

# Reduced TBCK a potential cause of bone dysmorphology in a mouse model of pediatric neurodegeneration



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### TBCK Syndrome

OVERVIEW, SYMPTOMS + HEALTH IMPACTS

TBCK SYNDROME IS A VERY RARE NEUROGENETIC DISEASE THAT WAS FIRST DESCRIBED IN MEDICAL LITERATURE IN 2016. MOST OF THE IDENTIFIED POPULATION IS CHILDREN + YOUNG ADULTS AS OF 2022.

**100**  
ESTIMATED NUMBER OF PATIENTS DIAGNOSED GLOBALLY

**22**  
AGE OF OLDEST KNOWN PATIENT

**SEVERE HYPOTONIA**  
Most patients have very low tone, contributing to additional health concerns.

**INTELLECTUAL + PHYSICAL DISABILITY**  
Most diagnosed patients require assistance with basic needs.

**ENDOCRINE SYSTEM**  
Thyroid dysfunction  
**EAR/NOSE/THROAT**  
**EYE/LOW VISION**

**DIVERSE POPULATION**  
-Large portion of population identify as a person of color  
-Varying mutations individual to patients  
-Founders mutation: Boricua Mutation

**AUTONOMIC FUNCTION**  
**MUSCULAR SYSTEM**  
Most patients have severe hypotonia.

**BRAIN + EPILEPSY**  
Seizures are a common symptom, impacting most patients. Families note seizures as the number one health concern. Neuro-degeneration is possible in some mutations.

**RESPIRATORY SYSTEM**  
Due to hypotonia (low tone) basic respiratory illnesses can be severe. Some patients require a tracheostomy.

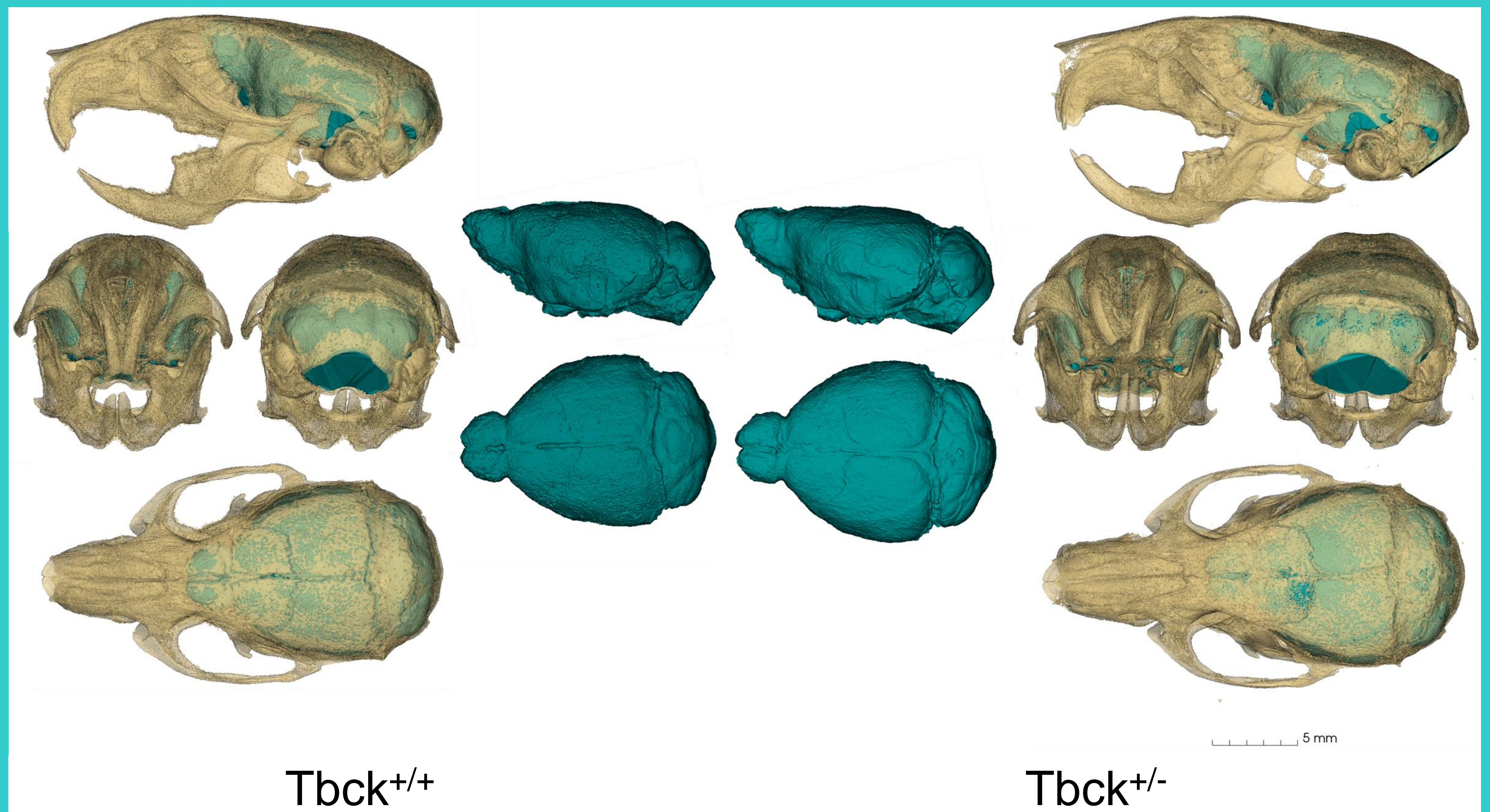
**DIAGNOSTIC CHALLENGES**  
With such a rare syndrome, there can be many barriers to diagnosis.

**GASTRO-INTESTINAL + LIVER**  
GI issues  
G-tubes are very common for patients

**AUTOSOMAL RECESSIVE DISEASE**  
**AUTISM**

**TBCK FOUNDATION**  
@tbckfoundation  
www.tbckfoundation.com

## TBCK deletion has system-wide effects specifically on bone



**Hypothesis:** Loss of TBCK negatively impacts bone health

### Methods:

- ❖ 89wk  $Tbck^{+/+}$  &  $Tbck^{+/-}$  mice  $n=7$ /group
- ❖ Micro CT endocast and cephalometrics
- ❖ Histology suture morphometrics

**Results:**  $Tbck^{+/-}$  skulls and sagittal sutures are wider and longer than  $Tbck^{+/+}$  skulls

**Conclusions:** There are effects of loss of TBCK beyond the brain.

**Future Directions:** Determine the bone cell type sensitive to TBCK levels

**Figure 1: Anatomy of adult mouse skull and endocast.** 3D reconstructions of  $Tbck^{+/+}$  (left) and  $Tbck^{+/-}$  (right) skulls and endocasts (center) in left lateral (top), anterior (middle left), posterior (middle right), and superior (bottom) views. Note longer, less domed calvarium in  $Tbck^{+/-}$  individuals. Also note incisor defects and skeletal malformations leading to malocclusion in  $Tbck^{+/-}$  mice. Scale = 5 mm

### Figure 2: Additional assessments of $Tbck^{+/+}$ and $Tbck^{+/-}$ adult skulls.

Endocast volume, calculated using 3Dslicer and Wrap Solidify, did not identify significant differences between genotypes which does not preclude potentially significant differences in brain shape (Left). Cephalometric assessment of calvaria determined  $Tbck^{+/-}$  mice have an elongated calvarium ( $p=0.044$ ) as compared to  $Tbck^{+/+}$  mice. No other measure used identified shape differences between genotypes perhaps indicating a need for a more global form assessment (middle). Skull growth site histomorphometrics indicated a significant increased in sagittal suture area (width  $p\leq 0.001$ , height  $p=0.047$ ) perhaps indicating changes to calvarial growth patterns (right).

