## SCID and Primary Immunodeficiency Fact Sheet

CIRM funds many projects seeking to better understand Severe Combined Immune Deficiency (SCID) and other primary immunodeficiency diseases to translate those discoveries into new therapies.

## Description

Primary immunodeficiencies are disease that compromise or destroy the immune system, leaving patients susceptible to serious infections. Typically, these diseases have genetic causes and many of them are rare. Severe combined immune deficiency or SCID is an example of a primary immunodeficiency.

SCID – also known as 'bubble boy disease' - is a rare genetic disorder, effecting one in 30,000 newborns. Left untreated the children die before the age of 2, and the only readily available treatment involves high-risk bone marrow transplants. Because these patients already have a compromised immune system, 10 to 20 percent don't survive the transplant.

Gene therapy has been used to correct the defect in certain types of SCID, but early gene modifying techniques resulted in some patients developing cancer. Newer gene therapy techniques appear to be safer but have been tried on fewer than 20 patients.

Researchers funded by California's stem cell agency are looking for a better alternative to help these children. They are trying to improve the safety of bone marrow transplant (BMT), which essentially uses the stem cells in bone marrow to give the children a new immune system that works properly. Most of the risk of current BMT procedures comes from the radiation or chemotherapy given to patients before the transplant to wipe out the patient's own stem cells that form immune cells. These regimens kill many types of cells beyond those intended and result in numerous toxic side effects.

### Clinical Stage Programs

**Stanford School of Medicine (X-linked SCID)**

This team proposes to replace SCID patients' dysfunctional immune cells with healthy ones using a safer form of bone marrow transplant (BMT). They plan to eliminate the bad cells with an antibody, a protein, that very specifically targets and eliminates blood forming stem cells. If successful, the procedure could open up similar BMT therapies to patients with other auto-immune diseases such as multiple sclerosis, lupus or diabetes that are generally not candidates for BMT currently. These diseases, while debilitating, are not immediately life-threatening and generally don't warrant the risks involved in BMT the way it is done today.

- Read more about this project
- Read about this clinical trial

**St. Jude Children's Research Hospital**

The team is using gene therapy to correct a genetic mutation in the blood stem cells of patients with X-linked SCID. The corrected stem cells are then transplanted back into the patient to restore their immune system's ability to produce healthy immune cells. This will allow the patient to fight off infections and will hopefully cure their disease.

- Read more about this project
- Read about this clinical trial

**University of California, Los Angeles (Chronic granulomatous disease and ADA-SCID)**

The team is developing a therapy for chronic granulomatous disease: a very rare primary immune deficiency disease that results in severe and recurrent infections that can impact quality and length of life. The UCLA team uses the patient's own genetically modified blood stem cells to create a new blood supply and immune system to eradicate the problem.

- Read more about this project
- Read about this clinical trial

UCLA is also developing a therapy for a form of SCID called adenosine deaminase (ADA)-deficient SCID. Patients with ADA-SCID lack an important enzyme called adenosine deaminase in their immune cells. Without this enzyme, toxic by-products build up in their immune cells and eventually kill them off leaving the patient susceptible to deadly infections. The group from UCLA will genetically modify patient blood stem cells to remove the disease-causing mutation and transplant these corrected stem cells back into the patient to create a new, healthy immune system.

- Read more about this project
- Read about this clinical trial

### CIRM Grants Targeting Immune Diseases including SCID

| Researcher name | Institution | Grant Title | Grant Type | Award Amount |
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| Nicholas Gascoigne | Scripps Research Institute | Role of Innate Immunity in hematopoeitic stem cell-mediated allograft tolerance | Transplantation Immunology | $1,705,554 |
| Jennifer Puck | University of California, San Francisco | Ex Vivo Transduction of the Human Artemis (DCLRE1C) cDNA by Lentiviral Vector AProArt into CD34+ Hematopoietic Cells for Artemis (ART)-Deficient Severe Combined Immunodeficiency (SCID) | Late Stage Preclinical Projects | $4,268,865 |
| Husein Hadeiba | Palo Alto Veterans Institute for Research | Application of Tolerogenic Dendritic Cells for Hematopoietic Stem Cell Transplantation | Transplantation Immunology | $733,061 |
| Donald Kohn | University of California, Los Angeles | Efficacy and safety of cryopreserved autologous CD34+ HSC transduced with EFS lentiviral vector encoding for human ADA gene in ADA-SCID subjects | Clinical Trial Stage Projects | $10,156,925 |
| David DiGiusto | City of Hope, Beckman Research Institute | Development of RNA-based approaches to stem cell gene therapy for HIV | Early Translational II | $3,097,160 |
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| Jeanne Loring | Scripps Research Institute | Thymus based tolerance to stem cell therapies | Transplantation Immunology | $1,108,921 | |
| Rosa Bacchetta | Stanford University | GENE EDITING FOR FOXP3 IN HUMAN HSC | Quest - Discovery Stage Research Projects | $984,228 | |
| John Zaia | City of Hope, Beckman Research Institute | ZINC FINGER NUCLEASE-BASED STEM CELL THERAPY FOR AIDS | Disease Team Research I | $14,536,969 | |
| Tippi MacKenzie | University of California, San Francisco | Maternal and Fetal Immune Responses to In Utero Hematopoietic Stem Cell Transplantation | Transplantation Immunology | $1,230,869 | |
| Stephen Gottschalk | St. Jude Children's Research Hospital | Lentiviral Gene Therapy for Infants with X-linked Severe Combined Immunodeficiency using Autologous Bone Marrow Stem Cells and Busulfan Conditioning | Clinical Trial Stage Projects | $11,924,780 | |
| Irvin Chen | University of California, Los Angeles | HPSC based therapy for HIV disease using RNAi to CCR5. | Disease Team Research I | $9,905,604 | |
| Anjana Rao | La Jolla Institute for Allergy and Immunology | Generation of regulatory T cells by reprogramming | Transplantation Immunology | $1,464,446 | |
| Leslie Meltzer | Orchard Therapeutics plc | Efficacy and safety of cryopreserved autologous CD34+ HSC transduced with EFS lentiviral vector encoding for human ADA gene in ADA-SCID subjects | Clinical Trial Stage Projects | $8,465,745 | |
| Michele Calos | Stanford University | Safe, efficient creation of human induced pluripotent stem cells without the use of retroviruses | New Cell Lines | $1,406,875 | |
| Ellen Robey | University of California, Berkeley | Human Immune System Mouse models as preclinical platforms for stem cell derived grafts | Transplantation Immunology | $1,005,605 | |
| Katja Weinacht | Stanford University | Regenerative Thymic Tissues as Curative Cell Therapy for Patients with 22q11 Deletion Syndrome | Quest - Discovery Stage Research Projects | $1,251,720 | |
| Irvin Chen | University of California, Los Angeles | Genetic modification of the human genome to resist HIV-1 infection and/or disease progression | SEED Grant | $616,800 | |
| Judith Shizuru | Stanford University | Purified allogeneic hematopoietic stem cells as a platform for tolerance induction | Transplantation Immunology | $1,233,275 | |
| Kinnari Patel | Rocket Pharmaceuticals, Inc. | LADICell | Clinical Trial Stage Projects | $6,567,085 | |
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| Thomas Lane | University of California, Irvine | Human Embryonic Stem Cells and Remyelination in a Viral Model of Demyelination | SEED Grant | $368,081 |
| Kenneth Weinberg | Stanford University | Engineered immune tolerance by Stem Cell-derived thymic regeneration | Transplantation Immunology | $1,271,729 |
| Rosa Bacchetta | Stanford University | IND-enabling activities for a Phase 1 Study of Autologous CD4LVFOXP3 T Cells in Subjects with IPEX Syndrome | Late Stage Preclinical Projects | $5,002,496 |
| Kenneth Weinberg | Stanford University | Embryonic stem cell-derived thymic epithelial cells | SEED Grant | $628,793 |
| Yang Xu | University of California, San Diego | Induction of immune tolerance to human embryonic stem cell-derived allografts | Transplantation Immunology | $1,192,680 |
| Irving Weissman | Stanford University | Prospective isolation of hESC-derived hematopoietic and cardiomyocyte stem cells | Comprehensive Grant | $2,471,386 |
| Judith Shizuru | Stanford University | A monoclonal antibody that depletes blood stem cells and enables chemotherapy free transplants | Disease Team Therapy Planning I | $90,147 |
| Samuel Pleasure | University of California, San Francisco | Human stem cell derived oligodendrocytes for treatment of stroke and MS | Comprehensive Grant | $2,459,235 |
| Morton Cowan | University of California, San Francisco | Gene Correction of Autologous Hematopoietic Stem Cells in Artemis Deficient SCID | Early Translational III | $3,862,367 |
| Steven Deeks | University of California, San Francisco | Anti-HIV duoCAR-T cell therapy for HIV infection | Clinical Trial Stage Projects | $8,970,732 |
| Zack Jerome | University of California, Los Angeles | Human Embryonic Stem Cell Therapeutic Strategies to Target HIV Disease | Comprehensive Grant | $2,401,903 |
| Judith Shizuru | Stanford University | A monoclonal antibody that depletes blood stem cells and enables chemotherapy free transplants | Disease Team Therapy Development - Research | $18,990,683 |
| Inder Verma | Salk Institute for Biological Studies | Curing Hematological Diseases | Early Translational I | $5,979,252 |
| Mark Anderson | University of California, San Francisco | Generation of a functional thymus to induce immune tolerance to stem cell derivatives | Basic Biology V | $1,191,000 |
| Mark Anderson | University of California, San Francisco | Stem cell differentiation to thymic epithelium for inducing tolerance to stem cells | Transplantation Immunology | $1,314,089 |
| Matthew Porteus | Stanford University | Pre-clinical development of gene correction therapy of hematopoietic stem cells for SCID-X1 | Preclinical Development Awards | $874,877 |

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| Jeffrey Bluestone | University of California, San Francisco | Stem cell tolerance through the use of engineered antigen-specific regulatory T cells | Transplantation Immunology | $1,152,768 | |
| Donald Kohn | University of California, Los Angeles | A Phase I/II, Non Randomized, Multicenter, Open-Label Study of G1XCGD (Lentiviral Vector Transduced CD34+ Cells) in Patients With X-Linked Chronic Granulomatous Disease | Clinical Trial Stage Projects | $7,083,364 | |
| Gay Crooks | University of California, Los Angeles | Engineering Thymic Regeneration to Induce Tolerance | Transplantation Immunology | $1,235,445 | |
| Donald Kohn | University of California, Los Angeles | Primary Immune Deficiency Treatment Consortium (PIDTC) Annual Scientific Workshop | Conference II | $29,807 | |
| Caroline Kuo | University of California, Los Angeles | Evaluation of Gene Therapy Approaches for Autosomal Recessive Hyper IgE Syndrome Due to Mutations in DOCK8 | Progression Award - Discovery Stage Research Projects | $234,000 | |
| Caroline Kuo | University of California, Los Angeles | Ex Vivo Gene Editing of Human Hematopoietic Stem Cells for the Treatment of X-Linked Hyper-IgM Syndrome | Therapeutic Translational Research Projects | $4,896,628 | |
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### Resources

- The Stem Cellar blogs about SCID and immune disease research
- Immune Deficiency Foundation
- NIH: SCID Fact Sheet
- SCID.net
- Find a clinical trial near you: NIH Clinical Trials database
- Family Caregiver Alliance
- National Family Caregivers Association

**Find Out More:**
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