

UPDATES



HARVARD
MEDICAL SCHOOL
MASSACHUSETTS
GENERAL HOSPITAL

from Dr. Faustman's Laboratory at Massachusetts General Hospital

Issue One: Fall 2005

Updates on the Clinical Trial

In order to begin the first part of the clinical trial, we had to develop a new blood test (also known as a blood assay) to evaluate how well the therapies to be tested are working. This assay must be highly reliable and accurate. To develop it, we have been building a machine that separates different types of blood cells. We will use the cells isolated by the machine to develop the assay that counts the number of defective white blood cells that are causing disease. We have installed the equipment needed for the cell separation and blood assay machinery at Massachusetts General Hospital. This machinery includes the robots and robotic arms that will perform steps on an assembly line. In addition, we continue to build a computer program and engineer the many sequential steps to separate white blood cells from red blood cells. There will likely be over

800 separate robotic steps to this process and both the movement of the robotic arms and engineer platforms will be designed and tested. Our goal is to have this equipment ready to ramp up the human clinical trial for 2007.

In addition, we're collecting blood samples from volunteers as far away as California and Manitoba, Canada, as they visit us here in Boston. The laboratory is using these samples to fine-tune the cell separation procedure and clinical trial assay.

The steps we are taking are critical for the upcoming trial. If we were to proceed without the blood test, it would be like giving insulin without ever being able to check blood sugar levels. We need to have a rapid blood test to know if we are correctly dosing the drugs we will be testing.

Corroborating Research: Good News from Other Labs

Every month it seems we learn of more research that points to the potential of regeneration of the insulin-secreting cells in the pancreas. From the American Diabetes Association's 65th Annual Scientific Sessions, held June 10–14, 2005, three abstracts further confirm and support some of the key points of our research:

- In *Evidence for Sustained Islet Turnover in Humans with Long-Standing Type 1 Diabetes* (Abstract # 1612-P), researchers found that even those with long standing type 1 diabetes have beta cells that continue to be destroyed, suggesting that concomitant new beta cell formation must be occurring. They concluded that type 1 diabetes may be reversible by targeted inhibition of beta cell destruction, a key concept in Dr. Faustman's work that will be tested in a clinical trial to be led by Dr. David Nathan.
- *Comparative Analysis of Therapies Tested in Animal Models of Type 1 Diabetes and Human Clinical Trials* (Abstract # 102-OR) identified several reasons that may account for past difficulties in translating type 1 diabetes research from mice to humans and showed that identifying the impact of dose and time on the efficacy of potential therapeutic agents such as bacillus Calmette-Guerin (BCG) may be critical to future clinical success. Dr. Faustman's major research efforts are to develop a human blood assay that will allow researchers to monitor the efficacy of BCG in terms of dose and timing of administration during clinical trials.
- Finally, *In Vitro Generation of Insulin-Producing Cells from Adult Spleen* (Abstract # 1642-P) provided support for Dr. Faustman's past research that identified the splenic stem cell that can form islets. Multiple labs have now confirmed the existence of this stem cell. This newest data shows that these cells can be grown in the lab, transplanted into diabetic mice, and reduce hyperglycemia in these mice.



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Events in NYC and London

I was invited to give two lectures this fall focusing on the regeneration of islets in type 1 diabetes.

The first invited lecture happened in September at the New York Academy of Sciences, where I spoke

to the Metropolitan Diabetes Society. The second lecture will take place in London in October at the Institute of Cell and Molecular Sciences at Queen Mary's School of Medicine.

Fundraising Update

The Iacocca Foundation's JoinLeeNow (www.joinleenow.org) got a big boost this summer. Most of you have seen by now that Mr. Iacocca is back on television doing commercials for Chrysler. The bigger news is that Chrysler has agreed to become the official sponsor of JoinLeeNow and will work with the Iacocca Foundation to raise the money for the clinical trials. JoinLeeNow has over \$6 million already committed. Mr. Iacocca was also on TV during the July 31st broadcast of *This Week* with George Stephanopoulos. Here's what he had to say:

"People ask me how we're doing...and now I've hit 80 and I'm running out of time. I made a commitment to my wife to try...to find a cure before I die. We have about 100 researchers in her name all over the world. Now, one of those researchers at Mass General had a 10-strike. Dr. Denise Faustman cured diabetes in mice about a year and a half ago, and once she cured it, she said, "Wow! Not only did I stop the disease, but once I stopped the disease in the mice, they started to regenerate new cells." So now it's simple: If you're a mouse, I got you covered. But how you will translate that to humans, that is tough. I think we're on the brink of a breakthrough, and that's why I'm pouring the coals on it. So now I'm about one third of the way there on the project. Chrysler and its dealers, thank God, will probably put me over the top. I'm in the neighborhood. I'm getting close."

Mr. Iacocca isn't the only one who is busy. Sue Root and Jackie Fusco held another bike ride September 24-25, "100 Miles for Human Trials." They started in Mystic, CT and finished here at the MGH. The numbers aren't in yet for this year, but last year they raised almost \$145,000. On September 17th, two separate motorcycle rides raised funds for the Nathan/Faustman clinical trial program. In Hendricks County, Indiana, *Dallas & Reid's Ride*, which raised over \$45,000, included an afternoon of music, field events, and food. In Redmond, Washington, the DOCS Foundation's sixth annual Ride & Cure raised over \$12,000 and included a concert featuring performances from Styx, Foreigner, and REO Speedwagon on the cliffs of the Columbia River.

I greatly appreciate the help of Mr. Iacocca and all of the JoinLeeNow volunteers. This clinical trial couldn't happen without them.

Keep in touch,

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