Transplanted Liver Cells Hold Hope for Treating Inherited Diseases

October 9 2009, By Marcia Goodrich

Mike Gibson

(PhysOrg.com) -- Mike Gibson, chair of the Department of Biological Sciences at Michigan Technological University, has spent most of his professional life trying to better understand genetic metabolic disorders that arise in children. With that knowledge, he is working to develop treatments in mice--including liver-cell transplants--that could one day be used to treat a variety of liver-based illnesses in people.

The genetic diseases Gibson studies are often dizzyingly complex, involving a cascade of biochemical reactions that go awry. While the knowledge gained by studying a single disease could help researchers develop a better treatment, it may also expand our fundamental understanding of physiology and be applied in the search for treatments of other hereditary maladies.

One of the conditions Gibson researches is maple syrup urine disease. People with the disease are unable to break down and metabolize three important amino acids, the building blocks of protein and essential for health. Urine in persons with this condition can smell like maple syrup.

Maple syrup disease is rare in the general population, found in about one in 200,000 individuals. But in the Amish and Mennonite communities, about one in 200 persons are affected. People with the disease must stick to a protein-restricted diet to avoid the buildup of the amino acids leucine, isoleucine and valine in their blood.

That can pose major problems for children and adolescents, says Gibson. “The diet is a challenge to implement and adhere to, and they don’t necessarily want to be told they can’t have a hamburger or pizza with their friends, which can lead to social stigmatization. Ingesting large amounts of protein can make these patients very ill quickly.” If amino acid levels rise too high, individuals can slip into a coma and even die without rapid attention.

The disease arises when defective liver cells don’t produce a key enzyme used to break down the amino acids. “We also know that patients with maple syrup disease have problems with neurotransmitters, like dopamine, which is key for controlling movement, and seratonin, which plays a role in everything from appetite to anxiety to sleep,” said Gibson.

Diet can control the disease, but it doesn’t cure it. “What drives this research is that even if maple syrup disease patients are treated for life and their amino acid levels are good, they may still show cognitive problems,” says Gibson.

He speculated that if healthy cells were put into the livers of people with the disease, those cells might proliferate and help restore sufficient enzyme to the liver to help normalize blood amino acid levels.

Gibson and his colleagues tested his theory in mice with maple syrup disease and found that after injecting a tiny amount of healthy cells into their livers, the level of the three amino acids in their bloodstream dropped about 70 percent. In addition, tests showed that the new cells could also be useful in restoring seratonin and dopamine to normal levels in the mice.

The positive effect was short-lived, Gibson said, but the results hold promise, for treating both maple syrup disease and other metabolic disorders with their roots in the liver.

Provided by Michigan Technological University (news : web)