Baraitser-Winter syndrome

Genes: ACTB and ACTG1

Clinical Features:
This rare autosomal dominant congenital disorder is characterized by ptosis, high-arched eyebrows, hypetelorism, ocular colobomata and predominant anterior lissencephaly[1]. Other common features are postnatal short stature, microcephaly, intellectual disability, seizures and hearing loss[1].

Genetics:
Baraitser-Winter syndrome is an autosomal dominant disorder. Many cases are sporadic and are likely due to new pathogenic missense variants.

Test Methods:
Using genomic DNA from the submitted specimen, the complete coding regions and splice site junctions of the genes on this panel are enriched using a proprietary targeted capture system developed by GeneDx for next-generation sequencing with CNV calling (NGS-CNV). The enriched targets are simultaneously sequenced with paired-end reads on an Illumina platform. Bi-directional sequence reads are assembled and aligned to reference sequences based on NCBI RefSeq transcripts and human genome build GRCh37/UCSC hg19. After gene specific filtering, data are analyzed to identify sequence variants and most deletions and duplications involving coding exons. For the *ACTB* gene, only large deletion/duplication events may be detected. Alternative sequencing or copy number detection methods are used to analyze regions with inadequate sequence or copy number data. Reportable variants include pathogenic variants, likely pathogenic variants and variants of uncertain significance. Likely benign and benign variants, if present, are not routinely reported but are available upon request.

Test Sensitivity:
In a cohort of 42 patients diagnosed with Baraitser-Winter syndrome 79% of patients harbored a mutation within the *ACTB* gene while the remaining 21% harbored a mutation within the *ACTG1* gene[2].

References:

1. Rivière et al. (2012) Nature Genetics 44 (4):440-4, S1-2 (PMID: 22366783)
2. Verloes et al. (2015) European Journal Of Human Genetics : Ejhg 23 (3):292-301 (PMID: 25052316)