

Dear Friends,

Thanks to the generosity and support of people like you, we are forging ahead to fulfill our mission of improving the lives of children and young adults affected by TANGO2 disease. Now in our third year, there are just over 100 known cases throughout the world from 18 different countries.

With the hiring of an experienced Executive Director, the multiple new research projects underway (see *pages 3 & 4*), combined with continuing research studies, we have hope for a better understanding of this disease and options for treatment or prevention.

Thank you for being a part of this journey. Please continue to follow our progress and support our work at www.tango2research.org.

Natural History Study Yields Answers Thanks to TANGO2 Families

A natural history is the single best avenue to study traits of TANGO2 and how these traits progress over time. A huge thank you to the TANGO2 families that have participated in the natural history study with researchers from Baylor College of Medicine (BCM).

Based on the data collected from patient histories, researchers at BCM have

- Determined that metabolic crisis are triggered predominantly by illness, decreased oral intake, and heat
- Gathered important information about the heart during a metabolic crisis and how to best treat patients
- Created an emergency protocol letter to bring to hospitals when seeking care

These findings have already helped children with TANGO2 who have had a crisis and may have potentially saved children from getting to a crisis stage. Please consider taking part in this important study.

Announcing and Welcoming Our Executive Director, Ann Geffen

It is with great pleasure that we introduce our new (and first) Executive Director, Ann Geffen, who enthusiastically accepted the reins of this position a few weeks ago. She will officially begin working in July.

Ann comes to us with over 10 years of experience in nonprofits where she has successfully managed fundraising campaigns, staff, programs, events, and more. Her most recent experience with the March of Dimes was managing national corporate partnerships with an expected income of over \$5 million.



She established her own nonprofit organization which demonstrates her go-getter attitude, willingness to tackle whatever comes up, and expertise in small nonprofits. Along with her vast experience, talents, motivation, and vision, Ann has a Master of Arts degree in Strategic Public Relations and a law degree.

She looks forward to working with the TANGO2 community to make a real difference in the lives of TANGO2 patients and families. Welcome, Ann!

TANGO2 Foundation Joins the Rare As One Project

Part of \$13.5 Million from the Chan Zuckerberg Initiative Against Rare Diseases

In February 2020 we received \$450,000 in funding from the Chan Zuckerberg Initiative (CZI) to continue our work to find treatments and a cure for TANGO2 disease. The two-year grant will help the Foundation accelerate the expansion of our research network and the development of a sustainable funding plan. We are one of 30 patient-led organizations receiving funding from CZI's [Rare As One Project](#). (continued on page 2)

Rare As One Project *(continued from page 1)*

The Network is guided by the belief that it's imperative to develop strong collaboration among scientists, researchers, clinicians and patient communities who are striving towards a common goal of better patient outcomes.

In March, these 30 organizations were scheduled to attend a kick-off event in San Francisco. However, like many events in 2020, it was held virtually instead. Over these past months, CZI has held on-line training sessions to help rare disease organizations like the TANGO2 Research Foundation. The Rare As One Network has been working together to build a road map for all rare disease organizations to follow. It is our hope that this collaborative effort led by CZI will fast-track our mission to improve the lives of those children and young adults affected by TANGO2 disease. In sum, through dedication to working together and sharing information and resources we aim to:

- Develop a collaborative research network to work together, learn from, and share information and resources
- Develop a sustainable funding stream
- Develop a comprehensive research agenda, and
- Transition from an all-volunteer organization to one with dedicated professionals focusing on this critically important work every day.

“We are proud to support patient-led organizations as they pursue diagnoses, information, and treatment options in partnership with researchers and clinicians.”

Priscilla Chan, CZI
Co-Founder & Co-CEO

About the Chan Zuckerberg Initiative

Founded by Dr. Priscilla Chan and Mark Zuckerberg in 2015, the Chan Zuckerberg Initiative (CZI) is a new kind of philanthropy that's leveraging technology to help solve some of the world's toughest challenges — from eradicating disease, to improving education, to reforming the criminal justice system. We strive to help build an inclusive, just and healthy future for everyone. *For more about CZI, visit www.chanzuckerberg.com.*

Smiles from Around the World



Thanks to Our Supporters... The TANGO2 Research Foundation Is Funding 5 New International Research Projects That Are Now Underway

For more details, visit <https://tango2research.org/research>



1 Researching Effects of TANGO2 on Heart Function Using Stem Cells

Christina Miyake, MD, MS

Lilei Zhang, PhD

Diana Milewicz, MD, PhD

Heinrich Taegtmeyer, MD, PhD

We believe that understanding the mechanism behind TANGO2 may be best studied by looking at the heart because the heart is affected in all children during crisis and because it demonstrates the most severe effects. We believe that TANGO2 may play an important role in maintaining energy for cardiac cells. By using cells from a child with TANGO2 disease, we will essentially be recreating stem cells from that child's body with all of their specific genetic information. When studied, these cells will provide insights into that specific child and the information can then be generalized to other children with the same genetic change.

2 Studying the Path from Biological Function to Therapeutic Strategies

Felix Distelmaier, MD

Michael Sacher, PhD

A prerequisite to devising a treatment plan for individuals with specific gene mutations is knowing what the affected protein does in a cell. In our current research project we focus on understanding the basic biological function of TANGO2 and the cellular physiological consequences of TANGO2 deficiency. We will apply a drug screening platform to search for chemical compounds that influence TANGO2 function and will be able to mitigate the effects of TANGO2 deficiency.

3 Searching for Patterns in Blood to Decrease Life-Threatening Crises

Claudia Soler-Alfonso, M.D., F.A.C.M.G.

Patients with TANGO2 Disorder can also present with life-threatening emergencies known as "metabolic crisis." Our research goal is to study TANGO2 patients to identify metabolic patterns in the blood that could give us an idea of why they experience episodes. The technique being used is a more comprehensive way to look at chemicals in the blood as it will identify hundreds of compounds instead of only a few dozen. Our research goal is to identify a specific metabolic profile in TANGO2 patients, with particular attention to vitamin levels and fatty acid oxidation markers. If a definite pattern of deficiency is proven, we may be able to give patients extra amounts of a given vitamin or other nutrients to make their symptoms better and prevent episodes altogether.

Meet Harrison



He lives with his Mum and Dad and dog Phoebe in Australia.

He loves cars and trucks, sandwiches, swimming, and ignoring the word "no."

He sounds like any other 2-year-old, except he has TANGO2 disease.

Please join our search for answers.

DONATE TODAY



New International Research Projects

(continued from page 3)

4 Investigating the Main Function of TANGO2 and Its Role in Energy

Lina Ghaloul-Gonzalez, MD

Jerry Vockley, MD, PhD

In preliminary experiments, I have shown that cells lacking TANGO2 protein have an impaired ability to generate energy from the mitochondria (the energy producing part of the cell). My experiments will examine the normal location of TANGO2 protein in cells and how that location is affected. Further studies will characterize energy production caused by TANGO2 mutations. These experiments will help us to better understand the consequences of TANGO2 deficiency on the body and to develop novel treatments for the disease.

5 Deciphering the Physiopathology of TANGO2 Disease

Pascale de Lonlay, MD, PhD

Edor Kabashi, PhD

Our goal is to create a mutant TANGO2 zebrafish using genetic engineering techniques which allows us to do molecular investigations and screen medicines at the same time. By using this approach, we expect to set the basis for the translation of potential drugs that will protect patients from rhabdomyolysis (muscle breakdown) and neurological regression during illness.

Parallels of Rare Disease and COVID-19



When I first heard people talking about their experiences with COVID-19, thanks to the abundance of media coverage, I immediately thought of how familiar it sounded. How the thoughts and feelings are echoed by those living with a rare disease. The anxiety from not having answers on how to treat or cure their loved one's life-threatening illness. The confusion from seeing new symptoms. The fear of an uncertain future. The hope for finding answers. The list goes on. I don't want to belittle the seriousness of COVID-19. I want to share the similarities of having a life-threatening illness and to encourage empathy for what rare disease families have been struggling with for many years.

The collaboration from around the world to help during this pandemic is amazing and heart warming. A significant amount of resources and money (both public and private) is put towards treating and curing COVID-19. The idea that "together we can beat this" raises my spirits. Can we harness this idea that together we can beat this and find answers to rare diseases like TANGO2? I sincerely hope so. Please join me in supporting the TANGO2 Research Foundation. *Thank you!*

What Is TANGO2 Disease?

TANGO2 disease is a very rare genetic disorder only discovered in 2016. Very little is known about it, but we do know it has no treatment or cure (yet), it is progressive, and it can be life threatening. Symptoms first appear at about 12 months and vary in number and severity. Many children may suffer from life-threatening abnormal heart rhythms and metabolic crises, intellectual and developmental delays, muscle weakness, seizures, and more.

The TANGO2 Research Foundation

Founded in 2017, the TANGO2 Research Foundation's mission is to lead the way in finding a cure for TANGO2 related disease. We will do this by helping to fund, coordinate and guide scientific research that leads to a better understanding of TANGO2 disease. We are a 501(c)(3) organization.

Web site: www.tango2research.org

Donate: www.tango2research.org/donations