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 mutations in the *ACVRL1, ENG,* or *SMAD4* gene

Related tests

Hereditary Hemorrhagic Telangiectasia (HHT) Panel, Sequencing Deletion/Duplication, 5 Genes 2009337

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

Hereditary Hemorrhagic Telangiectasia (*ACVRL1* and *ENG*) Sequencing and Deletion/Duplication with Reflex to Juvenile Polyposis (*SMAD4*) Sequencing and Deletion/Duplication 2009008

- Appropriate initial test for individuals with telangiectases clustered on face, hands, and mouth
  - In conjunction with recurrent nosebleeds
  - With or without internal arteriovenous malformations

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 mutation 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 mutation in *ACVRL1, ENG,* or *SMAD4* are expected to have a *BMP9* mutation
- Analytical sensitivity/specificity – 99%

Results

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

Limitations

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