impact genetics inc.
advancing genetic diagnostics

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Patient name:	--	**Referring specialist:**	--
		Contact person:	--
Date of birth:			
Medical record #:		**Institution:**	--
			Address:
Patient status:	*Confirmed clinical diagnosis*		*Fax:*
Family history:	*Positive family history*		
Date of report:			
Family #:			
Patient #:		**Copies to:**	*Name*
			Fax:

Test requested: *Hereditary Hemorrhagic Telangiectasia (HHT) genetic test - proband*

Test results

The patient's mutation has been identified.

Gene	Result
ENG	c.63delC (p.Thr22fs)
Methods Used: Multiplex ligation-dependent probe amplification (MLPA) and sequence analysis	

Interpretation

- This patient is affected with hereditary hemorrhagic telangiectasia (HHT), specifically with HHT type 1.
- Sequence analysis of this patient's blood sample identified a heterozygous deletion mutation, c.63delC (p.Thr22fs), in exon 1 of the *ENG* gene. This mutation is highly likely to cause HHT. The mutation is predicted to causes a frameshift in the protein sequence, leading to the formation of a premature termination codon and truncation of the ENG protein.

Guidance and recommendations

- We recommend that all reports be reviewed with a genetic counselor.
- The risk of inheriting this mutation is 50% for each of this patient's children. Any person who inherits this mutation is likely to develop HHT; a child who does not inherit the mutation has only the general population risk (1/8,000).
- Genetic testing for this mutation can be offered to this patient's children and any additional at risk relatives.

These results and the interpretation, including guidance and supplemental information, were reviewed and approved by:

Electronically signed by Hilary Racher, PHD FCCMG DABMGG, Laboratory Director, on MMM DD, YYYY at <time>
Electronically signed by Brenda Gallie, MD FRCSC, Medical Director, on MMM DD, YYYY at <time>

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--name--, --institution--, --city--

Details of Samples Tested

Patient Sample	Sample #	Collected	Received	Authorized/Test Started
Blood	##-####	MMM DD, YYYY	MMM DD, YYYY	MMM DD, YYYY

Supplemental Information

Test Methods (not all samples employ every method)**:**

- Sequence analysis of the entire coding region and flanking intronic regions for each exon of *ENG* (including a portion of the 5'UTR) and *ACVRL1*; and for exons 8–11 of *SMAD4*
- Gross deletion/duplication analysis was performed using quantitative multiplex PCR (QM-PCR) or multiplex ligation-dependent probe amplification (MLPA, SALSA MLPA P093-C1 HHT/PPH1 MRC Holland).
- Reverse-transcriptase PCR RNA analysis where indicated

Test method analytic sensitivity and specificity: As of Jan 27, 2017, Impact Genetics has identified definitive mutations for 89.7% of over 336 HHT families referred by clinicians, excluding individuals who exhibit less than three Curaçao criteria, and for whom no mutation was found.

Whenever possible, Impact Genetics banks DNA and RNA for future tests when a causative mutation is not found. Outside of human error, our mutation detection strategy shows 100% specificity.

Reporting: Non-pathogenic (benign) variants may not be included on reports but are available upon request. Classification of DNA variants may change over time as new information becomes available and where possible, reports will be re-issued if appropriate.

Test method limitations: Very low level mosaic mutation carriers may not be detected by our methods. Our methods can detect mutant levels as low as 12.5% mutant DNA for most mutation types. Most translocations or gross intronic re-arrangements cannot be detected by our methods. Deep intronic splice mutations cannot be detected by conventional DNA analysis, but may be detected by analysis of the mRNA transcript by reverse-transcriptase PCR using a fresh blood sample.

Notation: Mutations are described using HGVS (ver. 2.0) guidelines using the RefSeq accession # NM_000118.3 (*ENG*), NM_000020.2 *(ACVRL1*) and NM_005359.5 (*SMAD4*). For coding DNA sequences, the A of the ATG initiator codon is denoted as nucleotide 1.

General disclaimer: This test was developed and its performance characteristics determined by Impact Genetics. It has not been cleared or approved by the Food and Drug Administration. Each of Impact Genetics' molecular tests use a direct method of mutation detection and analysis is based on current knowledge of the genes. Characterization of a mutation in a family does not preclude the remote possibility that a second, unidentified mutation occurs in an individual patient. Moreover, it is possible for two relatives to have different gene mutations.

Additional Information for clinicians and patients regarding the test performed and hereditary hemorrhagic telangiectasia is available at impactgenetics.com.