A variant of NKH is uncovered

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People from around the country and the world turn to Johan Van Hove, MD, PhD, for advice on a rare metabolic disease known as NKH, which can disrupt the body in devastating and even deadly ways. Now, Van Hove, a University of Colorado medical school professor, has identified a new disease related to NKH, a finding that resolves previously baffling cases including the death of a Colorado girl.

"This opens the door," Van Hove said. "I am hopeful that it will eventually lead to major advances in dealing with these diseases."

The findings were published today in the journal *Brain*. The research team led by Van Hove, including scientists from the United States and five other countries, calls the new disease variant NKH.

The discovery is part of the new wave of personalized medicine being pioneered at CU and other institutions, in which researchers and doctors delve into the human genome to determine what is causing disease and use the information to try to fix the problem.

Van Hove has been on the trail of NKH for 22 years. Much of the funding for his research comes from families and others who have encountered the disease.

NKH, short for non-ketotic hyperglycinaemia, occurs in about one in 60,000 births. It involves the amino acid glycine, a building block for many functions including movement and brain activity. When a genetic mutation prevents the body from breaking down excess glycine, it can

cause brain problems including severe epilepsy and impaired intellectual development.

Scientists know the symptoms of NKH and also the genes that, when they malfunction, cause it. But a few patients worldwide had symptoms or glycine test results that were similar but did not quite match up.

One of those patients was a Colorado girl. She seemed fine until she was six months old. Then she began to lose muscle tone. She lost some control of her head movements. Seizures came next, along with a range of muscle twitches. By eight she lost her ability to walk. At the end, she spent most of her time curled in the fetal position.

Several years ago, at age 11, she died.

Researchers kept her genetic material, as they did with other patients who seemed to fall outside the NKH symptoms or who had molecular test results that were outside of the NKH pattern. The patients, some of whom are living, were scattered around the globe, in Australia, Lebanon, Canada and other countries as well as in the United States.

By looking into the genomes of this group of 11, Van Hove and his colleagues found that eight shared a genetic glitch different than the ones associated with NKH.

In other words, "this is a new disease," said Van Hove, who practices at Children's Hospital Colorado.

More testing is likely to reveal more such patients and, he said, may allow development of a new drug to make life better for patients with variant NKH.