July 1, 2024

Cure RTD Awards $160,000 AUS Grant to Dr. Anai Gonzalez-Cordero at the University of Sydney, Australia.

The Cure RTD Foundation has awarded a $160,000 AUS grant to Dr. Anai Gonzalez-Cordero for the project "Understanding the eye defects of RTD patients by developing iPSC-derived Retinal Organoids: a 3D model to test the efficacy of the AAV Gene Therapy."

Dr. Anai Gonzalez-Cordero

Organoids, which can reproduce complex tissue structures, are revolutionizing basic research and regenerative medicine. A human organoid is a miniature organ model grown from patient stem cells. Organoids are often called 'mini-organs' because they look and act similar to the tissues in actual organs. Organoids retain vital characteristics and functions of their tissue of origin and can be used to study disease progression and response to treatment, such as riboflavin and gene therapy.

Scientists worldwide have been racing to grow three-dimensional organoids for all kinds of tissues, because these organoids can mimic human development and disease in a dish. Thanks to Cure RTD funding, Dr. Anai Gonzalez-Cordero and Cecilia Mei are using a state-of-the-art tissue engineering platform at the University of Sydney to develop and study living organoids derived from RTD patient cells (also referred to as induced pluripotent stem cells or iPSc).

Two of the most common symptoms of RTD Type 2 are muscle weakness and vision loss. Muscle weakness associated with RTD is primarily caused by damage to motor neurons in the spinal cord and brain, and vision loss is primarily caused by damage to the optic nerve. As part of this study, living eye (retinal) and spinal organoid models are being grown from RTD patient stem cells to study the various factors and mechanisms causing RTD damage, as well as their response to gene therapy treatment.

Gene Therapy

In recent years, scientists have made important discoveries to unlock gene therapy's enormous potential in treating disease. Gene therapy, which replaces the mutated gene causing RTD (SLC52A2 gene), is a potential therapeutic option to halt RTD disease progression and hopefully reverse some of the symptoms and damage that has already occurred. Cure RTD is funding projects to test gene therapy on both RTD mice and iPSc-derived human motor neurons. In this project, a viral vector (AAV9) will carry healthy copies of the SLC52A2 gene to eye and spinal organoids derived from RTD patient stem cells to show the safety and effectiveness of the treatment. All of these gene therapy projects combined are necessary to demonstrate that gene therapy is an effective treatment for RTD, providing the rationale to initiate human clinical trials for individuals with RTD.

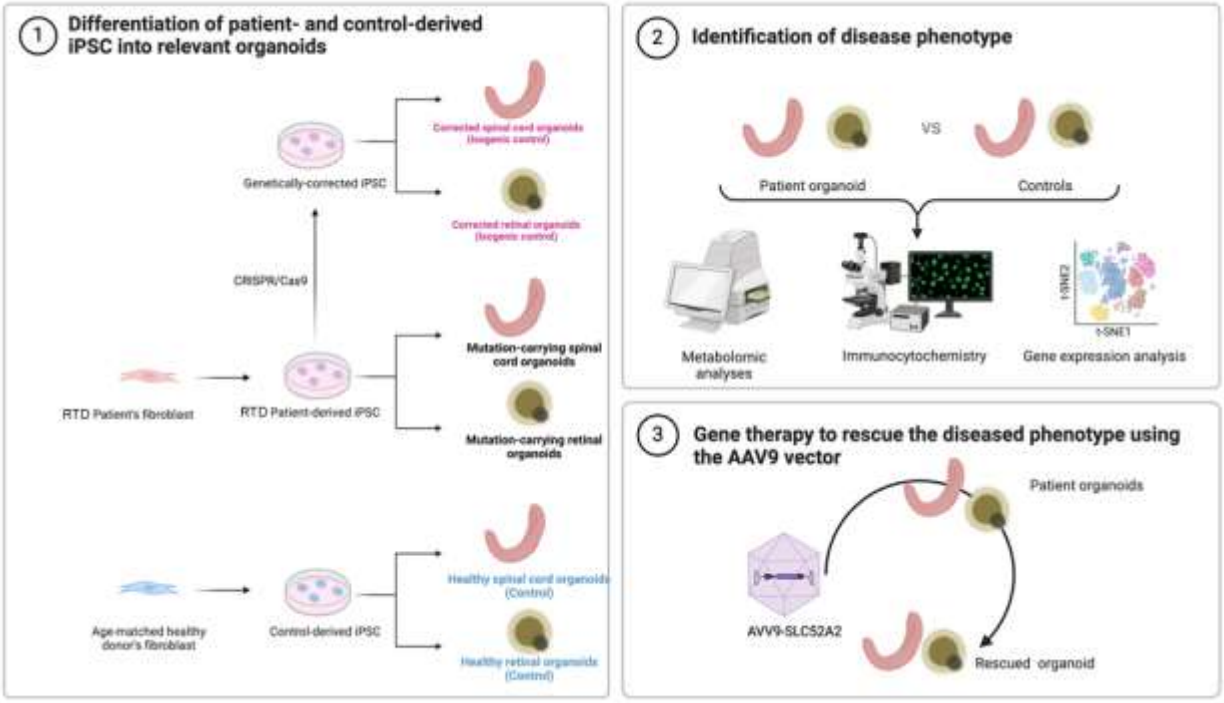
Meet Dr. Anai Gonzalez-Cordero

Dr. Anai Gonzalez-Cordero (PhD) leads the Children's Medical Research Institute (CMRI) Stem Cell Medicine Research Group and the Stem Cell and Organoid Facility at the Children's Hospital at Westmead in Australia. Dr. Gonzalez-Cordero joined the University of Sydney and CMRI in 2019 after working as a Research Fellow on the world-leading laboratory of Prof Robin Ali at the Institute of Ophthalmology, University College London, UK. Dr. Gonzalez-Cordero recently received the Metcalf Prize– the most prestigious stem cell research award in Australia – and is considered a world expert on retinal organoid modeling.

Meet Cecilia Mei

Cecilia Mei is in the final year of her PhD and has a Master of Science in Medical Biotechnology and Molecular Medicine. Before moving to Australia for this project, Cecilia was a PhD researcher at Dr. Claudia Compagnucci's lab at Bambino Gesu` Children's Hospital (OPBG) in Rome, Italy, where she studied the use of *AAV9/SLC52A2* gene therapy to rescue motoneurons (MNs) derived from induced pluripotent stem cells (iPSCs) of RTD Type 2 patients.

Experimental plan



What exactly is gene therapy?

In RTD and thousands of other rare diseases, a single gene mutation causes a protein to either malfunction or not be produced. This can cause death or destruction of specific cells that are crucial in vital functions. Gene therapy involves pairing healthy copies of the malfunctioning gene with a harmless virus called a "viral vector". Trillions of vector copies are made and then given to a person through a one-time injection. The healthy, normally functioning genes are incorporated into cells, which begin to correctly produce the missing or malfunctioning protein. In RTD, this malfunctioning protein would be the riboflavin transporter protein (RFVT). Researchers believe that gene therapy for RTD has the potential to not only halt disease progression but also reverse some of the symptoms and damage that has already occurred. Rather than managing disease, gene therapy aims to stop it permanently.

Cure RTD Research Funding

This grant to Dr. Anai Gonzalez-Cordero is part of Cure RTD's Basic Research and Drug Discovery programs that we are announcing for our 2024-2025 grant cycle.