

## Pulmonary/Critical Care Research at WFUBMC

Wake Forest University Baptist Medical Center is one of the premier research hospitals in the state of North Carolina. Its campus includes a children's hospital, a Level I trauma center, the Wake Forest Medical School, a pediatric Level I trauma center, and a large array of cutting-edge technology and research facilities. Located in Winston-Salem, it is renowned for providing top-level care to all who come through its doors. Additionally, it is one of 12 clinical centers in the prevention and early treatment of acute lung injury (PETAL) network currently researching Acute Respiratory Distress Syndrome (ARDS) and figuring out how best to tackle this dangerous problem.

ARDS is characterized by widespread inflammation in the lungs and buildup of fluid in the alveoli, the air sacs in the lungs typically filled with air, which prevents oxygen from diffusing into the bloodstream. ARDS is a serious illness, carrying a fatality rate of 20-50%, and often appears as a secondary result of a primary injury such as trauma or sepsis. Currently, there are few options for clinical management of ARDS patients. Dr. Clark Files is presently working with an animal model to test potential therapies for ARDS. Under Dr. Files' supervision, I had the extraordinary opportunity to contribute to this groundbreaking research.

Although I was only at the hospital for 6 weeks, I learned a substantial amount about the ARDS disease process and current research on treatments. Additionally, I presented on a paper regarding the molecular basis of disuse-induced atrophy in aged rats and how aerobic exercise may help prevent muscle wasting. The research for this presentation was essential in helping me understand the pathophysiology of ARDS, as well as giving me a chance to present to other

summer interns and several physicians. Following the presentation, I felt that I had gained significant background knowledge into the meaning behind our work in the laboratory.

ARDS can cause skeletal muscle wasting which is observable through elevated levels of several proteins, including Muscle Ring Finger 1 (MuRF1) and FoxO. The FoxO family of proteins is responsible for transcribing atrophy-related genes. The transcription of these genes results in increased expression of the E3-Ubiquitin Ligases Atrogin-1 and MuRF1. Elevated levels of these components of the ubiquitin-proteasome complex result in skeletal muscle wasting, and thus also serve as quantifiable markers of muscle damage in lung injury. Recently, new drugs have been developed to control the expression of these proteins in hopes of reducing the risk of tissue wasting in lung injured patients. In Dr. Files' lab, we tested one of these drugs. Lesion was induced via Lipopolysaccharide before administration of placebo or the experimental drug. Following a careful schedule of muscular stimulation, mice were sacrificed so that tissue, organ, and BAL (Broncho alveolar Lavage) samples could be harvested.

I, as well as two lab technicians, used western blotting and Image J software to quantify levels of FoxO and MuRF1 protein in mouse muscle tissue samples & BALs. Fluorescent microscopy was also employed to visualize localization of FoxO proteins. Although I wasn't able to follow the project to completion due to the limited timeframe, my work with western blotting, fluorescent microscopy, and protein quantification was an important part of this drug trial. Through my time here, I was able to greatly hone my skills in the lab. Whether it was staining a slide, preparing and running a western blot, or learning how to use a fluorescent microscope, I was able to add to the foundation of knowledge I built at Sewanee.

In addition to my time in the lab, I observed Dr. Files in a variety of clinical settings include the medical ICU, pulmonary clinic, and through various pulmonary consults throughout the hospital. Most of my previous exposure to medicine has been with the trauma unit and the emergency department. In those situations, the gap between thinking and acting is minimal. Patients often present in extremis and immediately are wheeled up to the OR with limited information. In the medical ICU and the pulmonary clinic, there is more deliberation. While rounding in the ICU with Dr. Files, our patients typically had an array of problems that required unique and dynamic treatment plans. I learned a lot from watching the residents and medical students present each patient to the attending physician (Dr. Files) while he would fire questions at them and quiz them on their knowledge. Certainly, I became more in-tune with the medical hierarchy. Perhaps most importantly, while discussing cases and radiography with the residents, I realized that I belong in medicine.