Gene sleuths use social media to help map a new disease

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(Medical Xpress)—By combining the modern tools of gene-sequencing and social media, a team of researchers has confirmed the identification of a new genetic disorder that causes severe impairments in children.

The new disease, called NGLY1 deficiency, is reported online in the March 20, 2014, issue of *Genetics in Medicine*, the journal of the American College of Genetics and Genomics. The study describes the disease in eight patients, confirming the work of Duke Medicine scientists who originally identified the genetic mutation in a single young patient in 2012.

Children with the genetic mutation have a distinctive inability to produce tears when they cry, but also have movement disorders, developmental delays and liver problems. The genetic defect is so rare that without social media, the eight affected children would have remained unknown to each other and to scientists, but instead were connected within months.

"After we got the original diagnosis, we worked really hard to find additional cases to confirm that we got it right," said senior author David Goldstein, Ph.D., director of the Center for Human Genome Variation at Duke. "While we were working hard but making slow progress, the original family was writing about their experience and connecting with others on social media. They were able to find several more potential patients to be tested. This experience really brought home to all of us just how important family engagement is to this work and how important

it is to think hard and long about every patient's genome."

Duke researchers and scientists across two continents worked to sequence the entire genomes and exomes of the individual patients, revealing the newly identified genetic defect that was shared among them all.

The mutation causes a deficiency of the N-glycanase 1 enzyme, which is crucial in the process of recycling misshapen proteins so their components can be reused. In children with a defective NGLY1 gene, the proteins build up, resulting in impairments.

"Because of the unusual clinical presentations - notably the absence of tears along with liver abnormalities - parents of other affected children in distant places recognized these features when they read social media posts by the original family," said co-lead author Vandana Shashi, M.D., a medical geneticist at Duke who evaluated the first patient. "This enabled other children to be quickly identified and diagnosed."

After the first patient underwent sequencing at Duke, since NGLY1 had not yet been associated with human disease and since this was the only patient with mutations in the gene, Goldstein and Shashi consulted the Ad Hoc Genetics Committee at Duke. Charged with the task of advising Duke researchers on scientific and ethical issues related to genomic research, the committee reviewed the clinical and genomic data on the patient and approved the communication of the NGLY1 mutations to the family as likely causing the child's clinical symptoms.

"The Ad Hoc committee recognized that this study was venturing into uncharted territory, and we wanted to make the right decision," said Nancy C. Andrews, M.D., Ph.D., dean of the Duke University School of Medicine who chaired the ad hoc committee at the time of the decision. "The guiding principle was that we had to do what was in the best

interests of the patient and his family. I am delighted that this was how it turned out, and that this important discovery also benefits other patients around the world."

Goldstein said work is now focused on finding potential therapies to treat the condition, and on identifying additional disorders that might be related.

"We don't know how NGLY1 deficiency is causing the neurological findings seen in the children we're treating," said Gregory Enns, MB, ChB, associate professor of genetics in pediatrics at the Stanford University School of Medicine and co-lead author of the paper. "Once the gene defect is found, that's when the work really begins."

Provided by Duke University