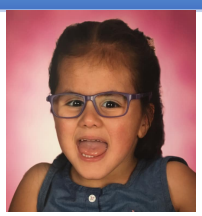
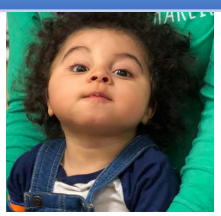
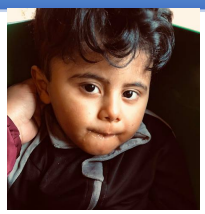
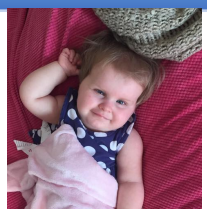
# TBCK Information Sheet



### *What is TBCK?*

TBCK or TBCK-related ID syndrome (named after the gene) is a rare neurogenetic disorder/disease with 40 reported cases worldwide. The disease impacts brain development and usually causes intellectual disability. TBCK is an autosomal recessive condition. The symptoms and conditions of TBCK vary depending on the person and specific variant.

TBCK stands for TBC1-domain-containing kinase. TBCK is associated with slowed mTOR functioning (a biological pathway). The mTOR pathway helps to regulate cell metabolism, growth, proliferation, and survival. Abnormalities in the mTOR pathway are associated with brain abnormalities, intellectual disability, epilepsy, and autism. Patients can have seizures, neurodegeneration, progressive neuromuscular weakness, and progressive coarse facial features similar of lysosomal storage disorders.

## COMMON SYMPTOMS

- Hypotonia
- Epilepsy
- Global developmental delay (moderate to profound)
- Intellectual Disability
- Hypothyroidism
- Vision impairment
- Dysphagia
- Respiratory insufficiency
- White matter changes, cerebellar atrophy, Thin corpus callosum
- Absent/severely delayed expressive language
- Osteopenia
- Hypercholesterolemia
- Frequent UTIs/nephrolithiasis
- Hyporeflexia/areflexia
- Coarse facies

### *Prevalence and Impact of TBCK*

Cases have been diagnosed through the Whole Exome Sequence. There is a range of genetic variants that have been recorded, with the full extent of symptoms for the disease being variable. Notably is a founder variant in the Caribbean region ("Boricua mutation" p.R126X) causing with severe disease, also known as TBCK-encephaloneuronopathy.

### *Diagnosis*

As more cases are being diagnosed a distinguishable clinical marker has emerged. All reported patients have biallelic variants in TBCK, which can be missed by Sanger sequencing and exome sequencing may miss these small exon-level deletions. It is recommended that both sequencing and deletion/duplication analysis should be performed. Also, neurophysiological studies show axonal motor neuropaty/neuronopathy in severely affected patients. CHOP research team has found urine oligosaccharide abnormalities.

### *Treatment for TBCK*

There is no known cure or treatment at this time. Therapies are highly recommended as well as evaluations for feeding, seizures, and respiratory insufficiency. Researchers have identified the potential treatment of supplementing with branch chain amino acids or leucine (one of the branch chain amino acids) but research has not begun.

Seizures should be monitored. There is no recommended antiepileptic, with some patients responding well to levetiracetam. Caution is advised for Valproate, biphosphonate infusion, and the ketogenic diet based on adverse outcomes in some patients. Patients can sometimes begin with provoked seizures (fever/illness) and then can progress to epilepsy. Patients should closely monitor aerial blood gases (ABGs) when patients are sick to avoid progression to seizures.

### *For Diagnosed Families*

You are not alone. There are researchers, families, and advocates that are dedicated to improving the lives of those impacted by TBCK. Scientists and medical professionals (with the help of our families) have identified these first steps:

- Get connected to CHOP Neurogenetics Department (tbckresearch@chop.edu)
- Sleep study (to check for sleep apnea and respiratory muscle weakness especially at night)
- Therapies
- EEG (to check for seizures, they can be subclinical and only detected on EEG; (see above on seizure treatment)
- Cholesterol and thyroid hormone levels monitoring
- Liver levels monitoring
- Swallow study (to evaluate for possible aspiration)



*Resources: Theo's Village: The TBCK Foundation, Neurogenetics Team of CHOP*