time allows, the study could extend to comparisons of Louisiana residents to the rest of US population and propose some public health approaches that could be used in the prevention and control of T2DM. No prior knowledge of T2DM or statistical modeling is expected.

5) **CURE student proposal from Dr. Edmond Kabagambe**
   Population studies in epidemiology
   (1 student)

Title: Omega-3 fat consumption, tissue levels and incidence of heart disease

In this project, the student will examine literature on dietary fat and heart disease and summarize findings from the literature. Next the student will formulate a question relating fat and heart disease. An analyst will perform statistical analyses and create results summarizing the association. The student will work with a mentor to interpret the data and propose additional analyses that could be done to improve the rigor of the study and validity of the findings. The student will write an abstract summarizing the findings and determine whether findings from literature are consistent findings from the dataset that was analyzed. The student and mentor will explore why the results from literature and their analyses are similar or different. No prior knowledge of nutrition, heart disease or statistical modeling is expected.