Loss of TBCK alters bone cell homeostasis resulting in altered bone morphology

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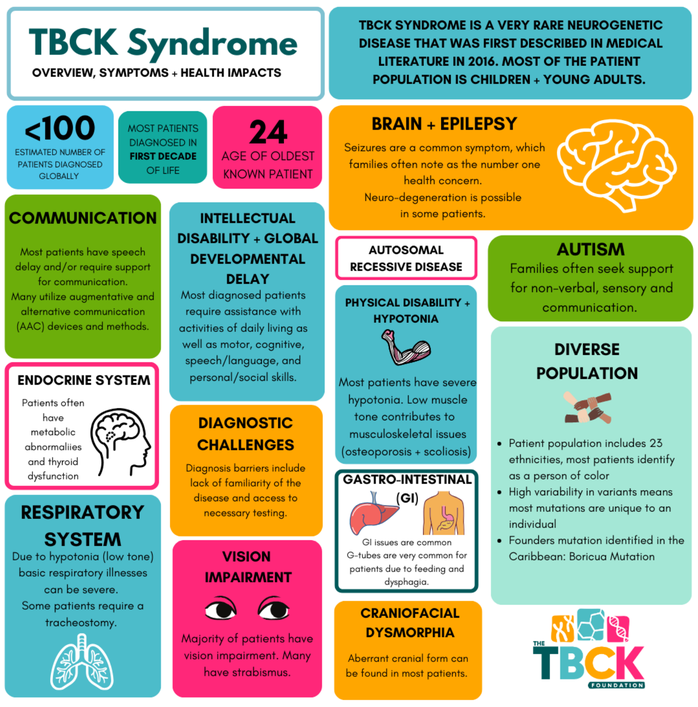

Hypothesis: Loss of TBCK negatively impacts bone health

Methods:

- Differentiate patient derived fibroblasts
- Compare gene expression
- 89wk Tbck$^{+/+}$ & Tbck$^{+/-}$ mice n=7/group
- Micro CT endocast and cephalometrics
- Histology suture morphometrics

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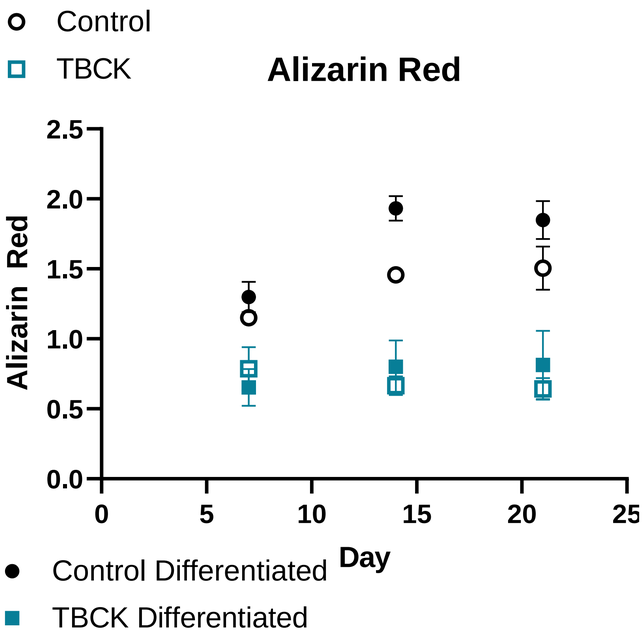
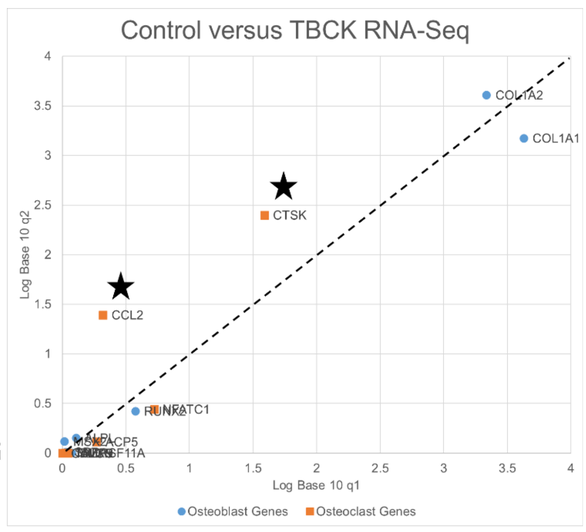
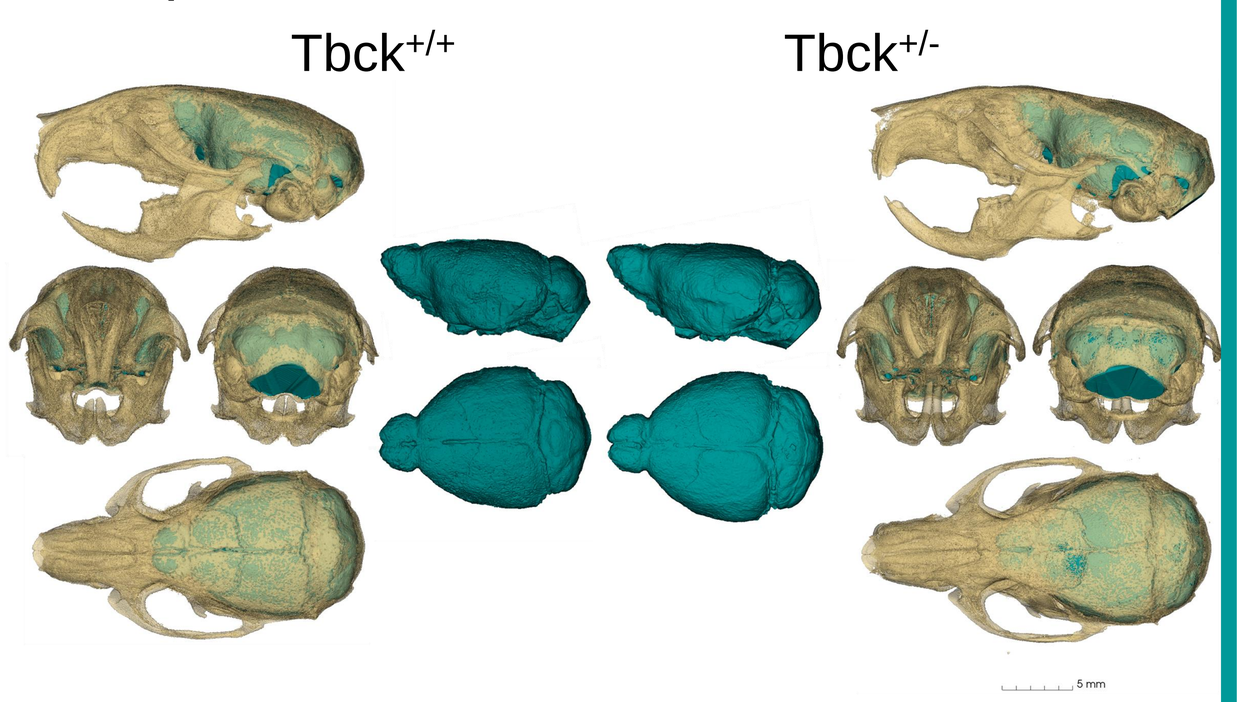
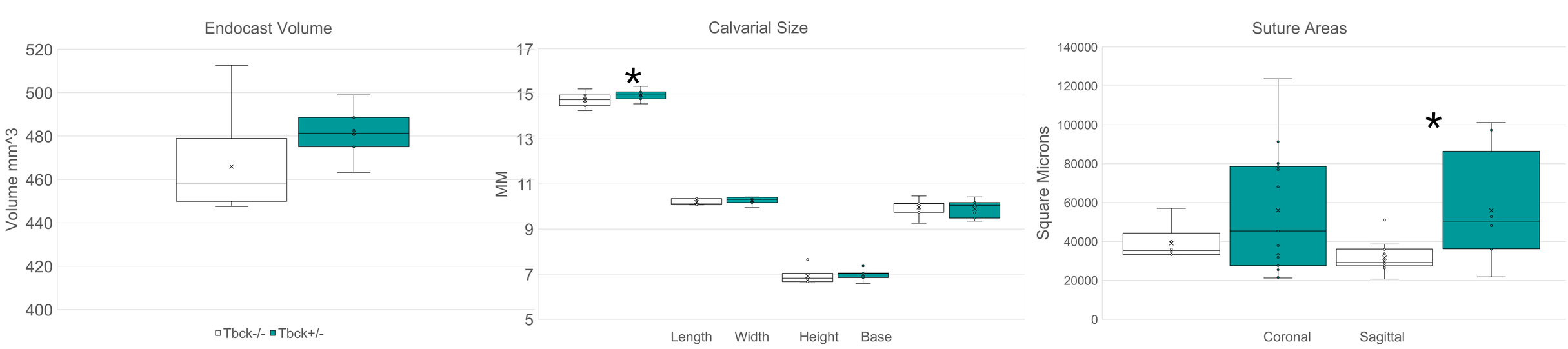
TBCK syndrome:
a rare multi-organ neurodegenerative disease
Durham et al 2023







TBCK deletion has system-wide effects specifically on bone



Figures: Top Left. Differentiation of patient derived fibroblasts using osteogenic media. n = 3 **Top Center.** Scatterplot of bone related gene expression in Control and TBCK samples. Stars highlight significantly differentially expressed osteoclast related genes. Genes along the dotted line indicate similar (unaffected by TBCK deficiency) gene expression. **Top Right.** 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. n = 7/genotype Scale = 5 mm **Bottom Left.** 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. **Bottom Center.** 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. **Bottom Right.** 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. n = 3/genotype for histology.

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