

Protein protects brain against compound in lead poisoning, liver disease

December 6 2007

Scientists have discovered that a protein known as PEPT2 protects the brains of mice from a naturally occurring but potentially toxic compound present in lead poisoning and in a class of liver diseases that can cause serious neurological complications.

Scientists at the University of Michigan found that when dosed with the compound called 5-aminolevulinic acid (5-ALA), mice without the PEPT2 protein died sooner, had neuromuscular dysfunction, and had up to 30 times higher concentrations of the toxic compound in their cerebrospinal fluid than did mice with the PEPT2.

PEPT2 is part of a class of membrane proteins called transporter proteins. The research focuses on understanding how these proteins work so that eventually, transporter proteins can be used to deliver different compounds to or from areas of the body in order to help fight diseases such as cancer.

"The findings suggest that the PEPT2 protein could work the same way in humans," said David Smith, U-M professor and chair of pharmaceutical sciences. "If that is the case, then PEPT2 may have relevance as a secondary genetic modifier of conditions such as acute hepatic porphyrias and lead poisoning, and in drug transport at the blood-brain barrier.

"We are looking at how to use the body's own machinery to get the compounds to where we want them to go," Smith said.

Naturally occurring in the body, the acid is involved in forming a substance called heme, which is a component of hemoglobin as well as many important enzymes. If there is an accumulation or an overproduction of 5-ALA in the body, however, it can become toxic. High concentrations of 5-ALA are present in people who have lead poisoning or hepatic porphyrias.

Source: University of Michigan

Citation: Protein protects brain against compound in lead poisoning, liver disease (2007, December 6) retrieved 27 April 2024 from <https://medicalxpress.com/news/2007-12-protein-brain-compound-poisoning-liver.html>

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