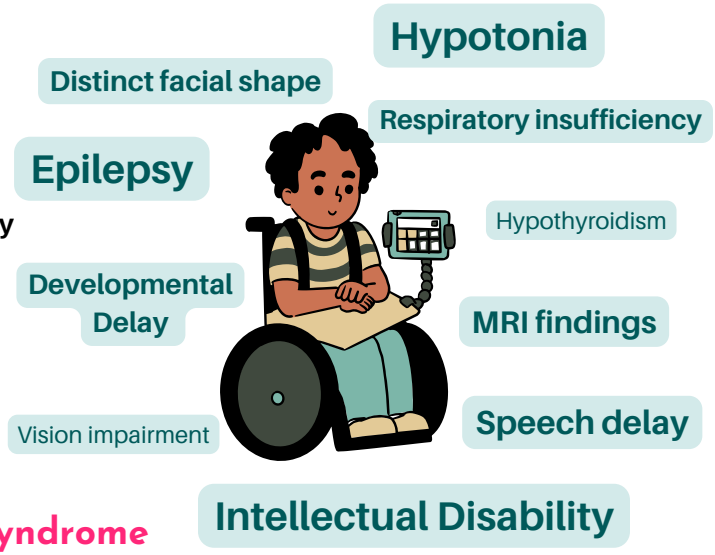
# TBCK TIDBITS

## What is TBCK Syndrome?

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

TBCK stands for TBC1-domain-containing kinase. TBCK Syndrome is associated with slowed mTOR functioning (a biological pathway regulating cell metabolism, growth, proliferation, and survival).




## Prevalence, Diagnosis, and Impact of TBCK Syndrome

More than 100 TBCK warriors have been identified across the globe. Cases are diagnosed with Whole Exome Sequencing. There is a range of genetic variants that have been recorded, with the full extent of symptoms for the disease being variable. Patients have balletic variants in *TBCK*, which can be missed by Sanger Sequencing and exome sequencing may miss small exon-level deletions. It is recommended that both sequencing and deletion/duplication analysis be performed. Neurophysiological studies show axonal motor neuropathy/neuronopathy in severely affected patients. Notably, a founder variant has been identified in the Caribbean region ("Boricua mutation" p.R126X) causing with severe disease, also known as TBCK-encephaloneuropathy.

## Treatment for TBCK Syndrome

There is no known cure or treatment at this time. Therapies are highly recommended as well as evaluations for feeding, seizures, and respiratory insufficiency. Research focused on patient outcomes is ongoing. Seizures should be monitored. There is no recommended anti-epileptic, with some patients responding well to levetiracetam. Caution is advised for Valproate, bisphosphonate infusion, and the ketogenic diet based on adverse outcomes. 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 Syndrome. Scientists and medical professionals (with the help of our families) have identified these first steps:

- Sleep study (to check for sleep apnea and respiratory muscle weakness especially at night)
- 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)
- Connect RARE-X