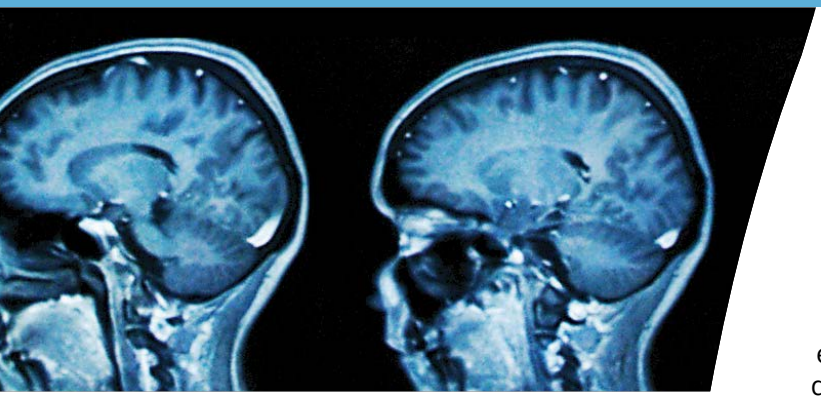
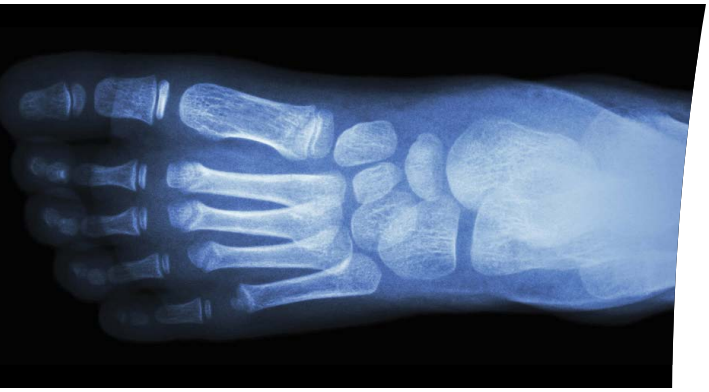
SOMA Gene Set

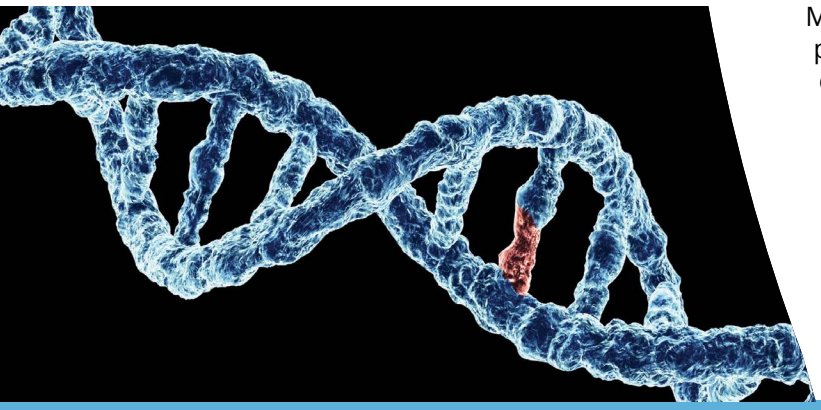
GENOMICS AND PATHOLOGY SERVICES
GPS@WUSTL™
CLINICAL TESTING • RESEARCH • EDUCATION





Orderable gene sets include:

- Somatic overgrowth
- *PIK3CA*-related overgrowth
- McCune Albright (GNAS)
- Nevus syndrome
- Curry - Jones syndrome
- Maffucci syndrome
- Rasopathies



Genomic profiling for Segmental Overgrowth, McCune Albright and related syndromes

Next-generation sequencing for efficient and cost-effective somatic variant analysis; germline variants also detected

Concise, expert interpretations by board-certified clinical genomicists

Expert consultation available to physicians in result interpretation and in other technical/clinical considerations

Testing covered by most insurance; preauthorization performed by GPS

Clinical utility

The **SOMA Gene Set** is designed to identify patients with diagnostic genetic mutations that underlie segmental overgrowth, McCune Albright and related syndromes.

The **PI3K/AKT/mTOR pathway** is critical in regulating cellular proliferation, mobility and survival. Variation in genes of this pathway can result in several disorders characterized by a wide range of phenotypes often making it difficult to make a **definitive diagnosis**.

Most commonly, disorders characterized by these phenotypes are a result of **somatic variants** - those occurring in only a proportion of the body's cells - rather than germline variants that are found in all cells of the body. As a result, testing for these disorders is strongly recommended from affected tissue.

Next-generation sequencing provides clinicians with a **powerful tool** to manage patients with these diagnostically challenging disorders.

Washington University Physicians
Washington University School of Medicine in St. Louis

07/28/15

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Indications for testing

Indications for referral include clinical features of the following:

- Bannayan-Riley-Ruvalcaba syndrome (BRRS)
- Cowden syndrome
- Congenital, lipomatous, overgrowth, vascular malformations, epidermal nevi and scoliosis/skeletal/spinal anomalies (CLOVES)
- Hemimegalencephaly
- Klippel-Trenaunay syndrome (KTS)
- McCune Albright syndrome (MAS)
- Macrocephaly–capillary malformation (M-CM)
- Megalencephaly-polymicrogyria-polydactyly-hydrocephalus (MPPH)
- Proteus syndrome
- Schimmelpenning-Feuerstein-Mims (Epidermal Nevus Syndrome)

Genes tested

Somatic Overgrowth Gene Set: *AKT1, AKT2, AKT3, BRAF, FGFR1, GNA11, GNAQ, HRAS, IDH1, IDH2, KRAS, MAP2K1, MAP3K3, MTOR, NRAS, PDGFRB, PIK3CA, PIK3R1, PIK3R2, PTEN, RASA1, SMO, TEK, TSC1 and TSC2.*
***PIK3CA*-Related Overgrowth Gene Set:** *PIK3CA.*

McCune Albright Gene Set: *GNAS.*

Nevus Gene Set: *BRAF, FGFR1, FGFR2, FGFR3, GNA11, GNAQ, HRAS, KRAS, MAP3K3, NRAS, PIK3CA and TEK.*

Curry-Jones Syndrome Gene Set: *SMO.*

Maffucci Syndrome Gene Set: *IDH1 and IDH2.*

Rasopathies Gene Set: *BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NF1, NRAS, PTPN11, RAF1, RIT1, SHOC2, SOS1 and SPRED1.*

Testing methodology

Tests are performed using targeted hybridization capture coupled with next-generation sequencing (NGS) in our CAP/CLIA labs for deep, comprehensive coverage of all coding exons of ordered genes. Types of variation detected include single nucleotide variants (SNVs) small insertions and deletions (indels).

This test is routinely performed using formalin fixed paraffin embedded (FFPE) or fresh tissues and is able to detect alterations under 10% allele frequency in affected tissues. A buccal swab may be tested if affected tissue is not available however sensitivity may be limited.

Results and interpretation

DNA sequence data are analyzed by GPS' clinically validated bioinformatics pipeline to identify and annotate genetic variants associated with segmental overgrowth syndromes.

Variants are interpreted by a board-certified clinical genomicist in the context of the patient's disease. Those that are most likely to account for the observed clinical phenotype based on evidence from the medical literature are highlighted. Results are returned to the ordering physician in a concise report.

Specimen requirements

Preferred specimen types include tissue from the affected area. In addition, 2-5 mL of peripheral blood in a lavender-top EDTA tube is also required to allow comparative study.

Acceptable materials for submission include disease involved tissue in the form of a formalin fixed paraffin embedded (FFPE) tissue block, fresh tissue in transport or tissue culture media or buccal swab. Acid decalcified samples and heparinized blood are not acceptible.

Kits for testing on peripheral blood and buccal cells are available upon request.

Turnaround time

The turnaround time for testing and interpretation is six to eight weeks from the time a specimen arrives.

Ordering

To order a test, submit a completed requisition form (available on our website) by fax or email. GPS performs insurance preauthorization.

In the case of archival specimens, GPS coordinates sample acquisition. If surgical pathology materials have to be requested from outside BJC HealthCare, include the release form. Please contact us for more information.

Selected references

Keppler-Noreuil KM, Sapp JC, et al. Clinical delineation and natural history of the PIK3CA-related overgrowth spectrum. Am J Med Genet A. 2014 Jul;164(7):1713-33.

Mirzaa GM, Rivière JB, Dobyns WB. Megalencephaly syndromes and activating mutations in the PI3K-AKT pathway: MPPH and MCAP. Am J Med Genet C Semin Med Genet. 2013 May;163C(2):122-30.

Rivière JB, Mirzaa GM, et al. De novo germline and postzygotic mutations in AKT3, PIK3R2 and PIK3CA cause a spectrum of related megalencephaly syndromes. Nat Genet. 2012 Jun 24;44(8):934-40.

Kurek KC, Luks VL, et al. Somatic mosaic activating mutations in PIK3CA cause CLOVES syndrome. Am J Hum Genet. 2012 Jun 8;90(6):1108-15.

Dumitrescu CE, Collins MT. McCune-Albright syndrome. Orphanet J Rare Dis. 2008 May 19;3:12.

Contact us to order a test or for more info

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