MedicalXpress

Stem cell researcher pioneers gene therapy cure for children with "Bubble Baby" disease

November 20 2014, by Peter M. Bracke

UCLA stem cell researchers have pioneered a stem cell gene therapy cure for children born with adenosine deaminase (ADA)-deficient severe combined immunodeficiency (SCID), often called "Bubble Baby" disease, a life-threatening condition that if left untreated can be fatal within the first year of life.

The groundbreaking treatment was developed by renowned stem cell researcher and UCLA Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research member Dr. Donald Kohn, whose breakthrough was developed over three decades of research to create a gene therapy that safely restores immune systems in children with ADA-deficient SCID using the patient's own cells with no side effects.

To date, 18 children with SCID have been cured of the disease after receiving the stem cell gene therapy in clinical trials at UCLA and the National Institutes of Health.

"All of the children with SCID that I have treated in these stem cell clinical trials would have died in a year or less without this gene therapy, instead they are all thriving with fully functioning immune systems" said Kohn, a professor of pediatrics and of microbiology, immunology and molecular genetics in Life Sciences.

To protect children born with SCID they are kept in isolation, in controlled environments because without an immune system they are extremely vulnerable to illness and infection that could be lethal.

"Other current options for treating ADA-deficient SCID are not always optimal or feasible for many children," said Kohn. "We can now, for the first time, offer these children and their families a cure, and the chance to live a full healthy life."

Defeating ADA-Deficient SCID: A Game-Changing Approach

Children born with SCID, an inherited immunodeficiency, are generally diagnosed at about six months. They are extremely vulnerable to infectious diseases, and in a child with ADA-deficient SCID even the common cold can prove fatal. The disease causes cells to not create an enzyme called ADA, which is critical for production of the healthy white blood cells that drive a normal, fully-functioning immune system. About 15 percent of all SCID patients are ADA-deficient.

Currently, the only treatments for these children include injecting them twice a week with the necessary enzyme, a life-long process that is very expensive and often doesn't return the immune system to optimal levels. These children also have the option to undergo bone marrow transplants from matched siblings, but matches are very rare or result in rejection of the transplanted cells which then turn against the child.

Since 2009 and over the course of a two multi-year clinical trials, Kohn and his team tested two therapy regimens on 18 children with ADA-deficient SCID. During the trials, the patient's blood stem cells were removed from their bone marrow and genetically modified to correct the defect. All of the 18 patients were cured.

Kohn used a virus delivery system that he first developed in his lab in the 1990s to insert the corrected gene that produces the missing enzyme necessary for a healthy immune system into the blood forming stem cells

in the bone marrow. The genetically corrected blood forming stem cells then produce T cells that will fight infection.

He and colleagues tested different viral vectors, modifying each and perfecting viral delivery as the best method to put the healthy ADA genes back into the bone marrow cells of the patients. With the newly-transplanted cells now able to produce the needed enzyme, they use the powerful self-renewal potential of stem cells to repopulate the blood stream and the child develops their own new, fully-functioning immune system.

"We were very happy that over the course of several clinical trials and after making refinements and improvements to the treatment protocol, we are now able to provide a cure for babies with this devastating disease using the child's own cells," said Kohn.

The next step is to seek FDA approval for the gene therapy in the hopes that all children with ADA-deficient SCID will be able to benefit from the treatment.

This cutting-edge research also lays the groundwork for the successful gene therapy to be clinically tested for treatment of sickle cell disease, with trials set to begin next year.

"We've been working for the last five years to take the success we've had with this stem cell gene therapy for SCID to sickle cell," said Kohn. "We now have the potential to take the gene that blocks sickling and get it into enough of a patient's stem cells to block the disease."

The Padilla-Vaccaro Family: One Child's Story

Only weeks after giving birth to fraternal twins in 2012, Alysia Padilla-Vaccaro quickly felt something was wrong with one of her daughters,

Evangelina, now two years old.

"I was told that it was the stress, or the fear of being a new mom, but I just knew something wasn't right," said Padilla-Vaccaro. "Then I was informed that Evangelina had absolutely no immune system. That anything that could make her sick, would kill her. It was literally the worst time of my life."

Alysia and her husband Christian, of Corona, California, brought Evangelina to see Dr. Kohn at UCLA. Soon after undergoing Dr. Kohn's stem cell gene therapy treatment, Evangelina's new immune system developed without side effects. Her T cell count began to rise and her ability to fight off illness and infection grew stronger.

Then Dr. Kohn told Alysia and Christian the good news. For the first time, they could hug and kiss their daughter and take Evangelina outside to meet the world.

"To finally kiss your child on the lips, to hold her, it's impossible to describe what a gift that is," Padilla-Vaccaro said. "I gave birth to my daughter, but Dr. Kohn gave my baby life."

Provided by University of California, Los Angeles