Clinical Features:
Temple-Baraitser syndrome [OMIM# 611816] is a rare neurodevelopmental disorder resulting in severe intellectual disability, abnormalities of thumb and big toe (hallux), and seizures in most cases [1]. Aplasia or hypoplasia of toe nails and the presence of a proximally implanted and distally broadened thumb and hallux are common features as well as characteristic radiographic findings of the fingers and toes [1, 3, 5]. Affected individuals may have mild dysmorphic facial features including a pseudo-myopathic facies, and demonstrate poor visual contact and autistic-like behaviors. Most individuals are delayed in their early milestones and seizures usually present in childhood or later [1, 3-5]. Some affected individuals have been reported with heart defects and gastrointestinal issues [4, 5].

Molecular Genetics:
Pathogenic variants in KCNH1 gene have been implicated as a causative etiology in Temple-Baraitser syndrome. KCNH1 codes for a voltage-gated potassium channel protein that is suggested to play a role in the regulation of cell proliferation and is likely fundamental to developmental processes. It is proposed that pathogenic variants in this gene disrupt cell proliferation and migration along with neuronal development. All reported pathogenic variants to date are missense variants, resulting in a gain of function of KCNH1, with a decreased activation threshold and delayed deactivation period [2]. Gain of function mutations in KCNH1 can also cause Zimmermann-Laband syndrome [OMIM# 135500] [6], which is characterized by gingival hyperplasia, dysplastic or absent nails, hypoplasia of distal phalanges, scoliosis, hepatosplenomegaly, hirsutism, and cartilaginous abnormalities of the nose and/or ears [7].

Inheritance:
KCNH1-associated disorders are autosomal dominant and the majority of pathogenic variants described to date have been de novo. Mosaic pathogenic KCNH1 variants have been identified in a subset of parents of children with Temple-Baraitser syndrome. These carriers of mosaic KCNH1 pathogenic variants typically have isolated seizures with no additional features of Temple-Baraitser syndrome [2]. Recurrence risk for parents of an affected child may depend on their carrier status.

Test Methods:
We offer full gene sequencing of all coding exons and intron/exon boundaries of KCNH1 by direct sequencing of amplification products in both the forward and reverse directions.

**KCNH1 sequencing**

- **Sample specifications:** 3 to 10cc of blood in a purple top (EDTA) tube
- **Cost:** $900
- **CPT codes:** 81406
- **Turn-around time:** 4 weeks

Results:
Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

*For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.*
References:


Committed to CUSTOMIZED DIAGNOSTICS, TRANSLATIONAL RESEARCH & YOUR PATIENTS’ NEEDS