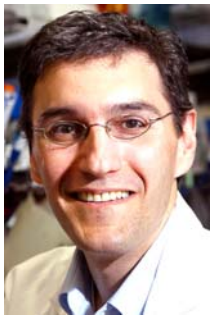
THE HARTWELL FOUNDATION

2010 Individual Biomedical Research Award

Review of Proposed Research

Investigator: **Patrick Seed, MD, Ph.D.**
Assistant Professor
Department of Pediatrics

Institution: **Duke University**



Proposal: **Interactions Between the Environment and Microbiome in Extremely Preterm Infants**

Dr. Seed seeks to prevent colonization of premature babies with dangerous microbes, through identification of the species and strains causing disease, and from where in the environment around the infant they originate. Differences among dominant strains in their potential for pathogen infectivity and relative capacity to overcome body defenses have major consequences not only for future risk of invasive disease, but metabolic and immunologic alterations, as well. To address the problem, he intends to conduct the first high resolution examination of sources and mechanisms of microbial transmission by which very premature infants are colonized. Each year, more than 63,000 infants are born very premature and face over 25 times greater chance of death in infancy. Infectious diseases of the bowel, bloodstream, urinary tract, and central nervous system are a severe threat, with high rates of illness and death that require care well out of proportion to less premature, or term infants. These infants consume over 35% of costs for health care in neonatal units, often in excess of $2,000 per day. Among low birth weight infants, invasive infections are an extremely serious problem. Despite widespread antibiotic use, about 40% of premature infants will have at least one serious infection, with mortality approaching 50%. Unfortunately, liberal antibiotic use promotes the emergence of antibiotic resistant microbes and thus exacerbates the situation. Remarkably, and perplexingly, many dominant pathogenic bacteria, fungi, and parasites can be found in the infant gut and represent a potential reservoir for infection. The problem is how to limit colonization of the infant gut with potentially dangerous microbes. To address this unmet need, Patrick seeks to learn which microbes are most suited to colonize and persist in very premature infants. The *environment* almost certainly provides the primary source of colonization, but considering the complexity of the intensive care unit the epidemiologic vectors for colonization are neither obvious nor unambiguous. In this regard, Patrick intends to pinpoint the sources for colonization by isolating and identifying microbes with different capacities to colonize and persist despite all of the medical therapies used for neonates in their early weeks of life. Without relying on traditional microbiological culturing techniques that capture only a tiny proportion of microbes in the environment, he will deploy ‘‘deep sequencing’’ to generate huge numbers of sequencing reads per instrument run to determine what species and strains are causing disease. If successful, eliminating colonization of the infant gut with potentially dangerous microbes or intentionally colonizing them with more benign microbes will provide antibiotic sparing alternatives with the potential to dramatically reduce the risk for invasive infections in this fragile population of newborns.