

## Stories of Hope: Liver Disease



If the trace of chocolate on **Vanessa Lupian's** lips didn't give the 6-year-old away, the candy wrappers on the bathroom floor would have.

"That's where my panic came in," her mother, Veronica Lupian said. The wrong food — almost any food — could land Vanessa in the hospital fighting for her life. Vanessa had a metabolic disease that narrowed the list of foods she was allowed to eat so drastically that dinnertime left her staring enviously at the food on her family's plates.

Sometimes she would ask for a smell.

Vanessa was born with Maple Syrup Urine Disease, which rendered her incapable of breaking down proteins, and often landed her in the hospital with life-threatening complications.

When Veronica Lupian learned a liver transplant could change everything, the risks frightened her. When she finally broached the subject with her daughter, Vanessa burst into tears. Veronica thought she had scared her daughter. She hadn't.

"Mom, this is the happiest day of my life!" she said. And at age 10, after getting a new liver, she had her first French fry.

Veronica Lupian looks forward to the day children with metabolic disorders have simpler options. It may be possible to repair genetic defects in a child's liver stem cells, for example. Those cells could populate the liver with cells capable of breaking down otherwise harmful molecules.

"I hope they can discover something less invasive, something that can help a child not go through what my child went through," she said. "That would be the greatest thing not only for the child, but for the parents."

- Watch the Spotlight on liver disease talks

### Toward a Cure: liver disease

The heart beats its own drum, and the brain crackles with constant dazzle, but the liver is the ultimate behind-the-scenes player.

accomplishing roles less glamorous but every bit as essential. Among its more than 500 humdrum-but-critical duties, it carries away waste, breaks down fat, stores energy, and clears poisons from the blood. When a genetic defect, such as the one that causes Maple Syrup Urine Disease, interrupts its functions, survival hangs in the balance.

Right now, a liver transplant is the only treatment for such a metabolic disease, says Holger Willenbring, MD, PhD, an associate professor of surgery at The Liver Center, University of California, San Francisco. But it is a solution with many challenges, starting with a lack of available organs. Further, the surgery comes with a lifetime of treatment to prevent the immune system from rejecting the organ. Those drugs, which have serious side effects, don't always work and sometimes people need a second transplant.

Willenbring and others, including collaborators at UC Davis, hope that stem cells can one day repair livers without the need for a transplanted organ.

"Cell therapy in the liver is a very realistic goal," Willenbring says. In previous experiments in animals scientists have introduced liver cells created from embryonic or reprogrammed adult cells and have found that those cells continue to function in their new surroundings. But those repairs, to date, are short lived. The introduced cells won't multiply and quickly vanish, the victims of competition from the individual's own liver cells.

Willenbring's lab is working to determine which adult cell types — such as those from fat — will most readily produce liver stem cells. Then he hopes to fix the disease-causing mutation, creating a suitable population of healthy cells for transplant.

The stem cells could be introduced into the patient's liver, where they would multiply and help the liver function normally again. Expanding the cells after transplantation is the key to maintaining liver function, Willenbring says. "We would like to have stable correction of the disease, which will also reduce the number of cells needed."

So far, stem cells have corrected liver failure in mice. "Preliminary data suggests it's going to be feasible to do this in humans, but we're not at that stage yet," Willenbring says.

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