BMP9-Related Telangiectasia Syndrome

Indications for Ordering

Diagnostic test for individuals suspected to have a telangiectasia syndrome

Test Description

Bidirectional sequencing of entire coding region and intron/exon boundaries of *BMP9/GDF2* gene

Tests to Consider

Primary Test

Telangiectasia Syndrome (*BMP9/GDF2*) Sequencing 2010015

- Diagnostic test for individuals suspected to have a telangiectasia syndrome in the absence of pathogenic variants in the *ACVRL1*, *ENG*, or *SMAD4* gene

Related Tests

Hereditary Hemorrhagic Telangiectasia (HHT) Panel, Sequencing and Deletion/Duplication 2009337

- Most comprehensive test to diagnosis a telangiectasia/arteriovenous malformation (AVM) disorder

RASA1-Related Disorders (*RASA1*) Sequencing and Deletion/Duplication 2007852

- Appropriate test for individuals with cutaneous capillary malformations, with or without telangiectasia and arteriovenous malformations

Familial Mutation, Targeted Sequencing 2001961

- Useful when a familial variant identifiable by sequencing is known

Disease Overview

Prevalence: ~1/5,000-10,000 for hereditary hemorrhagic telangiectasia (HHT)

- *BMP9*-related disorder: 1-2% of individuals with HHT

Symptoms

- Cutaneous telangiectasia located on face, mouth, hands, limbs and/or trunk
- Recurrent nosebleeds
- Solid organ arteriovenous malformations: unknown occurrence/incidence

Genetics

Gene: *BMP9*/*GDF2*

Inheritance: autosomal dominant

Function

- Encodes for protein called bone morphogenetic protein 9
- Involved in a common transforming growth factor-beta (TGFB)-signaling pathway with hereditary hemorrhagic telangiectasia genes *ACVRL1*, *ENG*, and *SMAD4*

Test Interpretation

Sensitivity/Specificity

- Clinical sensitivity: ~1-2% of individuals suspected to have a telangiectasia syndrome in the absence of a pathogenic variant in *ACVRL1*, *ENG*, or *SMAD4* are expected to have a *BMP9* variant
- Analytical sensitivity/specificity: 99%

Results

- Positive: pathogenic variant detected
  - Cause of telangiectasia syndrome identified
- Negative: no pathogenic variant detected
  - No etiology for telangiectasia identified
- Inconclusive: novel variant of uncertain clinical significance may be identified

Limitations

- Not detected:
  - Large deletions/duplications
  - Deep intronic variants
  - Regulatory region variants
- Diagnostic errors can occur due to rare sequence variations.
- Variants in other genes associated with telangiectasia syndromes will not be tested.