April 5, 2025

Cure RTD Awards $110,000 Grant to Dr. Claudia Compagnucci, at the Bambino Gesù Children's Research Hospital, Italy

Dr. Claudia Compagnucci

The Cure RTD Foundation has awarded a $110,000 USD grant to Dr. Claudia Compagnucci at the Bambino Gesù Children's Research Hospital (OPBG) in Rome, Italy, to support her project, "Unveiling the underpinning of mitochondrial bionergetics in RTD motoneurons and evaluation of Nerve Growth Factor treatment as therapeutic treatment." An additional $16,500 USD in funding has been contributed by our sister organization, Cure RTD Italia.

Riboflavin Transporter Deficiency (RTD) is marked by the degeneration of specific nerve cells in the spinal cord and brainstem, known as motor and sensory neurons. In this study, cells from five individuals with RTD Type 2 are reprogrammed into an embryonic-like state known as induced pluripotent stem cells (iPSCs). These iPSCs can provide an unlimited source of living human cells—such as motor neurons—that can be used to study the disease mechanisms underlying RTD and to evaluate the effectiveness of potential treatments.

Dr. Compagnucci has shown that motor neurons derived from RTD patient iPSCs display several abnormalities compared to those from healthy individuals, including disrupted energy metabolism, mitochondrial dysfunction, and cytoskeletal abnormalities. Although high-dose riboflavin treatment provides some improvement, it does not fully correct these defects—underscoring the need for additional and complementary therapeutic strategies.

This study will investigate complementary therapeutic strategies that could be combined with riboflavin to improve outcomes for individuals with RTD, using patient-derived motor neurons for evaluation.

One such strategy involves the use of Nerve Growth Factor (NGF), a protein essential for the growth, survival, and maintenance of specific nerve cells. NGF supports neuronal development during early life and helps preserve neuronal health in adulthood. It also aids in the repair of damaged neurons and enhances mitochondrial function, making it a promising candidate for treating neurodegenerative disorders such as Riboflavin Transporter Deficiency (RTD).

Additional therapeutic strategies under evaluation include hydroxybutyrate—a naturally occurring ketone that serves as an energy source for brain cells—and nicotinamide mononucleotide (NMN), a compound that enhances cellular energy production by increasing NAD^+ levels.

The study will use real-time imaging, functional assays, and metabolic analysis (via Seahorse XF Analyzer) to assess NGF's effects, potentially paving the way for a novel adjunct therapy to improve outcomes in RTD patients.

Meet Dr. Claudia Compagnucci

Who are you?
I'm a biologist at Bambino Gesù Children's Hospital (OPBG), working in the Unit of Neuromuscular and Neurodegenerative Disorders led by Dr. Enrico Bertini. I earned my PhD in Craniofacial Development from King's College London (UK). At OPBG, my research focuses on understanding the biological mechanisms that regulate neuronal development and function—both in health and in disease.

How did you first become involved in RTD research?
I became interested in the cellular and molecular biology of RTD when I joined OPBG in 2012. Our lab director, Dr. Enrico Bertini, co-authored one of the first published reports on RTD Type 2, which described a young boy with a genetically confirmed diagnosis. That early exposure sparked my long-term interest in the disorder.

What is your current role in RTD research?
I'm actively involved in uncovering the pathogenic mechanisms underlying RTD and testing various therapeutic approaches. Over the past 12 years, I've worked extensively on developing and refining iPSC-based models to better understand RTD at a cellular level. Our research has identified emerging disease mechanisms involved in RTD-related neurodegeneration and explored the biological basis for riboflavin supplementation as a treatment strategy.

Cure RTD Research Funding

The grant awarded to Dr. Compagnucci is part of Cure RTD's **Basic Research and Drug Discovery** initiatives for our 2025–2026 grant cycle.

Basic Research
This is the foundation of our research strategy. By funding basic science, we aim to better understand the biology and causes of RTD—critical steps in identifying effective therapeutic targets. These grants also support the development of tools and models to advance RTD research more broadly.

Drug Discovery
Building on insights from basic research, our drug discovery efforts focus on identifying and developing new treatment candidates that can move toward clinical testing. This funding is designed to accelerate progress and ensure that we are advancing treatments for all RTD types, age groups, and disease stages.