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

Genetic Diabetes & Hyperinsulinism Testing

At Washington University

Clinical Utility

Next generation sequencing can provide clinicians with a diagnosis for diseases that would otherwise be impossible to diagnose. This test is designed to identify alterations that underlie genetic forms of diabetes and hyperinsulinism.

Obtaining a genetic diagnosis can provide life changing results for patients and their families by directing treatment options or providing risk assessment for family members and future pregnancies. Additionally, patients found to have genetic forms of diabetes or hyperinsulinism may be able to participate in research studies (or clinical trials) aimed at understanding their disease or offering new therapies.

Genomic Profiling

Tests developed in concert with endocrinologists, medical geneticists, and researchers at Washington University School of Medicine in St. Louis.

Next-generation sequencing for efficient, cost-effective and robust germline variant detection.

Concise, expert interpretations by board-certified clinical genomicists, reported back to the ordering physician.

Professional consultation available to physicians in result interpretation, and other technical and clinical considerations.

Testing covered by most insurance; preauthorization performed by GPS laboratory personnel.

Orderable disease focused gene sets include:

- **Monogenic Diabetes and Maturity Onset Diabetes of the Young (MODY)** – *43 genes*
- **Permanent Neonatal Diabetes Mellitus (PNDM)** - 29 *genes*
- **Endoplasmic Reticulum (ER) Stress** – *5 genes*
- **Hyperinsulinism** – *18 genes*

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

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Genes Tested

Endoplasmic Reticulum (ER) Stress Gene Set (5 genes) - *CISD2, EIF2AK3, IER3IP1, INS, WFS1*

Hyperinsulinism Gene Set (18 genes) - *ABCC8, AKT2, CACNA1D, FOXA2, GCK, GLUD1, HADH, HNF1A, HNF4A, INSR, KCNJ11, KDM6A, KMT2D, PGM1, PMM2, SLC16A1, TRMT10A, UCP2*

Monogenic Diabetes and Maturity Onset Diabetes of the Young (MODY) Gene Set (43 genes) - *ABCC8, AGPAT2, AIRE, AKT2, APPL1, BLK, CEL, CISD2, CP, EIF2AK3, FOXP3, GATA4, GATA6, GCK, GLIS3, HFE, HNF1A, HNF1B, HNF4A, IER3IP1, INS, INSR, KCNJ11, KLF11, LRBA, MNX1, NEUROD1, NEUROG3, NKX2-2, PAX4, PAX6, PCBD1, PDX1, PLAGL1, PPARG, PTF1A, RFX6, SLC2A2, SLC19A2, STAT3, TRMT10A, WFS1, ZFP57*

Permanent Neonatal Diabetes Mellitus (PNDM) Gene Set (29 genes) - *ABCC8, CP, EIF2AK3, FOXP3, GATA4, GATA6, GCK, GLIS3, HNF1B, IER3IP1, INS, KCNJ11, LRBA, MNX1, NEUROD1, NEUROG3, NKX2-2, PAX6, PCBD1, PDX1, PLAGL1, PTF1A, RFX6, SLC2A2, SLC19A2, STAT3, TRMT10A, WFS1, ZFP57*

Testing Methodology

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

Results and Interpretation

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

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

Specimen types accepted include 2-5 mL peripheral blood in a lavender-top EDTA tube. Specimen kits are available upon request.

Please contact us or fill out the NGS supply order form available on our website at gps.wustl.edu/forms-and-resources.

Turnaround Time

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

Ordering

To order a test, submit a completed requisition form (available at gps.wustl.edu/forms-and-resources) by fax or email. GPS performs insurance preauthorization.

Ancillary Testing

Deletion/Duplication analysis via CGH (comparative genomic hybridization) for the *HNF1B* gene is performed as a send out for the Monogenic Diabetes and MODY Gene Set and the Permanent Neonatal Diabetes Mellitus (PNDM) Gene Set when NGS is negative.

Selected References

American Diabetes Association (2019) "Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019". Diabetes Care. 42:S13-S28.

Hattersley A, Bruining J, Shield J, Njolstad P, Donaghue KC (2009). "The diagnosis and management of monogenic diabetes in children and adolescents". Pediatric Diabetes. 12:33-42.

Naylor RN, John PM, Winn AN, Carmody D, Greeley SA, Philipson LH, Bell GI, Huang ES (2014). "Cost-effectiveness of MODY genetic testing: translating genomic advances into practical health applications". Diabetes Care. 37(1):202-209.

Contact us to order a test or for more info

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