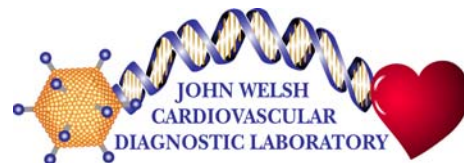


TGFBR2 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR
DIAGNOSTIC LABORATORY



Transforming growth factor-beta receptor type 2 (*TGFBR2*), which is composed of 7 exons and is located at 3p22, encodes a member of the serine/threonine protein kinase family and the TGF-beta receptor subfamily. The encoded protein is a transmembrane protein that has a protein kinase domain, forms a heterodimeric complex with type I TGF-beta receptor protein, and binds TGF-beta.

Multiple mutations in *TGFBR2* have been associated with Loeys-Dietz syndrome (LDS), which is characterized by hypertelorism, bifid uvula and/or cleft palate, and generalized arterial tortuosity with ascending aortic aneurysm and dissection. Other findings in multiple systems included craniosynostosis, structural brain abnormalities, mental retardation, congenital heart disease, and aneurysms with dissection throughout the arterial tree. Two types of LDS are distinguished: typical LDS (LDS type I) and probands presenting with vascular Ehlers-Danlos syndrome (LDS type II). *TGFBR2* mutations have also been identified in patients with Marfan syndrome type II (MFS2) and familial thoracic aortic aneurysm 3 (AAT3/TAAD2). Mutations in *TGFBR2* have been noted to demonstrate autosomal dominant inheritance with a variable clinical expression. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for *TGFBR2* mutations. Individuals will be tested by automatic fluorescent DNA sequencing of all 7 exons and 2 alternatively spliced exons 1A and 3A of the *TGFBR2* gene. Genetic counseling is recommended for all individuals in order to identify additional at-risk family members and to discuss reproductive issues.

REASONS FOR REFERRAL

- Molecular confirmation of the diagnosis of Loeys-Dietz syndrome, Marfan syndrome type II, or familial thoracic aortic aneurysm 3

METHODOLOGY

Genomic DNA will be analyzed for *TGFBR2* mutations by automatic fluorescent DNA sequencing of all 7 exons and 2 alternatively spliced exons 1A and 3A of the *TGFBR2* gene, as well as the exon/intron junctions and a portion of the 5' and 3' untranslated regions. Patient DNA will be sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members will be analyzed only for the familial mutation(s) by automatic fluorescent DNA sequencing.

SERVICE FEES

	<i>Direct and Institutional Billing</i>	<i>CPT Codes</i>
Index Case (Full Gene)	\$600 per sample	83891, 83898x10, 83904x20, 83912
Additional Family Members	\$200 per sample; known familial mutation only	83891, 83898, 83904x2, 83912

SENSITIVITY

DNA Sequencing Analysis: Approximately 95% detection of mutations in exons 1-7, 1A, and 3A of *TGFBR2*

SPECIMEN REQUIREMENTS

Blood (preferred): EDTA (purple-top) tubes: *Adult:* 5 cc *Child:* 5 cc *Infant:* 2-3 cc
Tissue: Frozen (preferred), RNAlater, Formalin-fixed, Paraffin embedded
Other Body Fluids: Call to inquire

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