Renal Disease Testing at Washington University

GENOMICS AND PATHOLOGY SERVICES
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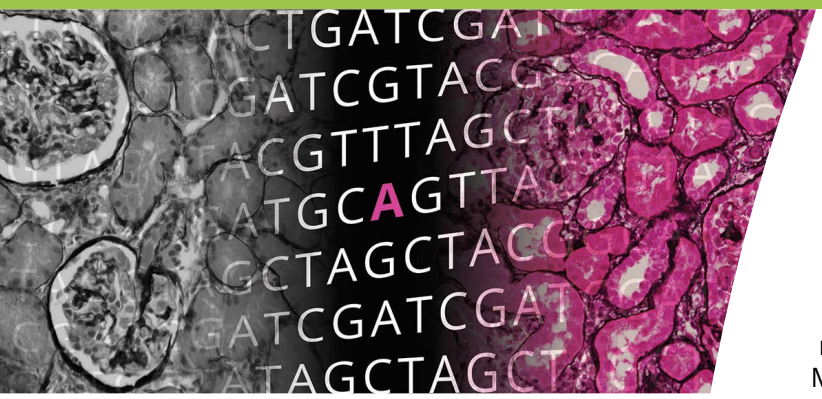
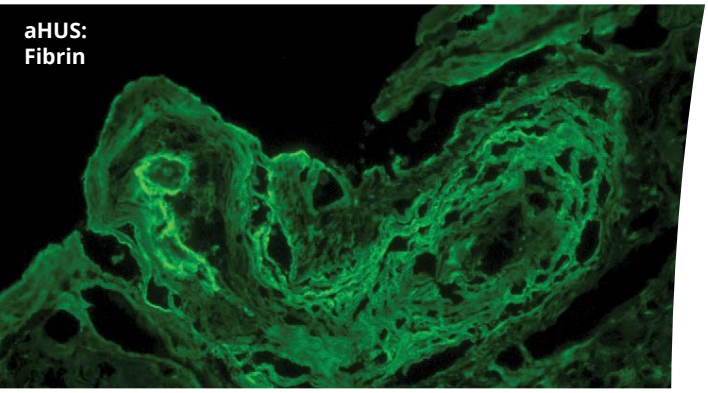
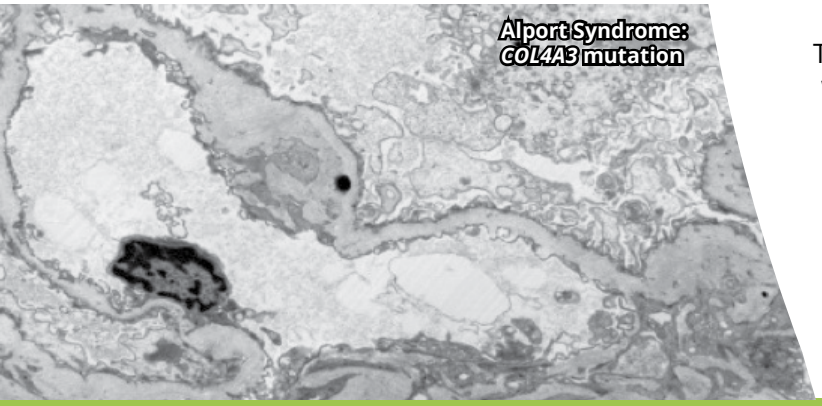
CLINICAL TESTING • RESEARCH • EDUCATION





Orderable gene sets include:

- **Alport Syndrome** *(3 genes)*
- **aHUS/TMA/C3 Glomerulopathy** *(13 genes & CFHR3-CFHR1 deletion)*
- **Cystic disease and Nephronopthisis** *(33 genes)*
- **Nephrotic Syndrome and Focal Segmental Glomerulosclerosis** *(52 genes)*



Genomic profiling for renal diseases

Tests developed in concert with immunobiologists and nephropathologists 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

Clinical utility

Tests are designed to identify patients with diagnostic genetic mutations that underlie renal disease.

Many times, a renal biopsy is simply not enough to make a **definitive diagnosis** – even when combined with the powerful ancillary techniques of immunofluorescence and electron microscopy.

This is particularly true for **pediatric patients** who present with steroid resistant nephrotic syndrome, and patients with suspected complement system abnormalities such as aHUS.

These next-generation sequencing tests provide clinicians with a **powerful tool** to manage patients with diagnostically challenging diseases.

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

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Genes tested

Alport Syndrome Gene Set (3 genes): *COL4A3, COL4A4, COL4A5.*

aHUS/TMA/C3 Glomerulopathy Gene Set (13 genes): *ADAMTS13, C3, CD46, CFB, CFH, CFHR1, CFHR2, CFHR3, CFHR4, CFHR5, CFI, DGKE, THBD; CFHR3-CFHR1* deletion by multiplex ligation-dependent probe amplification (MLPA).

Cystic disease and Nephronopthisis Gene Set (33 genes): *ACE, AGT, AGTR1, AHI1, BBS10, BICC1, CC2D2A, CEP290, CRB2, DNAJB11, EYA1, GANAB, GLIS2, HNF1B, INVS, IQCB1, MUC1, NEK8, NPHP1, NPHP3, NPHP4, PAX2, PKD1, PKD2, PKHD1, REN, RPGRIP1L, SIX5, TMEM67, TTC21B, UMOD, USH2A, XPNPEP3.*

Nephrotic Syndrome and Focal Segmental Glomerulosclerosis Gene Set (52 genes): *ACE, ACTN4, ADCK4 (COQ8B), ANLN, APOL1, ARHGAP24, ARHGDIA, CD2AP, CLCN5, COL4A3, COL4A4, COL4A5, COQ2, COQ6, CRB2, CUBN, EMP2, FAT1, INF2, ITGA3, ITGB4, KANK1, KANK2, KANK4, LAGE3, LAMB2, LMX1B, MAGI2, MEFV, MYH9, MYO1E, NEIL1, NPHS1, NPHS2, NUP10, NUP205, NUP93, OCRL, OSGEP, PDSS2, PLCE1, PTPRO, REN, SCARB2, SMARCAL1, TP53RK, TPRKB, TRPC6, TTC21B, WDR73, WT1, XPO5.*

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). *CFHR3-CFHR1* deletion is detected by MLPA. Reflex send out testing for deletion/duplication analysis via aCGH may be performed for cases negative by NGS (*COL4A5* for Alport panel and *CLCN5, COL4A5, NPHS1, NPHS2* for Cystic panel) or for cases where a single pathogenic variant is detected in a recssive gene.

Results and interpretation

DNA sequence data are analyzed by GPS' clinically validated bioinformatics pipeline to identify and annotate genetic variants associated with a variety of renal diseases.

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 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.

Selected References

Beck L, Bomback AS, et al. KDOQI US Commentary on the 2012 KDIGO Clinical Practice Guideline for Glomerulonephritis. Am J Kidney Dis. 2013;62(3):403-441.

Joshi S, Andersen R, et al. Genetics of steroid-resistant nephrotic syndrome: a review of mutation spectrum and suggested approach for genetic testing. Acta Paediatr. 2013 Sep;102(9):844-56.

Liapis H, Gaut JP. The renal biopsy in the genomic era. Pediatr Nephrol. 2013 Aug;28(8):1207-19.

Savige J, Gregory M, et al. Expert guidelines for the management of Alport syndrome and thin basement membrane nephropathy. J Am Soc Nephrol. 2013 Feb;24(3):364-75.

Fassett RG, Venuthurupalli SK, et al. Biomarkers in chronic kidney disease: a review. Kidney Int. 2011 Oct;80(8):806-21.

Contact us to order a test or for more info

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