

Severe Congenital Neutropenia Gene Set



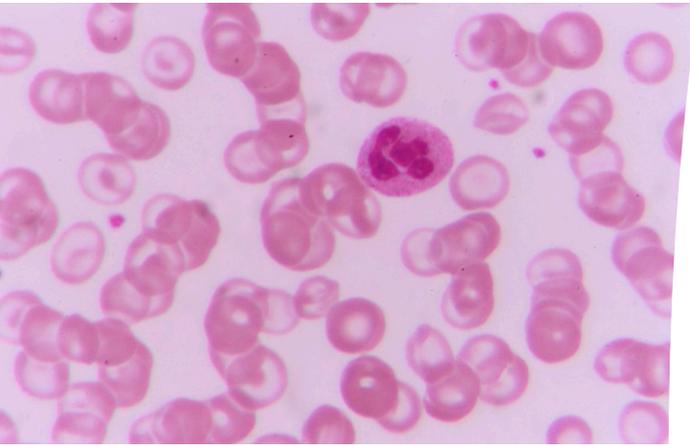
Genomic profiling for congenital neutropenia

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



Maximum information for definitive diagnoses

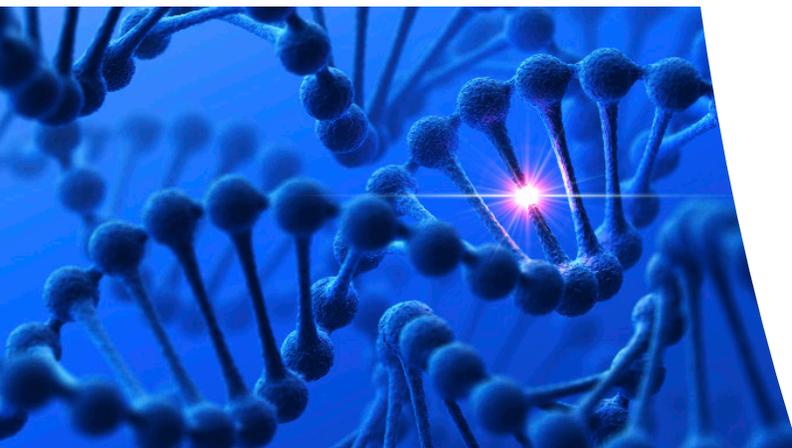
Clinical utility

The SCN Gene Set is designed to identify genetic mutations in individuals with symptoms consistent with Severe Congenital Neutropenia.

Many times, patients present with a variety of related phenotypes making diagnosis challenging. Targeted next-generation sequencing provides clinicians with a powerful tool to analyze multiple genes with clinical relevance to enhance the diagnostic yield of testing.

Identification of a pathogenic mutation can often be used to make a more definitive diagnosis, allowing for more appropriate patient management. It also enables tailored genetic counseling in both the patient and at-risk family members.

Over time, such analyses have the potential for genotype-phenotype correlations to be drawn and may enable disease-specific therapies.



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Indications for testing

Indications for testing include symptoms of congenital neutropenia, a family history of neutropenia, recurrent childhood infection, osteopenia, osteoporosis, childhood leukemia, childhood MDS, recurrent fever, recurrent sinusitis and recurrent gingivitis.

Genes tested

(48 genes): *AK2, AP3B1, ASXL1, CD40LG, CLPB, CSF3R, CXCR2, CXCR4, DNAJC21, DNM2, DOCK2, EFL1, EIF2AK3, ELANE, G6PC3, GATA1, GATA2, GFI1, GINS1, HAX1, IRAK4, JAGN1, KAT6A, KRAS, LAMTOR2, LYST, MYD88, NRAS, PGM3, PSTPIP1, RAB27A, RAC2, RUNX1, SBDS, SLC37A4, SMARCD2, SRP54, STK4, TAZ, TCIRG1, TCN2, TP53, USB1, VPS13B, VPS45, WAS, WDR1* and *WIPF1*.

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). Reflex testing for deletion/duplication analysis via aCGH may occur as a send out post sequencing for negative cases (*AP3B1, GATA2, HAX1, RAB27A, SLC37A4, TAZ, VPS13B, WAS*) or for cases where a single pathogenic variant is detected in a recessive gene.

Results and interpretation

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

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.

Turnaround time

The turnaround time for testing and interpretation of sequencing results is four weeks from the time a specimen arrives. If performed, deletion/duplication analysis may take an additional four weeks.

Specimen requirements

Specimen types accepted include 8 mL peripheral blood in lavender-top EDTA tubes. 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.

Ordering

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

Neutropenia patient registry

For information about the Severe Chronic Neutropenia International Registry (SCNIR) please visit depts.washington.edu/registry or call 1-800-726-4463.

Selected references

Makaryan V., Zeidler C., et al. (2015). "The diversity of mutations and clinical outcomes for ELANE associated neutropenia." *Curr Op Hematol*. 22:3-11.

Hauck, F. and C. Klein (2013). "Pathogenic mechanisms and clinical implications of congenital neutropenia syndromes." *Curr Opin Allergy Clin Immunol* 13(6): 596-606.

Xia, J., A. A. Bolyard, et al. (2009). "Prevalence of mutations in ELANE, GFI1, HAX1, SBDS, WAS and G6PC3 in patients with severe congenital neutropenia." *Br J Haematol* 147(4): 535-542.

Ancliff et al., (2006) Two novel activating mutations in the Wiskott-Aldrich syndrome protein result in congenital neutropenia. *Blood*. 108(7): 2182-2189.

NIH Genetics Home Reference:
ghr.nlm.nih.gov/condition/severe-congenital-neutropenia

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