

Hutchinson-Gilford Progeria Syndrome (HGPS) via *LMNA* Gene Sequencing (Test #347)

Brief Description and Genetics: Hutchinson-Gilford Progeria syndrome (HGPS; OMIM 176670) is an ultra rare genetic disorder characterized by features reminiscent of marked premature aging. Sequencing of exon 11 of the *LMNA* gene, revealed that 18 out of 20 classical cases of HGPS harbored an identical *de novo* (that is, newly arisen and not inherited) single-base substitution, c.1824C>T (p.Gly608Gly, GGC > GGT), within exon 11 (Eriksson et al., *Nature* 423: 293-298, 2003). One additional *de novo* case was identified with a c.1822G>A substitution (p.Gly608Ser, GGC > AGC) within the same codon. Both of these mutations result in activation of a cryptic splice site within exon 11, resulting in production of a protein product that deletes 50 amino acids near the carboxy terminus. Identification of the common p.Gly608Gly mutation has potential clinical significance for presymptomatic diagnosis in this population allowing the clinician to determine which patients carry the common mutation and therefore have an increased risk for developing HGPS.

Description of This Particular Test: This test involves bidirectional DNA sequencing of all 12 exons of the *LMNA* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on either side are sequenced. If specifically requested, we will sequence exon 11, containing the common Gly608Gly mutation, first before proceeding to the rest of the gene.

Reference Sequences: Genomic: NC_000001.9 mRNA: NM_170707.1 Protein: NP_733821.1

Indications for Test: Suspected Hutchinson-Gilford Progeria Syndrome.

Given the rarity and severity of this condition PreventionGenetics feels that it is important that all physicians ordering this testing for HGPS or other progeroid syndromes contact the Progeria Research Foundation (<http://www.progeriaresearch.org/>) for the latest information on treatment, research and patient support.

Sensitivity of Test: Unknown at present.

Turn Around Time: Maximum of 40 days.

Specimen Requirements: See bottom of page two of the Requisition Form.

Price: Sequencing of complete coding regions of *LMNA* Gene **\$ 590**

CPT Codes:

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x11	83898	\$ 160	Sequencing x11	83904	\$ 230
Separation	83894	\$ 50	Interpretation/Report	83912	\$ 80

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