THE HARTWELL FOUNDATION

2014 Individual Biomedical Research Award

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Omega-3 Fatty Acids as a Non-Invasive Therapy for the Prevention of Retinopathy of Prematurity

Every year in the United States, 517,000 infants are born early and before eye development is complete. About 16,000 of these infants will develop some degree of retinopathy of prematurity (ROP), where abnormal blood vessels grow in the retina (light sensitive tissue in the back of the eye). About 10% of ROP cases are so severe that they require high-risk invasive medical treatment like laser therapy, eye injections of medicines to alter abnormal blood vessel growth, or eye surgery, any of which may leave a baby blind if these interventions fail. Infants with ROP are at a greater lifetime risk of decreased contrast sensitivity, nearsightedness (myopia), lazy eye (amblyopia), crossed eyes (strabismus), and retinal detachment. Clearly, prevention would do the most to overcome the damage caused by ROP. While a correlation exists between oxygen, inflammation, lipid metabolism and abnormal blood vessel growth, the biochemical mechanisms responsible remain unclear. In the presence of excess oxygen, alterations in lipid metabolism contribute to an increase in tissue inflammation and suppression of an oxygen-sensing protein called prolyl hydroxylase, which leads to a reduction in the activity of a transcription factor known as hypoxia inducible factor (HIF). From recent reports, omega-3 fatty acids may work to enhance HIF activity. It is therefore provocative that recently published evidence suggests more omega-3 fatty acids in feeding formulae might act to prevent ROP. Unfortunately, nutrition in the American NICU contains mainly omega-6 fatty acids and consequently, premature infants do not receive the omega-3 fatty acids that usually build up in the fetus during the third trimester of pregnancy before eye development is complete. This is due to the lack of research on omega-3 fatty acids and their role in ROP. To address this need, Shira proposes a rigorous clinical trial to demonstrate that infants receiving omega-3 fatty acid therapy will produce more HIF, less pro-inflammatory factors, have normal growth of retinal blood vessels and therefore, have less ROP. To do so, she will compare lipid profiles of full-term infants and premature infants with and without ROP; determine the gene expression profiles of pro-inflammatory and angiogenic (blood vessel growth) genes in infants with and without ROP; and ascertain the severity of ROP as a function of omega-3 fatty acid therapy. If Shira is successful, the scientific evidence will support a link between omega-3 fatty acids and reduction of inflammation. If multi-centered clinical trials were subsequently to confirm her results, the ensuing benefit would lead to adoption of a new postpartum therapy in babies born prematurely, resulting in a transformative approach to prevent the devastating consequences of ROP.