MOUNT SINAI SCHOOL OF MEDICINE

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ESCO2 Testing in Roberts Syndrome

Clinical features:

Roberts syndrome is characterized by pre- and postnatal growth retardation, microcephaly, bilateral cleft lip and palate, and symmetric limb reduction. Mental retardation is reported in the majority of affected individuals and mortality is high among most of the severely affected fetuses and newborns.

Inheritance:

Roberts syndrome is a genetic disorder that has autosomal recessive inheritance, meaning that the risk to children born to two carrier parents is 25%.

Prevalence:

Roberts syndrome is rare; no accurate estimates of prevalence have been published. Carrier frequency is also unknown. Approximately 150 individuals of diverse racial and ethnic backgrounds have been reported. Parental consanguinity is common.

Reasons for referral:

1. Confirmation of a clinical diagnosis
2. Carrier testing of parents who have had a child affected with Roberts syndrome
3. Prenatal diagnosis

Test methodologies:

The diagnosis of Roberts syndrome typically relies upon cytogenetic testing of cells from the peripheral blood of individuals with suggestive clinical findings; however, mutations in the gene, *ESCO2*, have been identified in all Roberts syndrome patients tested. To perform mutation analysis, a blood sample is drawn (about 1 tablespoon) and DNA is obtained from the white blood cells. Next, the DNA sequence of the coding regions (exons 2-11) of the Roberts syndrome disease gene, *ESCO2*, is read and compared to that of the normal sequence. Prenatal testing is possible, if both parental mutations have been identified.

Test sensitivity and specificity:

The overall ability of this test to find an *ESCO2* mutation, if there is one, is ~98%. Different and variable mutations in *ESCO2* have been reported in families with Roberts syndrome. The abnormalities thus far reported in *ESCO2* are predicted to lead to loss of function, truncation of the protein, or a single amino acid change. If two previously reported mutations are detected, the diagnosis of Roberts syndrome is confirmed. To date, no other phenotypes (clinical manifestations) have been associated with mutations in *ESCO2*. There is a possibility of obtaining an inconclusive result. If a change is found that has not been reported before, it will be evaluated in the context of all findings, including what the predicted effect on the protein is, cytogenetic findings and what the change is, if any, on the other chromosome.