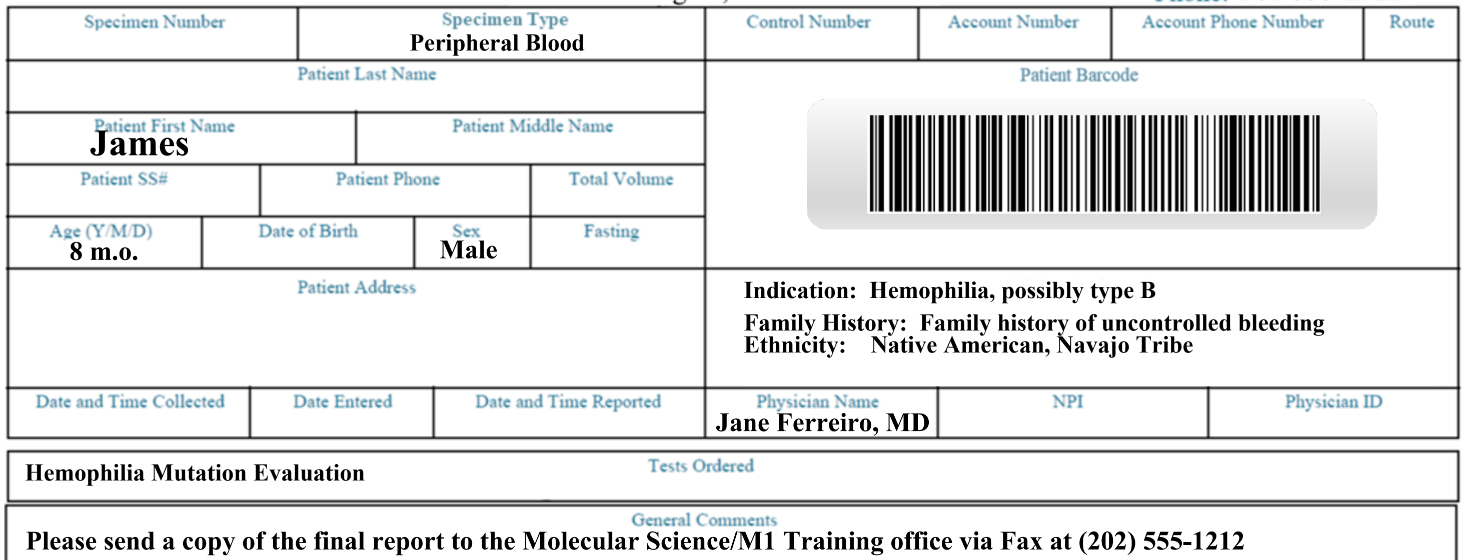
ClinGenLab
Clinical Testing Laboratory, Inc.

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 First Name: James

Patient Middle Name:

Patient SS#:

Patient Phone:

Total Volume:

Age (Y/M/D): 8 m.o.

Date of Birth:

Sex: Male

Fasting:

Patient Barcode

Patient Address:

Indication: Hemophilia, possibly type B
Family History: Family history of uncontrolled bleeding
Ethnicity: Native American, Navajo Tribe

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

Tests Ordered: **Hemophilia Mutation Evaluation**

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 DNA Hemophilia Mutation Evaluation

GENE	TEST RESULTS	EXPLANATION
F9 (Xq27.1)	Arg75Ter	**This result confirms the diagnosis of Hemophilia B**. This result should be interpreted in the context of clinical presentation and results of other laboratory tests (e.g., APTT, Factor IX Activity, Factor IX Inhibitor, etc.). A PCR/sequencing study has detected one copy of the Arg75Ter (F9: g.11409C>T, c.223C>T or p.Arg75Ter) variation. The Arg75Ter variation is a C to T change at nucleotide position 11409 of the F9 gene. This forms a premature stop (termination) codon at amino acid position 75 resulting in an abnormally short or truncated protein. As males have only one copy of the X chromosome, a variation in an X-linked gene renders the patient with only a mutated form of the gene. Thus, they are susceptible to the most severe form of the disease.
F8 (Xq28)	Negative	

INDICATIONS FOR TESTING

Individuals with a diagnosis of hemophilia B, appropriate at-risk female relatives of probands with identified mutations, and hemophilia B carriers with genetic counseling, are candidates for testing.

METHODOLOGY

Factor IX sequencing: All coding exons (1-8) and associated intron junctions of the Factor IX gene 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

Factor IX sequencing: From previous experience, we have been able to detect factor IX gene mutations in about 99% of individuals with the diagnosis of hemophilia B with specificity of mutation detection in probands and carrier detection is also estimated to be greater than 99%.

LIMITATIONS

The sequence analysis will not detect mutations located in regions of the Factor IX gene 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 (in females). Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance.

CLINICAL DESCRIPTION

Hemophilia B is characterized by deficiency in factor IX clotting activity that results in prolonged oozing after injuries, tooth extractions, or surgery, and delayed or recurrent bleeding prior to complete wound healing. This is an X-linked recessive bleeding disorder with an incidence of about 1 per 30,000 live male births. Hemophilia B affects males, however, all male offspring will be normal, and although all female offspring will be obligatory carriers, they rarely have symptomatic bleeding. In contrast, female offspring of carriers of hemophilia B have a 50% chance of being carriers themselves, and each male offspring has a 50% chance of being affected.

The age of diagnosis and frequency of bleeding episodes are related to the level of factor IX clotting activity. In severe hemophilia B, spontaneous joint or deep-muscle bleeding is the most frequent symptom. Individuals with severe hemophilia B are usually diagnosed during the first two years of life; without prophylactic treatment, they may average up to two to five spontaneous bleeding episodes each month. Individuals with moderate hemophilia B seldom have spontaneous bleeding; however, they do have prolonged or delayed oozing after relatively minor trauma and are usually diagnosed before age five to six years; the frequency of bleeding episodes varies from once a month to once a year. Individuals with mild hemophilia B do not have spontaneous bleeding episodes; however, without pre- and post-operative treatment, abnormal bleeding occurs with surgery or tooth extractions; the frequency of bleeding may vary from once a year to once every ten years. Individuals with mild hemophilia B are often not diagnosed until later in life. In any individual with hemophilia B, bleeding episodes may be more frequent in childhood and adolescence than in adulthood. Approximately 10% of carrier females are at risk for bleeding (even if the affected family member has mild hemophilia B) and are thus symptomatic carriers, although symptoms are usually mild. After major trauma or invasive procedures, prolonged or excessive bleeding usually occurs, regardless of severity.

REFERENCES

1. Yoshitake S, Schach BG, Foster DC, et al: Nucleotide sequence of the gene for human factor IX (antihemophilic factor B). Biochemistry 1985 July 2;24(14):3736-3750
2. Giannelli F, Green PM, Sommer SS, et al: Haemophilia B: database of point mutations and short additions and deletions-eighth edition. Nucleic Acids Res 1998 Jan 1;26(1):265-268
3. Ketterling RP, Bottema CD, Phillips JA 3rd, et al: Evidence that descendants of three founders constitute about 25% of hemophilia B in the United States. Genomics 1991 Aug;10(4):1093-1096

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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
James	

Patient SS#	Patient Phone	Total Volume

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

Patient Address

Indication: Hemophilia, possibly type B

Family History: Family history of uncontrolled bleeding
Ethnicity: Native American, Navajo Tribe

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

Tests Ordered
Hemophilia Mutation Evaluation

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 DNA Hemophilia Mutation Evaluation

GENE	TEST RESULTS	EXPLANATION
F8 (Xq28)	Arg15Ter	**This result confirms the diagnosis of Hemophilia A**. This result should be interpreted in the context of clinical presentation and results of other laboratory tests (e.g., APTT, Factor VIII Activity, etc.). A PCR/sequencing study has detected one copy of the Arg15Ter (F8:g.5214C>T, c.43C>T or p.Arg15Ter) variation. The Arg15Ter variation is a C to T change at nucleotide position 5214 of the F8 gene and 43 of the F8 mRNA transcript. This forms a premature stop (termination) codon at amino acid position 15 resulting in an abnormally short or truncated protein. As males have only one copy of the X chromosome, a variation in an X-linked gene renders the patient with only a mutated form of the gene. Thus, they are susceptible to the most severe form of the disease.
F8 (Xq28)	Negative	

INDICATIONS FOR TESTING

Individuals with a diagnosis of hemophilia B, appropriate at-risk female relatives of probands with identified mutations, and hemophilia B carriers with genetic counseling, are candidates for testing.

METHODOLOGY

Factor IX sequencing: All coding exons (1-8) and associated intron junctions of the Factor IX gene 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

Factor IX sequencing: From previous experience, we have been able to detect factor IX gene mutations in about 99% of individuals with the diagnosis of hemophilia B with specificity of mutation detection in probands and carrier detection is also estimated to be greater than 99%.

LIMITATIONS

The sequence analysis will not detect mutations located in regions of the Factor IX gene 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 (in females). Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance.

CLINICAL DESCRIPTION

Hemophilia B is characterized by deficiency in factor IX clotting activity that results in prolonged oozing after injuries, tooth extractions, or surgery, and delayed or recurrent bleeding prior to complete wound healing. This is an X-linked recessive bleeding disorder with an incidence of about 1 per 30,000 live male births. Hemophilia B affects males, however, all male offspring will be normal, and although all female offspring will be obligatory carriers, they rarely have symptomatic bleeding. In contrast, female offspring of carriers of hemophilia B have a 50% chance of being carriers themselves, and each male offspring has a 50% chance of being affected.

The age of diagnosis and frequency of bleeding episodes are related to the level of factor IX clotting activity. In severe hemophilia B, spontaneous joint or deep-muscle bleeding is the most frequent symptom. Individuals with severe hemophilia B are usually diagnosed during the first two years of life; without prophylactic treatment, they may average up to two to five spontaneous bleeding episodes each month. Individuals with moderate hemophilia B seldom have spontaneous bleeding; however, they do have prolonged or delayed oozing after relatively minor trauma and are usually diagnosed before age five to six years; the frequency of bleeding episodes varies from once a month to once a year. Individuals with mild hemophilia B do not have spontaneous bleeding episodes; however, without pre- and post-operative treatment, abnormal bleeding occurs with surgery or tooth extractions; the frequency of bleeding may vary from once a year to once every ten years. Individuals with mild hemophilia B are often not diagnosed until later in life. In any individual with hemophilia B, bleeding episodes may be more frequent in childhood and adolescence than in adulthood. Approximately 10% of carrier females are at risk for bleeding (even if the affected family member has mild hemophilia B) and are thus symptomatic carriers, although symptoms are usually mild. After major trauma or invasive procedures, prolonged or excessive bleeding usually occurs, regardless of severity.

REFERENCES

4. Yoshitake S, Schach BG, Foster DC, et al: Nucleotide sequence of the gene for human factor IX (antihemophilic factor B). Biochemistry 1985 July 2;24(14):3736-3750
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Specimen Number	Specimen Type	Control Number	Account Number	Account Phone Number	Route
	Peripheral Blood				

Field	Value
Patient Last Name	
Patient First Name	Raven
Patient Middle Name	
Patient SS#	
Patient Phone	
Total Volume	
Age (Y/M/D)	25 y.o.
Date of Birth	
Sex	Female
Fasting	
Patient Address	
Patient Barcode	
Date and Time Collected	
Date Entered	
Date and Time Reported	
Physician Name	Jane Ferreiro, MD
NPI	
Physician ID	

Indication: Hemophilia B carrier
Family History: Family history of uncontrolled bleeding
Ethnicity: Native American, Navajo Tribe

Tests Ordered: **Hemophilia Mutation Evaluation**

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 DNA Hemophilia Mutation Evaluation

GENE	TEST RESULTS	EXPLANATION
F9 (Xq27.1)	Arg75 Arg75Ter Heterozygous Carrier Status	**This result confirms the status of carrier for Hemophilia B**. This result should be interpreted in the context of clinical presentation and results of other laboratory tests (e.g., APTT, Factor IX Activity, Factor IX Inhibitor, etc.). A PCR/sequencing study has detected one Arg75Ter (F9: g.11409C>T, c.223C>T or p.Arg75Ter) variation. The Arg75Ter variation is a C to T change at nucleotide position 223 in the F9 gene. This forms a premature stop (termination) codon at amino acid position 75 resulting in an abnormally short or truncated protein. Female carriers of Hemophilia B have one normal X chromosome and one abnormal X chromosome. The normal X chromosome produces a certain amount of factor IX clotting factor. This protects carriers from the most severe form of hemophilia, however the levels of circulating clotting factors among carriers are very wide.
F8 (Xq28)	Negative	

INDICATIONS FOR TESTING
Individuals with a diagnosis of hemophilia B, appropriate at-risk female relatives of probands with identified mutations, and hemophilia B carriers with genetic counseling, are candidates for testing.

METHODOLOGY
Factor IX sequencing: All coding exons (1-8) and associated intron junctions of the Factor IX gene 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
Factor IX sequencing: From previous experience, we have been able to detect factor IX gene mutations in about 99% of individuals with the diagnosis of hemophilia B with specificity of mutation detection in probands and carrier detection is also estimated to be greater than 99%.

LIMITATIONS

The sequence analysis will not detect mutations located in regions of the Factor IX gene 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 (in females). Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance.

CLINICAL DESCRIPTION

Hemophilia B is characterized by deficiency in factor IX clotting activity that results in prolonged oozing after injuries, tooth extractions, or surgery, and delayed or recurrent bleeding prior to complete wound healing. This is an X-linked recessive bleeding disorder with an incidence of about 1 per 30,000 live male births. Hemophilia B affects males, however, all male offspring will be normal, and although all female offspring will be obligatory carriers, they rarely have symptomatic bleeding. In contrast, female offspring of carriers of hemophilia B have a 50% chance of being carriers themselves, and each male offspring has a 50% chance of being affected.

The age of diagnosis and frequency of bleeding episodes are related to the level of factor IX clotting activity. In severe hemophilia B, spontaneous joint or deep-muscle bleeding is the most frequent symptom. Individuals with severe hemophilia B are usually diagnosed during the first two years of life; without prophylactic treatment, they may average up to two to five spontaneous bleeding episodes each month. Individuals with moderate hemophilia B seldom have spontaneous bleeding; however, they do have prolonged or delayed oozing after relatively minor trauma and are usually diagnosed before age five to six years; the frequency of bleeding episodes varies from once a month to once a year. Individuals with mild hemophilia B do not have spontaneous bleeding episodes; however, without pre- and post-operative treatment, abnormal bleeding occurs with surgery or tooth extractions; the frequency of bleeding may vary from once a year to once every ten years. Individuals with mild hemophilia B are often not diagnosed until later in life. In any individual with hemophilia B, bleeding episodes may be more frequent in childhood and adolescence than in adulthood. Approximately 10% of carrier females are at risk for bleeding (even if the affected family member has mild hemophilia B) and are thus symptomatic carriers, although symptoms are usually mild. After major trauma or invasive procedures, prolonged or excessive bleeding usually occurs, regardless of severity.

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

Field	Value
Patient Last Name	
Patient First Name	Raven
Patient Middle Name	
Patient SS#	
Patient Phone	
Total Volume	
Age (Y/M/D)	25 y.o.
Date of Birth	
Sex	Female
Fasting	
Patient Address	
Patient Barcode	

Indication: Hemophilia B carrier

Family History: Family history of uncontrolled bleeding
Ethnicity: Native American, Navajo Tribe

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

Tests Ordered: **Hemophilia Mutation Evaluation**

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 DNA Hemophilia Mutation Evaluation

GENE	TEST RESULTS	EXPLANATION
F8 (Xq28)	Arg15 Arg15Ter Heterozygous Carrier Status	**This result confirms the status of carrier for Hemophilia A**. This result should be interpreted in the context of clinical presentation and results of other laboratory tests (e.g., APTT, Factor VIII Activity, etc.). A PCR/sequencing study has detected one copy of the Arg15Ter (F8:g.5214C>T, c.43C>T or p.Arg15Ter) variation. The Arg15Ter variation is a C to T change at nucleotide position 5214 of the F8 gene and 43 of the F8 mRNA transcript. This forms a premature stop (termination) codon at amino acid position 15 resulting in an abnormally short or truncated protein. Female carriers of Hemophilia A have one normal X chromosome and one abnormal X chromosome. The normal X chromosome produces a certain amount of factor IX clotting factor. This protects carriers from the most severe form of hemophilia, however the levels of circulating clotting factors among carriers are very wide.
F9 (Xq27.1)	Negative	

INDICATIONS FOR TESTING

Individuals with a diagnosis of hemophilia B, appropriate at-risk female relatives of probands with identified mutations, and hemophilia B carriers with genetic counseling, are candidates for testing.

METHODOLOGY

Factor IX sequencing: All coding exons (1-8) and associated intron junctions of the Factor IX gene 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

Factor IX sequencing: From previous experience, we have been able to detect factor IX gene mutations in about 99% of individuals with the diagnosis of hemophilia B with specificity of mutation detection in probands and carrier detection is also estimated to be greater than 99%.

LIMITATIONS

The sequence analysis will not detect mutations located in regions of the Factor IX gene 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 (in females). Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance.

CLINICAL DESCRIPTION

Hemophilia B is characterized by deficiency in factor IX clotting activity that results in prolonged oozing after injuries, tooth extractions, or surgery, and delayed or recurrent bleeding prior to complete wound healing. This is an X-linked recessive bleeding disorder with an incidence of about 1 per 30,000 live male births. Hemophilia B affects males, however, all male offspring will be normal, and although all female offspring will be obligatory carriers, they rarely have symptomatic bleeding. In contrast, female offspring of carriers of hemophilia B have a 50% chance of being carriers themselves, and each male offspring has a 50% chance of being affected.

The age of diagnosis and frequency of bleeding episodes are related to the level of factor IX clotting activity. In severe hemophilia B, spontaneous joint or deep-muscle bleeding is the most frequent symptom. Individuals with severe hemophilia B are usually diagnosed during the first two years of life; without prophylactic treatment, they may average up to two to five spontaneous bleeding episodes each month. Individuals with moderate hemophilia B seldom have spontaneous bleeding; however, they do have prolonged or delayed oozing after relatively minor trauma and are usually diagnosed before age five to six years; the frequency of bleeding episodes varies from once a month to once a year. Individuals with mild hemophilia B do not have spontaneous bleeding episodes; however, without pre- and post-operative treatment, abnormal bleeding occurs with surgery or tooth extractions; the frequency of bleeding may vary from once a year to once every ten years. Individuals with mild hemophilia B are often not diagnosed until later in life. In any individual with hemophilia B, bleeding episodes may be more frequent in childhood and adolescence than in adulthood. Approximately 10% of carrier females are at risk for bleeding (even if the affected family member has mild hemophilia B) and are thus symptomatic carriers, although symptoms are usually mild. After major trauma or invasive procedures, prolonged or excessive bleeding usually occurs, regardless of severity.

REFERENCES

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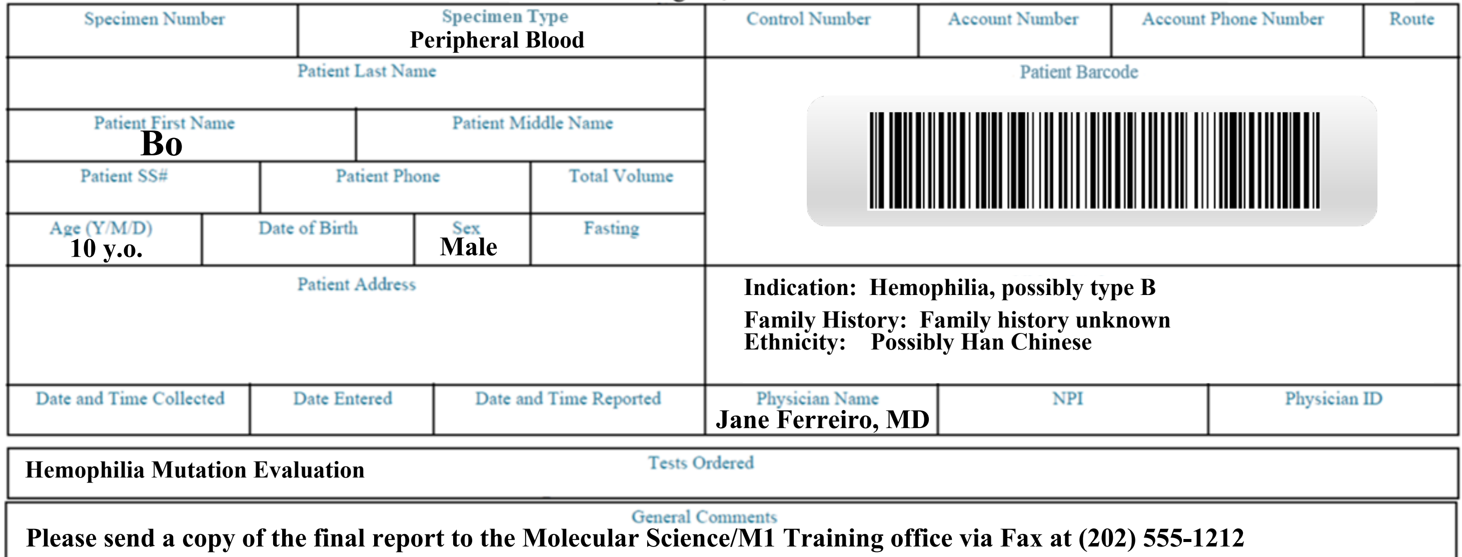
6. Ketterling RP, Bottema CD, Phillips JA 3rd, et al: Evidence that descendants of three founders constitute about 25% of hemophilia B in the United States. Genomics 1991 Aug;10(4):1093-1096



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

Patient Last Name:
Patient First Name: **Bo**
Patient Middle Name:
Patient SS#:
Patient Phone:
Total Volume:
Age (Y/M/D): **10 y.o.**
Date of Birth:
Sex: **Male**
Fasting:
Patient Address:
Patient Barcode

Indication: Hemophilia, possibly type B
Family History: Family history unknown
Ethnicity: Possibly Han Chinese

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

Tests Ordered: **Hemophilia Mutation Evaluation**

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 DNA Hemophilia Mutation Evaluation

GENE	TEST RESULTS	EXPLANATION
F9 (Xq27.1)	Asp110Gly	**This result confirms the diagnosis of Hemophilia B**. This result should be interpreted in the context of clinical presentation and results of other laboratory tests (e.g., APTT, Factor IX Activity, Factor IX Inhibitor, etc.). A PCR/sequencing study has detected one copy of the Asp110Gly (F9: g.15392A>G, c.329A>G or p.Asp110Gly) variation. The Asp110Gly variation is an A to G change at nucleotide position 15392 in the F9 gene. This encodes an amino acid at position 110 (glycine) that is different from the reference (aspartate) and may have implications on structure and or function of the resulting protein. As males have only one copy of the X chromosome, a pathogenic variation in an X-linked gene renders the patient with only a mutated form of the gene. Thus, they are highly susceptible to development of significant abnormal hemophiliac symptoms.
F8 (Xq28)	Negative	

INDICATIONS FOR TESTING

Individuals with a diagnosis of hemophilia B, appropriate at-risk female relatives of probands with identified mutations, and hemophilia B carriers with genetic counseling, are candidates for testing.

METHODOLOGY

Factor IX sequencing: All coding exons (1-8) and associated intron junctions of the Factor IX gene 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
Factor IX sequencing: From previous experience, we have been able to detect factor IX gene mutations in about 99% of individuals with the diagnosis of hemophilia B with specificity of mutation detection in probands and carrier detection is also estimated to be greater than 99%.

LIMITATIONS
The sequence analysis will not detect mutations located in regions of the Factor IX gene 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 (in females). Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance.

CLINICAL DESCRIPTION
Hemophilia B is characterized by deficiency in factor IX clotting activity that results in prolonged oozing after injuries, tooth extractions, or surgery, and delayed or recurrent bleeding prior to complete wound healing. This is an X-linked recessive bleeding disorder with an incidence of about 1 per 30,000 live male births. Hemophilia B affects males, however, all male offspring will be normal, and although all female offspring will be obligatory carriers, they rarely have symptomatic bleeding. In contrast, female offspring of carriers of hemophilia B have a 50% chance of being carriers themselves, and each male offspring has a 50% chance of being affected.

The age of diagnosis and frequency of bleeding episodes are related to the level of factor IX clotting activity. In severe hemophilia B, spontaneous joint or deep-muscle bleeding is the most frequent symptom. Individuals with severe hemophilia B are usually diagnosed during the first two years of life; without prophylactic treatment, they may average up to two to five spontaneous bleeding episodes each month. Individuals with moderate hemophilia B seldom have spontaneous bleeding; however, they do have prolonged or delayed oozing after relatively minor trauma and are usually diagnosed before age five to six years; the frequency of bleeding episodes varies from once a month to once a year. Individuals with mild hemophilia B do not have spontaneous bleeding episodes; however, without pre- and post-operative treatment, abnormal bleeding occurs with surgery or tooth extractions; the frequency of bleeding may vary from once a year to once every ten years. Individuals with mild hemophilia B are often not diagnosed until later in life. In any individual with hemophilia B, bleeding episodes may be more frequent in childhood and adolescence than in adulthood. Approximately 10% of carrier females are at risk for bleeding (even if the affected family member has mild hemophilia B) and are thus symptomatic carriers, although symptoms are usually mild. After major trauma or invasive procedures, prolonged or excessive bleeding usually occurs, regardless of severity.

REFERENCES

1. Yoshitake S, Schach BG, Foster DC, et al: Nucleotide sequence of the gene for human factor IX (antihemophilic factor B). Biochemistry 1985 July 2;24(14):3736-3750
2. Giannelli F, Green PM, Sommer SS, et al: Haemophilia B: database of point mutations and short additions and deletions-eighth edition. Nucleic Acids Res 1998 Jan 1;26(1):265-268
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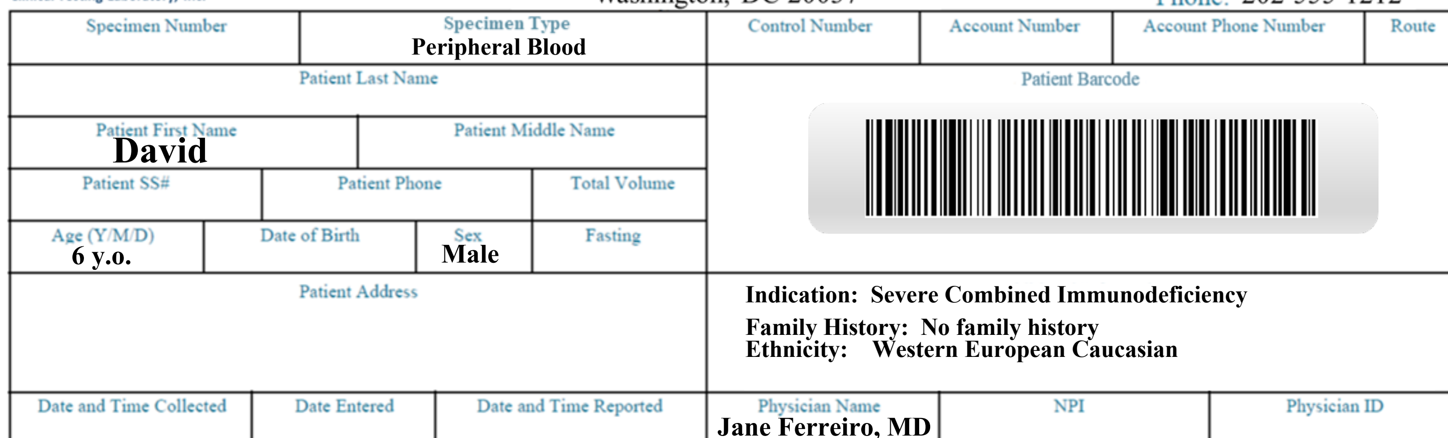
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Washington, DC 20037

Phone: 202-555-1212

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

Patient Last Name:
Patient First Name: David
Patient Middle Name:
Patient SS#:
Patient Phone:
Total Volume:
Age (Y/M/D): 6 y.o.
Date of Birth:
Sex: Male
Fasting:
Patient Address:
Patient Barcode

Indication: Severe Combined Immunodeficiency
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
Severe Combined Immunodeficiency (SCID): Three-gene Profile (IL2RG, ADA, IL7R)

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
IL2RG (Xq13.1)	Cys115Arg	**This result confirms the diagnosis of X-linked Severe Combined Immunodeficiency (SCID)**. 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 Cys115Arg (IL2RG: g.5939T>C, c.343T>C or p.Cys115Arg) variation. The Cys115Arg mutation is caused by a T to C change at nucleotide position 5939 in the IL2RG gene. This encodes an amino acid at position 115 (arginine) that is different from the reference (cysteine) and may have implications on structure and or function of the resulting 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.
ADA (20q13.12) IL7R (5p13.2)	Negative	No known pathogenic variant detected in these genes

INDICATIONS FOR TESTING

Individuals with a diagnosis of Severe Combined Immunodeficiency (SCID) 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 ADA, IL2RG, or IL7R mutations in about 99% of individuals with the diagnosis of Severe Combined Immunodeficiency (SCID) 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 ADA, IL2RG, or IL7R 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 (in females). Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance.

CLINICAL DESCRIPTION

Group of rare congenital disorders characterized by impairment of both humoral and cell-mediated immunity, leukopenia, and low or absent antibody levels. It is inherited as an X-linked or autosomal recessive defect. Mutations occurring in many different genes cause human Severe Combined Immunodeficiency (SCID).

-from MeSH

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Washington, DC 20037

Phone: 202-555-1212

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

Field	Value
Patient Last Name	
Patient First Name	Ashanthi
Patient Middle Name	
Patient SS#	
Patient Phone	
Total Volume	
Age (Y/M/D)	4 y.o.
Date of Birth	
Sex	Female
Fasting	
Patient Address	
Patient Barcode	

Indication: Severe Combined Immunodeficiency

Family History: No family history
Ethnicity: Sri Lanka – Southern Asia

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

Tests Ordered
Severe Combined Immunodeficiency (SCID): Three-gene Profile (IL2RG, ADA, IL7R)

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
ADA (20q13.12)	Gly216Arg Gly216Arg	**This result confirms the diagnosis of Severe Combined Immunodeficiency (SCID) due to Adenosine Deaminase Deficiency**. This result should be interpreted in the context of clinical presentation and results of other laboratory tests. A PCR/sequencing study has confirmed two copies of the Gly216Arg (ADA: g.33697G>A, c.646G>A or p.Gly216Arg) variation. The Gly216Arg mutation is caused by a G to A change at nucleotide position 646 in the ADA gene. This encodes an amino acid at position 216 (arginine) that is different from the reference (glycine) and may have implications on structure and or function of the resulting 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.
IL2RG (Xq13.1) IL7R (5p13.2)	Negative	No known pathogenic variant detected in these genes

INDICATIONS FOR TESTING

Individuals with a diagnosis of Severe Combined Immunodeficiency (SCID) 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 ADA, IL2RG, or IL7R mutations in about 99% of individuals with the diagnosis of Severe Combined Immunodeficiency (SCID) 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 ADA, IL2RG, or IL7R 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 (in females). Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance.

CLINICAL DESCRIPTION

Group of rare congenital disorders characterized by impairment of both humoral and cell-mediated immunity, leukopenia, and low or absent antibody levels. It is inherited as an X-linked or autosomal recessive defect. Mutations occurring in many different genes cause human Severe Combined Immunodeficiency (SCID).

-from MeSH

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

Field	Value
Patient Last Name	
Patient First Name	Jill
Patient Middle Name	
Patient SS#	
Patient Phone	
Total Volume	
Age (Y/M/D)	19 y.o.
Date of Birth	
Sex	Female
Fasting	
Patient Address	
Patient Barcode	

Indication: Congenital Muscular Dystrophy
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
Congenital Muscular Dystrophy Sequencing Panel

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)	Arg453 Arg453Trp	**This result confirms the diagnosis of Limb-Girdle Muscular Dystrophy type 1B**. 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 Arg453Trp (LMNA: g.58841C>T, c.1357C>T or p.Arg453Trp) variation. The Arg453Trp mutation is caused by a C to T change at nucleotide position 58841 in the LMNA gene. This encodes an amino acid at position 453 (tryptophan) that is different from the reference (arginine) and may have implications on structure and or function of the resulting 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.
Secondary Finding:		
LMNA (1q22)	Arg482 Arg482Trp	**This result suggests a diagnosis of Familial Partial Lipodystrophy, type 2**. 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 Arg482Trp (LMNA g.59412C>T, c.1444C>T or p.Arg482Trp) variation. The Arg482Trp mutation is caused by a C to T change at nucleotide position 159412 in the LMNA gene. This encodes an amino acid at position 482 (tryptophan) that is different from the reference (arginine) and may have implications on structure and or function of the resulting 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.

GENE	TEST RESULTS	EXPLANATION
EMD (Xq28) **FHL1 (Xq26.3)** **SYNE1 (6q25.2)** **SYNE2 (14q23.2)** **TMEM43 (3p25.1)**	Negative	No known pathogenic variant detected in these genes

INDICATIONS FOR TESTING
Individuals with a diagnosis of Emery-Dreifuss Muscular Dystrophy 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 EMD, FHL1, LMNA, SYNE1, SYNE2, or TMEM43 mutations in about 99% of individuals with the diagnosis of Emery-Dreifuss Muscular Dystrophy 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 EMD, FHL1, LMNA, SYNE1, SYNE2, or TMEM43 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
Emery-Dreifuss muscular dystrophy (EDMD) is characterized by the clinical triad of joint contractures that begin in early childhood, slowly progressive muscle weakness and wasting initially in a humero-peroneal distribution that later extends to the scapular and pelvic girdle muscles, and cardiac involvement that may manifest as palpitations, presyncope and syncope, poor exercise tolerance, and congestive heart failure. Age of onset, severity, and progression of muscle and cardiac involvement demonstrate both inter- and intrafamilial variability. Clinical variability ranges from early onset with severe presentation in childhood to late onset with slow progression in adulthood. In general, joint contractures appear during the first two decades, followed by muscle weakness and wasting. Cardiac involvement usually occurs after the second decade.

-from GeneReviews

Familial partial lipodystrophy type 1 (FPLD1), or Kobberling-type lipodystrophy, is characterized by loss of adipose tissue confined to the extremities, with normal or increased distribution of fat on the face, neck, and trunk (Kobberling and Dunnigan, 1986). For a general description and a discussion of genetic heterogeneity of familial partial lipodystrophy (FPLD), see 151660.

-from OMIM

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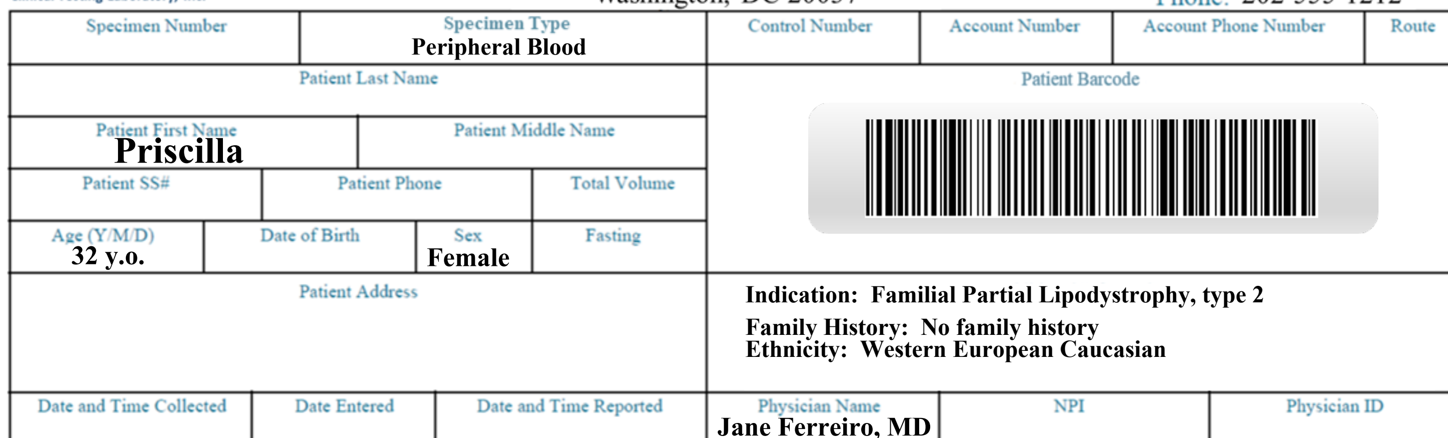

Specimen Number	Specimen Type	Control Number	Account Number	Account Phone Number	Route
	Peripheral Blood				

Field	Value
Patient Last Name	
Patient First Name	Priscilla
Patient Middle Name	
Patient SS#	
Patient Phone	
Total Volume	
Age (Y/M/D)	32 y.o.
Date of Birth	
Sex	Female
Fasting	
Patient Address	
Patient Barcode	

Indication: Familial Partial Lipodystrophy, type 2
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
LMNA Sequencing

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)	Arg482 Arg482Trp	**This result confirms the diagnosis of Familial Partial Lipodystrophy, type 2**. 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 Arg482Trp (LMNA g.59412C>T, c.1444C>T or p.Arg482Trp) variation. The Arg482Trp mutation is caused by a C to T change at nucleotide position 159412 in the LMNA gene. This encodes an amino acid at position 482 (tryptophan) that is different from the reference (arginine) and may have implications on structure and or function of the resulting 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-Guilford syndrome (HGPS), Congenital muscular dystrophy, LMNA-related (MDCL), or Familial partial lipodystrophy, type 1 (FPLD1) 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-Guilford syndrome (HGPS), Congenital muscular dystrophy, LMNA-related (MDCL), or Familial partial lipodystrophy, type 1 (FPLD1) 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

Familial partial lipodystrophy type 1 (FPLD1), or Kobberling-type lipodystrophy, is characterized by loss of adipose tissue confined to the extremities, with normal or increased distribution of fat on the face, neck, and trunk (Kobberling and Dunnigan, 1986). For a general description and a discussion of genetic heterogeneity of familial partial lipodystrophy (FPLD), see 151660.

-from OMIM

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

Field	Value
Patient Last Name	
Patient First Name	Sam
Patient Middle Name	
Patient SS#	
Patient Phone	
Total Volume	
Age (Y/M/D)	22 m.o.
Date of Birth	
Sex	Male
Fasting	
Patient Address	
Patient Barcode	

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

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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 First Name	Patient Middle Name
Jeff		

Patient SS#	Patient Phone	Total Volume

Age (Y/M/D)	Date of Birth	Sex	Fasting
46 y.o.		Male	

Patient Barcode

Patient Address

Additional Information
Indication: Suspected Hemochromatosis
Family History: No known 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
Hereditary Hemochromatosis Panel

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 Hereditary hemochromatosis

6 conditions tested:

- Hereditary hemochromatosis (type 1)
- Hemochromatosis type 2A
- Hemochromatosis type 2B
- Hemochromatosis type 3
- Hemochromatosis type 4
- Juvenile hemochromatosis

GENE	TEST RESULTS	EXPLANATION
HAMP	Negative	No known pathogenic variant detected
HFE	Pathogenic p.Cys282Tyr p.Cys282Tyr	**This result confirms the diagnosis of or predisposition for Hereditary hemochromatosis** (type 1). This result should be interpreted in the context of clinical presentation and results of other laboratory tests (e.g., serum transferrin-iron saturation and serum ferritin). A PCR/sequencing study has detected two copies of the Cys282Tyr (HFE g.10633G>A, c.845G>A, p.Cys282Tyr) variation. The Cys282Tyr mutation is a G to A change at nucleotide position 10633 in the HFE gene, 845 in the primary HFE transcript and results in a change from cysteine to tyrosine at amino acid position 282. In addition, 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.
HFE2	Negative	No known pathogenic variant detected
SLC40A1	Negative	No known pathogenic variant detected
TFR2	Negative	No known pathogenic variant detected

DISCLAIMER:
Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete. Rare polymorphisms exist that could lead to false negative or positive results. If results obtained do not match the clinical findings, additional testing should be considered.

ASSAY METHODS

Full-Gene Sequencing covers the full gene coding sequence, +/- 10 base pairs of adjacent intronic sequence, and other non-coding sequence positions containing select known pathogenic variants. Deletion/Duplication Analysis detects most intragenic deletions and duplications at single exon resolution. Rarely however, single-exon duplication events may be missed due to inherent sequence properties or isolated reduction in data quality.

CLINICAL DESCRIPTION

HFE-associated hereditary hemochromatosis (HFE-HH) is characterized by inappropriately high absorption of iron by the gastrointestinal mucosa. The phenotypic spectrum of HFE-HH is now recognized to include Those with clinical HFE-HH, in which manifestations of end-organ damage secondary to iron storage are present; Those with biochemical HFE-HH, in which the only evidence of iron overload is increased transferrin-iron saturation and increased serum ferritin concentration; and Non-expressing p.Cys282Tyr homozygotes in whom neither clinical manifestations of HFE-HH nor iron overload are present. Clinical HFE-HH is characterized by excessive storage of iron in the liver, skin, pancreas, heart, joints, and testes. In untreated individuals: early symptoms may include abdominal pain, weakness, lethargy, and weight loss; the risk of cirrhosis is significantly increased when the serum ferritin is higher than 1,000 ng/mL; other findings may include progressive increase in skin pigmentation, diabetes mellitus, congestive heart failure and/or arrhythmias, arthritis, and hypogonadism. Clinical HFE-HH is more common in men than women.

REFERENCES

- Rochette J, et al. Factors influencing disease phenotype and penetrance in HFE haemochromatosis. Human Genetics.2010;128(3):233–248.
- Whitlock EP, Garlitz BA, Harris EL, et al. Screening for hereditary hemochromatosis: a systematic review for the U.S. preventive services task force. Annals of Internal Medicine. 2006;145(3):209–223.
- Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS. Diagnosis and management of hemochromatosis: 2011 practice guideline by the American Association for the study of liver diseases. Hepatology. 2011;54(1):328–343.

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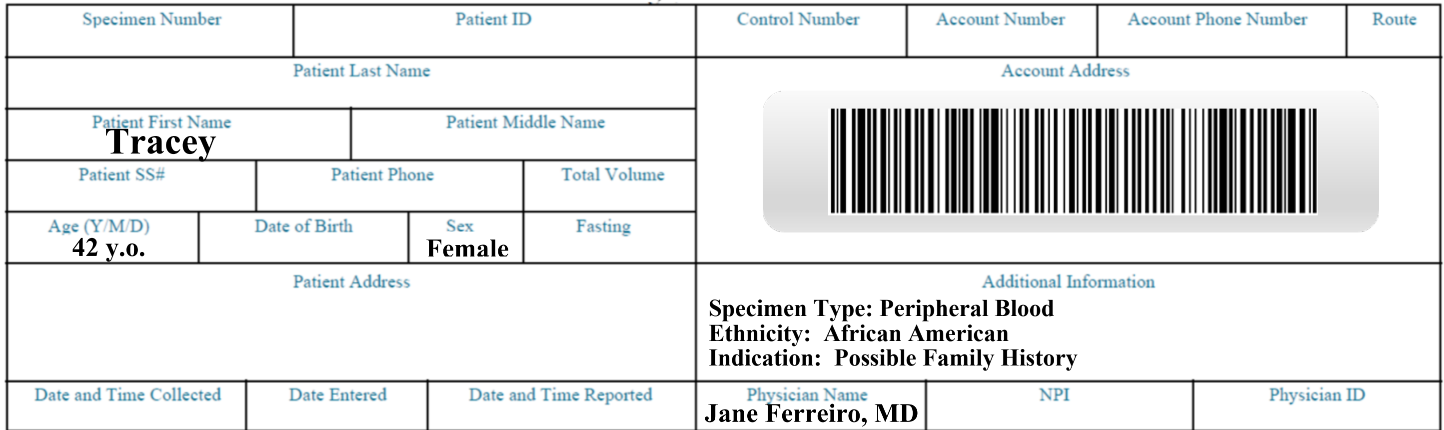
Phone: 510-555-1212



Specimen Number	Patient ID	Control Number	Account Number	Account Phone Number	Route

Patient Last Name:

Patient First Name: **Tracey**

Patient Middle Name:

Patient SS#: | Patient Phone: | Total Volume:

Age (Y/M/D): **42 y.o.** | Date of Birth: | Sex: **Female** | Fasting:

Account Address:

Patient Address:

Additional Information
Specimen Type: Peripheral Blood
Ethnicity: African American
Indication: Possible Family History

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

Tests Ordered
Malignant Hyperthermia Susceptibility Sequencing Panel

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 Malignant Hyperthermia Susceptibility

5 conditions tested:

- Malignant Hyperthermia Susceptibility, type 1
- Malignant Hyperthermia Susceptibility, type 5
- Central Core Disease
- Minicore Myopathy with External Opthalmoplegia
- Native American Myopathy

GENE	TEST RESULTS	EXPLANATION
CACNA1S	Negative	No known pathogenic variant detected
RYR1	L4824P | L4824P	**This result confirms the susceptibility for Malignant Hyperthermia type 1**. This result should be interpreted in the context of clinical presentation and results of other laboratory tests. A PCR/sequencing study has detected two copies of the NM_000540.2(RYR1):c.14471T>C (p.Leu4824Pro) variation. The L4824P mutation is encoded by a T to C change at nucleotide position 14471 in the RYR1 mRNA and results in a change from leucine to proline at amino acid position 4824 in the protein. In addition, this individual's result has important implications for other family members. Clinical evaluations should be considered and genetic counseling is recommended for at-risk individuals.
STAC3	Negative	No known pathogenic variant detected

DISCLAIMER:
Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete. Rare polymorphisms exist that could lead to false negative or positive results. If results obtained do not match the clinical findings, additional testing should be considered.

NGS method: We use a combination of Next Generation Sequencing (NGS) and Sanger sequencing technologies to cover the full coding regions of the listed genes plus ~20 bases of non-coding DNA flanking each exon. As required, genomic DNA is extracted from the patient specimen. For NGS, patient DNA corresponding to these regions is captured using an optimized set of DNA hybridization probes. Captured DNA is sequenced using Illumina's Reversible Dye Terminator (RDT) platform (Illumina, San Diego, CA, USA). Regions with insufficient coverage by NGS are covered by Sanger sequencing. All pathogenic, likely pathogenic, or variants of uncertain significance are confirmed by Sanger sequencing. aCGH method: As required, DNA is extracted from the patient specimen. Equal amounts of genomic DNA from the patient and a gender matched reference sample are amplified and labeled with Cy3 and Cy5 dyes, respectively. To prevent any sample cross contamination, a unique sample tracking control is added into each patient sample. Each labeled patient product is then purified, quantified, and combined with the same amount of reference product. The combined sample is loaded onto the designed array and hybridized for at least 22-42 hours at 65°C. Arrays are then washed and scanned immediately with 2.5 μM resolution. Only data for the gene(s) of interest for each patient are extracted and analyzed. If you would like to order a subset of these genes contact us to discuss pricing.

CLINICAL DESCRIPTION

Malignant hyperthermia is characterized by a rapid increase in temperature to 39-42 degrees C in response to inhalational anesthetics such as halothane or to muscle relaxants such as succinylcholine. [from HPO]