Pegylated enzyme helps in mice with urea cycle disorder

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A specially engineered, long-lasting form of the enzyme arginase, which converts arginine to ornithine, reduces levels of arginine in the blood after both single and repeated doses in mice with arginase deficiency said researchers led by those at Baylor College of Medicine in a report that appears in the journal *Human Molecular Genetics*.

When children lack adequate supplies of the enzyme arginase 1, they can suffer from spastic diplegia (or paralysis on corresponding parts of both sides of the body), intellectual disability, seizures and growth deficiency. This decrease in arginase activity causes a urea cycle disorder, but unlike other such disorders, this one does not typically result in recurrent and large amounts of ammonia in the blood. Arginine is an amino acid produced naturally in the body and has a significant effect on human brain chemistry.

However, elevations of arginine and its metabolites circulating in the blood are suspected to contribute to the neurologic features of this disorder, said Dr. Lindsay C. Burrage, assistant professor in the department of molecular and human genetics at Baylor and the first author of this report.

"Current therapeutic strategies make it challenging to reduce arginine levels to normal or near-normal levels," she said. For that reason, she and colleagues, including corresponding author Dr. Brendan H. Lee, chair of the department of molecular and human genetics at Baylor, thought that this new molecule called pegylated arginase 1 (made by Austin-based

Aeglea Biotherapeutics) might reduce the levels of arginine circulating in the blood stream. In fact, researchers have used this strategy in studies of cancer treatment.

In studies of both newborn and adult mice with arginase deficiency, the researchers found that the pegylated enzyme (also known as AEB1102) reduced arginine levels in the blood.

However, the mice in this study were more severely ill than humans with this disorder, said Burrage. For that reason, the treatment did not slow death.

"Our hope is that this enzyme might be used in treating patients with this enzyme deficiency by complementing current treatment strategies used to reduce the levels of arginine in the blood," she said.

Now that there is newborn screening for the disorder, she expects more cases to come to the attention of pediatricians earlier in a child's life.

More information: "Human recombinant arginase enzyme reduces plasma arginine in mouse models of arginase deficiency." *Hum. Mol. Genet*. first published online September 10, 2015 DOI: 10.1093/hmg/ddv352

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