THE HARTWELL FOUNDATION

2009 Individual Biomedical Research Award

Review of Proposed Research

Investigator: **De-Ann M. Pillers, MD, Ph.D.**
Professor
Department of Pediatrics

Institution: **The University of Wisconsin**

Proposal: **Genetics of the Innate Immune Response of the Infant as a Potential Biomarker for Premature Birth**

Dr. Pillers proposes to identify genetic risk factors in the developing fetus that predispose it to preterm birth. Changing pregnancy outcomes by identifying genetic risk factors for premature birth in the mother has long been studied without success, so this represents a new paradigm: infection of the membrane (chorioamnion) that surrounds the fetus in the womb is strongly associated with preterm birth and since the membrane develops from the embryo, genetic risk factors for premature birth should be closely associated with the genetic makeup of the baby, not the mother. The chorioamnion, along with the placenta and umbilical cord, is identifiable in the afterbirth. Each of these fetal membranes forms and appears together with the embryo, playing important roles in embryonic development. Except for a small maternal contribution to the placenta, the fetus and the chorioamnion are derived from the same cells at the time of conception, and thus share the same genetic complement; they overlap with each parent by only 50%. The prevention of premature birth is an unmet clinical need, as preterm infants are at greatest risk for medical problems, including cerebral palsy, developmental delays, hearing, vision deficits and asthma. The normal full term for pregnancy is 37-41 weeks gestation, with approximately 12.5% of all births (500,000 babies) each year in the United States recorded as premature. More than 70% of premature babies are born between 34 and 36 weeks gestation; about 12 percent are born between 32 and 33 weeks, and 16% at less than 31 weeks. While 25% of premature births are the result of early induction of labor or c-section, remarkably, the chorioamnion is thought to be a contributing factor in 25-40% of all premature births, with the frequency of infection inversely related to the gestational age. Despite all efforts, in half of all preterm births the cause of a woman delivering prematurely is still unknown. Thus, preterm birth remains the leading cause of newborn deaths and a major contributor to lifelong learning and physical disabilities. Based upon a discovery by Dr. Pillers for increased frequency of a polymorphism in Toll-like receptors (recognition sites for various bacterial and other infectious pathogens that *connect* the immune stimulus to the initiation of host defenses) among certain premature infants predisposed to serious infection, she now seeks to confirm the presence of a novel biomarker for prematurity. If successful, such a biomarker would predict which infants will be at risk of preterm birth and thereby enable early interventions for prevention.