CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

August 2022

BLOOD DISEASES

Alpha Thalassemia Major

UC San Francisco
Team Lead: Tippi MacKenzie
Dr. MacKenzie is using hematopoietic stem cells (HSCs) to treat babies in the womb who have alpha thalassemia major, a blood disorder that is almost always fatal. The HSCs are taken from the mother's bone marrow and transplanted into the baby before birth. The mother's cells are able to survive and correct the defect in the baby's blood cells, increasing the chances of a healthy birth and improving the chances of having effective treatments after birth.

Beta Thalassemia

Sangamo Therapeutics
Team Lead: Bettina Cockroft
UC San Francisco researchers aim to repair the damaged immune system of children born with severe combined immunodeficiency (SCID), a genetic blood disorder in which even a mild infection can be fatal. This trial will focus on SCID patients who have mutations in a gene called Artemis, the most difficult form of SCID to treat when using a standard bone marrow transplant from a healthy donor. The team will genetically modify the patient's own blood stem cells with a functional copy of Artemis, with the goal of creating a new blood system and restoring the health of the immune system.

Bone Marrow Transplant And Viral Infection

Children's Hospital of Los Angeles
Team Lead: Michael Pulsipher
Viral infection can lead to fatal complications in patients with weakened immune systems resulting from chemotherapy, bone marrow or cord blood transplant, and other forms of inherited or acquired disorders. A team at Children's Hospital of Los Angeles is testing the feasibility of providing these immune suppressed patients with engineered T-cells to fight these viruses. Donated virus-specific T-cells will be matched to the patient's immune system to help boost their ability to fight off these viruses and to provide longer-term anti-viral protection.

Chronic Granulomatous Disease

UCLA
Team Lead: Donald Kohn
Chronic granulomatous disease is a rare immune disorder that results in severe, recurrent infections that can impact quality and length of life. A team at UCLA uses the patient's own genetically modified blood stem cells to create a new blood supply and a healthy immune system, with the aim of curing patients with this disease.

Leukocyte Adhesion Deficiency-I (LAD-I)

Rocket Pharmaceuticals, Inc.
Team Lead: Dr. Kinnari Patel

Rocket Pharmaceuticals is using blood stem cells to treat infants with Leukocyte Adhesion Deficiency-I (LAD-I), a rare pediatric disease caused by a mutation in a specific gene that affects the body's ability to combat infections. The team will test a treatment that modifies an infant's own blood stem cells and inserts a functional version of the gene. These modified stem cells are then reintroduced back into the infant, with the hope of creating a new blood supply and repairing the immune system, thereby enabling the body to combat infections.

Severe Combined Immunodeficiency (SCID)

UCLA
Team Lead: Donald Kohn

A team at UCLA is using a patient's own blood stem cells to try and repair their damaged immune system. They will use what's called a lentiviral vector to deliver genetic material into the blood stem cells, correcting the genetic flaw that causes SCID. It's hoped this will create a new blood system and a healthy immune system.

Stanford University
Team Lead: Judith Shizuru

A team at Stanford proposes to replace SCID patients' dysfunctional immune cells with healthy ones using a safer form of bone marrow transplant (BMT). Current BMT procedures must use toxic chemotherapy to make space in the bone marrow for the healthy transplanted stem cells to engraft. The Stanford team will instead test a safe, non-toxic protein that targets and removes the defective 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.

St. Jude Children's Research Hospital
Team Lead: Stephen Gottschalk

St. Jude Children's Research Hospital is teaming up with UC San Francisco to repair the damaged immune system of children born with SCID. They will genetically modify the patient's own blood stem cells, with the goal of creating a new blood system and restoring the health of the immune system.

UC San Francisco
Team Lead: Morton Cowan

Researchers aim to repair the damaged immune system of children born with the genetic blood disorder SCID. This trial will focus on SCID patients who have mutations in a gene called Artemis, the most difficult form of SCID to treat when using a standard bone marrow transplant from a healthy donor. The team will genetically modify the patient's own blood stem cells with a functional copy of Artemis, with the goal of creating a new blood system and restoring the immune system.

CIRM

CALIFORNIA'S STEM CELL AGENCY

Sickle Cell Disease

Boston Children's Hospital (UCLA Trial Site) Team Lead: David Williams

Researchers will conduct a gene therapy clinical trial for sickle cell disease (SCD). The team will take a patient's own blood stem cells and insert a novel engineered gene to silence abnormal hemoglobin and induce normal fetal hemoglobin expression. The modified blood stem cells will then be reintroduced back into the patient. The goal of this therapy is to aid in the production of normal shaped red blood cells, thereby reducing the severity of the disease.

City of Hope (Severe Sickle Cell Disease)
Team Lead: Joseph Rosenthal

Scientists at the City of Hope are conducting a Phase 1 clinical trial testing a stem cell-based therapy for adult patients with severe sickle cell disease (SCD) - a chronic, debilitating blood disease. The therapy transplants blood-forming stem cells from a donor into a patient who has received a milder, less toxic chemotherapy treatment that removes some but not all of the patient's diseased bone marrow stem cells. This allows the donor stem cells to engraft and create a healthy supply of non-diseased blood cells without causing an immune reaction in the patient. The hope is that this treatment will cure patients with more severe forms of SCD who aren't able to benefit from currently available blood stem cell transplants that require the administration of more toxic chemotherapy drugs.

ExcellThera
Team Lead: Pierre Caudrelier

Sickle Cell Disease (SCD) is an inherited blood disorder caused by a single gene mutation that results in the production of "sickle" shaped red blood cells. It affects an estimated 100,000 people, mostly African American, in the US and can lead to multiple organ dam- age as well as reduced quality of life and life expectancy. Although blood stem cell transplantation can cure SCD fewer than 20% of patients have access to this option due to issues with donor matching and availability. Dr. Caudrelier is using umbilical cord stem cells from healthy donors, which could help solve the issue of matching and availability. In order to generate enough blood stem cells for trans- plantation, Dr. Caudrelier will be using a small molecule to expand these blood stem cells. These cells would then be transplanted into twelve children and young adults with SCD and the treatment would be monitored for safety and to see if it is helping the patients.

UCLA

Team Lead: Donald Kohn

A team at UCLA is genetically modifying a patient's own blood stem cells to produce a correct version of hemoglobin, the protein that is mutated in these patients, which causes abnormal sickle-like shaped red blood cells. These misshapen cells lead to dangerous blood clots, debilitating pain and even death. The genetically modified stem cells will be given back to the patient to create a new sickle cell-free blood supply.

UCSF

Team Lead: Mark Walters

A team at UCSF Benioff Children's Hospital Oakland will be conducting a clinical trial that uses CRISPR-Cas9 gene editing technology to correct the genetic mutation in the blood stem cells of patients with severe SCD. The corrected blood stem cells will then be reintroduced back into patients with the goal of correcting the defective hemoglobin and thus producing functional, normal shaped red blood cells.

BONE DISEASES

Infantile Malignant Osteopetrosis (IMO)

Rocket Pharmaceuticals

Team Lead: Gayatri Rao

IMO is a rare and life-threatening disorder that develops in infancy and is caused by defective bone cell function, which results in blindness, deafness, bone marrow failure, and death very early in life. The trial will use a gene therapy that targets IMO caused by mutations in the TCIRG1 gene. The team will take a young child's own blood stem cells and inserting a functional version of the TCIRG1 gene. The newly corrected blood stem cells are then introduced back into the child, with the hope of halting or preventing the progression of IMO in young children before much damage can occur.

Osteoarthritis

California Institute for Biomedical Research Team Lead: Kristen Johnson

Researchers at the California Institute for Biomedical Research (CALIBR) have been awarded $8.447 million to test KA34, a drug that, in preclinical tests, recruits stem cells to create new cartilage in areas damaged by osteoarthritis. CIRM funded the research that developed this technology and now this Phase 1 trial will test this stem cell directed treatment in people with osteoarthritis of the knee, hopefully slowing down or even halting the progression of the disease.

Osteonecrosis

UC Davis
Team Lead: Nancy Lane

A team at UC Davis is testing a drug that directs bone stem cells to the surface of the bone where they then develop new bone tissue and stimulate new blood vessel formation, two defects underlying osteonecrosis. Should this drug prove safe and show signs of effectiveness, it may be tested for the treatment of other bone diseases like osteoporosis.

CANCER, BLOOD

Acute Myeloid Leukemia (AML)

Forty Seven, Inc.
Team Lead: Mark Chao

Forty Seven Inc. is conducting a Phase 1b clinical trial for acute myeloid leukemia patients. Leukemia stem cells have a protein on their surface that enable them to evade being identified and destroyed by the patient's own immune system. This protein also helps these leukemia stem cells survive traditional therapies such as chemotherapy, enabling the cancer to lie dormant for a period before returning and causing the patient to relapse. The team is using a combination of a monoclonal antibody and the drug Azacitidine to make leukemia stem cells vulnerable to being attacked and destroyed by the immune system.

Nohla Therapeutics Inc.
Team Lead: Colleen Delaney

Nohla Therapeutics is testing a hematopoietic stem cell and progenitor cell therapy called NLA101 to help patients suffering from neutropenia, a condition that leaves people susceptible to deadly infections, after receiving chemotherapy for acute myeloid leukemia (AML). The company is currently launching a Phase 2 trial to test this treatment in adult AML patients that have received high-dose chemotherapy.

Acute Myeloid Leukemia (AML) and Chronic Myelomonocytic Leukemia (CMML)

Immune-Onc Therapeutics
Team Lead: Joseph Woodard

Immune-Onc Therapeutics is conducting a Phase 1 clinical trial for patients with acute myeloid leukemia (AML) and chronic myelomonocytic leukemia (CMML), both of which are types of blood cancer. The team will treat AML and CMML patients with an antibody therapy called IO-202 that targets leukemic stem cells. The antibody works by blocking a signal named LILRB4 whose expression is connected with decreased rates of survival in AML patients. The goal is to attain complete cancer remissions and prolonged survival.

B Cell Cancers

Stanford University

Team Lead: Crystal Mackall

Chimeric Antigen Receptor (CAR) T Cell Therapy is an innovative cancer therapy with very encouraging response rates in patients. The therapy works by isolating a patient's own T cells (a type of immune cell) and then genetically engineering them to recognize a protein on the surface of cancer cells, triggering their destruction. In some patients with B cell leukemias, however, cancer cells escape detection by the modified T cells and cause the cancer's reoccurrence. Researchers at the Stanford University School of Medicine have developed an engineered T cell designed to recognize not one, but two, cell surface proteins on cancer cells with the aim of enhancing a patient's response to the therapy and reducing the potential for relapse. In addition, some of the T cells will form memory stem cells that will survive for years and continue to survey the body, killing any new or surviving cancer cells.

Blood Cancer

Angiocrine Bioscience Inc.

Team Lead: Edward Kavalerchik

Angiocrine will use genetically engineered cells, derived from cord blood, to see if they can help alleviate or accelerate recovery from the toxic side effects of chemotherapy for people undergoing treatment for lymphoma and other aggressive cancers of the blood or lymph system.

Blood Stem Cell Transplants For Cancer Patients

Angiocrine Biosciences

Team Lead: Paul Finnegan

The Angiocrine team is developing a cell therapy aimed to improve the availability and engraftment of blood stem cell transplants for cancer patients who have had their cancerous bone marrow removed by chemotherapy. The cell therapy is made of blood stem cells and endothelial cells, which line blood vessels and are thought to improve the engraftment of the stem cell transplant. The hope is that this treatment will provide a safer, more tolerable and effective stem cell transplantation that will rebuild the patient's immune system cancer-free.

Blood Cancer – Stem Cell Transplant

Stanford:

Team Lead: Dr. Maria Grazia Roncarolo

This team will test an immunotherapy cell approach using a therapy that is enriched with specialized immune cells called type I regulatory T (Tr1) cells. These cells will be infused into the patient following the bone marrow transplant. Both the Tr1 cells and the bone marrow will come from the same donor. The hope is this will help provide the patient's immune system with these regulatory cells to combat life-threatening graft versus host disease and increase the success of treatment and bone marrow (HSCT) transplant.

Chronic Lymphocytic Leukemia (CLL)

UC San Diego (2 clinical trials)

Team Lead: Thomas Kipps

A team at UCSD is testing an antibody therapy called cirmtuzumab in a clinical trial study to treat a blood cancer, Chronic Lymphocytic Leukemia (CLL). The antibody recognizes and attaches to a protein on the surface of cancer stem cells. This attachment disables the protein which slows the growth of the leukemia and makes it more vulnerable to anti-cancer drugs. The team is also testing cirmtuzumab in combination with an approved cancer fighting drug called ibrutinib, to target cancer stem cells in a separate clinical trial. The aim is that combining cirmtuzumab with ibrutinib will improve cancer remission and long-term cancer control in patients.

Multiple Myeloma

Poseida Therapeutics

Team Lead: Matthew Spear

Poseida Therapeutics is testing the safety of a gene modified cell therapy to treat multiple myeloma, the abnormal growth of malignant plasma cells of the immune system. The company's technology is seeking to destroy these cancerous myeloma cells with an immunotherapy approach that uses the patient's own engineered immune system T cells to seek and destroy the myeloma cells.

CANCER, SOLID TUMORS

Brain Cancer (Malignant Glioma)

City of Hope

Team Lead: Christine Brown

A team at the City of Hope led by Dr. Christine Brown is pursuing a Phase 1 trial targeting an aggressive brain cancer called malignant glioma. City of Hope will re-engineer a patient's immune system central memory T cells (TCM cells) to express chimeric antigen receptors (CAR). These CAR-T cells will recognize a molecular marker on the surface of glioma cancer stem cells and kill the tumors.

Brain Cancer (Glioma)

Stanford
Team Lead: Crystal Mackall
This trial will focus on a treatment for children and young adults with glioma, a devastating, aggressive brain tumor that occurs primarily in children and young adults and originates in the brain. The team will modify a patient's own T cells, an immune system cell that can destroy foreign or abnormal cells. The T cells will be modified with a protein called chimeric antigen receptor (CAR), which will give the newly created CAR-T cells the ability to identify and destroy the brain tumor cells. The CAR-T cells will be re-introduced back into patients and the therapy will be evaluated for safety and efficacy.

Brain Metastases (HER2-Expressing)

City of Hope
Team Lead: Saul Priceman
A team at the City of Hope led by Dr. Saul Priceman is conducting a clinical trial for the treatment of breast cancer related brain metastases, which are tumors in the brain that have spread from the original site of the breast cancer, expressing high levels of a tumor protein called HER2. The therapy consists of a genetically-modified version of a patient's own T cells, which are an immune system cell that can destroy foreign or abnormal cells. The T cells are modified with a protein called a chimeric antigen receptor (CAR) that recognizes HER2. These modified T cells (CAR-T cells) are then infused into the patient's brain where they are expected to detect and destroy the HER2-expressing tumors in the brain.

Brain Tumors (Pediatric and Malignant)

City of Hope
Team Lead: Leo D Wang
City of Hope is conducting a Phase 1 trial for children with malignant brain tumors. The team will treat pediatric patients with aggressive brain tumors using chimeric antigen receptor (CAR) T cell therapy. The CAR T therapy involves obtaining a patient's own T cells, which are an immune system cell that can destroy foreign or abnormal cells and modifying them so that they are able to identify and destroy the brain tumors. The aim of this approach is to improve patient outcome.

Colon Cancer

Forty Seven, Inc.
Team Lead: Mark Chao

Forty Seven, Inc. has developed an antibody therapy to block a protein called CD47 that is found on the surface of cancer cells. CD47 acts as a 'don't eat me' signal that tells immune cells not to eliminate the cancer cells. When this 'don't eat me' signal is blocked by the antibody, the cancer cells are 'eaten' and eliminated by the patient's immune cells . Forty Seven, Inc. will combine the anti-CD47 antibody with cetuximab – a drug used in the treatment of solid tumors – to treat patients with advanced colorectal cancer, hitting it with a 1-2 punch to kill the tumors and prevent any recurrence.

Lung Cancer

UCLA
Team Lead: Steven Dubinett

The five-year survival rate for people diagnosed with the most advanced stage of non-small cell lung cancer (NSCLC) is between one and 10 percent. To address this devastating condition, UCLA researchers are using the patient's own immune system where their dendritic cells – key cells in our immune system – are genetically modified to boost their ability to stimulate their native T cells - a type of white blood cell - to destroy cancer cells. The investigators will combine this cell therapy with the FDA-approved therapy pembrolizumab (better known as Keytruda) a therapeutic that renders cancer cells more susceptible to clearance by the immune system.

Sarcomas and Advanced Solid Tumors

UCLA
Team Lead: Dr. Theodore Nowicki

A team at UCLA is using peripheral blood stem cells (PBSCs) and peripheral blood monocular cells (PBMCs) to treat patients with sarcomas and other advanced solid tumors, with an emphasis on patients with late stage or recurring tumor growth that have few options. The team will test a treatment that genetically modifies PBSCs and PBMCs to target these solid tumors. The gene modified stem cells, which have the ability to self-renew, provide the potential for a durable effect.

Skin Cancer and Other Hard-to-Treat Cancers

UCLA
Team Lead: Antoni Ribas

There are few options for patients whose cancers have metastasized, or spread, due to resistance to current therapies. This team is using gene editing technology to modify a patient's own immune system cells and blood-forming stem cells with the aim of creating a continuous supply of immune cells that can recognize and attack hard-to-treat cancers.

Solid Tumors

UCLA
Team Lead: Dennis Slamon

A team at UCLA is testing a drug for the treatment of cancer that works by blocking PLK4, a protein that is important in regulating cell growth, division and death. This protein is important for the survival of the cancer stem cell as well as the rest of the cells in a tumor. It is hypothesized that blocking this protein from working in the tumor may stop or even shrink tumor growth.

Colorectal, breast and ovarian cancer
BioEclipse;

BioEclipse combines two approaches - an immune cell called a cytokine-induced killer (CIK) cell and a virus engineered to kill cancer cells called an oncolytic virus (OV) - to create what they call "a multi-mechanistic, targeted treatment." They will use the patient's own immune cells and, in the lab, combine them with the OV. The cell/virus combination will then be administered back to the patient. The job of the CIK cells is to carry the virus to the tumors. The virus is designed to specifically attack and kill tumors and stimulate the patient's immune system to attack the tumor cells. The goal is to eradicate the primary tumor and prevent relapse and recurrence.

Head and Neck Cancer
UC Davis
Dr. Peter Belafsky

Dr. Peter Belafsky and his team at the University of California at Davis are developing a therapeutic approach using Autologous Muscle Derived Progenitor Cells (AMDC), cells derived from a biopsy of the patient's own muscle, elsewhere in the body. Those AMDCs are injected into the tongue of the patient, where they fuse with existing muscle fibers to increase tongue strength and ability to swallow.

CIRM

CALIFORNIA'S STEM CELL AGENCY

COVID-19

Acute Respiratory Distress Syndrome (ARDS)

UCSF
Team Lead: Michael Matthay

Dr. Matthay and his team at UCSF will be using Mesenchymal Stromal Cells (MSCs) for the treatment of acute respiratory distress syndrome (ARDS) in both COVID-19 positive and COVID-19 negative patients.

SARS-CoV-2

Celularity Inc.
Team Lead: Xiaokui Zhang

This trial will use blood stem cells obtained from the placenta to generate natural killer (NK) cells, a type of white blood cell that is a vital part of the immune system, and administer them to patients with COVID-19. NK cells play an important role in defense against cancer and in fighting off viral infections. The goal is to administer these cells to locate the active infection sites and destroy the virus-infected cells.

CIRM-FUNDED CLINICAL TRIALS

CIRM

CALIFORNIA'S STEM CELL AGENCY

City of Hope
Team Lead: John Zaia

Plasma is a component of blood that carries proteins called antibodies that are usually involved in defending our bodies against viral infections. Blood plasma from patients that have recovered from COVID-19, referred to as convalescent plasma, contain antibodies against the virus that can be used as a potential treatment for COVID-19. Dr. Zaia and his team at City of Hope will create the COVID-19 Coordination Program. It will partner with the medical teams at CIRM's Alpha Stem Cell Clinic Network, as well as infectious disease, pulmonary and critical care teams from medical centers and community hospitals across the state. Potential donors will be identified and thoroughly screened for eligibility per the established National and State blood banking safety requirements. Finally, the convalescent plasma will be collected from eligible donors and administered by licensed physicians to COVID-19 patients, who will be evaluated for response to the treatment and potential recovery.

DIABETES

Type 1 Diabetes

Caladrius Biosciences
Team Lead: Douglas Losordo

Researchers at Caladrius Biosciences will take cells, called regulatory T cells (Tregs), from the patient's own immune system, expand the number of those cells in the lab and return them to the patient to reduce the autoimmune attack on the insulin-producing cells in people with type 1diabetes.

UCSF
Team Lead: Peter Stock

This trial at UCSF aims to address current limitations in transplanting beta cells into patients. The trial will be using parathyroid glands to aid in the success and viability of the transplant procedure. Co-transplantation of islets and parathyroid glands, from the same donor, substantially increases beta cell survival, potentially enabling adequate long-term insulin production and removing the need for multiple donors. Additionally, the co-transplantation will occur in the patient's forearm, which allows for easier monitoring and improves the effectiveness and accessibility of islet transplants for patients.

ViaCyte, Inc. (2 clinical trials)
Team Lead: Howard Foyt

ViaCyte is developing cell therapies to replace lost beta cells for people with type 1 diabetes (T1D). The therapies are derived from human embryonic stem cells, which are partially matured into becoming pancreatic tissues (the type destroyed in T1D). The cells are inserted into a small pouch that is transplanted under the patient's skin. The transplanted cells will develop into fully matured beta cells that secrete the hormone insulin, which is needed to keep blood sugar levels at a healthy level. CIRM is funding ViaCyte's two Phase 1/2 trials testing different product candidates. The first product, VC-01, encapsulates the cells and protects them from the patient's immune system. The second product, VC-02, allows the patient's blood vessels to make direct contact with the implanted cells. VC-02 is being developed for patients with high-risk T1D.

EPILEPSY

Neurona Therapeutics

Dr. Cory Nicholas

Mesial temporal lobe epilepsy (MTLE) is one of the most common forms of epilepsy. Epileptic seizures are debilitating and increase the risk of a decreased quality of life, depression, anxiety and memory impairment.

Neurona has developed a therapy called NRTX-1001, consisting of a specialized type of neuronal cell derived from embryonic stem cells. These cells are injected into the brain in the area affected by the seizures where they release a neurotransmitter or chemical messenger that will block the signals in the brain causing the epileptic seizures. Pre-clinical testing suggests a single dose of NRTX-1001 may have a long-lasting ability to suppress seizures.

EYE DISEASE

Corneal Damage

UCLA

Team Lead: Sophie Deng

Limbal stem cell deficiency (LSCD) is a blinding corneal disease. LSCD is caused by a decrease in the number and/or function of limbal stem cells (LSCs), a type of stem cell that is needed to continuously regenerate tissue of the cornea, the clear front surface of the eye that refracts light entering the eye and is responsible for the majority of the optical power. Without adequate limbal cells, inflammation, scarring, eye pain, loss of corneal clarity and gradual vision loss can occur. This clinical trial will expand the patient's own remaining LSCs for transplantation and will use novel diagnostic methods to assess the severity of LSCD and patient responses to treatment.

Macular Degeneration

University of Southern California

Team Lead: Mark Humayun

Regenerative Patch Technologies and scientists at the University of Southern California and UC Santa Barbara, are growing specialized cells of the retina from embryonic stem cells, placing them on a single layer scaffold and implanting the combination device in the back of the eye to try to reverse blindness.

CIRM-FUNDED CLINICAL TRIALS

CIRM

CALIFORNIA'S STEM CELL AGENCY

Retinitis Pigmentosa

UC Irvine and jCyte, Inc. (3 clinical trials) Team Lead: Henry Klassen

A team at UC Irvine is using cells called retinal progenitor cells to repair the damage caused by this vision destroying disease. The cells are injected into the back of the eye and it's hoped they will help preserve the photoreceptors attacked by RP as well as generate new photoreceptors to replace those destroyed by the disease. We funded the Phase 1 clinical trial and are now funding two Phase 2 trials, one of which is testing a repeat injection in a previously treated eye.

Cedars-Sinai Medical Center
Team Lead: Clive Svendsen

A team at Cedars-Sinai Medical Center is using human neural progenitor cells (hNPCs) and transplanting them to the back of the eye of retinitis pigmentosa patients. The goal is that the transplanted hNPCs will integrate and create a protective layer of cells that prevent destruction of the adjacent photoreceptors.

HEART DISEASE

Duchenne Muscular Dystrophy-Associated Heart Disease

Capricor Therapeutics

Team Lead: Linda Marban

Capricor is using donor cells derived from the heart to treat patients suffering from Duchenne Muscular Dystrophy (DMD), a genetic disorder that leads to progressive muscle degeneration, including heart muscle. One of the leading causes of death for children with DMD is heart failure and the aim of this treatment is to help improve heart muscle outcomes for these patients.

Left-Sided Heart Failure (Resulting from a Heart Attack)

Stanford

Team Lead: Joseph Wu

This team will test a therapy for left-sided heart failure resulting from a heart attack. The major issue with this disease is that after a large number of heart muscle cells are killed or damaged by a heart attack, the adult heart has little ability to repair or replace these cells. Thus, rather than being able to replenish its supply of muscle cells, the heart forms a scar that can ultimately cause it to fail. The team will use human embryonic stem cells (hESCs) to generate cardiomyocytes (CM), a type of cell that makes up the heart muscle. The newly created hESC-CMs will then be administered to patients at the site of the heart muscle damage in a first in human trial. This initial trial will evaluate the safety and feasibility of the therapy, and the effect upon heart function will also be examined. The ultimate aim of this approach is to im- prove heart function for patients suffering from heart failure.

Pulmonary Hypertension

Cedars-Sinai Medical Center

Team Lead: Michael Lewis

A team at Cedars-Sinai Medical Center is using donor cells derived from the heart to reduce two hallmark symptoms of pulmonary hypertension: inflammation and high blood pressure in the blood vessels within the lungs. These conditions make the heart struggle to pump blood to the lungs and over time can ultimately lead to heart failure. The aim of this treatment is to delay the progression of the disease.

HIV-AIDS

HIV/AIDS

Calimmune, Inc.
Team Lead: Geoff Symonds

Calimmune is genetically modifying patients' own blood-forming stem cells (also known as bone marrow stem cells) so they can produce immune cells—the ones normally destroyed by the virus—that cannot be infected by the virus. The goal of this treatment is to enable the patients to clear their systems of the virus, effectively curing the disease.

City of Hope and Sangamo Therapeutics Team Lead: John Zaia

A team at City of Hope and Sangamo Therapeutics is testing a similar method to functionally cure people with HIV. But while Calimmune is using a technique called RNA interference to block the virus, City of Hope/Sangamo are using a technology called zinc finger nuclease – a kind of molecular scissors – to snip out the target gene.

UCSF
Team Lead: Dr. Steven Deeks

Dr. Deeks and his team will take a patient's blood and extract T cells, a type of. immune cell. The T cells are then genetically modified to express two different chimeric antigen receptors (CAR), which enable the newly created duo CAR-T cells to recognize and destroy HIV infected cells. The modified T cells are then reintroduced back into the patient.

AIDS-Related Lymphoma

UC Davis
Team Lead: Mehrdad Abedi

A team at UC Davis is taking a patient's blood forming stem cells and inserting three anti-HIV genes into them and then returning them to the individual to help rebuild their immune system. The anti-HIV genes are then passed on to all new immune system cells and make them resistant to HIV. Because AIDS-related lymphoma is linked to the constant immune cell stimulation caused by HIV infection, getting rid of the virus should prevent return of the cancer.

IMMUNE DISORDERS

Stanford

Team Lead: Dr. Rosa Bacchetta

Dr. Rosa Bacchetta and her team at Stanford University have developed a therapy using the patient's own natural CD4 T cells that, in the lab, have been genetically modified to express the FoxP3 gene and converted into Treg cells. Those cells are then re-infused into the patient with a goal of determining if this approach is both safe and beneficial. Because the cells come from the patients there will be fewer concerns about the need for immunosuppressive treatment to stop the body rejecting the cells. It will also help avoid the problems of finding a healthy donor and graft vs host disease.

KIDNEY DISEASE

Cystinosis

UC San Diego

Team Lead: Stephanie Cherqui

A team at UC San Diego will be using a gene therapy approach to modify a patient's own blood stem cells with a functional version of a defective CTNS gene that causes the rare disease Cystinosis. The defective CTNS gene causes abnormal accumulation of an amino acid called cystine in all cells of the body, which can lead to multi-organ failure, with some of earliest and most pronounced effects on the kidneys, eyes, thyroid, muscle, and pancreas. Basd on pre-clinical data, the approach is to reintroduce the corrected stem cells into the patient that give rise to blood cells that will reduce cystine buildup in affected tissues.

Dialysis

Humacyte, Inc. (2 clinical trials)

Team Lead: Jeffrey Lawson

Humacyte is using donor cells to create a bioengineered vein needed by people undergoing hemodialysis, the most common form of dialysis. In dialysis a person is connected to a machine that removes waste from their blood. The bioengineered vein is implanted in the arm and used to carry the patient's blood to and from their body during dialysis. Over time the patient's own stem cells start to populate this vein, in effect making it part of the patient's own body. In two separate clinical trials, the Humacyte product is being compared head-to-head with the current standard of care as well as a synthetic product that is used by some patients who are not candidates for the standard treatment.

CIRM-FUNDED CLINICAL TRIALS

Immune Tolerance in Kidney Transplant Patients

Medeor Therapeutics

Team Lead: Paulo Baroldi

Patients who receive kidney transplants must take life-long immunosuppressive drugs to prevent their immune system from rejecting the transplant. Over time, these drugs are toxic and can increase a patient's risk of infection, heart disease, cancer and diabetes. Medeor Therapeutics has developed a stem cell-based treatment they hope will eliminate the need for immunosuppressive drugs in kidney transplant patients. Blood-forming stem cells and immune cells from the organ donor are infused into the patient receiving the donor's kidney. By introducing the donor's immune cells into the patient, the patient's immune system is able to tolerate the donor's kidney, potentially eliminating the need for immunosuppressive drugs that are normally necessary to prevent transplant rejection. Medeor is currently testing this treatment in a Phase 3 clinical trial.

CIRM

CALIFORNIA'S STEM CELL AGENCY

Stanford University
Team Lead: Everett Meyer
This study will use a combination of healthy donor stem cells and the patient's own regulatory T cells (Tregs), to train the patient's immune system to accept the transplanted kidney and eliminate the need for immunosuppressive drugs. The initial group targeted in this clinical trial are people with what are called HLA-mismatched kidneys. This is where the donor and recipient do not share the same human leukocyte antigens (HLAs), proteins located on the surface of immune cells and other cells in the body. The hope is to eliminate the needs for immunosuppressive drugs and that the health of the patients will improve due to reduction in side effects associated with these drugs, and reduced likelihood of the body rejecting the transplanted organ.

Kidney Failure

Stanford University
Team Lead: Samuel Strober
A team at Stanford University will work with kidney transplant patients to see if injecting blood stem cells and T cells (which play an important role in the immune system) from the kidney donor into the kidney recipient can enable the recipient to bypass the need for a life-long dependence on immunosuppressant drugs.

NEUROLOGIC DISORDERS

Amyotrophic Lateral Sclerosis (ALS, Also Called Lou Gehrig's Disease)

Cedars-Sinai Medical Center
Team Lead: Clive Svendsen
A team at Cedars-Sinai is transplanting millions of genetically engineered stem cells into patients with a degenerative nerve disease called ALS. When transplanted, these cells become astrocytes, the support cells that keep nerve cells functioning. Due to the genetic modifications, the cells also deliver high doses of a growth factor which has been shown to protect nerve cells. The goal of this early-stage trial is to test the safety of this astrocyte replacement strategy in ALS patients.

Cedars-Sinai Medical Center
Team Lead: Clive Svendsen
A team at Cedars-Sinai is genetically engineered stem cells that will be transplanted into the motor cortex, an area of the brain responsible for voluntary movements. These transplanted cells then become astrocytes, a type of support cell that help keep nerve cells functioning. The astrocytes have been genetically altered to deliver high doses of a growth factor which has been shown to protect nerve cells. The goal of this approach is to protect the upper motor neurons controlling muscle function and meaningfully improve the quality of life for ALS patients.

CIRM-FUNDED CLINICAL TRIALS

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CALIFORNIA'S STEM CELL AGENCY

BrainStorm Cell Therapeutics
Team Lead: Ralph Kern

BrainStorm Therapeutics is using mesenchymal stem cells that are taken from the patient's own bone marrow. These stem cells are then modified to boost their production of neurotrophic factors, which are known to help support and protect neurons, the cells destroyed by ALS. The CIRM funding will enable the company to test this therapy, called NurOwn®, in a Phase 3 trial involving about 200 patients.

Myelomeningocele (MMC, Severe Form of Spina Bifida)

UC Davis
Team Lead: Diana Farmer

UC Davis will conduct a clinical trial of in utero repair of myelomeningocele (MMC), the most severe form of spina bifida. MMC is a birth defect that occurs due to. incomplete closure of the developing spinal cord, resulting in neurological damage to the exposed cord. This damage leads to lifelong lower body paralysis, and bladder and bowel dysfunction. The team will use placenta tissue to generate mesenchymal stem cells (MSCs). The newly generated MSCs will be seeded onto an FDA approved dural graft and the product will be applied to the spinal cord while the infant is still developing in the womb. The goal of this therapy is to help promote proper spinal cord formation and improve motor function, bladder function, and bowel function.

Parkinson's Disease

Brain Neurotherapy Bio
Team Lead: Krystof Bankiewicz

Brain Neurotherapy Bio is using a gene therapy approach to promote the production of a protein called GDNF, which is best known for its ability to protect dopaminergic neurons, the kind of cell damaged by Parkinson's Disease. The approach seeks to increase dopamine production in the brain, alleviating PD symptoms and potentially slowing down the disease progress.

Spinal Cord Injury

Lineage Cell Therapeutics
Team Lead: Francois Binette

Lineage uses cells derived from embryonic stem cells to heal the spinal cord at the site of injury. They mature the stem cells into cells called oligodendrocyte precursor cells that are injected at the site of injury where it is hoped they can repair the insulating layer, called myelin, that normally protects the nerves in the spinal cord.

STROKE

SanBio

Team Lead: Bijan Nejadnik

SanBio is carrying out a Phase 2 clinical trial using mesenchymal stem cells (MSCs) to help people suffering from chronic disability following a stroke. The MSCs are isolated from the bone marrow of healthy adult donors, and then modified to enhance their ability to promote recovery from injury by triggering the brain's natural regenerative ability. Patients with stroke can suffer from loss of mobility in certain parts of their body and the hope is that this therapy will rescue some of these problems.

Stroke (Chronic, Ischemic)

Stanford University

Team Lead: Gary Steinberg

This team will use neural stem cells (NSCs), a kind of stem cell that can form different cell types found in the brain. The NSCs, in turn, are derived from human embryonic stem cells (hESCs). hESCs can form virtually any human cell type. In a surgical. procedure, the team will inject the NSCs directly into the brains of chronic stroke patients. While the ultimate goal of the therapy is to restore loss of movement in patients, this is just the first step in clinical trials for the therapy. This first in human trial will evaluate the therapy for safety and feasibility and look for signs of efficacy in the form of im- proved movement.

Stanford University

Team Lead: Gary Steinberg

Gary Steinberg, M.D., Ph.D., and his team at Stanford University will use neural stem cells (NSCs), a kind of stem cell that can form different cell types found in the brain. The NSCs, in turn, are derived from human embryonic stem cells (hESCs) and these can form virtually any human cell type. In a surgical procedure, the team will inject the NSCs directly into the brains of chronic stroke patients. While the ultimate goal of the therapy is to restore loss of movement in patients, this is just the first step in clinical trials for the therapy. This first-in- human trial will evaluate the therapy for safety and feasibility and look for signs of efficacy in the form of improved movement.

Urethra

Wake Forest University Health Sciences

Team Lead: Dr. James Yoo

When a scar, or stricture, forms along the urethra it impedes the flow of urine and causes other complications. James Yoo, M.D., Ph.D., and his team at Wake Forest University Health Sciences will use epithelial and smooth muscle cells, taken from the patient's bladder, and layer them on to a synthetic tubular scaffold. The tube will then be surgically implanted inside the urethra.

The goal is for the progenitor cells to support self-renewal of the tissue and for the entire structure to become integrated into the surrounding tissue and become indistinguishable from it, restoring normal urinary function. Dr. Yoo and his team believe their approach has the potential to be effective for at least a decade.

CIRM-FUNDED CLINICAL TRIALS

CLOSED CLINICAL TRIALS

CANCER

Blood Cancers, Solid Tumors

Stanford University
Team Lead: Irving Weissman

A team at Stanford University is using a molecule known as an antibody to target cancer stem cells. This antibody can recognize CD47, a protein the cancer stem cells carry on their cell surface. The cancer cells use that protein to evade the component of our immune system that routinely destroys tumors. By disabling this protein, the team hopes to empower the body's own immune system to attack and destroy the cancer stem cells. The clinical trial testing this therapy has concluded and has led to another CIRM-funded trial by Forty-Seven, Inc.

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CALIFORNIA'S STEM CELL AGENCY

CLINICAL TRIALS LIST AUGUST 2022

Brain Cancer (Glioblastoma)

ImmunoCellular Therapeutics
Team Lead: Anthony Gringeri

ImmunoCellular Therapeutics is targeting six proteins that are found on the surface of cancer stem cells in glioblastoma, a brain cancer. Immune cells from the patient's own immune system are exposed to fragments of these cancer cell proteins in the lab. When returned to the patient's body, these immune system cells can now help the patient's immune system identify, and then hopefully kill, the cancer stem cells responsible for the tumor's recurrence and growth. This Phase 3 trial was suspended in June 2017 due to lack of sufficient financial resources.

Skin Cancer (Melanoma)

Caladrius Biosciences, Inc.
Team Lead: Robert Dillman

NeoStem, which later changed its name to Caladrius BioScience, ran a Phase 3 trial targeting cancer stem cells. These cells are believed to survive chemotherapy and other cancer-targeting treatments, and can cause a relapse by enabling tumors to grow and spread. This approach used the patient's own tumor cells to create a personalized therapy, one designed to engage the patient's own immune system and destroy the cancer. The trial was halted by Caladrius in January 2016 for business reasons.

HEART FAILURE

Capricor Therapeutics
Team Lead: Rachel Smith

In this trial, Capricor Therapeutics used donor cells derived from the heart to treat patients at risk for developing heart failure after a heart attack. In previous clinical studies, the cells appear to reduce scar tissue, promote blood vessel growth and improve heart function. This trial is ending after failing to achieve its primary goal of reduction of scar size in the heart.

HUNTINGTON'S DISEASE (Observational)

UC Davis
Team Lead: Vicki Wheelock

A team at UC Davis plans to use bone marrow derived mesenchymal stem cells to deliver a growth factor, called BDNF, to patients' brains in order to reduce the death of nerve cells that occurs in Huntington's Disease (HD). In preparation for such a clinical trial study, the team completed a CIRM-funded observational trial in a group of HD patients to study the progression of disease.

SPINAL CORD INJURY

Geron Corporation

Team Lead: Jane Lebkowski

Geron carried out a Phase 1 clinical trial to assess the safety and preliminary activity of escalating doses of human embryonic stem cell (hESC) derived oligodendrocyte progenitor cells for treatment of spinal cord injury. Five patients were treated, all safely and without any serious side effects, before the trial was halted by Geron for financial reasons. The work in this trial later has since been revived by Asterias.

CIRM-FUNDED CLINICAL TRIALS

CLINICAL TRIALS LIST AUGUST 2022

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CALIFORNIA'S STEM CELL AGENCY

INDEX