2006352 X-Chromosome Inactivation Analysis XCI

Interpretive Data:
Characteristics: Females usually have two copies of the X-chromosome, one of which becomes randomly inactivated early in embryonic development in a process known as lyonization. If either the paternally or maternally derived X-chromosome is preferentially inactivated, this results in a non-random or "skewed" pattern of X-chromosome inactivation (XCI). The pattern of XCI may vary among tissue types. XCI ratios of 50:50 to 79:21 may suggest random XCI, ratios of 80:20 to 100:0 suggest non-random XCI.
Cause: Non-random XCI may result by chance or from secondary cell selection in females who are heterozygous for X-chromosome rearrangements, carriers of pathogenic variants in X-linked genes, or affected with neoplastic disease.
Gene Tested: The androgen receptor (*AR*) gene on the X chromosome.
Clinical Sensitivity: Approximately 90 percent. An estimated 10-15 percent of females have skewed X-inactivation by chance. However, skewed XCI may be seen more frequently with increasing age.
Methodology: Methylation-sensitive restriction digest followed by PCR and fragment analysis.
Limitations: Testing is limited to XX females only. This assay will be uninformative in up to 20 percent of females due to homozygosity for the polymorphic *AR* gene locus analyzed. XCI patterns may differ among tissues; therefore, the XCI ratio reported is for the tissue type tested with a standard deviation 0.09 in random XCI; 0.06 in non-random XCI. Although this test will detect the methylation status of the X-chromosomes, it will not determine if the X inactivation pattern is associated with rearrangements of the X chromosome, pathogenic variants in X-linked genes or neoplastic disease. If a non-random XCI pattern is present, the parent of origin of the active X cannot be determined without testing parental samples. XCI ratios should not be used to predict prognosis for female carriers of X-linked disorders as variable expressivity may result due to other genetic or environmental modifiers. Because the level of XCI may differ in prenatal specimens and whole blood, this test is not recommended for prenatal diagnosis. Diagnostic errors can occur due to rare sequence variations.

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