

## Severe Congenital Neutropenia via *ELANE*, *HAX1*, *G6PC3*, *GFII* and *WAS* Gene Sequencing (Test #445)

**Brief Description of Clinical Features:** Severe Congenital Neutropenia (SCN; OMIM 202700) comprises a heterogeneous group of disorders of myelopoiesis with varying symptoms and patterns of inheritance. SCN is characterized by absolute neutrophil counts (ANC) consistently below 500/ $\mu$ l and severe systemic bacterial infections beginning in early infancy (see Boxer and Newburger *Pediatr Blood Cancer* 49:609-614, 2007). Symptoms include recurrent fevers, sinusitis, gingivitis and other soft tissue infections. SCN is a premalignant condition which can progress to myelodysplastic syndrome and acute myeloblastic leukemia (MDS/AML). The risk of malignancy increases upon G-CSF treatment (Gilman et al. *Blood* 36:576-585, 1970; Freedman et al. *Blood* 96:429-436, 2000; Rosenberg et al. *Blood* 107:4628-4635, 2006).

**Genetics:** Heterozygous mutations in the *ELANE* gene (OMIM 202700) are associated with 35%-63% of SCN cases (Rosenberg et al. 2006; Bellanne-Chantelot et al. *Blood* 103:4119-4125, 2004). Rare cases of autosomal dominant SCN arise from mutations in the *GFII* gene (OMIM 600871). Autosomal recessive forms of SCN have been linked to mutations in the *HAX1* (OMIM 605998) and *G6PC3* (OMIM 611045) genes, and X-linked SCN has been attributed to three different activating mutations in exon 9 of the *WAS* (OMIM 300392) gene. In general, mutations in *ELANE* correlate with a more severe expression of the disease (Bellanne-Chantelot et al. 2004).

**Description of This Particular Test:** This test involves bidirectional, full-gene DNA sequencing of the *ELANE*, *HAX1*, *G6PC3*, and *GFII* genes and exon 9 only of the *WAS* gene plus ~50 bp of flanking non-coding DNA on either side of each exon. The genes will be tested sequentially in the order specified by the client. The default gene order is shown in the following tables. Individual sequencing tests are also available for each gene (Tests #440, 443-446, 447).

**Reference Sequences:**

Gene:	SCN type:	Genomic: NC_	mRNA: NM_	Coding Exons	Protein: NP_	CCDS:
<i>ELANE</i>	Dominant	000019.9	001972.2	5	001963.1	12045.1
<i>GFII</i>	Dominant	000001.10	005263.3	6	005254.2	30773.1
<i>HAX1</i>	Recessive	000001.10	006118.3	7	006109.2	1064.1
<i>G6PC3</i>	Recessive	000017.10	138387.3	6	612396.1	11476.1
<i>WAS</i>	X-linked	000023.10	000377.2	12	000368.1	14303.1

**Indications for Test:** Patients with recurring bacterial infections, a family history of SCN, or neutropenia unrelated to other syndromes (e.g. Chediak-Higashi Syndrome, Hermansky Pudlak Syndrome, or Griscelli Syndrome).

**Sensitivity of Test:** Over 60% of SCN cases are attributed to mutations in *ELANE*, *HAX1*, *G6PC3*, *GFII*, or *WAS* (exon 9).

**Turnaround Time:** Maximum of 60 calendar days, although many tests are completed more rapidly.

**Specimen Requirements:** See page 4 of Requisition Form

**Price: Sequencing of *ELANE*, *GFII*, *HAX1*, *G6PC3*, and *WAS* (exon 9)**

Test	CPT Codes						Total
	83890	83891 x1	83898	83904	83894 x1	83912 x1	
<i>ELANE</i>	\$30	\$40	\$130 (x5)	\$200 (x5)	\$30	\$90	\$520
<i>GFII</i>	\$30	\$40	\$150 (x7)	\$220 (x7)	\$30	\$90	\$560
<i>HAX1</i>	\$30	\$40	\$130 (x5)	\$200 (x5)	\$30	\$90	\$520
<i>G6PC3</i>	\$30	\$40	\$140 (x7)	\$200 (x7)	\$30	\$90	\$530
<i>WAS</i> (exon 9)	\$30	\$40	\$25 (x1)	\$35 (x1)	\$15	\$45	\$190
<b>Full Panel</b>	\$30	\$40	\$640 (x25)	\$950 (x25)	\$80	\$230	\$1970*

\* When three or more of the genes are tested, a 15% discount will apply to the sum of the prices of the individual tests.

**Accreditation:** CLIA ID:52D1027685 (expires 1/18/13) CAP ID:7185561, AU ID:1407125 (expires 12/20/12)

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