INDIANA BIOSCIENCES RESEARCH INSTITUTE
CASE STUDY

Indiana Biosciences Research Institute collaboration helps discover a new genetic disease.

A collaborative research project led in part by the Indiana Biosciences Research Institute (IBRI) has resulted in the first description of a new monogenic disease, named, "DHPS Deficiency."

Dr. Teresa Mastracci, who leads the Regenerative Medicine and Metabolic Biology (RMMB) group in the IBRI Diabetes Center, and Dr. Wendy Chung, Kennedy Family Professor of Pediatrics in Medicine at Columbia University Vagelos College of Physicians and Surgeons, and their teams and collaborators, published a landmark study identifying the first human mutations in the deoxyhypusine synthase (DHPS) gene.

DHPS is an enzyme that is essential for the production of the unique amino acid, hypusine, which works in every cell of the body to help make proteins. The function of DHPS is essential for life. The mutations identified in the patients in the study cause a reduction in DHPS enzyme activity, which leads to clinical symptoms, including neurodevelopmental delay and seizures.

The study, which began in mid-2017, identified five people, mostly children, from four unrelated families, who all developed similar if not identical symptoms of an unknown cause until the identification of common DHPS mutations.

The research study was published Jan. 17, 2019, in the *American Journal of Human Genetics*: "Recessive Rare Variants in Deoxyhypusine Synthase, an Enzyme Involved in the Synthesis of Hypusine, Are Associated with a Neurodevelopmental Disorder."

This work is significant not only because it is the first description of a new monogenic disease, but as a result of the study's publication, researchers will be able to find other affected individuals and families from around the world, as well as direct their research toward finding an effective treatment so that one day, testing for DHPS Deficiency can be included when infants are screened for genetic diseases.

As with so many rare genetic diseases, the more researchers can collaborate to advance the understanding of how these diseases occur and affect the body, the closer they will come to translating their findings into therapies that reduce the burden of disease for all patients.

The large collaborative team included scientists and medical professionals from Columbia University Irving Medical Center, the Indiana Biosciences Research Institute (IBRI), Indiana University School of Medicine, NYU Langone Health, GeneDx, University of Calgary, Duke University Medical Center, Ann & Robert H. Lurie Children's Hospital of Chicago, Feinberg School of Medicine at Northwestern University and the National Institutes of Health (NIH).

The families affected by this disease were very supportive of Drs. Mastracci and Chung's work, which was essential to the success of the study. In the relatively short time the researchers were working together, the DHPS Foundation was also formed. The Foundation continues to help get the word out and supports other families living with this disease. More at www.dhpsfoundation.org.

Drs. Mastracci and Chung are also involved in a larger research consortium that includes groups from around the world that are studying similar rare cell disorders.

DISCOVERY WITH PURPOSE

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