Richard H. Finnell, Ph.D., DABMGG

Dr. Richard H. Finnell is a Professor in the Center for Precision Environmental Health in the Department of Molecular and Cell Biology and in the Department of Medicine at Baylor College of Medicine. A pediatric geneticist, he has long been involved in investigating genetic susceptibility to environmentally induced birth defects, applying stem cell technology to the detection of potential teratogenic compounds in efforts to prevent these birth defects, developing mouse models to understand the pathogenesis of the malformations, and using highly innovative approaches to treating these disabilities. During his 39^{+}-year career, he has authored over 330 peer-reviewed publications in journals such as *Science, Nature Genetics, Nature Cell Biology, PNAS* and *Developmental Cell*. His early work with murine embryonic stem cells helped establish the dire embryonic consequences of folate deficiency during embryonic development. The Finnell laboratory is focused on how folic acid transport may be a target of selected human teratogens such as the anti-retroviral drug dolutegravir, or in other instances modifies the impact of teratogenic agents on embryonic development. This work takes advantage of his clinical training in medical genetics, as well as a background grounded in developmental and molecular biology and teratology. The Finnell Laboratory have been fortunate to receive continuous NIH funding for decades to support innovative research on birth defect prevention.

Managing High Risk Pregnancies: Can Precision Science/Medicine Come to the Rescue? The presentation will highlight the promise of precision medicine that is informed by genomic analysis coupled with high level genetic counseling in reducing the occurrence of complex congenital defects. Specifically, for the half of the talk, I will focus on the management of the pregnant epileptic mother, or women who receive anti-epileptic medication for other clinical indications. Medications such as Depakote (VPA; Valproic Acid), have been the most commonly prescribed AED globally, despite having the most significant teratogenic potential amongst the clinically available AEDs. In the Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study, 20% of VPA exposed children showed major congenital malformations (MCMs) or resulted in fetal death (Meador, et al., *Neurology* 2006). Yet like most teratogens, VPA and other anti-epileptic medications only compromise development in a small percentage of exposed infants. These represent challenging genetic counseling situations that could benefit from an infusion of genomic technology. In an effort to better manage AED-complicated pregnancies in order to prevent preventable birth defects, we are attempting to define a genetic signature of risk for mother-infant pairs exposed to VPA during pregnancy. Based on our recently published study (Chen et al., *Cell Research* 2018) that builds on the Omnigenic Model of Inheritance whereby susceptibility to various health conditions is linked not to just a few "core" genes, but rather involves almost all expressed genes throughout the genome, it is possible that NTD risk associated with VPA exposure can be quantified and explained by a defined genomic signature. The second half of the presentation will consider the role of the environment in compromising pregnancy outcomes and how identification and application of this approach to high risk mothers can one day prevent preventable birth defects.