Clinical Features:
Roberts syndrome (RBS) [OMIM #268300], also known as Roberts-SC phocomelia syndrome [OMIM #269000], is characterized by pre- and postnatal growth retardation, mental retardation, limb (tetraphocomelia or hypomelia) and hand malformations (oligodactyly, syndactyly, or clinodactyly), and craniofacial abnormalities (lip/palate clefting, micrognathia, hypertelorism, exophtalmos, down-slanting palpebral fissures, and ear malformations). Less common findings are cardiovascular, renal, gastrointestinal, splenogonadal, and genital abnormalities. Neoplasms, nerve paralysis, Moya-Moya disease, and stroke are seen only rarely. Severity varies even within families, ranging from spontaneous abortions or stillbirths in severe cases to no intellectual impairment in milder ones (1).

Molecular Genetics and Cytogenetics:
At the cytogenetic level, RBS cells exhibit premature separation of centromeres (PCS) and ‘puffing’ of other heterochromatic regions, resulting in a railroad track appearance of most chromosomes (1). Although its underlying etiology is still being debated (2, 3), PCS has been linked to mutations in the ESCO2 (establishment of cohesion 1 homolog 2) (4). ESCO2 is a member of the conserved Eco1/Ctf7 family of acetyltransferases involved in the establishment of cohesion between sister chromatids and in double-stranded DNA repair (4).

The ESCO2 gene [OMIM#609353] maps to chromosome 8p21.1. Its genomic DNA is 30.3 kbps in length and includes 11 exons (4). Out of 26 ESCO2 mutations reported to date, 88% lead to premature stop codons within the acetyltransferase domain located in the C-terminal end of ESCO2 (2). About 46% of identified mutations occur in exon 3, which represents 45% of the entire coding sequence of ESCO2 and harbors two repeat length mutational hotspots 23 and 21 nucleotides in length (2). No clear genotype-phenotype correlations have been reported. Cellular and cytogenetic phenotypes do not appear to differ between missense and other types of mutations.

Inheritance & Epidemiology:
RBS is a rare autosomal recessive condition reported in about 100 cases worldwide (1). With each pregnancy, parents of an affected child have a 25% chance of having another child with RBS, a 50% chance of having a carrier of one of ESCO2 mutation, and a 25% chance of having a non-carrier. Ethnic bias has not been reported. Penetrance appears to be complete (1, 2, 4).

Test methods:
We offer mutation analysis of all 10 coding exons and intron/exon boundaries of ESCO2 by direct sequencing of amplification products in both the forward and reverse directions. We also offer deletion/duplication analysis of the ESCO2 gene by oligonucleotide array-CGH to identify copy number changes involving one or more exons. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by this methodology. Array-CGH will not detect low level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory.

ESCO2 sequencing analysis
Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $1000
CPT codes: 81405
Turn-around time: 4 weeks
**ESCO2 deletion/duplication analysis**

Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube

Cost: $1000

CPT codes: 81404

Turn-around time: 4 weeks

**Results:**

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

**References:**


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**Committed to CUSTOMIZED DIAGNOSTICS, TRANSLATIONAL RESEARCH & YOUR PATIENTS’ NEEDS**