MOLECULAR AND CELLULAR MECHANISMS LEADING TO SIMILAR PHENOTYPES IN DOWN AND FETAL ALCOHOL SYNDROMES

Jeffrey P. Solzak[1] (Feng Zhou[2] and Randall J. Roper[1])

[1]Department of Biology, Indiana University Purdue University Indianapolis, 723 W. Michigan St. LD220C, Indianapolis, IN 46202

[2]Department of Anatomy and Cell Biology, Indiana School of Medicine, 635 Barnhill Drive, MS 509, Indianapolis, IN 46202

Down syndrome (DS) and Fetal Alcohol Syndrome (FAS) are two leading causes of birth defects with phenotypes ranging from cognitive impairment to craniofacial abnormalities. These syndromes have an estimated occurrence of 1/750 and 1/1000 live births, respectively. While DS originates from the trisomy of human chromosome 21 and FAS from excess alcohol consumption, many of the defining characteristics for these two disorders are stunningly similar. Our research of the published literature has identified more than 20 similarities in DS and FAS phenotypes including precise craniofacial and neurological abnormalities. We hypothesize that the similar phenotypes in these two syndromes are caused by disruptions in common molecular and cellular pathways. To test our hypothesis we are examining morphometric, genetic, and cellular phenotypes during development of DS and FAS mouse models. Our preliminary evidence indicates that during early development, expression of *Dyrk1a* and *Rcan1* (two genes found in three copies in individuals with DS) is dysregulated in the craniofacial and neurological precursors of both DS and FAS as compared to normal control embryos. Using immuocytochemistry, we are analyzing cellular properties of neurological development in DS embryos and comparing deficiencies found between trisomic and normal mice to those found in FAS embryos at similar stages. These results will further define molecular and cellular alterations leading to DS and FAS phenotypes and provide mechanisms to target for potential pharmacotherapy.