

# Chromosome Breakage Analysis—Fanconi Anemia

*FOR THE IDENTIFICATION OF CHROMOSOME BREAKAGE AND RADIAL FIGURES, THE HALLMARK FEATURES OF FANCONI ANEMIA-RELATED CHROMOSOME BREAKAGE REPAIR DEFICIT*

## Test Highlights

Fanconi anemia (FA) is a clinically and genetically heterogeneous disease caused by mutations in one of 15 different genes involved in DNA repair. Regardless of disease severity, the hallmark feature of FA is the presence of chromosome breakage.

### Clinical Background

- FA is characterized by growth retardation, physical malformations, and hematological disorders.
- FA is associated with defects in DNA repair caused by mutations in at least 15 different genes: *BRCA2*, *BRIPI*, *FANCA*, *FANCB*, *FANCC*, *FANCD2*, *FANCE*, *FANCF*, *FANCG*, *FANCI*, *FANCL*, *FANCM*, *PALB2*, *RAD51C*, and *SLX4*.
- An increased rate of spontaneous chromosomal breakage is observed in cells from affected persons after exposure to clastogenic agents.

### Disease Overview

- Most patients (60% to 75%) with FA have one or more characteristic physical abnormalities, including malformations of the thumbs, forearms, eyes, ears, heart, and kidneys. In addition, they often have short stature and pigmentary changes.
- Bone marrow failure resulting in anemia, pancytopenia, thrombocytopenia, or leucopenia usually occurs before age 10.
- Cancer is common in affected individuals.

### Epidemiology

- The incidence of FA in all populations is approximately one in 360,000 births, with a carrier frequency of one in 300.
- Approximately one in 89 persons of Ashkenazi Jewish heritage is a carrier of a mutation in *FANCC*.
- Other populations, such as Spanish Gypsy and black South African, have an increased carrier risk of approximately one in 100.

### Genetics

- 15 different known complementation groups
- Most are inherited in an autosomal recessive manner
- *FANCB* is inherited in an X-linked recessive manner

### Indications for Ordering

- Test is appropriate for patients with:
  - Characteristic physical anomalies
  - Progressive bone marrow failure
  - Adult-onset aplastic anemia with red cell macrocytosis and elevated hemoglobin F levels
  - Solid tumors presenting at an atypically young age and in the absence of other risk factors
  - Unusually toxic reactions to chemotherapy or radiation
- As 25% to 40% of affected individuals have no physical abnormalities, testing is recommended for asymptomatic siblings of an affected individual or asymptomatic offspring of known carriers.

### Additional Ordering Notes:

Test is performed by the Stanford Hospitals and Clinics Cytogenetics Laboratory.

### Interpretation

- Results are reported as the number of cells with radial figures.
- The average number of breaks per cell (in cells without radials) is also reported.
- Mitomycin-C (MMC) culture: interpreted relative to a normal control.
- Diepoxybutane (DEB) culture: interpreted relative to established DEB breakage rates.
- Negative: absent radial figures and <0.5 breaks/cell.
- Positive: multiple radials and >1.0 breaks/cell.
- Ambiguous: few or no radials and 0.5–1.0 breaks/cell.

### Limitations

Carriers cannot be detected by this test.

### Methodology

- Stimulated culture with clastogenic stress, unbanded breakage analysis.

- Peripheral blood is cultured with a T-cell mitogen, phytohemagglutinin, in the presence and absence of DEB and MMC, bifunctional DNA interstrand cross-linking agents.
- A total of 50 cells in metaphase from both cultures are scored and analyzed for chromosomal breakage as well as the formation of radials.

### Related Test

Chromosome Analysis – Breakage, Ataxia Telangiectasia, Whole Blood ([2005749](#))

### References

1. Auerbach AD. Fanconi anemia diagnosis and the diepoxybutane (DEB) test. *Exp Hematol.* 1993;21:731–3.
2. Cervenka J, et al. Mitomycin C test for diagnostic differentiation of idiopathic aplastic anemia and Fanconi anemia. *Pediatrics.* 1981;67:119–27.
3. Cohen, MM, et al. The identification of Fanconi anemia genotypes by clastogenic stress. *Am J Hum Genet.* 1982;34:794–810.

### Test Information

**0097688**      **Chromosome Analysis, Breakage Syndrome Analysis**

For specific collection, transport, and testing information, refer to the ARUP website at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).

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