March 22, 2019

Cure RTD has awarded a $32,949 grant to Dr. Manoj Menezes, MD and PhD, at The Children's Hospital at Westmead (CHW) in Sydney, Australia

Dr. Manoj Menezes

Cure RTD has awarded a $32,949 grant to Dr. Manoj Menezes, MD and PhD, at The Children's Hospital at Westmead (CHW) in Sydney, Australia for his project "Generating a RFVT2 C.elegans model of neuronal degeneration."

Over the past few years it has become clear that riboflavin treatment merely slows the disease progression of riboflavin transporter deficiency (RTD) rather than completely halting disease progression in a some patients. In addition, the long-term outcomes for all RTD patients on riboflavin treatment alone remain unknown. Hence, there is a great need to identify complementary, novel therapeutic strategies that can act synergistically with riboflavin treatment to halt RTD disease progression.

While it is known that the riboflavin transporters RFVT2 and RFVT3 are responsible for the transport of riboflavin in the body, the exact mechanism by which riboflavin deficiency causes neuronal damage in RTD is not understood. The development of an animal model with RTD will enable the investigation of these mechanisms, in an effort to subsequently develop novel therapeutic strategies for RTD.

In this proposal, Dr. Manoj Menezes and his team will develop an animal model of RTD using Caenorhabditis elegans (roundworms) to clarify the underlying mechanism of neuronal injury in RTD. Areas of investigation in this model will include neuronal and muscle morphology, mitochondrial function, synaptic transmission, life span as well as motor and sensory behaviors. This will be the first RTD animal model to carry the genetic mutations which are the human equivalent to SLC52A2 gene mutations causing RTD type 2.

Meet Dr. Manoj Menezes

Dr Manoj Menezes is considered an international expert in the pathophysiology and therapy of RTD, having published several research papers describing its phenotype, pathophysiology and use of disease-modifying therapy. Dr. Manoj Menezes completed his MD in Paediatrics from MS University, Baroda, India and completed his PhD in inherited peripheral neuropathies including RTD from the University of Sydney. He is a Staff Specialist in Neurology and Neurogenetics at CHW and a Clinical Senior Lecturer at the CHW Clinical School at The University of Sydney. He is also Director of the Peripheral Neuropathy Management Clinic, CHW and co-team leader of the Neuropathy Group at the Kids Neuroscience Centre, Kids Research.

How will this project work?

Caenorhabditis elegans (C. elegans) is one of the most widely used animal model systems to address questions in neurobiology. C. elegans possess a simple, but extremely well-defined nervous system that functions similarly to mammalian systems. In this project, C. elegans will be generated carrying mutations in the worm riboflavin transporter gene (rtf-1), which is the human equivalent for the SLC52A2 gene causing RTD type 2. This model will enable the study of neurons and other areas affected by RTD at different developmental stages.

What is the significance of this study?

Findings from this study have the potential to significantly impact our understanding of how mutations in the SLC52A2 genes cause neuronal damage in individuals with RTD. This animal model may help identify novel pathways for therapeutic intervention, leading to the development of complementary novel therapeutic strategies that can act synergistically with riboflavin treatment to halt RTD disease progression. In addition, once validated this animal model can be used for future studies to test novel compounds to treat RTD.

Cure RTD Research Funding

This grant to Dr. Manoj Menezes is part of Cure RTD's Basic Research and Drug Discovery programs that we are currently announcing for our 2019-2020 grant cycle.

Basic research is the first step in our comprehensive research model. We fund basic research to investigate the biology and cause of RTD in order to identify the most effective treatment strategies.