**Faculty Profile**

Joseph Alcorn, PhD is an Associate Professor in the Department of Pediatrics who joined the faculty of The University of Texas Medical School at Houston in July 1998.

My research focus has been the lung, with particular interest in the pulmonary surfactant proteins. These developmentally-regulated proteins have crucial roles in the function and defense of the lung. Surfactant protein B (SP-B) is absolutely required for the ability of pulmonary surfactant to reduce alveolar surface tension. Premature-born infants have underdeveloped lungs and reduced levels of SP-B, predisposing them to Respiratory Distress Syndrome (RDS), the leading cause of neonatal morbidity and mortality in developed countries. Surfactant protein A (SP-A) is a component of the innate immune system with major roles in defense of the lung against invasive pathogens, such as viruses and bacteria, and in modulation of inflammation of the lung.

One of the goals of my research is to understand the molecular mechanisms underlying post-transcriptional regulation of these proteins. Antenatal administration of glucocorticoids is the prescribed therapy to augment fetal lung development and to increase SP-B gene expression (through increased stability of SP-B mRNA). However, glucocorticoids are detrimental to neuronal development and can lead to cerebral palsy. Our research objective is to define how steroids increase SP-B mRNA stability with the ultimate goal of circumventing the use of steroids in augmenting SP-B expression. We have defined a 30 nucleotide-long element in the 3′-untranslated region of SP-B mRNA with dual functions; it acts to reduce mRNA stability in the absence of glucocorticoids and increases SP-B mRNA stability in the presence of glucocorticoids. We have identified a primate-specific protein, RBMXL3, with a role in the latter function. Currently we are identifying the proteins that bind the element in the absence of glucocorticoids and reduce mRNA stability.

The other research is to define the potential role of SP-A in a common disease of premature infants, necrotizing enterocolitis (NEC). NEC is caused by inflammation in the gut resulting from multiple stimuli and leads to destruction of the small intestine. Since SP-A is known to modulate inflammation, clear of bacteria and interact with toll-like receptor 4 (TLR4), and these same factors have a role in NEC, we hypothesized that SP-A may ameliorate NEC. Using a rat pup model of NEC (with generous help from the Drs. Marc Rhoads and Yuying Liu), we have found that oral administration of purified SP-A reduces the occurrence of NEC as well as the mortality and inflammation associated with NEC. Our current research focuses on defining the precise mechanism by which SP-A acts to reduce NEC with the ultimate goal to develop therapeutic strategies that can be applied in the NICU.