



CLIA #: 52D1027685 • CAP #: 7185561  
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## LEOPARD Syndrome via *PTPN11* Gene Sequencing (Test #377)

**Brief Description:** LEOPARD Syndrome (OMIM 151100) is a rare disorder with symptoms that overlap substantially with Noonan Syndrome (OMIM 163950) and to a lesser degree with Neurofibromatosis 1 (OMIM 162200). LEOPARD Syndrome is characterized by skin pigmentation abnormalities including lentigines and café au lait patches, characteristic facial features, heart defects (particularly hypertrophic cardiomyopathy), and deafness (Legius et al. J Med Genet 39:571-574, 2002; Sarkozy et al. J Med Genet 41:e68, 2004). Other less common features include short stature, mental retardation, and abnormal genitalia.

**Genetics:** Like Noonan Syndrome, LEOPARD Syndrome is caused by autosomal dominant mutations in the *PTPN11* gene. Unlike Noonan Syndrome, LEOPARD Syndrome mutations appear to deactivate the gene product (SHP2 protein) (Jopling et al. PLOS Genetics 3:e225, 2007). Parents of LEOPARD patients are often asymptomatic, and *de novo* mutations are common. LEOPARD Syndrome may also be caused by mutations in the *RAF1* gene (Pandit et al. Nat Genet 39:1007-1012, 2007). *RAF1* mutations, however, appear to be much less frequent than *PTPN11* mutations. Genotype-phenotype connections are just beginning to be made (see for example Limongelli et al. Am J Med Genet A 146:620-628, 2008).

**Description of This Particular Test:** Testing for LEOPARD Syndrome is performed at PreventionGenetics in two tiers. Tier 1 involves sequencing of the complete coding regions plus about 50 bp of flanking DNA on each side of exons 7, 12 and 13 in the *PTPN11* gene. If Tier 1 is negative, we go on to Tier 2 which involves sequencing of the remaining twelve *PTPN11* exons. Note that the Tier 1 LEOPARD Syndrome *PTPN11* exons are different from the Tier 1 Noonan Syndrome *PTPN11* exons. PreventionGenetics also offers sequencing of single *PTPN11* exons for confirmation of research results and for testing in relatives of patients with known mutations.

**Reference Sequences:** Genomic: **NC\_000012.10** mRNA: **NM\_002834.3** protein: **NP\_002825.3**

**Indications for Test:** Candidates for this test are patients with symptoms consistent with LEOPARD Syndrome and their family members.

**Sensitivity of Test:** Mutations in the *PTPN11* gene have been identified in 88% of LEOPARD Syndrome patients (Sarkozy et al. 2004), higher than in Noonan Syndrome.

**Turn Around Time:** Maximum of 40 days.

**Specimen Requirements:** See page 4 of the Requisition Form.

**Prices:** Tier 1 only **\$370** Tiers 1 and 2 **\$890**

**CPT Codes:**

Codes	Description	Tier 1 Only	Tier 1 + Tier 2
83890	Ascertainment	\$ 30 (x1)	\$ 30 (x1)
83891	DNA Isolation	\$ 40 (x1)	\$ 40 (x1)
83898	Amplification	\$100 (x3)	\$260 (x15)
83904	Mutation Ident by Sequencing	\$110 (x3)	\$400 (x15)
83894	Separation	\$ 30 (x1)	\$ 60 (x1)
83912	Interpretation and Report	\$ 60 (x1)	\$100 (x1)
<b>Totals:</b>		<b>\$370</b>	<b>\$890</b>

**Accreditation Info.** CLIA ID #: **52D1027685** (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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