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# Drosophila study hints at diet-based treatment for NGLY1 deficiency

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Researchers studying *Drosophila* fruit flies have found that in flies, providing a common dietary supplement prevents death caused by Pngl deficiency, the fly analog of the human genetic disorder N-Glycanase 1 (NGLY1) deficiency. Findings were reported at the American Society of Human Genetics (ASHG) 2016 Annual Meeting in Vancouver, B.C.

NGLY1 deficiency, a rare, autosomal recessive disease, was first defined four years ago and has been diagnosed in about 60 individuals worldwide, explained Clement Y. Chow, PhD, Assistant Professor in the Department of Human Genetics at the University of Utah and lead author on the study. People with this disease experience developmental delays, difficulty with movement, problems with liver function, and alacrima, the inability to produce tears. Symptoms are severe, starting from birth, and patients tend to live for less than ten years.

It is caused by a lack of the enzyme NGLY1, which plays an important role in degrading misfolded proteins in the cell. Researchers believe that without NGLY1, these proteins accumulate in the cell's cytoplasm, remaining bound to and depleting the cell's supply of GlcNAc, a sugar available widely as the dietary supplement N-acetylglucosamine. NGLY1 is remarkably consistent across species, and the *Drosophila* analog Pngl is thought to play a similar, equally critical role in flies. In a cohort of flies engineered to lack a functional copy of Pngl, just 18 percent survive to adulthood.

"Because GlcNAc is non-toxic and so widely available, we thought we'd

try providing flies with it as a supplement to restore the cell's supply," Dr. Chow said. He and his colleagues treated a cohort of Pngl-deficient flies with GlcNAc from birth. In this group, nearly 70 percent survived to adulthood.

While the results are dramatic, many steps remain before this approach could be tested for potential implementation in humans, Dr. Chow cautioned. The study took place in a *Drosophila* flies, and there are key differences between fly and human biology to consider. In addition, the flies were given GlcNAc supplement since birth. This would be nearly impossible in humans, who are severely affected even as infants and are unlikely to be diagnosed for at least the first several months of life.

"Even if such a treatment could alleviate symptoms, it would not be a cure - patients would still be unable to produce NGLY1," he added.

Nevertheless, the researchers are hopeful about its potential. They are starting to study the pathway involved to better understand how GlcNAc restores proper cell function in flies and whether it might have the same effect in humans. They are also exploring testing the treatment in mice.

**More information:** Dr. Chow will present his research on Thursday, October 20, 2016, from 11:30-11:45 a.m., in Room 302 of the Vancouver Convention Centre, West Building.

Provided by American Society of Human Genetics