

# Chromosome Analysis— Breakage, Ataxia Telangiectasia, Whole Blood

## *TO DETECT AN INCREASED RATE OF CHROMOSOMAL BREAKAGE OR REARRANGEMENT IN INDIVIDUALS WITH ATAXIA TELANGIECTASIA*

### Test Highlights

Chromosomal breakage syndromes, such as ataxia telangiectasia (AT), are caused by defects in DNA repair genes. When the chromosomes of these individuals are analyzed under specific conditions, chromosomal breakage and/or rearrangements are observed at rates above those of controls.

### Clinical Background

- AT is characterized by truncal ataxia, oculocutaneous telangiectasia, severely depleted levels of intracellular ATM protein, elevated serum alpha-fetoprotein concentrations, immunodeficiency, radiosensitivity, and increased rates of malignancy (usually leukemia or lymphoma).
- AT is an autosomal recessive disorder that is associated with defects in DNA repair caused by mutations in the *ATM* gene at 11q22.3.
- An increased rate of chromosomal breakage is observed in chromosomes of affected persons.

### Disease Overview

- Patients with classic AT develop progressive cerebellar dysfunction between one and four years of age.
- Acquired chromosome abnormalities involving 2p12, 7p13, 7q34, 14q11.2, 14q32, 22q11.2, and 22q13.2 are commonly seen.
- Cancer risk is approximately 35%–40% in affected individuals. Lymphoma and leukemia are most commonly seen in children. However, an increased risk for solid tumors in older affected individuals has been observed.
- Cancer risk, especially for breast cancer, in carriers of an AT mutation is increased four times over that of the general population.
- Non-classic AT includes adult-onset AT and AT with early-onset dystonia.

### Epidemiology

The incidence of AT in the United States is approximately 1/40,000 to 1/100,000 live births.

### Indications for Ordering

- Individuals who present with characteristic neurological anomalies

- Asymptomatic siblings of an affected individual or asymptomatic offspring of known carriers
- Children under age five years with malignancy should be evaluated for AT before starting chemotherapy or radiotherapy, since conventional doses of either can be fatal in affected individuals.

### Additional Ordering Notes

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

### Interpretation

- Results are reported as the average number of rearrangements per cell.
- Results include number of cells with rearrangement of common AT loci.

### Limitations

- Carriers cannot be detected by this test.
- A normal result does not rule out a diagnosis of AT.

### Methodology

- Peripheral blood is cultured for 72 hours, stimulated with phytohemagglutinin (PHA), and stained to identify the chromosome banding pattern.
- A total of 50 cells in metaphase are scored and analyzed for chromosomal breakage. Results are compared with those from a normal control.

### Related Test

Chromosome Analysis, Breakage Syndrome Analysis (0097688)

## References

1. Lavin MF. Ataxia-telangiectasia: from a rare disorder to a paradigm for cell signaling and cancer. *Nat Rev Mol Cell Biol.* 2008;9:759–769.
2. Porcedda P, et al. Impaired elimination of DNA double strand break-containing lymphocytes in ataxia telangiectasia and Nijmegen breakage syndrome. *DNA Repair.* 2006;5(8):904–913.
3. Concannon P. ATM heterozygosity and cancer risk. *Nat Genet.* 2002;32:89–90.
4. Geoffroy-Perez B, et al. Cancer risk in heterozygotes for ataxia-telangiectasia. *Int J Cancer.* 2001;93:288–293.

## Test Information

### 2005749 Chromosome Analysis, Breakage, Ataxia Telangiectasia, Whole Blood

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).

## AUTHORS

Danielle LaGrave, MS, CGC

Sarah South, PhD