Cincinnati Children's

Cytogenetic Laboratory
Molecular Genetics Laboratory
TTDS Laboratory

Shipping Instructions

Please enclose test requisition with sample. All information must be completed before sample can be processed.

- All samples must be clearly labeled with the patient's name and birth date and initialed by the phlebotomist.
- All samples should be wrapped, cushioned against breakage and sealed in a plastic bag before placement in the shipping container.
- All samples should be sent at room temperature. Do not allow to freeze.
- Samples should be sent by overnight carrier to arrive Monday through Thursday.

Ship to:
Cytogenetics &
Molecular Genetics Laboratory
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229

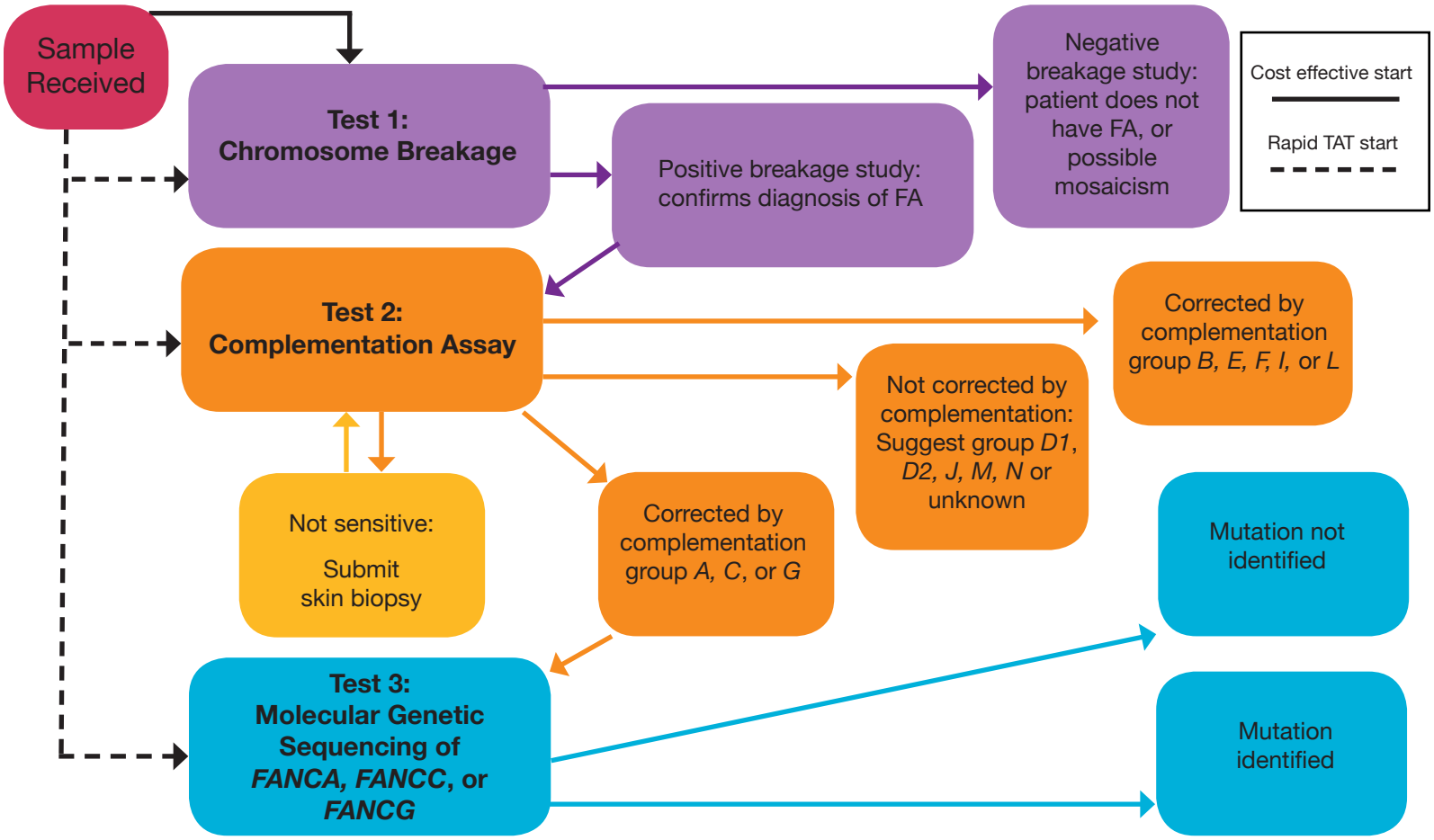
What is Fanconi Anemia?

Fanconi Anemia (FA) is a rare genetic disorder characterized by progressive aplastic anemia and an increased risk of developing various childhood cancers including: rare forms of leukemia, brain tumors, skin cancer, and other solid tumors. The disease can be caused by loss of function in any of at least 16 genes which correlate with 16 different complementation groups. The complementation groups include *A, B, C, D1* (aka *BRCA2*), *D2, E, F, G, I, J, L, M* and *N*. The most commonly reported FA genes are *FANCA, FANCC*, and *FANCG*, which are reported in 85% of patients. FA is usually inherited as an autosomal recessive disorder; however, *FANCB* is X-linked.

Indications:

Genetic testing for Fanconi Anemia is indicated in young patients with aplastic anemia, arm and/or thumb, cardiac, central nervous system, genitourinary, kidney, and/or skeletal system anomalies, hyper-pigmentation, small size, and/or bleeding disorders.

For more information call 513-636-4474



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Tests 1, 2, & 3 can be ordered individually, concurrently or sequentially

Test 1: Chromosome Breakage - When exposed to DNA cross-linkage agents the chromosomes of FA patients will break and form abnormal patterns.

Methodology: Lymphocytes are stimulated and cultured from peripheral blood. Baseline breakage, without a DNA damaging agent, is recorded. Then, DNA damaging agents Mitomycin C(MMC) and Diepoxybutane(DEB) are added and breakage is recorded. Twenty-five baseline metaphase cells and 50 cells each from MMC and DEB culture conditions are evaluated concurrently against a control.

Sensitivity/Specificity: Chromosome breakage in the presence of DEB is the most specific tool when testing for FA and is considered diagnostic.

Turn around: 14 days

Specimen: 5-10mL peripheral blood in sodium-heparin (green-top)

Test 2: Complementation – For patients with FA confirmed by positive DEB/MMC induced chromosome breakage studies, complementation analysis seeks to identify the patient's complementation group.

Methodology: **Tier 1:** Establish Cell line. **Tier 2:** Complementation analysis begins with testing for the most common groups *A*, *C* and *G*. **Tier 3:** If the sample is not complemented with *A*, *C* or *G*, a *FANCD2* Western blot is performed. **Tier 4:** If indicated, testing continues with complementation analysis for groups *E*, *F* and *L* (and *B* for male patients). Complementation analysis for *FANCI* is available for skin fibroblast samples only. A complementation group is identified when drug induced cell cycle arrest is corrected by addition of a specific FA gene vector.

Sensitivity/Specificity: Groups *A*, *C*, *G*, *E*, *F*, *L* and *B* account for 90% of FA patients in the US. Approximately 15-20% of cell lines derived from the blood of patients with FA are not sensitive to Melphalan and will not yield complementation results (skin biopsy may be required). In this lab, a complementation group has been identified in >60% of viable, sensitive cell lines.

Turn around: If tiers 2 through 4 are done sequentially, TAT is 3-6 months for groups *A*, *C*, and *G* (85%) or approximately a year for groups *E*, *F*, *L* and *B*. **If tiers are done concurrently, total TAT is 6-9 months.**

Specimen: 3ml of peripheral blood collected in ACD (yellow top tube. Fresh sample may be needed for reflex.) OR skin biopsy OR EBV transformed lymphoblastic cell line OR primary fibroblast cell line.

Test 3: Molecular – For patients with positive complementation analysis for *FANCA, FANCC*, or *FANCG,* sequencing is used to find the specific mutations. Carrier detection for patients with a family history of FA, prenatal diagnosis of an at-risk fetus and pre-implantation genetic diagnosis are also possible.

Methodology: Testing is performed by PCR-based sequencing of the entire coding regions and intron/exon boundaries of the *FANCA, FANCC*, or *FANCG* genes. If preceded by complementation analysis, only the indicated gene is sequenced. If ordering molecular testing only, testing can be done sequentially or concurrently . Targeted analysis for the *FANCC* common IVS4+4 A>T mutation is available for patients of Ashkenazi Jewish descent.

Sensitivity: DNA sequencing is over 99% sensitive for the detection of nucleotide base changes, small deletions, and insertions in the regions analyzed. 85% of individuals with FA have mutations in one of these three genes.

Turn around: 4 weeks for *FANCC/FANCG*, 6 weeks for *FANCA.* **Each gene can be run individually, concurrently or sequentially.**

Specimen: 3mL whole blood in EDTA (lavender top tube). Cytobrushes are required for analysis in patients who have undergone bone marrow transplantation. Other sample types may be acceptable; please call 513-636-4474 for additional information.

Please call 1-866-450-4198 with any billing or CPT questions.