

## Costello Syndrome via *HRAS* gene testing

Costello Syndrome is a multiple congenital anomaly and mental retardation syndrome that overlaps phenotypically with Noonan Syndrome and with Cardio-Facio-Cutaneous Syndrome. Symptoms include short stature, curly hair, thick and loose skin of the hands and feet, papillomata around the nose and mouth, mental retardation, cardiomyopathy, and benign tumors. Aoki et al. (*Nature Genetics*, 37:1038-1040, 2005) found heterozygous, *de novo* mutations in the *HRAS* gene in 12 of 13 Costello Syndrome patients. The mutations were all located in either codon 12 or 13 of exon 2. In a second publication, Gripp, et al., (*Am.J.Med.Genet. Epub* 2005.) demonstrated *de novo* exon 2 mutations and 33 out of 40 Costello Syndrome patients with the mutations again located in either codon 12 or 13. No causative mutations were found by either group elsewhere in the *HRAS* gene

The coding region for *HRAS* is entirely contained within four exons (exons 2, 3, 4 and 6). Clinical testing for causative *HRAS* mutations is done at PreventionGenetics by sequencing exon 2. There is currently no evidence clinically that causative mutations occur elsewhere in the gene. PreventionGenetics will also sequence exons 3, 4 and 6 on a research basis only if specifically requested. Our test involves the complete sequencing in both directions of the coding region of these exons plus additional non-coding, flanking DNA. Turn around time for our test is generally less than 2 weeks.

### Specimen Requirements

- Collect 2-5 ml of whole blood in EDTA (purple top tube) or ACD (yellow top tube). 5 ml is the preferred volume.
- Only one blood tube is required for multiple tests.
- Ship whole blood specimens at room temperature.
- Do not freeze blood.
- During hot weather, include a frozen ice pack in the shipping container. Do not allow the ice pack to come in direct contact with the specimen tube.
- In cold weather, include an unfrozen ice pack to help moderate extremes in temperature. The DNA in whole blood is stable for at least 48 hours at 21°C, 5-7 days at 4°C.

### Sequence analysis of Costello Syndrome via *HRAS* gene exon 2 testing

**\$230.00**

Molec Diag, Ascertainment	83890
Molec Diag, Isolation	83891
Molecular Diag, Amplif	83898
Mutat Id By Seq, Seg	83904
Molecular Diag, Separation	83894
Interpretation And Report	83912

Sequence analysis of the *HRAS* gene exons 3, 4, and 6 is available on a research basis only.  
Please contact PreventionGenetics for additional information concerning research testing.

**Accreditation Info. CLIA ID #: 52D1027685** (expires 1/18/07) (CAP#: 7185561, AU ID: 1407125 expires 12/20/06)

### Ship to:

Attn: Diagnostics Lab  
PreventionGenetics LLC  
3700 Downwind Drive  
Marshfield, WI 54449 USA  
Phone: 715-387-0484

### Contact for info:

Dr. Eric W. Johnson  
Director, Molecular Diagnostics and BioBanking  
715-387-0484  
clinicaltesting@preventiongenetics.com  
FAX: 715-384-3661