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

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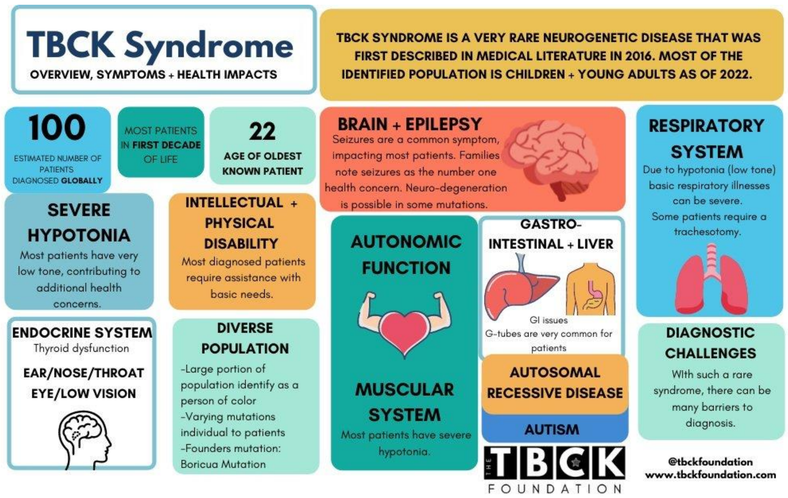

Hypothesis: Loss of TBCK negatively impacts bone health

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

TBCK deletion has system-wide effects specifically on bone

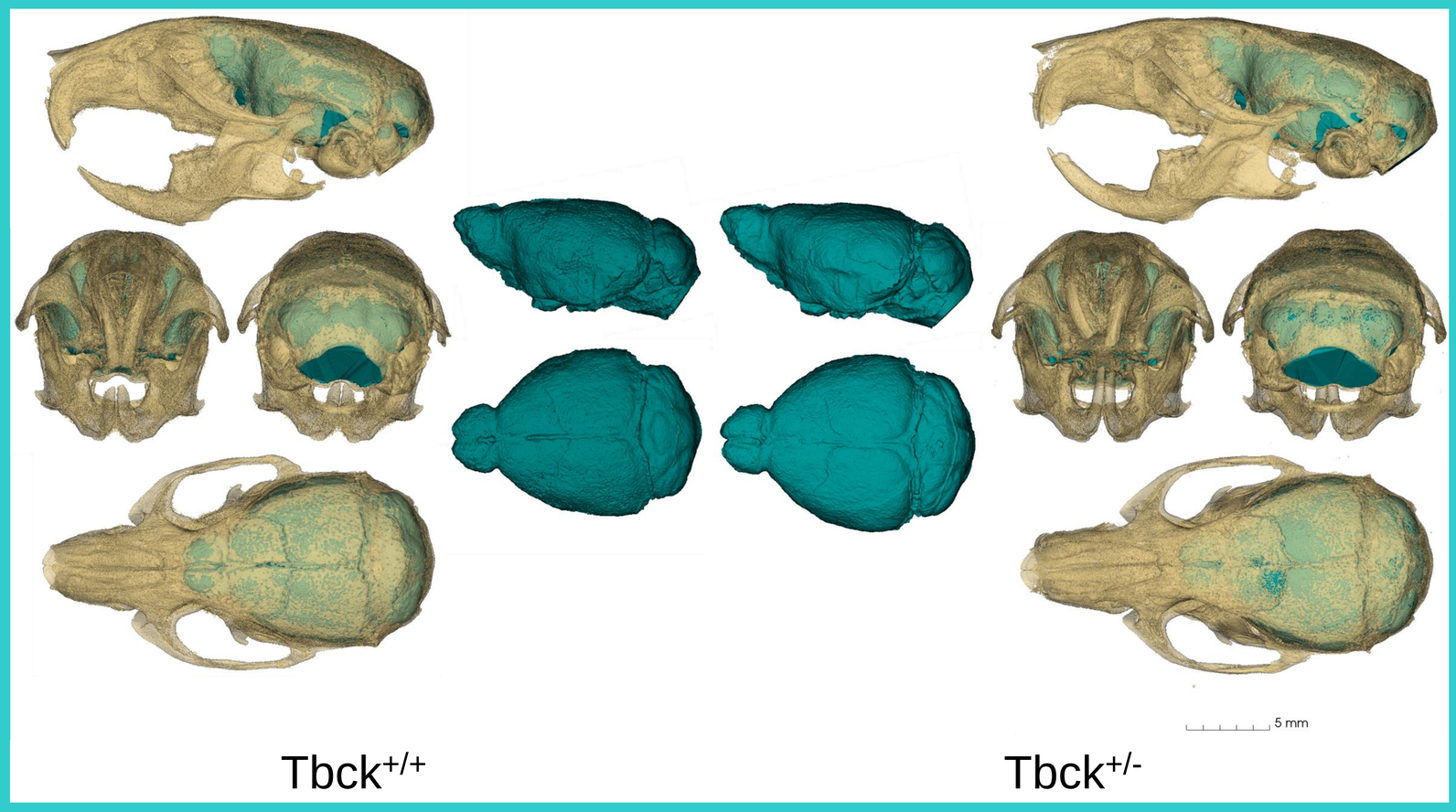

Figure 1: Anatomy of adult mouse skull and endocast. 3D reconstructions of Tbck$^{+/+}$ (left) and Tbck$^{+/-}$ (right) skulls and endocasts (center) in left lateral (top), anterior (middle left), posterior (middle right), and superior (bottom) views. Note longer, less domed calvarium in Tbck$^{+/-}$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

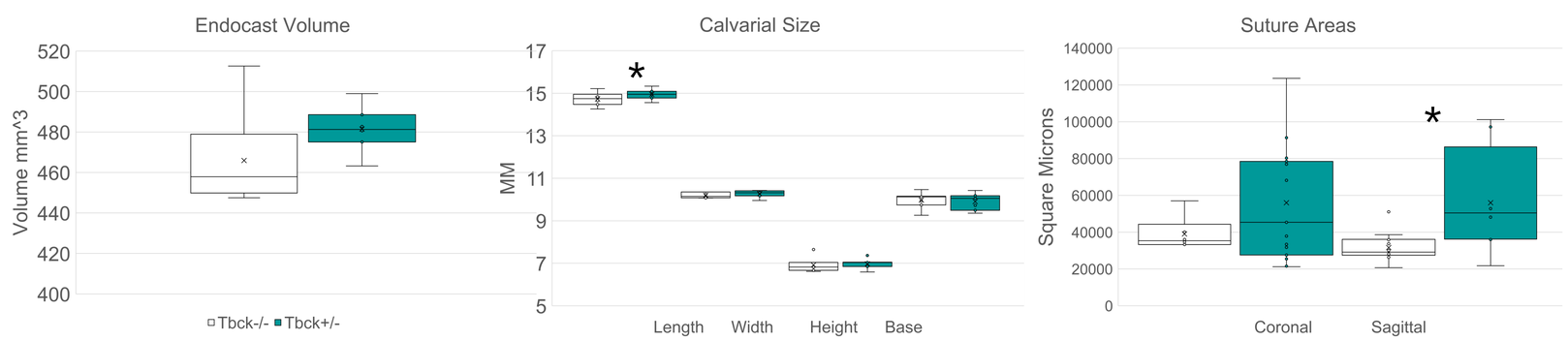

Figure 2: Additional assessments of Tbck$^{+/+}$ and Tbck$^{+/-}$ adult skulls. Endocast volume, calculated using 3DSlicer and Wrap Solidify, did not identify significant differences between genotypes which does not preclude potentially significant differences in brain shape (Left). Cephalometric assessment 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≤0.001, height p=0.047) perhaps indicating changes to calvarial growth patterns (right).