ClinGenLab
Clinical Testing Laboratory, Inc.

Clinical Testing Lab of Washington
2150 Pennsylvania Avenue NW
Washington, DC 20037
Phone: 202-555-1212

Specimen Number	Specimen Type	Control Number	Account Number	Account Phone Number	Route
	Peripheral Blood				

Patient Last Name	Patient Barcode

Patient First Name	Patient Middle Name
Sam	

Patient SS#	Patient Phone	Total Volume

Age (Y/M/D)	Date of Birth	Sex	Fasting
22 m.o.		Male	

Patient Address	Indication: Progeria Family History: No family history Ethnicity: Western European Caucasian

Date and Time Collected	Date Entered	Date and Time Reported	Physician Name	NPI	Physician ID
			Jane Ferreiro, MD		

Tests Ordered
Hutchinson-Gilford Progeria Syndrome (HGPS) via the LMNA Gene

General Comments
Please send a copy of the final report to the Molecular Science/M1 Training office via Fax at (202) 555-1212

Clinical test results for Severe Combined Immunodeficiency (SCID)

GENE	TEST RESULTS	EXPLANATION
LMNA (1q22)	Gly608 Gly608=	**This result confirms the diagnosis of Hutchinson-Gilford Progeria Syndrome (HGPS)**. This result should be interpreted in the context of clinical presentation and results of other laboratory tests. A PCR/sequencing study has confirmed one copy of the Gly608= (LMNA: g.59412C>T, c.1824C>T or p.Gly608=) variation. The Gly608= mutation is caused by a C to T change at nucleotide position 1824 in the LMNA gene. While this does not result in an altered encoded amino acid (=), it has been reported that the nucleotide variant impacts post-transcriptional processing of the mRNA transcript. The presence of the variant induces the use of a novel/cryptic splice donor site within exon 11 at position 1818. This is ligated directly to the reference splice acceptor site of exon 12, resulting in the deletion of encoded amino acid residues 607 to 656. Furthermore, loss of this protein region has been shown to prevent full post-translational processing (proteolytic cleavage) of the protein. This individual's result has important implications for other family members. Clinical and laboratory evaluations should be considered for at risk individuals. Genetic counseling is recommended for at risk individuals.

INDICATIONS FOR TESTING
Individuals with a diagnosis of Hutchinson-Gilford progeria syndrome with genetic counseling, are candidates for testing.

METHODOLOGY
Gene sequencing: All coding exons and associated intron junctions are analyzed by direct DNA sequence analysis using an automated fluorescent sequencing machine. When a mutation is detected, confirmation is carried out on an independent amplification of PCR using a second prep (B-prep) by sequencing in the opposite direction. If no mutation is found, sequence analysis is performed in both directions.

PERFORMANCE
Gene sequencing: From previous experience, we have been able to detect LMNA mutations in about 99% of individuals with the diagnosis of Hutchinson-Gilford progeria syndrome with specificity of mutation detection in probands detection is also estimated to be greater than 99%.

LIMITATIONS
The sequence analysis will not detect mutations located in regions of LMNA that are not analyzed (non-coding exon regions, intron regions other than the splice junctions, and upstream and downstream regions). The sequencing method also will not detect gross genetic alterations including most duplications, inversions, or deletions. Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance.

CLINICAL DESCRIPTION
Hutchinson-Gilford progeria syndrome encompasses a spectrum of clinical features that typically develop in childhood and resemble some features of accelerated aging. Although signs and symptoms vary in age of onset and severity, they are remarkably consistent overall. Children with Hutchinson-Gilford progeria syndrome (HGPS) usually appear normal at birth. Profound failure to thrive occurs during the first year. Characteristic facies, with receding mandible, narrow nasal bridge and pointed nasal tip develop. During the first to third year the following usually become apparent: partial alopecia progressing to total alopecia, loss of subcutaneous fat, progressive joint contractures, bone changes, nail dystrophy, and abnormal tightness and/or small soft outpouchings of the skin over the abdomen and upper thighs, and delayed primary tooth eruption. Later findings include low-frequency conductive hearing loss, dental crowding, and partial lack of secondary tooth eruption. Additional findings present in some but not all affected individuals include photophobia, excessive ocular tearing, exposure keratitis, and Raynaud phenomenon. Motor and mental development is normal. Death occurs as a result of complications of severe atherosclerosis, either cardiac disease (myocardial infarction) or cerebrovascular disease (stroke), generally between ages six and 20 years. Average life span is approximately 14.6 years.

-from GeneReviews