

## X-Chromosome Inactivation Studies

---

### DESCRIPTION

- Random inactivation of most genes on one X chromosome early in female development normally achieves dosage compensation between the single X chromosome in males and the two copies in females.
- This test determines the percentage methylation (inactivation) of the two X chromosomes relative to each other. If the results show non-random inactivation, the parent of origin of the active X cannot be determined without samples from the patient's parents.

### REASONS FOR REFERRAL:

- Testing is helpful in assessing females with sex-linked recessive disorders (e.g., Duchenne muscular dystrophy) who may manifest symptoms due to non-random X inactivation. Female carriers of a variety of X-linked disorders, especially those involving immune function (e.g. SCIDS), have been shown to have non-random X inactivation, as have carriers in some X-linked mental retardation families.

### METHOD OF ANALYSIS:

- DNA from the patient is amplified by PCR and analyzed by high-resolution gel electrophoresis in a laser-induced fluorescence capillary electrophoresis system with internal standard. The androgen receptor (AR) locus is evaluated because it is polymorphic for the number of CAG repeats (over 90% of the female population has two different alleles). Inactivation is assessed by predigestion of the sample with an enzyme sensitive to methylation, followed by PCR and quantitative analysis of the AR allele ratios (Allen et al., *Am J Hum Genet*, 1992, 51:1229-1239).
- Results are reported within 3 weeks or less of receipt of sample.

### REFERENCE RANGES:

- Females show results ranging from 100% non-random (only one allele amplifies) to random inactivation (equal amplification of the 2 alleles). Skewed X-inactivation occurs when allele peak ratios after digestion are 80:20, ratios of 90:10 or more are considered extreme skewing.
- If the patient is homozygous at the AR locus, the study is inconclusive.

### SAMPLE REQUIREMENTS:

- For DNA testing, 5 to 10 milliliters of blood (minimum 1 ml) in EDTA (purple top) tubes should be sent by overnight carrier at room temperature.
- Prenatal testing: Please contact the laboratory.

### TEST CPT CODES:

CPT 83891 DNA extraction  
CPT 83892 DNA enzymatic digestion X 2  
CPT 83894 DNA separation X 2  
CPT 83898 DNA amplification  
CPT 83912 DNA interpretation and report

*Discounts from list price are available for institutional billing under contractual arrangement with the laboratory. Contact Ellen Livers at 800-447-6614 ext 7523.*