OVERGROWTH PANEL

Background: Overgrowth syndromes encompass a variety of different diseases and are associated with both germline and somatic mutations in several different genes. This testing targets 8 genes associated with overgrowth, as well as other overlapping and non-overlapping clinical features.

Somatic mutations in AKT1 (OMIM 164730) are associated with Proteus syndrome. Mutations in AKT2 (OMIM 164731) are associated with hemihypertrophy with pseudohyperinsulinism. Somatic mutations in PIK3CA (OMIM 171834) are associated with CLOVES syndrome and macrodactyly. Mutations in AKT3 (OMIM 611223) and PIK3R2 (OMIM 603157) are associated with megalencephaly. Mutations in CDKN1C (OMIM 600856) are associated with familial cases of Beckwith-Wiedemann syndrome. Somatic, mosaic mutations in GNAQ (OMIM 600998) are associated with non-syndromic port-wine stains, as well as Sturge-Weber syndrome. Mutations in MTOR (OMIM 601231) are associated with hemimegalencephaly.

Most mutations in the genes above that result in the above diagnoses are somatic in their origin. These mutations are often mosaic and typically poorly detected in the blood and better detected in a clearly affected tissue (skin, muscle, adipose, CNS)

Assay: Multiplex PCR and Next Generation Sequencing on IonTorrent PGM platform.

Testing assesses specific regions related to overgrowth in the following 8 genes: AKT1, AKT2, AKT3, CDKN1C, GNAQ, MTOR, PIK3CA, PIK3R2 (Overgrowth version 1.0)

Utility: Confirmation of a clinical diagnosis, prognostic evaluation, clinical management.

Sensitivity: Testing targets specific gene mutations or exons of the genes listed above and does not detect mutations that are outside of the targeted area. Testing does not completely sequence every exon of each one of the 8 genes. The limit of detection is 1% at 1000X sequencing coverage and 10% at 200X coverage. This technology cannot reliably detect mutations at coverage below 100X coverage. Confirmation of mutations is performed by repeat sequencing of independent replicate sample.

Turn around: 6-8 weeks

Fee: $2500

CPT codes: 81479

12/22/2014