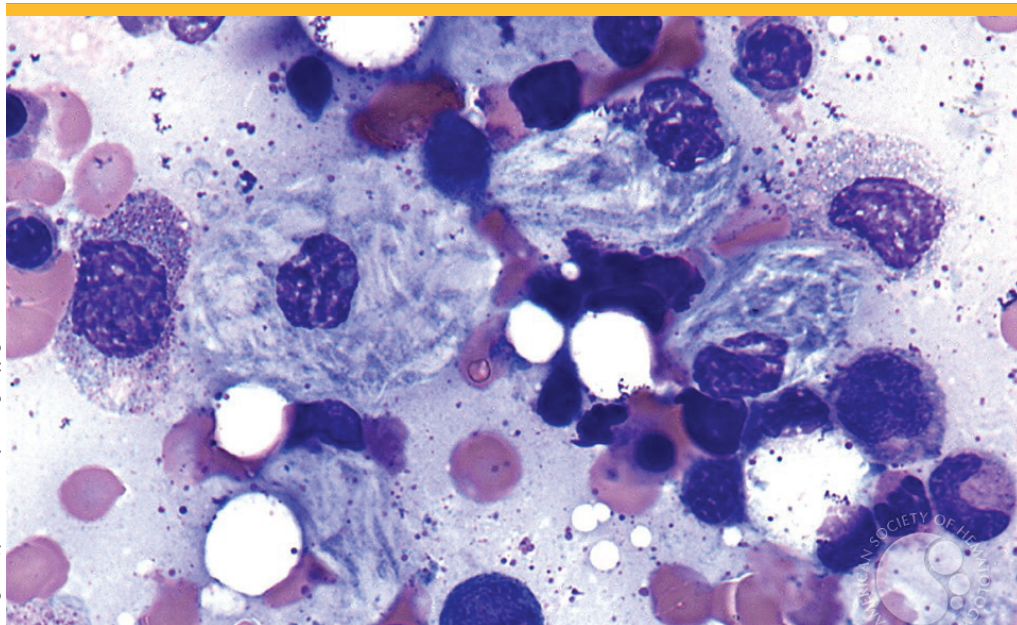


# Innovative cellular and gene therapy programs treat pediatric diseases



*Bone marrow sample from a patient with Gaucher disease stained to show the cell nuclei.*

**Ever since UCLA** opened one of the nation's first bone marrow transplant units in 1973, doctors in the gene and cellular therapy programs have been leading the way in researching treatments and cures for debilitating childhood diseases. Today, Mattel Children's Hospital UCLA is a world leader in developing and conducting several groundbreaking gene-therapy clinical trials.

The Program for Cellular Therapeutics in the Division of Pediatric Hematology/Oncology is working in conjunction with the UCLA Human Gene and Cell Therapy Program, the UCLA Children's Discovery & Innovation Institute and the Pediatric Bone Marrow Transplant Program to develop safer and innovative treatments for children who suffer from these life-threatening diseases.

## Severe combined immunodeficiency (SCID)

UCLA's Program for Cellular Therapeutics has been conducting gene-therapy clinical trials for adenosine deaminase (ADA) deficiency or ADA-SCID. This "bubble-baby disease" weakens the immune system, making it difficult for children to fight off even mild infections. ADA-SCID is lethal if left untreated.

Donald B. Kohn, MD, director of the UCLA Human Gene and Cell Therapy Program, and his colleagues performed the basic laboratory research to improve gene delivery to blood-forming stem cells, developed clinical protocols and received all local and national regulatory approvals.

## Lowering transplant rejection risk

The standard of care for a number of childhood illnesses is bone marrow transplantation, in which a patient's diseased blood cells are replaced with healthy donor cells. Transplants are most likely to be successful when the donor cells come from a close relative. Unfortunately, 70 percent of patients don't have a familial match. "The odds of graft-versus-host disease, a complication in which donor cells attack the recipient's body, go up dramatically when using cells from an unrelated donor," says Ami J. Shah, MD, director of the Program for Cellular Therapeutics at Mattel Children's Hospital UCLA.

Cellular and gene therapies use the patient's own (autologous) cells. "There is less risk of rejection when using a patient's own cells," explains Dr. Shah. "The cells are genetically modified in a laboratory and then transplanted back into the patient where it is hoped that they will multiply and start to kill diseased cells."

Thanks in large part to their dedicated research into cellular and gene therapies, UCLA doctors have been tapped to spearhead several groundbreaking clinical trials aimed at treating genetic diseases.

Since 2009, approximately 20 children have been treated at UCLA using gene therapy for ADA deficient SCID.

Another clinical trial under way targets X-SCID, a form of SCID that affects only boys. Mattel Children's Hospital UCLA is one of only three hospitals nationwide selected by the National Institute of Allergy and Infectious Diseases to participate in this trial.

## Adrenoleukodystrophy (ALD)

Mattel Children's Hospital UCLA is also one of only three hospitals in the nation participating in a gene-therapy clinical trial aimed at stopping the progression of ALD. This genetic disorder damages the myelin sheath that surrounds and insulates nerve cells in the brain. ALD affects movement, thinking, hearing, vision, swallowing and other body functions. Bone marrow transplants are helpful for a select group of patients with inherited blood diseases; however, gene therapy may be able to treat the same diseases with fewer complications since it uses the patient's own blood-forming stem cells, which are a perfect match for each patient.

## Sickle cell disease

A team of UCLA doctors led by Dr. Kohn was the first to develop a breakthrough gene therapy to treat sickle cell disease, the most commonly inherited blood disorder in the United States. As a result of the team's findings, the first human trial of stem-cell gene therapy for sickle cell disease is currently under way at UCLA. The gene therapy introduces a gene with anti-sickling properties into the hematopoietic (blood-producing) stem cells taken from patients' bone marrow. The modified stem cells are transplanted back into the patient where they may begin to create an ongoing source of healthy red blood cells that do not sickle. The trial is currently open to those age 18 years and older.

## Leukemia and lymphoma

UCLA pediatric hematologist/oncologist Satiro De Oliveira, MD, and his team from the Program for Cellular Therapeutics are working to genetically engineer cancer patients' healthy immune cells (T cells) and blood stem cells so they recognize and attack cancerous cells when reintroduced back into the body, targeting chemotherapy-resistant forms of leukemia and lymphoma. Another study is focused on modifying cells to target specific viruses known to increase the risk of death from infections following bone marrow transplantation.

## Generating a new immune system

The immune system functions poorly after chemotherapy and transplantation. Gay M. Crooks, MD, associate director of the Broad Stem Cell Research Center, seeks to uncover how human immune cells develop from bone marrow stem cells to find new ways to improve the immune system. The Crooks laboratory is also developing ways to engineer a transplantable thymus to permanently produce healthy T cells that suppress inflammation and fight infection.

## Participating Physicians

### Donald B. Kohn, MD

Professor of Microbiology, Immunology and Molecular Genetics (MIMG) and Pediatrics  
Director, UCLA Human Gene Medicine Program

### Theodore B. Moore, MD

Chief, Professor and Clinical Director  
Division of Pediatric Hematology/Oncology  
Director, Pediatric Blood and Marrow Transplant Program

### Ami J. Shah, MD

Professor of Pediatrics  
Division of Pediatric Hematology/Oncology  
Director, Program for Cellular Therapeutics

### Gay M. Crooks, MD

Professor of Pathology and Laboratory Medicine and Pediatrics  
Associate Director  
Broad Stem Cell Research Center

### Satiro De Oliveira, MD

Assistant Professor of Pediatrics  
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