

ADVANCING TREATMENTS FOR MUSCULAR DYSTROPHY



Located at UW Medicine at South Lake Union, ISCRM brings together researchers from many disciplines for collaboration and discovery.

A Quick Primer: Stem Cells

Because stem cells can develop (differentiate) into other, more specific cells, such as heart cells or neuro-retinal cells, they show great medical potential for replenishing and repairing tissues throughout the body. There are several types, including:

Human embryonic stem cells: derived from fertilized eggs left unused after *in vitro* fertilization. These cells have a great capacity for differentiation.

Adult stem cells: unspecialized cells found in low numbers within many adult tissues. Compared to embryonic cells, their ability to differentiate is more limited.

Induced pluripotent stem cells (iPSCs): adult stem cells that, with the addition of genes or drugs, can be induced to resemble embryonic stem cells and then differentiate into any cell type.

FOUNDED IN 2006, the Institute for Stem Cell and Regenerative Medicine (ISCRM) at the University of Washington brings together more than 140 people from various medical disciplines and institutions. Together, they're pursuing the promise of stem cells in repairing or regenerating damaged tissue. With stem cell medicine, ISCRM's scientists see the opportunity to make great strides in treating diseases, injuries and conditions such as heart disease, blindness, cancer, Alzheimer's disease and other conditions that affect millions of people worldwide.

Researchers at ISCRM are using gene and stem cell therapies to reverse the devastating effects of **Duchenne muscular dystrophy (DMD)**. The result of an inherited gene mutation, DMD affects 1 out of every 3,500 newborn males. The most common form of muscular dystrophy, DMD causes progressive muscle weakness. Children with DMD lose the ability to walk by their early to mid-teens, and as the disease progresses, it causes heart failure, breathing problems and premature death. There is currently no cure for it or any other form of muscular dystrophy — the only therapeutic options available are palliative care measures to improve quality of life.

Our experts, Drs. Chamberlain, Childers, Mack, Reyes and Ruohola-Baker, are performing groundbreaking research that utilizes both stem cells and gene therapies to reveal **new treatment options for patients suffering from Duchenne MD**, as well as other forms of MD. What follows is a brief overview of their projects, as well as a **request for support** for resources that will help UW Medicine develop stem cell and gene therapies for patients worldwide.

Using Stem Cells and Gene Therapy to Defeat Muscular Dystrophy

Through a combination of stem cell and gene therapies, the muscular dystrophy research team utilizes a multifaceted approach to improve muscle functioning and life expectancy for patients with DMD. An early breakthrough in the **Chamberlain Lab** demonstrated that damaged genes leading to DMD could be replaced in all muscles of the body using a non-infectious virus — work that is now moving toward clinical trials (see the illustration on the following page). Building on that discovery, the **Ruohola-Baker and Reyes Labs** are now studying MD in mice and fruit flies, which led to a related breakthrough — the identification of molecules that dramatically enhance the regenerative capacity of muscles.

Researchers at ISCRM are also exploring how adult and induced pluripotent stem cells can be used to treat MD. Investigators are developing methods for tissue replacement as well as studying MD through a “disease-in-a dish” approach. The **Childers and Mack Labs** use urine cells from patients with DMD to generate stem cells. These stem cells are then differentiated into beating heart cells in a petri dish, which allows researchers to study the cardiac defect associated with MD.

Opportunities for Partnership

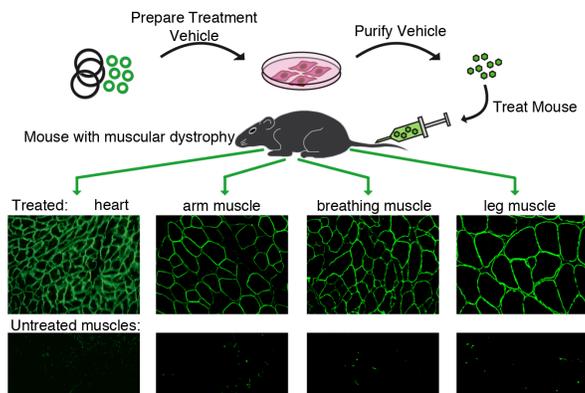
Reversing the damage caused by DMD could dramatically improve and lengthen the lives of those living with the disease. Currently, the research team is testing new gene and stem cell therapies in pre-clinical trials with animals. With contributions from members of the community, ISCRM intends to:

Begin clinical trials (in humans) for a groundbreaking new gene therapy for Duchenne MD. Described on the previous page, this new gene therapy has the potential to completely reverse the effects of DMD and restore normal muscle function. More importantly, the results of this trial will establish the infrastructure necessary to pursue additional trials for the other eight forms of MD.

Gifts would underwrite the recruitment of a part-time nurse-clinician experienced in enrolling participants in clinical trials, the development of an upper-limb device for participants to evaluate their strength, laboratory costs associated with production of the therapeutic agent, and large-animal safety studies needed to obtain FDA approval for clinical trials.

Develop alternative drug therapies. The team is in the process of identifying two approaches to drug therapy for patients with DMD. One approach will focus on identifying drugs that increase the amount of muscle stem cells, help existing muscle fibers maintain a healthy size and reduce muscle degeneration. The other drug therapy will be targeted at correcting heart failure.

Gifts would underwrite the recruitment of a full-time scientist needed to further develop the high-throughput drug-discovery screening program.



Therapy for MD entails delivering a therapeutic agent (i.e., a new gene, stem cell or drug) to each muscle. After several weeks, each muscle in the treated mice began making a protein (shown in green) that was previously absent due to their condition. As a result, their muscle degeneration was halted and normal functioning returned. ISCRM researchers are ready to test this therapeutic approach in clinical trials with humans.

Your Support

If you are interested in helping ISCRM make strides in the fight against MD, or if you wish to learn more about the institute's work, please contact Jim Boyle at boyleje@uw.edu or 206.543.7252 or visit depts.washington.edu/isCRM. Thank you for your interest.

Key Faculty

Jeffrey Chamberlain, Ph.D., UW Professor, Departments of Neurology, Biochemistry and Medicine-Medical Genetics; McCaw Endowed Chair in Muscular Dystrophy

Martin Childers, D.O., Ph.D., UW Professor, Department of Rehabilitation Medicine

David Mack, Ph.D., UW Assistant Professor, Department of Rehabilitation Medicine

Morayma Reyes, M.D., Ph.D., UW Assistant Professor, Department of Pathology

Hannele Ruohola-Baker, Ph.D., UW Professor, Department of Biochemistry; Adjunct Professor, Departments of Biology and Genome Sciences; Associate Director, ISCRM