March 23, 2019

Cure RTD Awards $50,000 Grant to Maria Barile, PhD at the University at Bari Aldo Moro, Italy

The Cure RTD Foundation has awarded a $50,000 USD grant to Maria Barile, PhD at the University of Bari Aldo Moro in Italy for the project "Alterations of Riboflavin Transport and Metabolism in Riboflavin Transporter Deficiency (RTD)".

Cesare Indiveri, PhD

Maria Barile, PhD

This grant will be used to fund three separate projects, conducted by two academic research teams, all working together to understand the effects of mutations in SLC52 genes causing RTD at the molecular levels. The two teams are led by Maria Barile, PhD at the University of Bari Aldo Moro in Italy, and Cesare Indiveri, PhD at University of Calabria, Italy.

RTD type 2 is caused by mutations in the SLC52A2 gene, which encode for the riboflavin transporter protein RFVT2. Although RFVT2 have been shown to be responsible for transport of riboflavin across cell membranes it remains unclear why lack of this protein specifically damages sensory and motor neurons. It is Prof. Barile's hypothesis that the absorption of riboflavin in neuronal cells mediated by RFVT2 is the limiting step of biosynthesis of FAD (Flavin Adenine Dinucleotide), which is an essential cofactor of more than 100 enzymes collectively known as flavoproteins. Flavoproteins are crucial for energy metabolism in neurons and are mostly located in the mitochondria. It is expected that defects in RFVT2 will be the cause of alterations in the whole content of flavin cofactors and mitochondrial bioenergetics, which can result in cellular damage.

Despite the importance of the issue, very little is understood about RFVT2's role, and the functional consequence of various SLC52 mutations, on mechanisms of transport and metabolism of riboflavin in neurons, as well as the biogenesis of adequate amounts of intracellular flavoproteins. This proposal plans to help address these important questions using several unique model systems, including an animal model and cell samples from individuals with RTD. These findings can provide the fundamental steps necessary toward the improvement of therapies or design of novel drugs for RTD.

Meet Maria Barile

Maria Barile has a broad background in enzymology and riboflavin metabolism. She is an Associate Professor of Biochemistry and Researcher at the University of Bari Aldo Moro in Italy. She has been involved in numerous national and international projects over the past 20 years, which have focused on the characterization of human enzymes involved in riboflavin metabolism, as well as in the pharmacological and clinical aspects of riboflavin therapy. She has published 63 peer-reviewed publication and her research group was responsible for cloning the human gene responsible for FAD synthase.

Meet Cesare Indiveri

Cesare Indiveri is an expert in the field of membrane transporters biology with over 120 peer-reviewed publications in top journals including Nature and Cell. He is currently the Director of the Department of DiBEST (Biologia Ecologie Scienze della Terra) and Full Professor in Biochemistry at University of Calabria in Italy. Cesare Indiveri's research group has been focused mainly on transporters of nutrients such as amino acids, carnitine and riboflavin with specialization in the measurement of transport activity in intact cells, in isolated organelles and in artificial membrane systems called proteoliposomes.

How will this project work?

These research teams will use several unique model systems to address the questions noted above including:

1) Motor neurons developed using induced pluripotent stem cells (iPSCs) from individuals with RTD type 2 and type 3.

2) A novel C. Elegans (Roundworm) model in which specific genes related to flavin homeostasis are silenced.

3) A model in which the riboflavin transporter RFVT2 is reconstituted in proteoliposomes, which are systems used to mimic lipid membranes.

What is the significance of this study?

These tissues and model systems have the potential to significantly impact the understanding that RFVT2 play in RTD disease processes and may identify novel pathways for therapeutic intervention that could complement RTD-targeting therapies.

Cure RTD Research Funding

This grant to Prof. Maria Barile is part of Cure RTD's Basic Research and Drug Discovery programs that we're 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. We also use this funding to develop tools that facilitate RTD research.