

Fanconi Anemia Panel via Sequencing of the *FANCA*, *FANCC* and *FANCG* Genes (Test #720)

Brief Description of Clinical Features: Fanconi Anemia (FA) (OMIM 227650) is characterized by a range of congenital abnormalities, bone marrow failure (aplastic anemia), pancytopenia, and predisposition to cancers (especially acute myelogenous leukemia (AML)). FA is primarily considered a blood disease, but all systems of the body can be affected. Other features commonly observed include radial ray defects (absent thumb or radius), skin pigmentation defects, short stature, microphthalmia, renal and urinary tract defects, genital defects (males), mental retardation, gastrointestinal malformations (atresia), congenital heart disease, and hearing and central nervous system defects (Tischkowitz and Hodgson *J Med Genet* 40:1-10, 2003; Dokal *Baillieres Best Pract Res Clin Haematol* 13:407-425, 2000). About one-third of FA patients have no obvious congenital abnormalities and are diagnosed only after developing hematological problems or after a family member is diagnosed (Giampietro et al. *Am J Med Genet* 68:58-61, 1997). In FA cells, chromosomes are hypersensitive to cross linking agents and highly susceptible to chromosome breakage, a hallmark of FA (Sasaki and Tomomura *Cancer Res* 33:1829-1836, 1973).

Genetics: FA is a genetically heterogeneous autosomal recessive disorder. To date, 14 FA or FA-like genes have been discovered, but ~ 86% of all cases are attributed to mutations in three genes: *FANCA* (OMIM 607139) (~ 60%), *FANCC* (OMIM 227645) (~ 16%), and *FANCG* (OMIM 602956) (~ 10%) (Auerbach *Mutat Res* 668:4-10, 2009). In the United States and Europe, the incidence of FA is around 3 per million and the carrier frequency is between 1 in 600 and 1 in 100 (see <http://www.fanconi.org/>). FA is found in all ethnic groups and appears equally among males and females. There is little genotype-phenotype correlation; even within families a large degree of phenotypic variation exists. However, patients with *FANCA* null mutations, or specific mutations in *FANCC* and *FANCG* often display the most severe phenotypes (Faivre et al. *Blood* 96:4064-4070, 2000).

Description of This Particular Test: This test involves bidirectional DNA sequencing of the *FANCA*, *FANCC*, and *FANCG* genes plus ~50 bp of flanking non-coding DNA on either side of each exon. The genes are tested sequentially in the order specified by the client. Tests for the individual genes are also available (see Test Descriptions by Gene).

Reference Sequences:

Gene:	Exons	Genomic: NC_	mRNA: NM_	Protein: NP_	CCDS:
<i>FANCA</i>	43	000016.9	000135.2	000126.2	32515.1
<i>FANCC</i>	15	000009.11	000136.2	000127.2	35071.1
<i>FANCG</i>	14	000009.11	004629.1	004620.1	6574.1

Indications for Test: Patients with clinical features of FA, individuals with a family history of FA, and patients that develop aplastic anemia at any age even if they present no other physical abnormalities.

Sensitivity of Test: *FANCA*, *FANCC* and *FANCG* pathogenic mutations account for ~ 86% of all FA cases.

Turnaround Time: Maximum of 50 calendar days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Price: Sequencing of *FANCA*, *FANCC* and *FANCG* Genes

Test	CPT Codes						Total
	83890	83891	83898	83904	83894	83912	
<i>FANCA</i>	\$30 (x1)	\$40 (x1)	\$620 (x42)	\$930 (x42)	\$90 (x1)	\$130 (x1)	\$1840
<i>FANCC</i>	\$30 (x1)	\$40 (x1)	\$240 (x14)	\$370 (x14)	\$50 (x1)	\$90 (x1)	\$820
<i>FANCG</i>	\$30 (x1)	\$40 (x1)	\$240 (x14)	\$370 (x14)	\$50 (x1)	\$90 (x1)	\$820
Panel*	\$30 (x1)	\$40 (x1)	\$1000 (x70)	\$1510 (x70)	\$190 (x1)	\$190 (x1)	\$2960*

*When two or three genes in the Panel are tested, the price will be 85% of the sum of the individual gene prices.

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

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