Research Statement – Miguel M. Leiva Juarez, MD, MSE

Applicant: Miguel M. Leiva Juarez, MD, MSE
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Background

Since the start of medical school I have been interested in understanding the aspects of physiology and pathophisiology to be able to find novel solutions to clinical challenges for the benefit of patients.

My academic background focuses on clinical, basic, translational and physical bases of cardiothoracic physiology and pathophysiology. As a clinician I am exposed to the everyday challenges in management of patients with advanced surgical disease. This has allowed me to identify complications and find areas of opportunity for innovation. At the same time, I have been exposed to both clinical and basic research which includes the *in vitro*, *ex-vivo* and *in vivo* design and testing of hypothesis to understand both the epidemiologic and pathophysiologic basis of disease down to the cellular level. Furthermore, my training in biomedical engineering includes the design, modelling, testing, marketing, and regulatory planning of medical devices. This provides the potential to design solutions to everyday problems and be able to coordinate with experts in different disciplines to achieve a common goal. As a senior surgical resident I have also developed the leadership skills to guide a team and delegate, particularly during situations of high acuity. In addition, while being a postdoctoral fellow, I would be in charge of the development of hypothesis, experimental design, and coordination with research assistants to test the hypothesis.

Past work

During medical school and throughout my postdoctoral fellowship at the Department of Pulmonary Medicine at the MD Anderson Cancer Center I investigated the use of *toll*-like receptor (TLR) ligands to induce innate epithelial resistance to pathogens in the lung. Research provided novel insights into the ability of epithelial cells, in parallel to immune cells, to deliver long-lasting immunity in response to pathogen recognizing receptor stimulation. In brief, mice and cells pre-stimulated with a combination of agonists for TLR 2/6 and TLR 9 prior to infection with bacteria, fungi or viruses resulted in improved survival and decreased viable pathogens. This therapy has proven safe during Phase I clinical trials and currently being tested in Phase II studies for prevention of pneumonia among immunocompromised hosts.

In addition to the above contributions, I have collaborated with the cardiac surgery team at the Southampton University Hospital in the United Kingdom to investigate the results of commonly performed cardiac procedures and elucidate interventions to improve outcomes. These have included optimal therapies for coronary artery bypass surgery as well as aortic valve replacement interventions using both open and minimally invasive techniques.

Current and future work

My current research focuses on the effects of different interventions on outcomes prior to or after thoracic surgery with a primary focus on lung transplantation. Our main effort is understanding the role of foregut function on long term outcomes after tranplant. Prior data from our and other groups have suggested an association of measured bile acids in airways of transplanted lungs and adverse outcomes after lung transplantation. Both the quantity and type of these bile acids correlate with increased mortality and earlier development of chronic rejection. Furthermore, these molecules correlate with both an inflammatory and lipidomic signature that is predictive of allograft dysfunction. Conversely, we have shown that anti-reflux procedures to decrease the amount of refluxed enteric contents improve survival after transplant. This overall provides one of the first reliable clinical biomarkers for early detection of chronic rejection, providing a tool for risk stratification and potential early treatment to prolong allograft function. These are currently being validated in a multicenter study.

Lung transplantation is limited by an eventual allograft dysfunction due to chronic rejection. Future efforts in elucidating the pathophysiology of retrograde aspiration of enteric contents may clarify the progression and mechanisms in chronic lung allograft dysfunction, which remain poorly understood. At the same time, validating the use of clinical biomarkers such as bile acid levels may provide a method of identifying patients at high risk for transplant dysfunction allowing a taylored approach to maximize the life span of the graft. These tools have the potential to be used outside of the field of transplant to manage treatment and prognosis of patients with aspiration pneumonia or pneumonitis.

Physicians have the responsibility of not only treating but also finding solutions for the everyday clinical challenges. It is my goal to continue to bring clinical problems to the bench and back to the clinical field to improve patient outcomes.