Titre: An induced pluripotent stem cell model of Prader-Willi syndrome

Dr. Lalande's areas of research interests are the role of epigenetics in disease and development, including control of gene expression in stem cells, and genomic imprinting and its association with neurogenetic disorders. Epigenetics refers to the study of heritable changes in gene function that occur without an alteration in DNA sequence. The Lalande lab is currently studying Angelman syndrome (AS), one of the better-known causes of mental retardation. AS is a neurogenetic disorder passed exclusively through the maternal germline because of the epigenetic process called genetic imprinting. Individuals with AS fail to inherit a normal active maternal copy of the gene encoding ubiquitin protein ligase E3A (UBE3A). Only the maternal copy of UBE3A is active in brain with the paternal copy being silenced due to imprinting. The loss of UBE3A in the brain of AS patients causes the accumulation of proteins in the brain that result in the clinical problems in AS. The accumulating proteins have not yet been discovered, and the Lalande lab is attempting to identify the targets of UBE3A. For these studies, the Lalande lab has developed techniques to knockout UBE3A in stem cells and then produce neurons from the UBE3A-negative stem cells. The researchers are also investigating the molecular process that silences the paternal UBE3A allele in the brain using a mouse model of the disease. This work is supported by the Physicians Health Services endowment.