

May 13, 2023

## Cure RTD Awards \$120,000 Grant to Maria Barile (PhD) and Cesare Indiveri (PhD)

The Cure RTD Foundation has awarded a \$120,000 USD grant to Maria Barile, PhD at the University of Bari Aldo Moro in Italy and Cesare Indiveri, PhD at University of Calabria, Italy for the project “Putting RFVTs in the correct place/environment: the relevance of interactions with proteins and modulators to RTD”.



*Cesare Indiveri, PhD*    *Maria Barile, PhD*

This two-year 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. These teams of researchers, led by Maria Barile, PhD, and Cesare Indiveri, PhD possess broad backgrounds in protein biochemistry, cell biology, and metabolism, with specific expertise in studying Rf homeostasis and transporters of nutrients in human cells.

RTD type 2 is caused by mutations in the SLC52A2 gene, which encode for the riboflavin transporter protein RFVT2. RFVT2 is responsible for transport of riboflavin across cell membranes. Previous studies by this team have demonstrated how various mutations in the SLC52A2 gene result in reduced function of the RFVT2 transport. The main aim of this project is to gain further insights into the structure and functional relationships ensuring correct functioning of RFVT2. The end goal of these projects is to help fill the existing gaps in the knowledge of the structure/function relationships in riboflavin transporters allowing for improving therapies or designing novel drugs.

Very little is currently 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 various cell samples from individuals with 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 over 65 peer-reviewed publications 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) Using cell lines (erythrocytes/lymphocytes/monocytes) extracted from blood samples from individuals with RTD.
- 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 2023-2024 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.