PedsFocus

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NEONATOLOGY/GASTROENTEROLOGY

The Benefits of Human Milk Oligosaccharides for the Breastfed Infant

The Bode laboratory at the University of California, San Diego School of Medicine is dedicated to research on human milk oligosaccharides. These complex sugars comprise the third most abundant component of human breast milk and are not present in infant formula. The lab is working to understand how these complex sugars benefit the breastfed infant and potentially, the breastfeeding mother.

Recently, the lab discovered in animal studies that specific oligosaccharides protect from necrotizing enterocolitis and is now testing whether these results translate to the human infant.The lab has also discovered that certain oligosaccharides correlate with a reduced risk of mother-to-child HIV transmission through breastfeeding; the researchers are now testing whether these results can predict and reduce the risk of transmission from an HIV-infected mother to her uninfected child. Additionally, the lab has discovered that oligosaccharides block certain viruses, bacteria and protozoan parasites that cause severe infections and kill thousands of infants and young children around the world and is now testing whether these oligosaccharides can be used to treat these deadly infections or prevent them from occurring. Finally, the lab has begun to use human milk stem cells to elucidate how oligosaccharides are synthesized in the mammary gland—one of the few biosynthetic pathways in humans that remains to be explored.

For more information visit www.bodelab.com.

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NEUROLOGY

Mutations in BCKD-kinase Lead to a Potentially Treatable Form of Autism with Epilepsy

Joseph Gleeson, MD, and colleagues at the University of California, San Diego and Yale University Schools of Medicine have identified mutations in the BCKDK gene as the cause of a potentially treatable recessive syndrome characterized by autism, intellectual disability and epilepsy (*Science*, published online 6 September 2012; doi:10.1126/science.1224631). The scientists performed exome sequencing in two consanguineous families, each presenting with two siblings with autism and other neurodevelopmental phenotypes and a segregation pattern consistent with autosomal recessive inheritance. In both families, they found that the affected siblings harbored homozygous loss-of-function mutations in BCKDK. Further analyses of in-house exome data led to the identification of a third consanguineous family with two affected siblings harboring a homozygous missense mutation in BCKDK. The kinase encoded by BCKDK acts as a negative regulator of the branched-chain ketoacid dehydrogenase complex, which catalyzes the degradation of branched-chain amino acids.

Consistent with the human findings, adult BCKDK-knockout mice developed neurological phenotypes, including tremors and seizures, accompanied by reduced levels of branched-chain amino acids in the brain and other tissues. Notably, placing these knockout mice on a diet enriched in branched-chain amino acids reversed these neurological phenotypes, suggesting that humans with BCKDK mutations could benefit from similar dietary supplementation.

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PULMONARY/RESPIRATORY MEDICINE

Molecular Regulation of Fibroblast Phenotypes in Pulmonary Fibrotic Disease

The Hagood Laboratory investigates the molecular regulation of fibroblast phenotypes in pulmonary fibrotic disease and lung alveolarization, undertaking basic cellular and molecular investigation of processes in chronic lung remodeling. James Hagood, MD, also has a special interest in childhood interstitial lung disease, a collection of rare disorders that cause diffuse alterations in the lungs. Recent data has shown that many of the molecular pathways that control the development of the lung in infancy and childhood are re-expressed in idiopathic pulmonary fibrosis (IPF) and other lung diseases in adults.

Dr. Hagood's lab recently made the observation that epigenetic regulation, which has been shown to control such diverse processes as obesity and cancer, is also important in lung fibrosis. In particular, the researchers found that hypermethylation of the promoter for Thy-1, a critical modulator of cellular phenotypes and regulator of vascular permeability at sites of inflammation, affects the lung fibroblast fibrogenic process. These epigenetic modifications appear to represent a reversible mechanism in fibrosis that offers the possibility of new therapeutic options for IPF and related disorders.

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