

# Children's Hospital Oakland Scientists Conduct First-Ever Gene Editing Inside a Human Body




**For the first time, researchers have infused a person's blood with gene-editing tools, aiming to treat his severe inherited disease.**

This week, a UCSF Benioff Children's Hospital Oakland's adult patient underwent a landmark gene editing therapy – marking the first time that genome editing has been done inside a human body in an effort to change the DNA of a patient with a rare genetic disease.

The gene editing treatment is part of a clinical trial between UCSF Benioff Children's Hospital Oakland and Sangamo Therapeutics – an "in vivo" genome editing therapy for people with mucopolysaccharidosis type II (MPS II), also known as Hunter syndrome.

The trial, being lead in at the hospital by UCSF Benioff Oakland's Paul Hartz, M.D. whose patient, Brian Madeux, had previously participated in other clinical trials for MPS II and who is a long-term patient of Dr. Hartz.

"We are proud to be part of this groundbreaking trial and it is our hope that the gene editing therapy will produce benefits to our patient and other MPS patients that will greatly contribute to an improved quality of life. We are grateful to our patient Brian for being the first person to participate in the trial," said Dr. Hartz, M.D., a pediatric gastroenterologist and a principal investigator for the study at the UCSF Benioff Children's Hospital Oakland.

The clinical trial aims to treat MPS II by using genome editing to insert a corrective gene into a precise location in the DNA of liver cells with the goal of enabling a patient's liver to produce a lifelong and stable supply of an enzyme he or she currently lacks.

Without that enzyme, people with MPS II suffer a debilitating buildup of toxic carbohydrates in cells throughout their body. Approximately one in 100,000 to one in 170,000 people are born with MPS II. Many people with MPS II receive weekly infusions of enzyme replacement therapy (ERT), the current standard-of-care treatment. Within a day of receiving ERT, however, IDS quickly returns to near undetectable levels in the blood.

"Even with regular infusions of ERT, which has markedly improved functional health outcomes, patients endure progressive damage to heart, bones, and lungs. Many patients with MPS II die of airway obstruction, upper respiratory infection or heart failure before they reach the age of 20," said Dr. Hartz.

"Living with Hunter's Syndrome is not a pain-free life. I have pain every second of the day," said Madeux. "I have learned to manage my issues as they arise, through the help of doctors and by staying active. There are people dealing with far worse. I go day by day. I actually thought I wouldn't live past my early 20's, but the way I lived my life has surely helped me to live longer. Being an athlete growing up and working in the hospitality industry has helped."

He decided to participate in the groundbreaking study because he wanted to give something back to others living with inherited conditions like him, "I am willing to take the minimal risk of changing my own DNA if it will prolong my life and help scientists find cures for humankind".

The therapy is part of Phase 1/2 clinical trial ("the CHAMPIONS study") evaluating SB-913, an investigational in vivo genome editing therapy. SB-913 makes use of Sangamo's zinc finger nuclease (ZFN) genome editing technology to insert a corrective gene into a precise location in the DNA of liver cells. To restrict editing to liver cells, the ZFNs and the corrective gene are delivered in a single intravenous infusion using AAV vectors that target the liver. The ZFNs enter the cells as inactive DNA instructions in a format designed only for liver cells to unlock. Once "unlocked", the ZFNs then identify, bind to and cut the DNA in a specific location within the albumin gene. Using the cells' natural DNA repair processes, liver cells can then insert the corrective gene for IDS at that precise location.

"For the first time, a patient has received a therapy intended to precisely edit the DNA of cells directly inside the

## News

**UCSF Benioff Children's Hospitals in Oakland and San Francisco To Begin Cutting Edge Stem-Cell Trials at CIRM-Funded Alpha Stem Cell Clinics**

UCSF Benioff Children's Hospitals in Oakland and San Francisco To Begi...

**UCSF Benioff Children's Hospital Study of Elite NBA Players Re-affirms Positive Impact of Playing Multiple Youth Sports**

Study of Elite NBA Players Re-affirms Positive Impact of Playing Multiple Yo...

**Children's Hospital Oakland Scientists Conduct First-Ever Gene Editing Inside a Human Body**

For the first time, researchers have infused a person's blood with gene-edit...

body. We are at the start of a new frontier of genomic medicine," said Dr. Sandy Macrae, CEO of Sangamo Therapeutics.

The CHAMPIONS study is an open-label clinical study designed to assess the safety, tolerability and preliminary efficacy of the SB-913 investigational genome editing therapy in up to nine adult males with MPS II.

UCSF Benioff Children's Hospital Oakland's gastroenterology research group, under the direction of Dr. Paul Hartz, is focused on translational and clinical research on the treatment of lysosomal storage diseases focused primarily on the mucopolysaccharidoses.

The mucopolysaccharidoses (MPS) are a group of 11 rare genetic disorders in the lysosomal storage disease (LSD) family, each caused by the absence or reduced function of lysosomal enzymes needed to break down glycosaminoglycans (GAGs). GAGs are long chains of carbohydrate constituents of bone, cartilage, and connective tissue. In the absence of lysosomal enzyme function, these GAGs collect in the cells and connective tissues and result in progressive cellular damage and organ system dysfunction. The mucopolysaccharidoses share many clinical features but have varying degrees of severity.

Treating these patients has depended on medical and surgical care, with hematopoietic stem cell transplantation as the only cure.

Since 2003, enzyme replacement therapy (ERT) has been approved for MPS I, II and VI provide specific therapy administered intravenously. Dr. Hartz participated in the clinical trials for MPS II and VI that led to FDA approval. Dr. Hartz lead one of only two US sites that participated in a longitudinal, multicenter, multinational natural history study for MPS IVA or Morquio A. He was also PI of one the US sites for the phase 3, randomized, placebo-controlled trial of enzyme replacement therapy that lead to the U.S. Food and Drug Administration (FDA) approval of a drug for patients with MPS IVA (Morquio A syndrome).

In addition to these trials, Dr. Hartz and his colleagues have participated in the NIH-sponsored Lysosomal Disease Network studies and enrolled patients into a longitudinal study of brain disease in MPS I and II.

#### STAY CONNECTED:



#### DIRECTIONS

#### SECTIONS

Departments & Clinics  
Physician Directory  
Refer a Patient  
Medical Education  
Research  
Giving  
Calendar

#### INFORMATION FOR

Referring Physicians  
Patients & Families  
Visitors  
Healthcare Professionals  
Media  
Job Seekers  
Vendors  
Donors

#### ABOUT US

About Children's Hospital  
Notice of Privacy Practices  
100 Year History  
Our Stories  
Children's Research Institute  
Graduate Medical Education  
Careers  
Contact Us

#### I'D LIKE INFORMATION ON

Volunteering  
My Child's Condition  
Finding a Doctor  
eCards  
Bill Pay  
Calendar  
Donations  
Paginas en Espanol

#### ABOUT THIS SITE

Site Map  
Disclaimer, Usage & Privacy

#### ASSOCIATED SITES

www.UCSFBenioffChildrensSF.org  
www.CHORI.org  
Give.UCSFBenioffChildrens.org  
www.CHOnext100.org  
www.100AmazingYears.org



© 2018 UCSF Benioff Children's Hospital Oakland  
747 52nd Street, Oakland, CA 94609  
510-428-3000

