

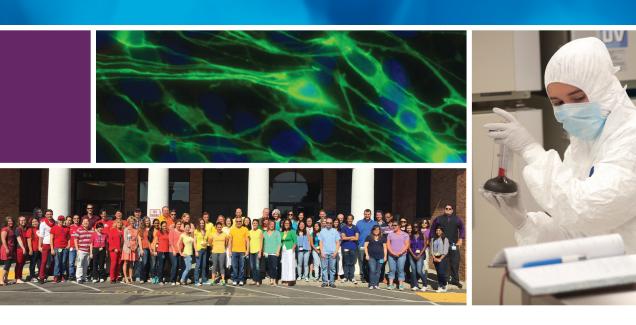
UC Davis Stem Cell Program







UC Davis' Stem Cell Program brings together physicians, research scientists, biomedical engineers and a range of other experts and collaborative partners at its Institute for Regenerative Cures, which is located on the university's Sacramento campus. The \$62 million facility, which was supported by the California Institute for Regenerative Medicine (CIRM), is the hub for collaborative, team-oriented science that is advancing breakthrough discoveries designed to bring stem cell therapies and cures to patients everywhere.



Support for IND-enabling studies

The institute has everything researchers need to take their projects from early stages to the successful submission of an Investigational New Drug (IND) application. It includes one of the largest, most advanced academic Good Manufacturing Practice facilities in the nation, enabling researchers to safely process cellular and gene therapies for clinical trials. It also includes a showerin, disease-free vivarium with immune deficient and humanized mouse cores, as well as cores for vector production, karyotyping, stem cell culturing, mesenchymal stem cell expansion and transduction, teratoma assays, and quality control and quality assurance. Staff members, which include an experienced regulatory team, have extensive involvement in stem cell and gene therapy clinical trials. In addition, the institute is home to the California Umbilical Cord Blood Collection Program.

Unique research capabilities

The university's stem cell research efforts benefit from being located on a campus with a nationally-designated comprehensive cancer center, a renowned neurodevelopmental institute, state-of-the-art imaging programs, a Clinical and Translational Science Center, and an academic medical center that is at the forefront of advanced patient care. With UC Davis' School of Veterinary Medicine, its humanized and transgenic mouse research research facility, and the California National Primate Research Center in nearby Davis, the Stem Cell Program has a unique range of research options that few other programs in the nation can offer.

Combining basic science and clinical medicine

One of the keys to the UC Davis program is the integration of basic science and clinical medicine. Stem cell researchers are collaborating with clinicians on clinical trials involving peripheral artery disease, osteoporosis, Huntington's disease and a number of other conditions. Bringing together disease-specific teams that include a full range of clinical knowledge and laboratory experience can be an important catalyst for stem cell discoveries and breakthroughs.

Clinical trials

UC Davis has nearly a dozen ongoing or recently completed stem cell and regenerative medicine clinical trials, with many more in the pipeline. Seven of its pending clinical trials – for peripheral artery disease, Huntington's disease, osteoporosis, chronic wounds, spina bifida, dysphagia, and heart attack – are funded by the state's stem cell agency.

Disease teams

UC Davis currently has approximately 150 faculty members conducting stem cell-related research as part of more than a dozen different disease teams. Each of these teams is comprised of leading researchers and clinicians who are exploring the most promising approaches for advancing patient health. A balanced stem cell research portfolio, including both adult and pluripotent stem cell research, allows UC Davis scientists to quickly adapt to new discoveries in this ever-changing field. Many current studies are aimed at comparing various types of stem cells to determine which are the safest and most effective.



Bladder disease (repair and bioengineered bladders)

■ Blood and autoimmune disorders (*scleroderma*, *MS*)

Burns and non-healing ulcers (skin and chronic wound repair)

Eye degeneration/blindness (vision regeneration)

Hearing loss (inner ear cilia repair)

Heart disease (infarction and stroke repair)

HIV (gene-modified stem cells treatment)

Kidney disease (repair and regeneration)

 Liver disease (repair and regeneration; bioengineered livers)

Lung disease (repair and regeneration)

 Neurodegenerative disease (Huntington's, Parkinson's, Alzheimer's, ALS)

 Neurodevelopmental disorders (autism spectrum, fragile X, FXTAS)

Osteoporosis (bone repair and cartilage regeneration)

 Peripheral artery disease (revascularization to prevent amputation)

Spina bifida (placental stem cell treatment)

Swallowing disorders (stem cell therapy for dysphagia)

Tumor stem cells (cell-based immunotherapy for cancer)



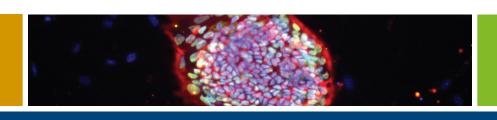
Disease team examples

HUNTINGTON'S DISEASE – With funding from CIRM, the team is moving forward with groundbreaking plans to conduct what they hope will be the first stem cell gene therapy trial for Huntington's disease. The planned clinical trial involves mesenchymal stem cells being used as delivery agents for BDNF (brain derived neurotrophic factor), a neural growth factor. In the pipeline is exciting gene editing research that has the potential to treat the aggressive juvenile form of the disease.

OSTEOPOROSIS AND OSTEONECROSIS – The team is working to increase the effectiveness of a patient's own bone-forming mesenchymal stem cells. They have developed a drug that directs the stem cells to go to the bone surface and form new bone, a great advance over current therapies that are costly and inconvenient. The team wants to determine if the compound LLP2A-Ale can bring stem cells to the area of dead bone and stimulate the formation of new blood vessels and new bone formation. If the treatment is effective, it could prevent the need for joint replacements in young adults.

CRITICAL LIMB ISCHEMIA – This work uses mesenchymal stem cells derived from healthy bone marrow donors that are bioengineered to produce a revascularizing factor. The cells are injected into the legs of critical limb ischemia patients where they are expected to migrate to oxygen-deficient areas in the patient's diseased limbs. UC Davis Vascular Center has one ongoing stem cell clinical trial and is also developing a novel therapeutic in collaboration with researchers at Reina Sofia University Hospital in Cordoba, Spain.

HEART DISEASE – With heart disease being the nation's number-one cause of death and disability, this UC Davis team is working with bone-marrow derived mesenchymal stem cells, in combination with a bioengineered framework known as an extracellular matrix, to regenerate damaged heart tissue, prevent heart disease and restore cardiac function. The cardiac team has completed one clinical trial with stem cells and the novel bioengineered "stem cell patch" is next in the pipeline.



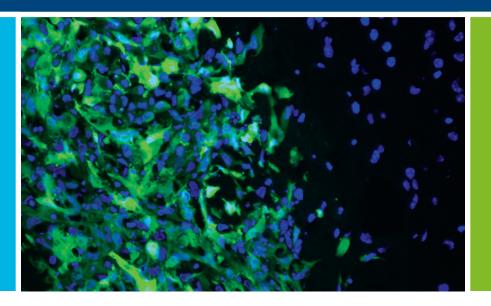
SPINA BIFIDA – The UC Davis team is developing a placental stem cell therapy for spina bifida, the common and devastating birth defect that causes lifelong paralysis as well as bladder and bowel incontinence. With support from CIRM, they are investigating a unique treatment that can be applied in utero – before a baby is born – in order to reverse spinal cord damage. The head of the Spina Bifida team previously conducted a national trial to treat Spina Bifida in babies still in the womb and the new proposed therapy plans to add stem cells to the framework of that therapy.

CHRONIC DIABETIC WOUNDS - The team, which includes a dermatologist, initially developed a potential treatment using mesenchymal stem cells and an FDA-approved scaffold to help regenerate dermal tissue and restart the healing process. They are now refining the therapeutic techniques and creating a biological bandage for use in diabetic wound repair and hope to launch human clinical trials within three years.

HIV – Using modified human stem cells, the HIV disease team has developed a gene-therapy strategy that in animal models shows promise as a functional cure for the human immunodeficiency virus that causes AIDS. The achievement, which involves an improved technique to purify populations of HIV-resistant stem cells, opens the door for a human clinical trial that was recently approved by the U.S. Food and Drug Administration.

SWALLOWING AND AIRWAY DISORDERS - UC Davis research and clinical specialists are working to develop a safe and effective treatment for patients suffering from severe airway stenosis. They are exploring the use of a tissue-engineered airway scaffold with stem/progenitor cells from the patients themselves. Members of the team are also investigating an innovative therapy for the treatment of dysphagia, infusing adult human muscle stem cells into the tongues of those with the swallowing disorder to increase tongue muscle strength.





TRAUMATIC BRAIN INJURY – New UC Davis research has shown that cells known as astrocytes, long considered mere 'housekeeping' cells because of their supportive roles to neurons, are actually much more sophisticated. By creating a highly purified population of astrocytes and proving both their therapeutic benefits and safety, the team hopes these cells could be used to restore brain function for conditions such as stroke, Alzheimer's disease, epilepsy, traumatic brain injury, cerebral palsy and spinal cord injury.

DEBILITATING CARTILAGE CONDITIONS – Working with biomedical engineers, researchers are working to develop a cellular therapy using stem cells created from an individual's own skin, known as autologous skin-derived stem cells, which have shown great promise in animal models. For anyone suffering from osteoarthritis or other debilitating cartilage conditions, using stem cells to regenerate new tissue could have enormous quality-of-life and economic benefits.

DISC DEGENERATION – UC Davis scientists and surgeons have been part of the first national clinical study to examine whether a single injection of adult stem cells directly into diseased lumbar discs can repair and regenerate them, relieve chronic low-back pain and possibly avert spine surgery. The study established the safety and potential efficacy of using mesenchymal precursor cells to treat diseased lumbar discs and relieve back pain.



MACULAR DEGENERATION – The team has conducted a pilot clinical trial on the feasibility and safety of an intravitreal autologous bone marrow stem cell therapy to treat people with irreversible vision loss from retinal degenerative conditions and retinal vascular disorders (dry age-related macular degeneration, retinitis pigmentosa, retinal vein occlusion, hereditary maculopathy or diabetic retinopathy). Two of the patients had significantly improved vision, as the team has recently published.

Tissue engineering

A primary focus of the Stem Cell Program is tissue engineering using decellularized tissue and stem cells for the following bioengineering investigations:

- Heart repair in adults
- Septal defect repair in neonates
- Liver repair
- Kidney repair
- Cartilage repair
- Bladder repair

- Bone repair, post MVA
- Non-healing ulcer treatment
- Burns, using skin sheets
- Breast reconstruction after mastectomy
- Facial and tissue reconstruction after gunshot or other injury





Good Manufacturing Practice facility

UC Davis' Good Manufacturing Practice facility in Sacramento features six manufacturing rooms with Class 10,000, multi-use cleanroom capabilities. It offers an associated product scale-up and testing lab. Unique features include a GMP-grade FACS sorter, switchable positive-negative room pressurization for gene therapy vector manufacturing, and a hot cell for clinical grade PET reagent manufacturing. This state-of-the-art facility currently manufactures products for university investigators as well as other academic and industry partners.

You can help

Many diseases and injuries have the promise of healing through the body's own system. UC Davis stem cell researchers and clinicians are still learning about body restorative powers. Seed funding, of any amount, can be the crucial catalyst that leads to grant-funded stem cell research and human clinical trials.

- Hearing loss
- Neurodegenerative disease
- Heart disease
- Bladder disease
- Chronic wounds
- Peripheral vascular disease
- Cancer relapse

- Eye disease
- Lung disease
- Osteoporosis
- Kidney disease
- Liver disease
- Blood disorders
- Immune system disorders



"UC Davis has strong, brilliant people who are dedicated to turning stem cells into cures. By working together, scientists, physicians, patient advocates and families will improve health and health care for all."

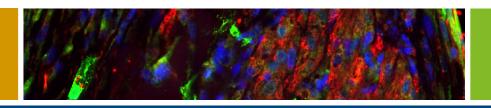
JAN NOLTA, DIRECTOR, UC DAVIS STEM CELL PROGRAM
UC DAVIS INSTITUTE FOR REGENERATIVE CURES

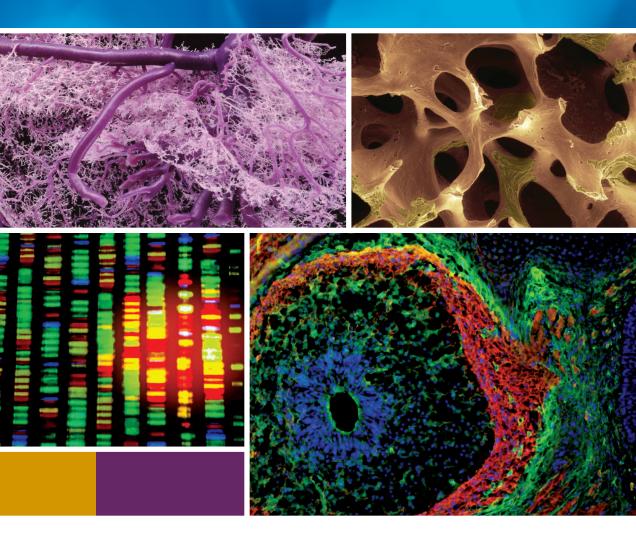
How you can help

With the ability to repair damaged tissue and develop into specialized cells and organs, stem cells are having a major impact in health care now and will only be more important in the future. Research into stem cell therapies is in full motion throughout the university, and private support can help our researchers leverage funding opportunities at national, state and community levels. With your generosity and our passion for finding innovative cures, we can continue to advance efforts to bring research and therapies to those in our own community, and around the world. Learn more about the UC Davis Stem Cell Program or make a gift to regenerative medicine research by contacting Mary Boivin-McGhee, senior director of development, at 916-734-1820 or mboivinmcghee@ucdavis.edu.

Stem Cell Program Contacts

Jan A. Nolta, Ph.D., Director janolta@ucdavis.edu 916-703-9300 Geralyn Annett, C.L.S, Clinical Research Director gmannett@ucdavis.edu 916-703-9318 Delia Roberts, Manager daroberts@ucdavis.edu 916-703-9311







healthsystem.ucdavis.edu/stemcellresearch/ourteam 916-703-9300

14-0281 (9/15)