

April 25, 2018

Cure RTD Awards \$61,700 Grant to Claudia Compagnucci, PhD, at the Bambino Gesù Children's Research Hospital, Italy



Claudia Compagnucci, PhD

The Cure RTD Foundation has awarded a \$61,700 USD grant to Claudia Compagnucci, PhD, at the Bambino Gesù Children's Research Hospital (OPBG) in Rome, Italy, for her project "Modelling Riboflavin Transporter Deficiency With Human-Induced Pluripotent Stem Cells." An additional \$25,000 USD has also been provided personally by directors of the Cure RTD Foundation towards this project.

Riboflavin Transporter Deficiency (RTD) is characterized by a loss of specific cells in the spinal cord and brainstem called motor and sensory neurons. As part of this study, skin cells (fibroblasts) obtained from individuals with RTD Type 2 and 3 are reprogrammed back into an embryonic-like pluripotent state, called induced pluripotent stem cells (iPSCs). These iPSCs can then be used for the development of an unlimited source of living human cells, such as motor neurons, for investigating the pathogenetic mechanisms in RTD and also the response to various treatments, such as riboflavin and antioxidants.

Dr. Compagnucci has shown that motor neurons developed using iPSCs from individuals with RTD have several abnormalities compared to motor neurons derived from healthy individuals. These abnormalities include reduced axon elongation and perturbation in the neurofilament composition. When these RTD motor neurons are treated with high-dose riboflavin, they are only partially rescued, suggesting the need to develop complementary novel therapeutic strategies.

In this proposal, Dr. Compagnucci will build upon these preliminary results to better understand the pathogenetic mechanisms in RTD and investigate complementary novel therapeutic strategies, which can lead to new and improved treatment approaches for individuals with RTD.

Meet Dr. Compagnucci

Who are you?

I am a Biologist at Bambino Gesù Children's Hospital (OPBG) working in the Unit of Neuromuscular and Neurodegenerative Disorders led by Dr. Enrico Bertini. I obtained my PhD in Craniofacial Development at King's College London (UK). At OPBG my main research interest is to unveil the biological mechanisms regulating neuronal development and function in health and disease.

How did you first become involved with RTD research?

I first became interested in the cellular and molecular biology that characterizes RTD when I moved to OPBG in 2012. Our lab director, Dr. Enrico Bertini, was an author of one of the first research reports about RTD Type 2, which described a young boy with genetically confirmed RTD.

What is your current role in RTD research?

I am currently involved in characterizing RTD pathogenetic mechanisms and testing various protocols for treatment of RTD. Over the past 6 years I have worked to characterize the modelling of iPSCs in order to deepen our knowledge of the system and be able to use iPSCs to model RTD. In our research so far we have discovered emerging pathogenetic mechanisms in RTD neurodegeneration, and investigated the biological rationale behind riboflavin supplementation. We have found that although riboflavin is important to ameliorate the RTD phenotype it is not sufficient to fully rescue the cells. Since riboflavin supplementation has some limits in rescuing all of the disease features in our models I am interested in developing complementary novel therapeutic strategies.

What do you hope to learn from this research project?

I hope to determine other biological mechanisms altered in the neurons derived from the patients' iPSCs and to characterize the molecular and cellular features when cells are treated with combined riboflavin and antioxidants.

How will this project work?

Patients' iPSCs will be differentiated into motor neurons. The main focus of our investigation will be on the cytoskeletal features of these motor neurons, since cytoskeletal dynamics are fundamental to build functional neuronal networks and particularly in motor neurons to extend and maintain neurites for long distances. In addition to this, we will study the redox features of RTD cells and look for possible amelioration of the RTD phenotype following treatment with riboflavin plus combinations of antioxidants.

What is the significance of your study?

Based on the available literature and our preliminary results, the combination of riboflavin and antioxidants supplementation could provide a sound foundation for future patient therapies, aimed at progressively ameliorating RTD manifestations. Furthermore, working on patients' specific iPSCs may allow us to develop custom therapies, considering individual variability of pathogenic mechanisms and responses to drug treatment. Therefore, this study may lead to life improvement for individuals with RTD.

Cure RTD Research Funding

This grant to Dr. Compagnucci is part of Cure RTD's Basic Research and Drug Discovery programs that we're currently announcing for our 2018-2019 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. We also use this funding to develop tools that facilitate RTD research.

Drug discovery converts what we have learned about the causes and biology of RTD through basic research into new drug candidates and treatment approaches that can be tested in clinical trials. This funding will be used strategically to help accelerate research, and to ensure we are developing treatments for all types, ages, and stages of RTD.