People and programs that keep the school healthy and vibrant



THE RACE IS ON

BUYING TIME FOR TPI RESEARCH

BY SARA WHITLOCK

When JT Borofka was 5 months old, he was diagnosed with a metabolic condition called triosephosphate isomerase (TPI) deficiency. Though his parents, Tara and Jason Borofka, had been taking him to doctors since he turned pale at 2 months old, the diagnosis was far from a relief. Tara Borofka remembers one doctor saying, "I would rather tell you that your child has cancer than tell you that your child has this."

The triosephosphate isomerase enzyme is an essential part of glycolysis—a primary energy production pathway for our bodies. In TPI deficiency, the enzyme is destabilized by a mutation and degraded. Children with this condition have lifelong anemia and develop severe progressive neuromuscular degeneration. Most die by age 5.

JT's doctors scoured the Internet to find Michael Palladino, professor of pharmacology and chemical biology at the University of Pittsburgh. "As far as I know, I'm the only one where TPI deficiency is a major focus in my lab," Palladino says. He identified a mutant fruit fly that is the only animal model of TPI deficiency and is using it to find drug targets that could help the TPI enzyme continue to produce energy. Early identification has been promising, and, according to Palladino, "If we find any one of the 2,000 or so available FDA-approved drugs" to hit their targets, "a clinician could use one of those almost immediately." However, money is an issue.

After JT's diagnosis, the Borofkas flew from their home in Salinas, Calif., where they both are professional anglers, to Pittsburgh to meet Palladino. When they learned that only part of his funding could be used for TPI research, the Borofkas decided to raise a million dollars for him. "We will do a fundraiser every weekend if we have to," Tara Borofka says. So far, they have raised $200,000 and channeled it to Palladino's work through a fund set up for them by the University of Pittsburgh.

Palladino says the Borofkas have been especially effective parent advocates: "They are used to media and social media as professional anglers. And JT is currently healthy, so they are not consumed with his medical care, only worrying about his future." JT, who is now more than a year old, is an exception because early genetic screening identified his condition before he showed neurological symptoms.

Now, he's on a special diet—similar to the keto diet—that helps Palladino's mutant fruit flies live longer; and so far, it's slowing the progression of JT's symptoms, too.

"He's a happy kid," Tara Borofka says. "Just being in one of our cars and holding the steering wheel makes him happy for like 30 minutes." If Palladino's team can find a drug that works, she says, maybe he'll be a racecar driver someday. ■

NATE LANGER/UPMC



Palladino with JT Borofka. JT's family is supporting Palladino's efforts to find a treatment for TPI.

SOUND APPROACH

Private gifts can help researchers move an idea, or discovery, from the lab into the clinic. For instance, support from donors propelled Thanos Tzounopoulos's work forward to better understand tinnitus, an often maddening disease where people perceive an incessant ringing noise. If everything proceeds as planned, patients may soon be able to try an experimental therapy. Pitt's Tzounopoulos is the UPMC Endowed Professor of Auditory Physiology and vice chair of research for otolaryngology.



2009
Thanos Tzounopoulos develops an animal model of tinnitus.

2011
Tzounopoulos determines that the root of chronic tinnitus exists in a structure of the brain.

2013
The Tzounopoulos lab identifies a molecular target for correcting tinnitus. A potassium channel is not working properly.

2015
Pitt chemist Peter Wipf starts working with Tzounopoulos to modify an existing drug, a potassium channel activator, which has the potential to reduce or remove phantom sound.

2017
Work continues to more specifically target potassium channels and reduce other side effects to make a therapy safer for public consumption.

2019–2021
Preclinical testing begins to determine safety for human trials. An Investigational New Drug application will be submitted as a requirement for clinical trials to begin.