

Using Genetic Testing for Diagnosis of Loeys-Dietz Syndrome (LDS)

Indications:

- Clinical diagnosis or family history of LDS
- Clinical symptoms consistent with Marfan Syndrome, but in absence of ectopia lentis and after exclusion of *FBN1* mutations
- Clinical symptoms consistent with vascular Ehlers-Danlos Syndrome, after exclusion of *COL3A1* mutations

Benefits:

Genetic testing for LDS-related *TGFBR1* or *TGFBR2* mutations can:

- confirm a clinical diagnosis of LDS and identify the familial mutation
- help to distinguish LDS from Marfan Syndrome, to indicate
 - the need for surgical intervention at an earlier age and/or a smaller degree of aortic dilation than recommended for Marfan patients.
 - an increased risk of arterial aneurysms away from the aortic root
- help to distinguish LDS from vascular Ehlers-Danlos Syndrome, to guide the use of prophylactic surgery, which is recommended for LDS, but not for vascular Ehlers-Danlos Syndrome
- allow targeted genetic family testing (once the familial mutation is known),
 - to identify pre-symptomatic mutation carriers who should take preventative measures and undergo regular monitoring for symptoms of aortic dilation
 - to exclude a highly increased risk of LDS in pre-symptomatic family members who do not carry the familial mutation

Background:

- Loeys-Dietz syndrome (LDS) is a systemic connective tissue disorder with cardiovascular, skeletal, and cutaneous manifestations that shows clinical overlap with Marfan Syndrome and/or vascular Ehlers-Danlos Syndrome.
- LDS is caused by mutations in the genes *TGFBR1* (25%) or *TGFBR2* (75%).
- Morbidity and mortality in LDS are largely due to complications from aortic aneurysms and dissections and can be reduced by surgical intervention.
- Aortic aneurysms associated with LDS are typically more aggressive than those associated with Marfan Syndrome and can lead to dissection and/or rupture at an earlier age and a smaller degree of dilation.
- Arterial aneurysms associated with LDS are not limited to the aortic root and may not be detectable by echocardiography alone.
- LDS is associated with a high risk of pregnancy related complications, including uterine rupture.

References: 1. Loeys BL et al (2006) N Engl J Med 355:788. 2. Aalberts JJJ et al (2008) Neth Heart J 16:299. 3. Loeys, BL, Dietz HC. GeneReviews, <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=loeys-dietz>, accessed 06/14/09

Ordering Information: Please see other side.

Ordering Information for Loeys-Dietz Syndrome (LDS) Testing

Indications for Testing

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Ordering Information for Single Gene Tests

Gene(s)	Test Code
<i>TGFBR1</i>	190602
<i>TGFBR2</i>	190603

Ordering Information for Multi-Gene Panels*

<i>TGFBR1, TGFBR2</i>	190698
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Family Testing (single amplicon)

Family Testing is available for both genes. Please contact Client Services at 1-866-647-0735 for requirements.

Test Methodology

- Amplification by polymerase chain reaction (PCR); sequencing of entire protein-coding region

NOTE: Specimens must be accompanied by a completed consent form. In the case of family tests (ie, known mutations), a copy of the result of the first patient tested in the family (the index case) must be submitted unless that test was performed at Correlagen. Other family members are subsequently tested for the specific mutation found in the first patient tested.

For test information, sample requirements, or to request a sample shipping kit, please contact Client Services at 1-866-647-0735 or visit us on the web at www.correlagen.com.