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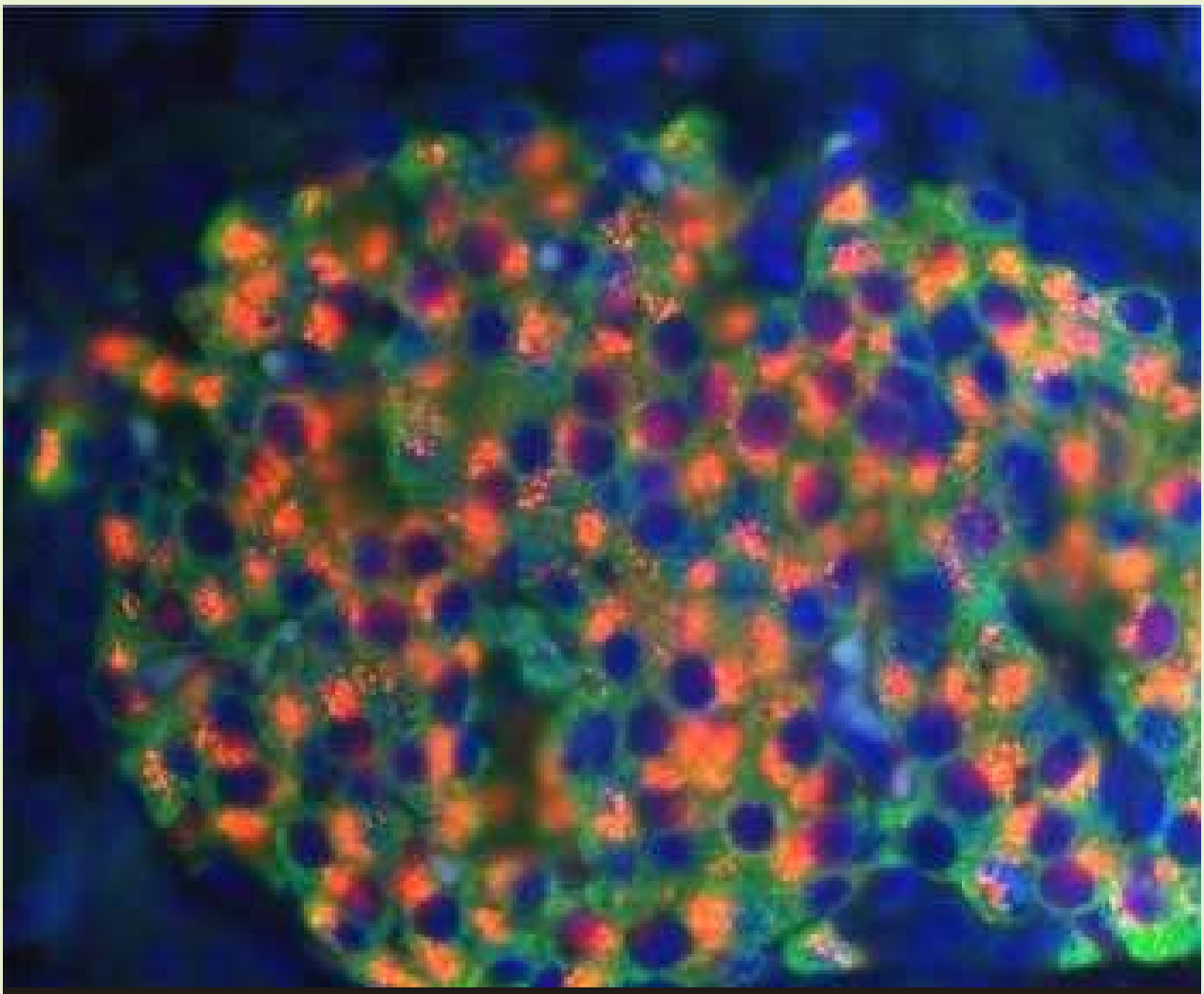

Insulin-secreting beta cells

Cord blood may preserve insulin levels in children with type 1 diabetes

Umbilical cord blood may safely preserve insulin production in children newly diagnosed with type 1 diabetes, as per findings from a small national pilot study presented Monday (June 25) at the American Diabetes Associations 67th Scientific Sessions in Chicago.

University of Florida scientists sought to determine whether it is feasible to use a patients own cord blood stem cells to neutralize the bodys autoimmune attack on the pancreas and help restore the organs ability to make insulin, which regulates how the body uses sugar and other nutrients for energy.

This is the first attempt at using cord blood as a potential treatment for type 1 diabetes. We hope these cells can either lessen the immune systems attack on the pancreas or possibly introduce stem cells that can differentiate into insulin-producing cells, said pediatric endocrinologist Dr. Michael Haller, an assistant professor of medicine at UFs College of Medicine.

While this is a relatively small study we can confidently say this is safe, and we have seen metabolic and immunologic changes to suggest there may be benefit, Haller said. Its not curing diabetes, but this is a first step to help us learn more and get us moving in the right direction.

Scientists got the idea in part from a patients father who had read that researchers elsewhere were able to reverse diabetes in mice by taking bone marrow from one animal and infusing it into its identical sibling without using chemotherapy or radiation treatment. And in the lab, researchers have been able to coax stem cells isolated from cord blood into making insulin. The man asked UF scientists whether giving a patient his or her own cord blood could have a similarly positive effect.

We thought this was a very reasonable question and would be a safe approach as long as we refrained from using chemotherapy, radiation treatment or

manipulating the cells. Since there are a lot more people out there who are banking cord blood than there were five years ago, we felt this approach would become increasingly attractive, Haller said.

A decade ago less than 1 percent of Americans were banking cord blood; today, that figure has grown to about.4 percent and is rising, Haller said. Cord blood is rich with cells that help regulate the immune system but until now has typically been used to restore a patients immune system after therapys for leukemia or lymphoma.

UF scientists identified children recently diagnosed with type 1 diabetes whose families banked their. umbilical cord blood at birth. Most were still producing a small amount of insulin. The scientists then gave seven patients ages 2 to 7 intravenous infusions of stem cells isolated from their own cord blood. (They have since treated an additional four children.) The patients were reviewed for the next two years to measure how much insulin they were making on their own and to assess blood sugar levels and the function of key immune system cells.

In the first six months, they mandatory significantly less insulin -- on average 0.45 versus 0.69 units of insulin per kilogram per day -- and maintained better control of blood sugar levels than children of comparable age with type 1 diabetes who were randomly selected from the clinic population. The scientists also noted that the children who received cord blood infusions had higher levels of regulatory immune cells in their blood six months after the infusion, on average 9 percent of the total cell volume compared with 7.21 percent at the time of infusion.This isnt a cure-all. We believe that giving these cells is essentially providing some immunotherapy and downregulating the autoimmunity these patients have, Haller said. Realistically, we hope to protect whats left of their insulin-production for an extended period of time. We think the immune regulation hypothesis is more likely than the hypothesis that stem cells are forming insulin producing cells on their own.

The idea would be to intervene and repair any early damage during the honeymoon period a number of patients enjoy -- the first several months after diagnosis during which insulin needs are minimal, he added.Our groups concept is that we wont be able to cure diabetes without a combination treatment approach, Haller said. Its nave to believe that with one agent were going to reverse a very complicated disease like type 1 diabetes. We probably need to go at it with multiple drugs to attack the various facets of the disease. Curing type 1 diabetes may require a similar approach to treating AIDS or cancer. The care of patients with these complex diseases did not markedly improve until combination therapies were administered. I suspect it will be the same with diabetes.

The Juvenile Diabetes Research Foundation and the National Institutes of Health funded the study, with support from UFs Clinical Research Center. UF scientists next plan to enroll up to 23 patients who will receive cord blood infusions. They also will seek to improve on the small metabolic and immunologic advantages theyve noted so far, possibly by testing the addition of one of the a number of drugs currently being used in other type 1 diabetes trials.We need to decide which agent will work well when combined with the cord blood, Haller said. Right now we are not manipulating the cells. We are simply infusing the cord blood. In addition to adding other drugs, we may need to see if we can take the key cells from cord blood and safely manipulate them to improve on our findings.The application of human cord blood in the therapy of type 1 diabetes is of extreme importance, said Colin P. McGuckin, a professor of regenerative medicine at Britains University of Newcastle upon Tyne Medical School.

The work carried out in the University of Florida has led the field in showing that cord blood contains cells which can quieten the immune system attack on the patients pancreas, McGuckin said. We know that cord blood contains very specialized cells which are there to stop rejection of the placenta of the child to the mother during pregnancy, and these are likely to be the ones which are useful for therapy in type 1 diabetes. Together with our work, showing that beta cells producing insulin can be formed using cord blood, we are on track to help diabetes patients in the future. The first step, though, has to be quietening

the immune system attack, and this is why the work in Gainesville is so important.

Epidemiological Reviews, Brach et al., 2000; 22(2): 218-227

Age, Gender Time: In the U.S., the prevalence of type 1 diabetes approximates 2 per 1000 for children less than age 20 years (27). This rate is higher than those reported for other childhood chronic disorders, such as cystic fibrosis, juvenile arthritis, etc. The onset of type 1 diabetes can occur at any age, **but it is usually diagnosed during childhood and adolescence, with a peak incidence around the time of puberty**. **This pattern has been reported for most populations throughout the world.**