

Appendix B

Database II

**One page description of genetic tests for non-cancer conditions with
some applicability to the Medicare population**

1. Gene Symbol: FGFR3 Chromosomal Locus: 4p16.3
2. Protein Name: Molecular gene testing of the Fibroblast growth factor receptor 3 (FGFR3) gene
3. Disease: Achondroplasia
4. Description: All individuals who have a single copy of the altered *FGFR3* have achondroplasia (100% penetrance). Achondroplasia is characterized by abnormal bone growth that results in short stature with disproportionately short arms and legs, a large head, and characteristic facial features with frontal bossing and mid-face hypoplasia. In infancy, hypotonia is typical, and acquisition of developmental motor milestones is often delayed. Intelligence and life span are usually normal.
5. Purpose: Confirmatory diagnostic and Prenatal Diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; sequence analysis
9. Other Diseases: Hypochondroplasia; FGFR related craniosynostosis; Severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN dysplasia); Thanatophoric dysplasia
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: 8/9/06
 - “Achondroplasia (limit to humans)”=1447 citations
 - “Fibroblast growth factor receptor 3”=633 citations
 - “Achondroplasia (limit to humans) and Fibroblast growth factor receptor 3”=147 citations

1. Gene Symbol: ALAD Chromosomal Locus: 9q34
2. Protein Name: Delta-aminolevulinic acid dehydratase (Porphobilinogen synthase)
3. Disease: Acute Hepatic Porphyria
4. Description: Mutations in the ALAD gene (aminolevulinate, delta-, dehydratase) cause ALAD deficiency porphyria
5. Purpose: Biochemical testing only
6. Availability: Mayo Clinic Biochemical genetic laboratory
7. Specimen: ND
8. Methodology: Analyte, Enzyme assay
9. Other Diseases: None
10. Clinical use(s): This disorder is very rare; fewer than 10 cases have ever been reported worldwide
11. Source of Information: GeneTests.org, Mayo Clinic
12. Exploratory Medline Search (10/27/06):
 - a. "Porphyria\$" = 7265 citations
 - b. "ALAD" = 454 citations
 - c. "Porphyria\$" and "ALAD" = 24 citations (limit to human)

1. Gene Symbol: ADA Chromosomal Locus: 20q13.11
2. Protein Name: Adenosine deaminase
3. Disease: Adenosine Deaminase Deficiency
4. Description: Adenosine deaminase (ADA) deficiency is a systemic purine metabolic disorder that primarily affects lymphocyte development and function.
5. Purpose: Diagnostic – late onset
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: [Enzyme assay](#), [Analysis of the entire coding region: Sequence analysis](#)
9. Other Diseases: None
10. Clinical use(s): Unclear
11. Source of Information: GeneTests.org
12. Exploratory Medline Search (10/27/06):
 - a. “Adenosine Deaminase Deficiency” = 356 citations
 - b. “ADA” = 5037 citations
 - c. “Adenosine Deaminase Deficiency” and “ADA” = 115 citations

1. Gene Symbol: AMPD1 Chromosomal Locus: 1p21-p13
2. Protein Name: AMP Deaminase 1
3. Disease: Adenosine Monophosphate Deaminase 1 or Exercise-Induced Myopathy
4. Description: Inherited disorder of muscular energy metabolism typically affecting skeletal muscle. The typical symptoms are exercise induced muscle pains, cramps and/or early fatigue. The vast majority of the patients are homozygous for the C34-T gene mutation in the AMPD1 gene
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Enzyme assay
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear. Symptoms can be treated by intake of D-ribose at the time of symptoms
11. Source of Information: GeneTests.org, Athena diagnostics (Reference Lab)
12. Exploratory Medline Search (10/27/06):
 - a. "Adenosine Monophosphate Deaminase" or "AMP Deaminase" = 891 citations
 - b. "AMPD1" = 69 citations
 - c. "a" and "AMPD1" = 60 citations (limit to human)

1. Gene Symbol: ABCD1 Chromosomal Locus: Xq28
2. Protein Name: ATP-binding cassette sub-family D member 1
3. Disease: Adrenoleukodystrophy, X-Linked
4. Description: An X-linked recessive disorder characterized by the accumulation of saturated very long chain fatty acids in the lysosomes of adrenal cortex and the white matter of central nervous system occurring almost exclusively in the males. Clinical features include the childhood onset of ataxia; neurobehavioral manifestations; hyperpigmentation; adrenal insufficiency; seizures; muscle spasticity; and dementia. The slowly progressive adult form is called adrenomyeloneuropathy. The defective gene ABCD1 is located at Xq28, and encodes the adrenoleukodystrophy protein (ATP-BINDING CASSETTE TRANSPORTERS).
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analyte, Enzyme assay
9. Other Diseases: None
10. Clinical use(s) for the Medicare: Unclear (early onset). Corticosteroid replacement therapy is essential for the treatment of individuals with X-ALD in whom adrenal insufficiency is identified. Physical therapy, management of urologic complications, and family and vocational counseling are of value for men with adrenomyeloneuropathy.
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/26/06)
 - a. "Adrenoleukodystrophy" = 1567 citations
 - b. "ABCD1" = 163 citations
 - c. "Adrenoleukodystrophy" and "ABCD1" = 132 citations (limit to humans)

1. Gene Symbol: HMBS Chromosomal Locus: 11q23.
2. Protein Name: Porphobilinogen deaminase
3. Disease: Acute Intermittent Porphyria
4. Description: An autosomal dominant porphyria that is due to a deficiency of hydroxymethylbilane synthase in the liver, the third enzyme in the 8-enzyme biosynthetic pathway of heme. Clinical features are recurrent and life-threatening neurologic disturbances, abdominal pain, and elevated level of aminolevulinic acid and porphobilinogen in the urine. When a potentially disease-causing *HMBS* mutation is not associated with symptoms, AIP is said to be "latent."
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Mutation scanning, Analysis of the entire coding region: Sequence analysis
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Testing is not useful in predicting if or when individuals who inherit the *HMBS* mutation will become symptomatic Identification of individuals at risk for AIP, however, alters management because avoidance of known risk factors and other measures may be helpful in preventing acute attacks and other symptoms
11. Source of Information: GeneTests.org, OVID MEDLINE
12. Exploratory Medline Search (10/27/06):
 - a. "Acute Intermittent Porphyria" = 1239 citations
 - b. "HMBS" = 38 citations
 - c. "Acute Intermittent Porphyria" and "HMBS" = 24 citations (limit to humans)

1. Gene Symbol: NOTCH2 Chromosomal Locus: 11p13-p11
2. Gene Symbol: JAG1 Chromosomal Locus: 20p12
3. Protein Name: Neurogenic locus notch homolog protein 2, Jagged-1
4. Disease: Alagille syndrome
5. Description: Alagille syndrome is a multisystem disorder. Studies of families with multiple affected members and/or *JAG1* mutations have demonstrated a wide spectrum of clinical variability ranging from life-threatening liver or cardiac disease to only subclinical manifestations (i.e., butterfly vertebrae, posterior embryotoxon, or characteristic facial features).
6. Purpose: Diagnostics
7. Availability: Clinical Laboratories
8. Specimen: Blood
9. Methodology: [Sequence analysis and FISH metaphase](#)
10. Other Diseases: None
11. Clinical use(s): The prevalence of Alagille syndrome has been estimated to be one in 70,000 live births. Molecular testing of *JAG1* is helpful if the proband's family is interested in clarification of the genetic status of at-risk relatives and/or in prenatal diagnosis
12. Source of Information: GeneTests.org
13. Exploratory Medline Search (10/26/06):
 - a. "Alagille syndrome" = 508 citations
 - b. "JAG1" or "NOTCH2" = 427 citations
 - d. "Alagille syndrome" and ("JAG1" or "NOTCH2") = 88 citations (limit to human)

1. Gene Symbol: GNAS (GNAS1) Chromosomal Locus: 20q13.2
2. Protein Name: Guanine nucleotide-binding protein G(s), alpha subunit
3. Disease: Albright Hereditary Osteodystrophy
4. Description: Albright hereditary osteodystrophy (AHO) is a syndrome including short stature, obesity, rounded face, subcutaneous ossifications and characteristic shortening and widening of long bones in the hands and feet. Also associated with resistance to PTH or parathyroid hormone (a syndrome called pseudohypoparathyroidism type 1a or PHP1a) and to other hormones (thyroid-stimulating hormone or TSH in particular). PHP1a is characterized by hypoparathyroid manifestations (hypocalcemia, hyperphosphoremia) and elevated PTH levels, indicating resistance to the hormone.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Sequence analysis of select exons
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear
11. Source of Information: GeneTests.org
12. Exploratory Medline Search (10/27/06):
 - a. "Albright Hereditary Osteodystrophy" = 91 citations
 - b. "GNAS" or "GNAS1" = 169 citations
 - c. "Albright Hereditary Osteodystrophy" and "b" = 197 citations (limit to human)

1. Gene Symbol: HGD Chromosomal Locus: 3q21-q23
2. Protein Name: Homogentisate 1,2-dioxygenase
3. Disease: Alkaptonuria
4. Description: Alkaptonuria is caused by deficiency of homogentisate 1,2-dioxygenase, an enzyme that converts homogentisic acid (HGA) to maleylacetoacetic acid in the tyrosine degradation pathway. The three major features of alkaptonuria are the presence of homogentisic acid in the urine, ochronosis (bluish-black pigmentation in connective tissue), and arthritis of the spine and larger joints.
5. Purpose: Biochemical testing Confirmatory diagnostic testing and carrier testing
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear
11. Source of Information: GeneTests.org
12. Exploratory Medline Search (10/30/06):
 - a. "Alkaptonuria" = 558 citations
 - b. "HGD" = 213 citations
 - c. "Alkaptonuria" and "HGD" = 5 citations (limit to human)

1. Gene Symbol: MAN2B1 Chromosomal Locus: 19cen-q12
2. Protein Name: Lysosomal alpha-mannosidase
3. Disease: Alpha -mannosidosis
4. Description: *MAN2B1* is the only gene associated with alpha-mannosidosis. A milder type 1 recognized after age ten years with absence of skeletal abnormalities, myopathy, and slow progression. Type 2 and 3 are associated with early symptoms, progression and early death
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis, sequence analysis, analyte, enzyme assay
9. Other Diseases: n/d
10. Clinical use(s) for the Medicare: Unclear
11. Source of Information: GeneTests.org
12. Exploratory Medline Search (10/30/06):
 - a. "Alpha -mannosidosis" = 240 citations
 - b. "MAN2B1" = 1 citation
 - c. "Alpha -mannosidosis" and "MAN2B1" = 1 citations (limit to human)

1. Gene Symbol: SGCA; Chromosomal Locus: 17q12-q21.3
2. Protein Name: Alpha-sarcoglycan
3. Disease: Limb-Girdle Muscular Dystrophy: Alpha-Sarcoglyopathy
4. Description: Mutations in the SGCA gene have been associated with Alpha-Sarcoglyopathy (a subset of Limb-Girdle Muscular Dystrophy). Findings range from early-childhood onset with severe progression to later onset with milder progression
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: DNA sequencing, targeted mutation analysis, and mutation scan
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Unclear (mostly young onset)
 - a. Genetic testing may be used to identify milder form of late onset disease
11. Source of Information: GeneTests.org, Athena Diagnostics
12. Exploratory Medline Search:
 - a. "Limb-Girdle Muscular Dystrophy.mp. or exp Muscular Dystrophies, Limb-Girdle"=534
 - b. "LGMD2D.mp."=21
 - c. a and b = 14

1. Gene Symbol: HBA1, HBA2, HBZ Chromosomal Locus: 16pter-p13.3
2. Protein Name: Hemoglobin alpha chain, Hemoglobin zeta chain
3. Disease: Alpha-thalassemia
4. Description: The clinically significant [phenotypes](#) of α -thalassemia are Hb Bart hydrops fetalis syndrome and HbH disease. HBA1, the gene encoding α_1 -globin, and HBA2, the gene encoding α_2 -globin, are the two genes associated with α -thalassemia.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Deletion/duplication analysis, Analysis of the entire coding region: Sequence analysis, Analysis of the entire coding region: Sequence analysis, Sequence analysis of select exons
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, Comprehensive Genetic Services, SC Molecular Diagnostic Laboratory
12. Exploratory Medline Search (10/30/06):
 - a. "Alpha-thalassemia" = 2982 citations
 - b. "HBA1" or "HBA2" or "HBZ" = 12908 citations
 - c. "Alpha-thalassemia" and "b" = 72 citations (limit to human)

1. Gene Symbol: ALMS1 Chromosomal Locus: 2p13
2. Protein Name: ALMS1 protein
3. Disease: Alstrom Syndrome
4. Description: Alström syndrome is characterized by cone-rod dystrophy, obesity, progressive sensorineural hearing impairment, dilated cardiomyopathy, the insulin resistance syndrome, and developmental delay. ALMS1 is the only gene currently known to be associated with Alström syndrome. Molecular genetic testing of the ALMS1 gene is estimated to detect mutations in 25-40% of individuals.
5. Purpose: diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: [Sequence analysis of select exons](#)
9. Other Diseases: n/d
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, Centro Genetica Clinica
12. Exploratory Medline Search (10/31/06):
 - a. "Alstrom Syndrome" 67 citations
 - b. "ALMS1" = 15 citations
 - c. "Alstrom Syndrome" and "ALMS1" = 10 citations (limit to human)

1. Gene Symbol: APP Chromosomal Locus: 21q21
2. Protein Name: Amyloid beta A4 protein
3. Disease: Alzheimer Disease Type 1 (Early-onset familial AD)
4. Description: Alzheimer disease (AD) is characterized by adult-onset slowly progressive dementia associated with diffuse cerebral atrophy on neuroimaging studies. It is the most common form of dementia, but fewer than 2% of families with AD have early-onset familial AD (EOFAD), in which symptoms consistently occur before the age of 65 years. Three forms of EOFAD caused by mutations in one of three genes (*APP*, *PSEN1*, *PSEN2*) are recognized. Alzheimer disease type 1 (AD1) is caused by mutations in the (*APP*) gene, which encodes the amyloid precursor protein.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons, Preimplantation genetic diagnosis
9. Other Diseases: n/d
10. Clinical use(s): Unclear
11. Source of Information: GeneTests.org, Hospital Clinic
Centro de Diagnostico Biomedico
12. Exploratory Medline Search (10/31/06):
 - a. "Alzheimer Disease" = 54431 citations
 - b. "APP" or "Amyloid beta-Protein Precursor" = 9616 citations
 - c. "Alzheimer Disease" and "b" = 5516 citations (limit to human)

1. Gene Symbol: PSEN1 Chromosomal Locus: 14q24.3
2. Protein Name: Presenilin 1
3. Disease: Alzheimer Disease Type 3 (Early-onset familial AD)
4. Description: Alzheimer disease (AD) is characterized by adult-onset slowly progressive dementia associated with diffuse cerebral atrophy on neuroimaging studies. It is the most common form of dementia, but fewer than 2% of families with AD have early-onset familial AD (EOFAD), in which symptoms consistently occur before the age of 65 years. Three forms of EOFAD caused by mutations in one of three genes (*APP*, *PSEN1*, *PSEN2*) are recognized. Alzheimer disease type 3 (AD3) is caused by mutations in *PSEN1*, the gene encoding the proteint presenilin 1.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Cerebrospinal Fluid and/or blood
8. Methodology: Mutation scanning, Targeted mutation analysis, Sequence analysis.
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset type) may be useful for diagnostic purposes
11. Source of Information: GeneTests.org, Hospital Clinic; Centro de Diagnostico Biomedico
12. Exploratory Medline Search 10/31/06:
 - a. "Alzheimer Disease" = 54431 citations
 - b. "PSEN1" or "presenilin 1" = 2217 citations
 - c. "Alzheimer Disease" and "b" = 1544 citations (limit to human)

1. Gene Symbol: PSEN2 Chromosomal Locus: 1q31-q42
2. Protein Name: Presenilin 2
3. Disease: Alzheimer Disease Type 4
4. Description: Alzheimer disease (AD) is characterized by adult-onset slowly progressive dementia associated with diffuse cerebral atrophy on neuroimaging studies. It is the most common form of dementia, but fewer than 2% of families with AD have early-onset familial AD (EOFAD), in which symptoms consistently occur before the age of 65 years. Three forms of EOFAD caused by mutations in one of three genes (*APP*, *PSEN1*, *PSEN2*) are recognized.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Mutation scanning, Sequence analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: useful for diagnostic purposes
11. Source of Information: GeneTests.org, Lab. "Dr. F. Echevarne"Department of Genetics_
12. Exploratory Medline Search (11/3/06):
 - a. " Alzheimer Disease" = 54529 citations
 - b. "PSEN2" = 78 citations
 - c. "Alzheimer Disease" and "PSEN2" = 58 citations (limit to human)

1. Gene Symbol: GSN Chromosomal Locus: 9q34
2. Protein Name: Gelsolin precursor, plasma
3. Disease: Amyloidosis V
4. Description: Amyloidosis V is an inherited, and degenerative disease, linked by the common theme of abnormal protein folding and deposition of AMYLOID. As the amyloid deposits enlarge they displace normal tissue structures, causing disruption of function. It results from the deposits of gelsolin.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories (Outside US)
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: n/d
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information (11/3/06):
 - a. "Amyloidosis" = 16551 citations
 - b. "GSN" = 1516 citations
 - c. "Amyloidosis" and "GSN" = 112 citations (limit to human)

1. Gene Symbol: KCNJ2 Chromosomal Locus: 17q23.1-q24.2
2. Protein Name: Inward rectifier potassium channel 2
3. Disease: Andersen Syndrome Type 1
4. Description: Andersen-Tawil syndrome (referred to as ATS in this entry) is characterized by a triad of distinctive dysmorphic features: episodic flaccid muscle weakness (i.e., periodic paralysis), ventricular arrhythmias and prolonged QT interval, and common anomalies such as low-set ears, ocular hypertelorism, small mandible, fifth digit clinodactyly, syndactyly, short stature, and scoliosis. In the first or second decade, affected individuals present with either cardiac symptoms (palpitations and/or syncope) or weakness that occurs spontaneously following prolonged rest or following rest after exertion. KCNJ2, encoding the inward rectifier potassium channel 2 protein, Kir2.1, is the only gene associated with ATS.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood or tissue
8. Methodology: Analysis of the entire coding region: Mutation scanning, Sequence analysis of select exons
9. Other Diseases: n/d
10. Clinical use(s) for the Medicare: unclear (early onset)
11. Source of Information: GeneTests.org, IRCCS Fondazione Salvatore Maugeri Molecular Cardiology Laboratories
12. Exploratory Medline Search (11/3/06):
 - a. "Andersen Syndrome" or "Andersen-Tawil" = 32 citations
 - b. "KCNJ2" = 57 citations
 - c. "a" and "KCNJ2" = 19 citations (limit to human)

1. Gene Symbol: HP Chromosomal Locus: 16q22.1
2. Protein Name: Haptoglobin
3. Disease: Anhaptoglobinemia
4. Description: Anhaptoglobinemia referring to lack of expression of the haptoglobin gene or Hp 0-0
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis, Deletion/duplication analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: ND
11. Source of Information: GeneTests.org
12. Exploratory Medline Search (11-06-06):
 - a. "Anhaptoglobinemia" = 15 citations
 - b. "Haptoglobin" or "HP" = 12178 citations
 - c. "Anhaptoglobinemia" or "b" = 6 citations

1. Gene Symbol: APOC2 Chromosomal Locus: 19q13.2
2. Protein Name: Apolipoprotein C-II
3. Disease: Apolipoprotein C-II Deficiency
4. Description: Apolipoprotein C-II deficiency is caused by mutation in the APOC2 gene. Clinically and biochemically, apoC-II deficiency closely simulates lipoprotein lipase deficiency, or hyperlipoproteinemia type I, and is therefore referred to as hyperlipoproteinemia type IB.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Deletion/duplication analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, Center for Nephrology and Metabolic Disorders Laboratory for Molecular Diagnostics
12. Exploratory Medline Search (11/06/06):
 - a. "Apolipoprotein C-II Deficiency" = 31 citations
 - b. "APOC2" = 103 citations
 - c. "Apolipoprotein C-II Deficiency" and "APOC2" = 0 citations

1. Gene Symbol: APOE Chromosomal Locus: 19q13.2
2. Protein Name: Apolipoprotein E
3. Description: Type III hyperlipoproteinemia (broad beta disease) should be considered in all patients with elevation of both serum cholesterol and triglycerides. The DNA test for this lipid disorder accurately determines the apolipoprotein E (apo E) genotype. The apo E genotype E2/E2 is diagnostic of type III hyperlipoproteinemia in individuals who have elevated serum cholesterol and triglycerides and accumulation of the abnormal lipoprotein β -VLDL. Type III hyperlipoproteinemia is associated with accelerated atherosclerosis, coronary heart disease and peripheral vascular disease.
4. Purpose: Diagnostic and prenatal diagnosis
5. Availability: Clinical Laboratories
6. Specimen: Blood
7. Methodology: Targeted mutation analysis
8. Disease: Cardiovascular Disease Risk Factor (Apolipoprotein E)
9. Other Diseases: None
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, Kimball Genetics, Inc.
12. Exploratory Medline Search (11/06/06):
 - a. "cardiovascular diseases" = 1318759 citations
 - b. "Apolipoproteins E" or "APOE" = 10704 citations
 - c. "cardiovascular diseases" and "b" = 1789 citations (limit to human)

1. Gene Symbol: FGD1 Chromosomal Locus: Xp11.2
2. Protein Name: FYVE, RhoGEF and PH domain containing protein 1
3. Disease: Aarskog Syndrome (facio-digito-genital syndrome)
4. Description: Aarskog syndrome is due to mutations in the FGD1 gene, a Rho/Rac guanine exchange factor localized to Xp11.21. Males present with short stature, hypertelorism, small scrotum and joint hyperextensibility. Carrier females tend to be shorter than non-carriers and usually have subtle facial features. Males can have mild cognitive impairment.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, replication analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, Molecular Diagnostic Laboratory
12. Exploratory Medline Search (11-07-06):
 - a. "Aarskog Syndrome' or faciodigitogenital syndrome" = 88 citations
 - b. "FGD1" = 39 citations
 - c. "FGD1" = 10 citations (limit to human)

1. Gene Symbol: Gene Symbol: RYR2 Chromosomal Locus: 1q42.1-q43
Gene Symbol: DSP Chromosomal Locus: 6p24
Gene Symbol: PKP2 Chromosomal Locus: 12p11
2. Protein Name: Ryanodine receptor 2, Plakophilin-2 (Ryanodine receptor 2, Desmoplakin)
3. Disease: Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy, Autosomal Dominant
4. Description: Autosomal dominant arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is a progressive disorder characterized by fibrofatty replacement of the myocardium that predisposes to ventricular tachycardia and sudden death in young individuals and athletes. The three genes known to be associated with autosomal dominant ARVD/C are: *RYR2* (locus name ARVD2), which encodes the cardiac ryanodine receptor protein; *DSP* (locus name ARVD8), which encodes the protein desmoplakin; and *PKP2* (locus name ARVD9), which encodes the desmosomal protein plakophilin-2.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Analysis of the entire coding region: Mutation scanning, Deletion/duplication analysis, linkage analysis
9. Other Diseases: Catecholaminergic polymorphic ventricular tachycardia, ARVD8/Carvajal syndrome
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, Johns Hopkins Hospital
DNA Diagnostic Laboratory
12. Exploratory Medline Search (11-09-06):
 - a. "Arrhythmogenic Right Ventricular Dysplasia" = 531 citations
 - b. "PKP2" or "DSP" or "RYR2" = 2065 citations
 - c. "Arrhythmogenic Right Ventricular Dysplasia" and "b" = 21 citations (limit to human)

1. Gene Symbol: SACS Chromosomal Locus: 13q12
2. Protein Name: Sacsin
3. Disease: autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS)
4. Description: SACS is the only gene known to be associated with autosomal recessive spastic ataxia of Charlevoix-Saguenay. ARSACS (**autosomal recessive spastic ataxia of Charlevoix-Saguenay**) is characterized in individuals born in Quebec Province by early-onset (age 12-18 months) difficulty in walking and gait unsteadiness. Onset is often delayed until the juvenile and even adult age range in individuals with ARSACS born outside the Province of Quebec. Individuals with ARSACS born in the Province of Quebec become wheelchair bound at the average age of 41 years; cognitive skills are preserved in the long term as individuals remain able to perform daily living tasks late into adulthood. Death commonly occurs in the sixth decade.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: ND
8. Methodology: Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, Hospital Sainte-Justine
Biologie Moleculaire
12. Exploratory Medline Search (11-07-06):
 - a) "ARSACS" or "Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay" = 35 citations
 - b) "SACS" = 3889 citations
 - c) "a" and "SACS" = 19 citations (limit to human)

1. Gene Symbol: APTX Chromosomal Locus: 9p13.3
2. Protein Name: Aprataxin
3. Disease: Ataxia with Oculomotor Apraxia 1
4. Description: Ataxia with oculomotor apraxia type 1 (AOA1) is characterized by childhood onset of slowly progressive cerebellar ataxia, followed by oculomotor apraxia and a severe primary motor peripheral axonal motor neuropathy. *APTX* is the only gene associated with AOA1.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Linkage analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: unclear
11. Source of Information: GeneTests.org, Cyprus Institute of Neurology and Genetics
Molecular Genetics Department D-Neurogenetics
12. Exploratory Medline Search (11-07-06):
 - a) "Ataxia" or "Oculomotor Apraxia 1" = 21242 citations
 - b) "APTX" = 48 citations
 - c) "a" and "APTX" = 39 citations (limit to human)

1. Gene Symbol: SETX Chromosomal Locus: 9q34
2. Protein Name: Probable helicase senataxin
3. Disease: Ataxia with Oculomotor Apraxia 2
4. Description: Ataxia with oculomotor apraxia type 2 (AOA2) is characterized by onset between ten and 22 years of age, cerebellar atrophy, axonal sensorimotor neuropathy, oculomotor apraxia, and elevated serum concentration of alpha-fetoprotein (AFP). AOA2 is associated with mutations in the gene *SETX*, which encodes the protein senataxin.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: unclear (early onset)
11. Source of Information: GeneTests.org, University of Rostock
Neurobiological Laboratory, Department of Neurology
12. Exploratory Medline Search (11-07-06):
 - a) "Ataxia" or "Oculomotor Apraxia 2" = 11203 citations
 - b) "SETX" = 15 citations
 - c) "a" and "SETX" = 8 citations (limit to human)

1. Gene Symbol*: CFH Chromosomal Locus: 1q32
Gene Symbol*: IF Chromosomal Locus: 4q25
Gene Symbol*: MCP Chromosomal Locus: 1q32
2. Protein Name: Protein Name: Complement factor H
Protein Name: Complement factor I
Protein Name: Membrane cofactor protein
3. Disease: Atypical Hemolytic-Uremic Syndrome
4. Description: Approximately 50% of patients with aHUS have mutations in one of the complement control proteins: factor H, factor I, or membrane cofactor protein (MCP). Atypical hemolytic uremic syndrome may become a chronic condition, and patients with aHUS may experience repeated attacks of the disorder. Children with aHUS are much more likely to develop chronic serious complications such as kidney failure and severe high blood pressure.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Deletion/duplication analysis
9. Other Diseases: ND
10. Clinical use(s): Unclear (early onset) Complement regulatory protein deficiency impacts treatment decisions as patients with aHUS have a recurrence rate in renal transplants of ~50%, whereas those with factor H mutations have an even higher risk (~80%).
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (8/10/06)
 - a. "Atypical hemolytic uremic syndrome"=139 citations
 - b. "Complement factor"=14162 citations
 - c. "Atypical hemolytic uremic syndrome" and "Complement factor"(limit to humans)=43 citations

1. Gene Symbol: LMNA Chromosomal Locus: 1q21.2
2. Protein Name: Lamin-A/C
3. Disease: Atypical Werner Syndrome
4. Description: Werner's syndrome is a progeroid syndrome caused by mutations at the WRN helicase locus. Some features of this disorder are also present in laminopathies caused by mutant LMNA encoding nuclear lamin A/C.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood, isolated DNA, cultured cells
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: Emery-Dreifuss Muscular Dystrophy, Dilated Cardiomyopathy, Cardiomyopathy with Conduction Defects, Partial Lipodystrophy, Charcot-Marie-Tooth, Mandibuloacral Dysplasia, Hutchinson-Gilford Progeria Syndrome
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org
12. Exploratory Medline Search:
 - a) "Atypical Werner Syndrome"=17 citations
 - b) "Lamin-A/C"=310 citations
 - c) "Atypical Werner Syndrome" and "Lamin-A/C"=2 citations

1. Gene Symbol: AIRE Chromosomal Locus: 21q22.3
2. Protein Name: Autoimmune regulator
3. Disease: Autoimmune Polyendocrinopathy Syndrome Type 1/Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy
4. Description: Type I is characterized by childhood onset and chronic mucocutaneous candidiasis (candidiasis and chronic mucocutaneous) and organ-specific antibodies against a variety of endocrine glands. Presence of at least one of the three characteristic component diseases such as Chronic mucocutaneous candidiasis, hypoparathyroidism, primary adrenal insufficiency of autoimmune polyglandular syndrome type 1 (APS1) in children age ten or younger.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Sequence analysis of select exons, Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (8/9/06)
 - a) "Autoimmune Polyendocrinopathies" = 476 citations
 - b) "Autoimmune regulator"=111 citations
 - c) "Autoimmune Polyendocrinopathies" and "Autoimmune regulator"=60 citations (limit to human)

1. Gene Symbol: TGFBI Chromosomal Locus: 5q31
2. Protein Name: Transforming growth factor-beta-induced protein ig-h3
3. Disease: Avellino Corneal Dystrophy
4. Description: The mutated keratoepithelin adhesion protein forms amyloidogenic intermediates that precipitate in the cornea, causing a progressive opacification. These diseases are usually inherited and do not affect other parts of the body. They may begin early in life, but can also manifest with age.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: ND
8. Methodology: Sequence analysis, Linkage analysis, Sequence analysis of select exons, Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) in the Medicare population: unclear (early to late onset)
11. Source of Information: GeneTests.org
12. Exploratory Medline Search:
 - a) "Hereditary Corneal dystrophies"=2171 citations
 - b) "TGFBI"=67 citations
 - c) "Hereditary Corneal dystrophies" and "TGFBI"=44 citations (limit to human)

1. Gene Symbol: VMD2 Chromosomal Locus: 11q13
2. Protein Name: Bestrophin-1
3. Disease: Best Vitelliform Macular Dystrophy
4. Description: Best vitelliform macular dystrophy is a slowly progressive macular dystrophy with onset generally in childhood and sometimes in later teenage years. Age of onset and severity of vision loss are variable. *VMD2* is the only gene known to be associated with Best vitelliform macular dystrophy
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis, linkage analysis, Mutation scanning, Targeted mutation analysis
9. Other Diseases: bull's-eye maculopathy, autosomal dominant vitreoretinopathopathy associated with nanophthalmos, Adult vitelliform macular dystrophy
10. Clinical use(s) for the Medicare: unclear (early onset)
11. Source of Information: GeneTests.org, Uppsala University Children's Hospital Rudbeck Laboratory
12. Exploratory Medline Search (11-08-06):
 - a) "Best Vitelliform Macular Dystrophy" = 22 citations
 - b) "VDM2" = 88 citations
 - c) "Best Vitelliform Macular Dystrophy" and "VDM2" = 8 citations (limit to human)

1. Gene Symbol: MANBA Chromosomal Locus: 4q22-q25
Gene Symbol: MANBB Chromosomal Locus: Chromosome 4
2. Protein Name: Beta-mannosidase
3. Disease: Beta-Mannosidosis
4. Description: Beta-Mannosidosis is an autosomal recessive disorder caused by deficiency of the lysosomal enzyme beta-mannosidase. The most common features of β - Mannosidosis include: mental retardation, speech impairment, low muscle tone, recurrent respiratory infections, and hearing loss. Some affected individuals may also have a purplish-red rash called angiokeratomas and tortuosity of conjunctival vessels.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Enzyme assay, analyte
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, Emory University Emory Biochemical Genetics Laboratory
12. Exploratory Medline Search: n/d
 - a) "Beta-Mannosidosis" = 372 citations
 - b) "MANBA" or "MANBB" = 2 citations
 - c) "Beta-Mannosidosis" and "b" = 0 citations

1. Gene Symbol: HBB Chromosomal Locus: 11p15.5
2. Protein Name: Hemoglobin beta chain
3. Disease: Beta-Thalassemia
4. Description: Beta-thalassemia is a common monogenic disease caused by mutations in the human beta-globin gene (HBB), many of which are differentially represented in human subpopulations stratified by ethnicity.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood, cultured cells, isolated DNA
8. Methodology: Sequence analysis, Targeted mutation analysis, linkage analysis, Deletion/duplication analysis, Mutation scanning
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: GeneTests.org, ARUP Laboratories, Inc.
ARUP Laboratories
12. Exploratory Medline Search:
 - a) "Beta-Thalassemia" = 5823 citations
 - b) "HBB" = 337 citations
 - c) "Beta-Thalassemia" and "HBB" = 14 citations (limit to human)

1. Protein Name: Cytochrome P450 4V2
2. Gene Symbol: CYP4V2 Chromosomal Locus: 4q35.1
3. Disease: Bietti Crystalline Retinopathy (Bietti crystalline corneoretinal dystrophy)
4. Description: Bietti crystalline corneoretinal dystrophy (BCD) is an autosomal recessively inherited disorder characterized by tiny yellowish glittering retinal crystals, choroidal sclerosis, and crystals in the peripheral cornea, associated with progressive night blindness. Mutations of the CYP4V2 gene, a novel family member of the cytochrome P450 genes on chromosome 4q35, have recently been identified in patients with BCD.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Mutation scanning, Linkage analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear
11. Source of Information: GeneTests.org, Institute of Research in Ophthalmology
Laboratory of Molecular Ophthalmology
12. Exploratory Medline Search (11-09-06):
 - a) "Bietti Crystalline" = 14 citations
 - b) "CYP4V2" = 10 citations
 - c) "Bietti Crystalline" and "CYP4V2" = 6 citations (limit to human)

1. Protein Name: Caspase recruitment domain protein 15
2. Gene Symbol: CARD15 Chromosomal Locus: 16q12
3. Disease: Blau Syndrome
4. Description: Mutations in the caspase recruitment domain family, member 15 (CARD15) gene have been identified in several families with a rare condition called Blau syndrome. This disorder is characterized by inflammation of the eye (uveitis), early-onset arthritis, unusual curvature of the fingers (camptodactyly), and a persistent skin rash. Researchers have found at least two CARD15 mutations in people with Blau syndrome.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis
9. Other Diseases: Crohn's disease
10. Clinical use(s) for the Medicare: Unclear
11. Source of Information: GeneTests.org, Chapman Institute/Center for Genetic Testing at Saint Francis, Genetics Laboratory
12. Exploratory Medline Search (11-09-06):
 - a) "Blau Syndrome" = 46 citations
 - b) "CARD15" = 592 citations
 - c) "Blau Syndrome" and "CARD15" = 23 citations (limit to human)

1. Gene Symbol: FOXL2 Chromosomal Locus: 3q23
2. Protein Name: Forkhead box protein L2
3. Disease: Blepharophimosis, Ptosis, and Epicanthus Inversus
4. Description: Classic blepharophimosis syndrome (BPES) is a complex eyelid malformation invariably characterized by four major features: blepharophimosis, ptosis, epicanthus inversus, and telecanthus. FOXL2 is the only gene currently known to be associated with BPES.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Deletion/duplication analysis; FISH-metaphase; Array genomic hybridization
9. Other Diseases: Premature ovarian failure
10. Clinical use(s) for the Medicare: Unclear
11. Source of Information: GeneTests.org, Ghent University Hospital
Molecular Genetics Laboratory
12. Exploratory Medline Search (11-09-06):
 - a) "Blepharophimosis and Ptosis" or "Epicanthus Inversus" = 177 citations
 - b) "FOXL2" = 78 citations
 - c) "a" and "FOXL2" = 32 citations (limit to human)

1. Gene Symbol: OPN1LW Chromosomal Locus: Xq28
Gene Symbol: OPN1MW Chromosomal Locus: Xq28
2. Protein Name: Red-sensitive opsin, Green-sensitive opsin
3. Disease: Blue-Mono-Cone-Monochromatic Type Colorblindness
4. Description: ND
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: ND
11. Source of Information: GeneTests.org, University Eye Hospital Tuebingen
Molecular Genetics Laboratory
12. Exploratory Medline Search (11-09-06):
 - a) "Blue-Mono-Cone-Monochromatic Type Colorblindness" = 0 citations
 - b) "OPN1LW" = 1 citation
 - c) "OPN1MW" = 0 citation

1. Gene Symbol: TGFB1 Chromosomal Locus: 19q13.1
2. Protein Name: Progressive Diaphyseal Dysplasia
3. Disease: Camurati-Engelmann Disease
4. Description: Camurati-Engelmann disease (CED) is characterized by hyperostosis of the long bones and the skull, proximal muscle weakness, severe limb pain, a wide-based, waddling gait, and joint contractures. TGFB1 is the only gene known to be associated with CED.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis
9. Other Diseases: Ribbing Disease
10. Clinical use(s) for the Medicare: unclear
11. Source of Information: GeneTests.org, University of Antwerp
Department of Medical Genetics - Van Hul Lab
12. Exploratory Medline Search (11-09-06):
 - a) "Camurati-Engelmann Disease" = 82 citations
 - b) "TGFB1" = 165 citations
 - c) "Camurati-Engelmann Disease" and "TGFB1" = 13 citations (limit to human)

1. Gene Symbol: MT-TL1 Chromosomal Locus: Mitochondrial
2. Protein Name: Mitochondrial tRNA leucine 1
3. Disease: Cardiomyopathy with or without Skeletal Myopathy
4. Description: Any structural or functional disease of heart muscle that is marked especially by hypertrophy of cardiac muscle, by enlargement of the heart, by rigidity and loss of flexibility of the heart walls, or by narrowing of the ventricles but is not due to a congenital developmental defect, to coronary atherosclerosis, to valve dysfunction, or to hypertension.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, HUSLAB
Laboratory of Molecular Genetics
12. Exploratory Medline Search (11-12-06):
 - a) "Cardiomyopathy" = 59451 citations
 - b) "MT-TL1" = 0 citationsa

1. Gene Symbol: CPT2 Chromosomal Locus: 1p32
2. Protein Name: Carnitine O-palmitoyltransferase II
3. Disease: Carnitine Palmitoyltransferase II Deficiency
4. Description: Carnitine palmitoyltransferase II (CPT II) deficiency is a disorder of long chain fatty acid oxidation. The three clinical presentations are: lethal neonatal form, severe infantile hepatocardiomyopathy form, and myopathic form that is usually mild and often of adult onset. CPT II deficiency is caused by mutations in the *CPT2* gene that reduce activity of the enzyme CPT II.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis, Targeted mutation analysis; Analyte, Enzyme assay
9. Other Diseases: None
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, Baylor Research Institute
Institute of Metabolic Disease
12. Exploratory Medline Search (11-12-06):
 - a) "Carnitine Palmitoyltransferase II Deficiency" = 385 citations
 - b) "CPT2" = 45 citations
 - c) "Carnitine Palmitoyltransferase II Deficiency" and "CPT2" = 22 citations (limit to human)

1. Protein Name: Calsequestrin, cardiac muscle isoform
2. Gene Symbol: CASQ2 Chromosomal Locus: 1p13.3-p11
3. Disease: CASQ2-Related Catecholaminergic Polymorphic Ventricular Tachycardia
4. Description: Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited arrhythmogenic disease characterized by cardiac electrical instability exacerbated by acute activation of the adrenergic nervous system. There are two genes currently known to be associated with CPVT are *RYR2* and *CASQ2*.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood, tissue, or buccal swab
8. Methodology: Sequence analysis, Mutation scanning
9. Other Diseases: Unknown
10. Clinical use(s) for the Medicare: unclear (early onset)
11. Source of Information: GeneTests.org, Baylor College of Medicine John Welsh Cardiovascular Diagnostic Laboratory
12. Exploratory Medline Search (11-12-06):
 - a) "Catecholaminergic Polymorphic Ventricular Tachycardia" = 78 citations
 - b) "CASQ2" = 22 citations
 - c) "Catecholaminergic Polymorphic Ventricular Tachycardia" and "CASQ2" = 9 citations (limit to human)

1. Protein Name: Extracellular calcium-sensing receptor
2. Gene Symbol: CASR Chromosomal Locus: 3q13.3-q21
3. Disease: CASR-Related Disorders (Familial Hypercalciuric Hypercalcemia (HHC1/FHH), Neonatal Severe Primary Hyperparathyroidism (NSHPT), Hypocalcemia, Autosomal Dominant (ADH), Hypoparathyroidism, Familial Isolated (FIH))
4. Description: The calcium-sensing receptor is expressed in multiple tissues including the parathyroid glands, kidneys, bone marrow, osteoclasts, breast, thyroid C-cells, gastrin-secreting cells in the stomach, intestine and some areas of the brain. One of its major functions is to regulate calcium balance via changes in parathyroid and renal function. This receptor may also have a role in cellular response to changes in the extracellular environment.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood or buccal swab
8. Methodology: Sequence analysis, Deletion/duplication analysis, Linkage analysis, mutation scanning
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear
11. Source of Information: GeneTests.org, Center for Nephrology and Metabolic Disorders
Laboratory for Molecular Diagnostics
12. Exploratory Medline Search (11-13-06):
 - a) "Familial Hypercalciuric Hypercalcemia" or "Neonatal Severe Primary" or "Autosomal Dominant Hypocalcemia" or "Familial Isolated Hypoparathyroidism" = 3976 citations
 - b) "CASR" = 742 citations
 - c) "a" and "CASR" = 71 citations (limit to human)

1. Gene Symbol: GJB1 Chromosomal Locus: Xq13.1
2. Protein Name: Gap junction beta-1 protein
3. Disease: Charcot-Marie-Tooth Neuropathy Type X
4. Description: Charcot-Marie-Tooth neuropathy type 1 (CMT1) is a demyelinating peripheral neuropathy characterized by distal muscle weakness and atrophy, sensory loss, and slow nerve conduction velocity (NCV). It is usually slowly progressive and often associated with pes cavus foot deformity and bilateral foot drop. Affected individuals usually become symptomatic between five and 25 years of age. Fewer than 5% of individuals become wheelchair dependent. Life span is not shortened. GJB1 is the only gene known to be associated with Charcot-Marie-Tooth neuropathy type X. Molecular genetic testing of the *GJB1* (*Cx32*) gene detects about 90% of cases.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood or extracted DNA
8. Methodology: Sequence analysis, Mutation scanning, linkage analysis
9. Other Diseases: None
10. Clinical use(s) for the Medicare: unclear (early onset)
11. Source of Information: GeneTests.org, 2nd School of Medicine Charles University, Dept of Child Neurology DNA Laboratory
12. Exploratory Medline Search (11-12-06):
 - a) "Charcot-Marie-Tooth Neuropathy Type X" = 66 citations
 - b) "GJB1" = 51 citations
 - c) "Charcot-Marie-Tooth Neuropathy Type X" and "GJB1" = 6 citations (limit to human)

1. Gene Symbol: CHM Chromosomal Locus: Xq21.2
2. Protein Name: Rab proteins geranylgeranyltransferase component A 1
3. Disease: Choroideremia
4. Description: Choroideremia (CHM) is characterized by progressive chorioretinal degeneration in affected males and milder signs in carrier females. Typically, symptoms in affected males evolve from night blindness to peripheral visual field loss, with central vision preserved until late in life. Although carrier females are generally asymptomatic, signs of chorioretinal degeneration can be observed with careful fundus examination. These signs become more readily apparent after the second decade. CHM is the only gene to date associated with choroideremia.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis, Targeted mutation analysis, Linkage analysis
9. Other Diseases: None
10. Clinical use(s) for the Medicare: unclear (early onset)
11. Source of Information: GeneTests.org, HUSLAB Laboratory of Molecular Genetics
12. Exploratory Medline Search (11-13-06):
 - a) "Choroideremia" = 179 citations
 - b) "CHM" = 488 citations
 - c) "horoideremia" and "CHM" = 76 citations (limit to human)

1. Gene Symbol: CYBA Chromosomal Locus: 16q24
Gene Symbol: CYBB Chromosomal Locus: Xp21.1
Gene Symbol: NCF1 Chromosomal Locus: 7q11.23
Gene Symbol: NCF2 Chromosomal Locus: 1q25
2. Protein Name: Cytochrome b-245 light chain, Cytochrome B-245 heavy chain, Neutrophil cytosol factor 1, Neutrophil cytosol factor 2
3. Disease: Chronic Granulomatous Disease
4. Description: Chronic Granulomatous Disease is associated with the CYB gene mutations. Patients with CGD typically experience recurrent infections caused by bacterial and fungal pathogens.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis, Deletion/duplication analysis, Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, GeneDx, Inc
12. Exploratory Medline Search (11-12-06):
 - a) "Chronic Granulomatous Disease" = 274081 citations
 - b) "CYBA" or "CYBB" or "NCF1" or "NCF2" = 499 citations
 - c) "Chronic Granulomatous Disease" or "b" = 160 citations (limit to human)

1. Gene Symbol: RPS6KA3 Chromosomal Locus: Xp22.2-p22.1
2. Protein Name: Ribosomal protein S6 kinase alpha-3
3. Disease: Coffin-Lowry Syndrome
4. Description: Coffin-Lowry syndrome is an X-linked mental retardation condition caused by mutations in the protein kinase gene, RSK2 (aka RPS6KA3), localized to Xp22. Males present with moderate to severe developmental delay, coarse facies, large soft hands with short tapering fingers, hypotonia, joint hyperextensibility and skeletal changes. Carrier females have mild mental impairment and short stature, coarse face, prominent lips, soft fleshy hands with thick tapering fingers.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood or buccal swab
8. Methodology: Sequence analysis, replication analysis, Mutation scanning
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, City of Hope
Clinical Molecular Diagnostic Laboratory
12. Exploratory Medline Search (11-13-06):
 - a) "Coffin-Lowry Syndrome" = 145 citations
 - b) "RPS6KA3" = 13 citations
 - c) "Coffin-Lowry Syndrome" and "RPS6KA3" = 5 citations (limit to human)

1. Gene Symbol: ABCA4 Chromosomal Locus: 1p21-p13
2. Protein Name: Retinal-specific ATP- binding cassette transporter
3. Disease: Cone-Rod Dystrophy, Type 3
4. Description: Cone-rod retinal dystrophy (CORD) characteristically leads to early impairment of vision. An initial loss of color vision and of visual acuity is followed by nyctalopia (night blindness) and loss of peripheral visual fields. One form of cone-rod dystrophy is caused by mutation in the ABCA 4 gene.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: sequence analysis, Mutation scanning
9. Other Diseases: n/d
10. Clinical use(s) for the Medicare: Unclear (early onset)
11. Source of Information: GeneTests.org, The Netherlands Institute for Neuroscience
Molecular Ophthalmogenetics Laboratory
12. Exploratory Medline Search (11-12-06):
 - a) "Cone-Rod Dystrophy" = 217 citations
 - b) "ABCA4" = 138 citations
 - c) "Cone-Rod Dystrophy" and "ABCA4" = 25 citations (limit to human)

1. Gene Symbol: CTH Chromosomal Locus: 1p31.1
2. Protein Name: Cystathionine gamma-lyase
3. Disease: Cystathioninuria
4. Description: Cystathioninuria, an autosomal recessive phenotype with no striking pathologic features, is characterized by abnormal accumulation of plasma cystathionine, leading to increased urinary excretion. Because of the inconsistency and wide variety of disease associations, cystathioninuria is considered to be a benign biochemical anomaly. Cystathioninuria can result from mutations in CTH encoding cystathionine gamma lyase.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analyte
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Unclear
11. Source of Information: GeneTests.org, Massachusetts General Hospital
Amino Acid Disorder (Neurochemistry) Lab
12. Exploratory Medline Search (11-13-06):
 - a) "Cystathioninuria" = 106 citations
 - b) "CTH" = 187 citations
 - c) "Cystathioninuria" and "CTH" = 3 citations (limit to human)

1. Gene Symbol: HSPB8 Chromosomal Locus: 12q24-qter
2. Protein Name: Heat-shock protein beta-8
3. Disease: Distal hereditary motor neuropathy type II (dHMN2)
4. Description: Distal hereditary motor neuropathy type II (dHMN2) is caused by mutation in the gene encoding heat-shock 22-kD protein-8. Distal hereditary motor neuropathy type II is an autosomal dominant disorder of lower motor neurons characterized by distal muscle weakness. The disorder is also referred to as distal spinal muscular atrophy (dSMA) and spinal muscular atrophy of the Charcot-Marie-Tooth type.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratory (only one outside US)
7. Specimen: ND
8. Methodology: Sequence analysis
9. Other Diseases: ND
10. Clinical use(s): Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (8/10/06)
 - a) "Type II Distal Hereditary Motor Neuropathy"=15
 - b) "HSPB8"=39
 - c) "Type II Distal Hereditary Motor Neuropathy" and "HSPB8"=2

1. Protein Name: Presynaptic protein SAP 102
2. Gene Symbol: DLG3 Chromosomal Locus: Xq13.1
3. Disease: DLG3-Related X-Linked Nonsyndromic Mental Retardation
4. Description: *DLG3* is the first XLMR gene that is linked directly to NMDA receptor-mediated signaling and synaptic plasticity. Irrespective of the mechanism, altered synaptic plasticity due to abnormal NMDA receptor signaling offers a plausible mechanism to explain the mental deficit observed in individuals with *DLG3* mutations.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (8/11/06)
 - a) "X-Linked Nonsyndromic Mental Retardation"= 42 citations
 - b) "DLG3"= 28 citations
 - c) "X-Linked Nonsyndromic Mental Retardation" and "DLG3"= 1 citations

1. Gene Symbol: EFEMP1 Chromosomal Locus: 2p1
2. Protein Name: EGF-containing fibulin-like extracellular matrix protein 1
3. Disease: Doyme Honeycomb Retinal Dystrophy
4. Description: The gene and protein is identified as mutated in both Doyme's and Malattia leventinese forms of macular degeneration. The Doyme's disease usually becomes manifest in early childhood. The protein is called EGF-containing fibrillin-like extracellular matrix protein, and the gene is called EFEMP. The same amino acid substitution mutation is present in individuals with Doyme's or Malattia leventinese macular degeneration, which suggests that the two diseases have a common cause.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories (only one in US)
7. Specimen: ND
8. Methodology: Analysis of the entire coding region: Mutation scanning, Analysis of the entire coding region: Sequence analysis, Targeted mutation analysis
9. Other Diseases: Malattia leventinese forms of macular degeneration
10. Clinical use(s) for the Medicare: Unclear (early onset). Clinical confirmation of mutations and pre-symptomatic testing
11. Source of Information: Genetests.org; eyesight.org
12. Exploratory Medline Search: (8/14/06)
"Doyme Honeycomb Retinal Dystrophy.mp. or exp Retinal Degeneration"=17130
"exp Extracellular Matrix Proteins/ or EGF-containing fibulin-like extracellular matrix protein 1.mp."=100508
"1 and 2" (limit to humans)=150

1. Gene Symbol: DPYS Chromosomal Locus: 8q22
2. Protein Name: Dihydropyrimidase
3. Disease: Dihydropyrimidinase Deficiency
4. Description: A deficiency of the enzyme dihydropyrimidase leads to the accumulation and excretion in the urine of the substrates for the enzyme, dihydrouracil and dihydrothymine. Onset is in early childhood
5. Purpose: Diagnostic
6. Availability: Clinical Laboratory (outside US)
7. Specimen: ND
8. Methodology: Sequence analysis, enzyme assay, analyte
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (8/14/06)
“Dihydropyrimidase deficiency”=29
“DYPS”=0

1. Gene Symbol: GCH1 Chromosomal Locus: 14q22.1-q22.2
2. Protein Name: GTP cyclohydrolase I
3. Disease: GTP Cyclohydrolase 1-Deficient Dopa responsive dystonia
4. Description: GTPCH1-deficient DRD is inherited in an autosomal dominant manner. This disorder typically presents with gait disturbance resulting from foot dystonia, later development of parkinsonism, and diurnal fluctuation of symptoms. The age of onset is 6 y
5. Purpose: Diagnostic (also presymptom)
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis; Southern blot/quantitative PCR
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org; genedx.com
12. Exploratory Medline Search (11-13-06):
 - a) "Dopa responsive dystonia" = 263 citations
 - b) "GCH1" = 52 citations
 - c) "Dopa responsive dystonia" and "GCH1" = 29 citations (limit to human)

1. Gene Symbol: ABCC2 (CMOAT1) Chromosomal Locus: 10q24
2. Protein Name: Canalicular multispecific organic anion transporter 1
3. Disease: Dubin Johnson Syndrome
4. Description: Dubin Johnson is a benign disease and patients present with predominantly conjugated chronic hyperbilirubinemia that was not associated with hemolysis. The disorder occurs in all races and nationalities and both sexes. Dubin-Johnson syndrome is induced by mutations in the ABCC2/MRP2 gene encoding the canalicular transporter for conjugated bilirubin.
5. Purpose: Diagnostic and to differentiate from other types of liver disease
6. Availability: Clinical Laboratories
7. Specimen: ND
8. Methodology: Analyte
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Unclear because of a benign nature of the disease
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-13-06):
 - a) "Dubin Johnson" = 359 citations
 - b) "ABCC2" or "CMOAT1" = 226 citations
 - c) "Dubin Johnson" and "b" = 16 citations (limit to human)

1. Gene Symbol: LMNA Chromosomal Locus: 1q21.2
2. Protein Name: Lamin-A/C
3. Disease: Dilated cardiomyopathy
4. Description: Mutations in the LMNA gene are associated with dilated cardiomyopathy. The phenotype of individuals with LMNA gene mutations can range from a classical Emery-Dreifuss muscular dystrophy (EDMD) phenotype to isolated dilated cardiomyopathy.
5. Purpose: Diagnostic, prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis, PCR
9. Other Diseases: EDMD, limb-girdle muscular dystrophy (type 1B), Charcot-Marie-Tooth disorder Type 2, Dunnigan familial partial lipodystrophy, Hutchinson-Gilford progeria syndrome, atypical Werner syndrome, and mandibuloacral dysplasia
10. Clinical use(s) for the Medicare population: Unclear (early onset)
 - a) Testing for individuals with clinical features of EDMD
11. Source of Information: GeneTests.org, University of Minnesota Fairview Diagnostics Laboratories, City of Hope Clinical Molecular Diagnostic Laboratory
12. Exploratory Medline Search: (10/24/06)
 - a. "Dilated cardiomyopathy.mp. or exp Cardiomyopathy, Dilated" = 6427
 - b. "exp Lamin Type A/ or LMNA.mp." = 466
 - c. a and b (limit to humans) = 65

1. Gene Symbol: TOR1A Chromosomal Locus: 9q34
2. Protein Name: Torsin A
3. Disease: Early onset primary dystonia (DYT1)
4. Description: Early-onset primary dystonia (DYT1) typically presents in childhood or adolescence (early-onset); adult onset occurs in a minority of individuals with DYT1. Dystonic muscle contractions causing posturing of a foot, leg, or arm are the most common presenting symptom. DYT1 is diagnosed by genetic testing of TOR1A gene revealing a 3-base pair GAG deletion in most affected individuals.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Targeted mutation analysis, Linkage analysis
9. Other Diseases: None
10. Clinical use(s): ND
11. Source of Information: GeneTests.org, Athena Diagnostics Inc
[Reference Lab](#)
12. Exploratory Medline Search (11-13-06):
 - a) "Dystonia Musculorum Deformans" or "Early onset primary dystonia" = 669 citations
 - b) "TOR1A" = 21 citations
 - c) "a" and "TOR1A" = 9 citations (limit to human)

1. Gene Symbol: FBN1 Chromosomal Locus: 15q21.1
2. Protein Name: Fibrillin-1
3. Disease: Ectopia Lentis, Isolated
4. Description: Ectopia lentis, isolated is a dominantly inherited disorder caused by mutations in the FBN1 gene. The disorder is characterized by congenital lens dislocation. The lens may be dislocated in any direction.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: aortic aneurysms, Marfan syndrome
10. Clinical use(s): n/d
11. Source of Information: GeneTests.org, Baylor College of Medicine
John Welsh Cardiovascular Diagnostic Laboratory
12. Exploratory Medline Search (11-13-06):
 - a) "Ectopia Lentis" = 341 citations
 - b) "FBN1" = 220 citations
 - c) "Ectopia Lentis" and "FBN1" = 23 citations (limit to human)

1. Gene Symbol: COL1A1 Chromosomal Locus: 17q21.3-q22
Gene Symbol: COL1A2 Chromosomal Locus: 7q22.1
2. Protein Name: Collagen alpha 1(I) chain, Collagen alpha 2(I) chain
3. Disease: Ehlers-Danlos Syndrome, Arthrochalasia Type
4. Description: Ehlers-Danlos syndrome (EDS) is a connective tissue disorder composed of numerous subtypes with distinct genetic and clinical findings. In general, EDS is characterized by joint hypermobility, skin hyperextensibility and tissue fragility. The Arthrochalasic type is caused by mutations leading to the skipping of exon 6 in either COL1A1 (EDS VIIA) or COL1A2 (EDS VIIB). The Arthroclalasic type is characterized by severe generalized joint hypermobility with recurrent subluxations and congenital hip dislocation.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood, extracted DNA, or Confluent cells
8. Methodology: Analysis of the entire coding region: Sequence analysis, Sequence analysis of select exons, Protein analysis
9. Other Diseases: ND
10. Clinical use(s): ND
11. Source of Information: GeneTests.org, Center for Human Genetics
Bioscientia GmbH
12. Exploratory Medline Search (11-13-06):
 - a) "Ehlers-Danlos" = 1903 citations
 - b) "COL1A1" or "COL1A2" = 575 citations
 - c) "Ehlers-Danlos" and "b" = 34 citations (limit to human)

1. Gene Symbol: COL5A1 Chromosomal Locus: 9q34.2-q34.3
Gene Symbol: COL5A2 Chromosomal Locus: 2q31
2. Protein Name: Collagen alpha 1(V) chain, Collagen alpha 2(V) chain
3. Disease: Ehlers-Danlos syndrome, Classic Type
4. Description: Ehlers-Danlos syndrome is a group of disorders that affect connective tissues, which are tissues that support the skin, bones, blood vessels, and other organs. Defects in connective tissues cause the signs and symptoms of Ehlers-Danlos syndrome, which vary from mildly loose joints to life-threatening complications. People with the classic form of Ehlers-Danlos syndrome experience wounds that split open with little bleeding and leave scars that widen over time to create characteristic shallow "cigarette paper" scars. The COL5A1 gene provides instructions for making a component of collagen. Collagens form a family of proteins that strengthen and support many tissues in the body, including skin, ligaments, bones, tendons, muscles, and the space between cells and tissues called the extracellular matrix.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood, skin biopsy
8. Methodology: Targeted mutation analysis
9. Other Diseases: None
10. Clinical use(s): ND
11. Source of Information: GeneTests.org, University of Washington
Collagen Diagnostic Laboratory
12. Exploratory Medline Search (11-13-06):
 - a) "Ehlers-Danlos" = 1903 citations
 - b) "COL5A1" or "COL5A2" = 68 citations
 - c) "Ehlers-Danlos" and "b" = 27 citations (limit to human)

1. Gene Symbol: PLOD1 Chromosomal Locus: 1p36.3-p36.2
2. Protein Name: Procollagen-lysine, 2-oxoglutarate 5-dioxygenase 1
3. Disease: Ehlers-Danlos syndrome, kyphoscoliotic form
4. Description: Ehlers-Danlos syndrome is a group of disorders that affect connective tissues, which are tissues that support the skin, bones, blood vessels, and other organs. Defects in connective tissues cause the signs and symptoms of Ehlers-Danlos syndrome, which vary from mildly loose joints to life-threatening complications. People with the kyphoscoliosis form of Ehlers-Danlos syndrome experience severe, progressive curvature of the spine that can interfere with breathing. Ehlers-Danlos syndrome is caused by mutations in the PLOD1 gene, resulting in the production of a nonfunctional version of the lysyl hydroxylase 1 enzyme. Several other mutations introduce premature stop signals that prevent the gene from making any functional enzyme. A loss of lysyl hydroxylase 1 activity impairs cross-linking between collagen molecules. This disruption in the network of collagen fibrils weakens connective tissues.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analyte
9. Other Diseases: None
10. Clinical use(s): ND
11. Source of Information: GeneTests.org, ARUP Laboratories, Inc.
ARUP Laboratories
12. Exploratory Medline Search (11-13-06):
 - a) "Ehlers-Danlos" = 1903 citations
 - b) "PLOD1" = 7 citations
 - c) "Ehlers-Danlos" and "PLOD1" = 4 citations (limit to human)

1. Gene Symbol: COL3A1 Chromosomal Locus: 2q31.2
2. Protein Name: Collagen pro α 1(III)
3. Disease: Ehlers-Danlos syndrome, vascular type
4. Description: Ehlers-Danlos syndrome (EDS) is a connective tissue disorder composed of numerous subtypes with distinct genetic and clinical findings. In general, EDS is characterized by joint hypermobility, skin hyperextensibility and tissue fragility. The vascular type represents the most severe form of the disorder. Patients frequently suffer rupture of the arteries and intestine. The vascular type is caused by defects in COL3A1.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood, skin biopsy
8. Methodology: Analysis of the entire coding region: Sequence analysis, Sequence analysis of select exons, Protein analysis
9. Other Diseases: ND
10. Clinical use(s): ND
11. Source of Information: GeneTests.org, Connective Tissue Gene Tests
12. Exploratory Medline Search (11-13-06):
 - a) "Ehlers-Danlos" = 1903 citations
 - b) "COL3A1" = 148 citations
 - c) "Ehlers-Danlos" and "COL3A1" = 71 citations (limit to human)

1. Gene Symbol: TAZ Chromosomal Locus: Xq28
2. Protein Name: Tafazzin
3. Disease: Endocardial Fibroelastosis
4. Description: Endocardial fibroelastosis is characterized by diffuse thickening of the left ventricular endocardium secondary to proliferation of fibrous and elastic tissue. The TAZ gene provides instructions for producing a group of proteins called tafazzins. Tafazzins seem to have two distinct functions in cells and tissues. First, tafazzins play a role in the maintenance of the inner membrane of the mitochondria inside of cells. Specifically, these proteins are involved in maintaining levels of a specific type of fat (lipid) called cardiolipin. Adequate levels of cardiolipin are essential for energy production in the mitochondria.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Targeted mutation analysis
9. Other Diseases: Barth syndrome, X-linked dilated cardiomyopathy
10. Clinical use(s): n/d
11. Source of Information: GeneTests.org, Baylor College of Medicine
John Welsh Cardiovascular Diagnostic Laboratory
12. Exploratory Medline Search (11/27/06):
 - a) "Endocardial Fibroelastosis" = 849 citations
 - b) "TAZ" = 203 citations
 - c) "Endocardial Fibroelastosis" and "TAZ" = 3 citations (limit to human)

1. Gene Symbol: NR2E3 Chromosomal Locus: 15q23
2. Protein Name: Photoreceptor-specific nuclear receptor
3. Disease: Enhanced S-Cone Syndrome
4. Description: This protein is part of a large family of nuclear receptor transcription factors involved in signaling pathways. Nuclear receptors have been shown to regulate pathways involved in embryonic development, as well as in maintenance of proper cell function in adults. Members of this family are characterized by discrete domains that function in DNA and ligand binding. This gene encodes a retinal nuclear receptor that is a ligand-dependent transcription factor. Defects in this gene are a cause of enhanced S cone syndrome.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: ND
10. Clinical use(s): ND
11. Source of Information: GeneTests.org, University of Antwerp
Department of Medical Genetics - Wuyts Lab
12. Exploratory Medline Search (11-13-06):
 - a) "S-cone" = 235 citations
 - b) "NR2E3" = 31 citations
 - c) "S-cone" and "NR2E3" = 15 citations (limit to human)

1. Gene Symbol: CACNA1A Chromosomal Locus: 19p13
Gene Symbol: CACNB4 Chromosomal Locus: 2q22-q23
2. Protein Name: Voltage-dependent L-type calcium channel beta-4 subunit, Voltage-dependent P/Q-type calcium channel alpha-1A subunit
3. Disease: Episodic ataxia type 2
4. Description: Episodic ataxia type 2 (EA2) typically starts in childhood or early adolescence (range two to 32 years). EA2 is characterized by paroxysmal attacks of ataxia, vertigo, and nausea typically lasting minutes to days in duration. Attacks can be associated with dysarthria, diplopia, tinnitus, dystonia, hemiplegia, and headache. About 50% of individuals with EA2 have migraine headaches. The genes CACNA1A and CACNB4 are known to be associated with EA2.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: Familial hemiplegic migraine, Spinocerebellar ataxia type 6,
10. Clinical use(s): ND
11. Source of Information: GeneTests.org, Horizon Molecular Medicine, LLC
12. Exploratory Medline Search (11-14-06):
 - a) "Episodic ataxia type 2" = 89 citations
 - b) "CACNA1A" or "CACNB4" = 350 citations
 - c) "Episodic ataxia type 2" and "b" = 55 citations (limit to human)

1. Gene Symbol: GJB3 Chromosomal Locus: 1p35.1
Gene Symbol: GJB4 Chromosomal Locus: 1p35.1
2. Protein Name: Gap junction beta-3 protein (Connexin 31), Gap junction beta-4 protein (Connexin 30.3)
3. Disease: Erythrokeratoderma variabilis
4. Description: Several GJB3 mutations have been identified in people with erythrokeratoderma variabilis (EKV), a skin disorder characterized by areas of abnormally thickened skin and temporarily reddened patches. These mutations change one of the protein building blocks (amino acids) used to make connexin 31. The altered protein probably interferes with the assembly of gap junctions, or it disturbs the normal function of the gap junction by leaving the channel continuously open. It remains unclear how GJB3 mutations disrupt the growth and maturation of skin cells and cause erythrokeratoderma variabilis.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood, buccal swab
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: nonsyndromic deafness, autosomal dominant, nonsyndromic deafness, autosomal recessive
10. Clinical use(s): ND
11. Source of Information: GeneTests.org, GeneDx, Inc
12. Exploratory Medline Search (11-14-06):
 - a) "Erythrokeratoderma variabilis" = 28 citations
 - b) "GJB3" or "GJB4" = 103 citations
 - c) "Erythrokeratoderma variabilis" and "b" = 8 citations (limit to human)

1. Gene Symbol: FECH Chromosomal Locus: 18q21
2. Protein Name: Ferrochelatase
3. Disease: Erythropoietic protoporphyria
4. Description: More than 80 different mutations in the FECH gene have been identified in individuals with a form of porphyria called erythropoietic protoporphyria. These mutations greatly reduce the activity of ferrochelatase when they occur in one of the two copies of the FECH gene in each cell. To show signs and symptoms of the disorder, however, a person must also have a particular version of the other copy of the gene. This variant gene, called a low-expression allele, reduces enzyme activity even further. Low levels of enzyme activity allow protoporphyrin (a byproduct of heme production) to build up in the body. High levels of protoporphyrin in the skin cause sun sensitivity characteristic of erythropoietic protoporphyria, and increased levels of this substance in the liver can result in liver damage.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analyte
9. Other Diseases: None
10. Clinical use(s): ND
11. Source of Information: GeneTests.org, Mayo Clinic
Biochemical Genetics Laboratory
12. Exploratory Medline Search (11-14-06):
 - a) "Erythropoietic protoporphyria" = 11 citations
 - b) "FECH" = 43 citations
 - c) "Erythropoietic protoporphyria" and "FECH" = 0 citations

1. Gene Symbol: GLA; Chromosomal Locus: Xq22
2. Protein Name: Alpha-galactosidase A
3. Disease: Fabry Disease
4. Description: Fabry disease is an X-linked lysosomal storage disorder resulting from the deficient activity of the lysosomal hydrolase, alpha-galactosidase A. As a result of the enzymatic defect, there is progressive accumulation of neutral glycosphingolipids with terminal alpha-galactosyl moieties (predominantly GL-3) in visceral tissues and body fluids. The enzyme is encoded by the *GLA* gene which is localized to Xq22.1. Affected individuals present with vascular skin lesions (angiokeratoma), acroparesthesias, hypohydrosis, and corneal and lenticular opacities.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Mutation scanning; Analysis of the entire coding region: Sequence analysis; Analyte; Enzyme assay; Deletion/duplication analysis; replication analysis (X-chromosome inactivation study); Targeted mutation analysis; Protein truncation testing (PTT)
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (10/3/06):
 - a) "Fabry Disease" = 1581 citations
 - b) "GLA" = 2247 citations
 - c) "Fabry Disease" and "GLA" = 27 citations (limit to humans)

1. Gene Symbol: ND; Critical Region: D4Z4; Chromosomal Locus: 4q35
2. Protein Name: None listed
3. Disease: Facioscapulohumeral muscular dystrophy
4. Description: The classic form of facioscapulohumeral dystrophy (FSHD) is inherited in an autosomal dominant fashion. The responsible gene has been mapped to chromosome 4q35. The disorder is causally related to a short repeat array that remains after deletion of an integral number of tandemly arrayed 3.3 kb repeat units (called D4Z4) in the 4q35 region.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Deletion/duplication analysis; linkage analysis
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-14-06):
 - a) "Facioscapulohumeral muscular dystrophy" = 177 citations
 - b) "D4Z4" = 70 citations
 - c) "Facioscapulohumeral muscular dystrophy" and "D4Z4" = 46 citations (limit to human)

1. Gene Symbol: F11; Chromosomal Locus: 4q35
2. Protein Name: Coagulation factor XI
3. Disease: Factor XI deficiency
4. Description: The defect is characterized by autosomal inheritance, minor bleeding episodes, severe protracted bleeding after surgical procedures, abnormal prothrombin consumption, prolonged PTT and recalcification times, and abnormal factor XI assay. The gene, F11, encodes coagulation factor XI of the blood coagulation cascade.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-14-06):
 - a) "Factor XI deficiency" = 509 citations
 - b) "F11" = 478 citations
 - c) Factor XI deficiency and "F11" = 9 citations (limit to human)

1. Gene Symbol: F13A1 Chromosomal Locus: 6p25-p24
2. Test Name: Coagulation factor XIII A chain
3. Disease: Factor XIII deficiency (Fibrin Stabilizing Factor, A Subunit)
4. Description: Factor XIII is the last enzyme generated in the blood coagulation cascade. Most cases of factor XIII deficiency are associated with alterations in the gene that encodes the catalytic A subunit of this factor. A minority of cases are due to defects of the carrier B subunit
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-15-06):
 - a) "Factor XIII deficiency" = 473 citations
 - b) "F13A1" = 48 citations
 - c) "Factor XIII deficiency" and "F13A1" = 0 citations

1. Gene Symbol: KCNQ1 Chromosomal; Locus: 11p15.5
2. Protein Name: Potassium voltage-gated channel subfamily KQT member 1
3. Disease: Familial atrial fibrillation
4. Description: Familial atrial fibrillation is a heart condition that causes a fast, irregular beating of the upper chambers of the heart (the atria). This abnormal heartbeat can lead to stroke and sudden death. The KCNQ1 gene belongs to a large family of genes that provide instructions for making potassium channels. These channels, which transport positively charged potassium atoms (ions) into and out of cells, play a key role in a cell's ability to generate and transmit electrical signals. In cardiac muscle cells, this mutation appears to increase the flow of potassium ions through the channel formed by the KCNQ1 protein. The enhanced ion transport alters the heart's normal rhythm, resulting in atrial fibrillation.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory (outside US)
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Mutation scanning, Sequence analysis of select exons
9. Other Diseases: Jervell and Lange-Nielsen syndrome, Romano-Ward syndrome, short QT syndrome, acquired long QT syndrome, SIDS
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/23/06)
 - a. "exp Atrial Fibrillation/ or familial atrial fibrillation.mp."=10444 citations
 - b. "exp KCNQ1 Potassium Channel/ or KCNQ1.mp."=492 citations
 - c. a and b (limit to humans) = 11 citations

1. Gene Symbol: SLC26A3 Chromosomal Locus: 7q22-q31.1
2. Protein Name: Chloride anion exchanger
3. Disease: Familial Chloride Diarrhea (CLD, Congenital Secretory Diarrhea, Chloride Type)
4. Description: Congenital chloride diarrhea (CLD) is an autosomal recessive disorder of intestinal electrolyte absorption. It is characterized by persistent secretory diarrhea resulting in polyhydramnios and prematurity prenatally, and dehydration, hyponatremia, hyperbilirubinemia, abdominal distention, and failure to thrive immediately after birth. CLD is caused by mutations in the solute carrier family 26, member 3 gene (SLC26A3, alias CLD or DRA), which encodes a Na⁺-independent Cl⁻/HCO₃⁻ (or OH⁻) exchanger. SLC26A3 is a member of the SLC26 sulfate permease/anion transporter family and it is expressed mainly in the apical brush border of intestinal epithelium. The only extraintestinal tissues showing SLC26A3 expression are eccrine sweat glands and seminal vesicles.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-14-06):
 - a) "Familial Chloride Diarrhea" = 626 citations
 - b) "SLC26A3" = 48 citations
 - c) "Familial Chloride Diarrhea" and "SLC26A3" = 19 citations (limit to human)

1. Gene Symbol: TNFRSF1A; Chromosomal Locus: 12p13.2
2. Protein Name: Tumor necrosis factor receptor superfamily member 1A
3. Disease: Familial Hibernian fever (TRAPS, Familial Periodic Fever)
4. Description: TRAPS is inherited in an autosomal dominant manner. The disorder usually presents in childhood, and is characterized by fevers that last from a few days to several weeks; abdominal symptoms (pain, diarrhea/constipation, occasionally peritonitis), pleuritic involvement, arthralgia, myalgia, conjunctivitis/periorbital edema, and tender migratory erythematous skin lesions. Mutations are identified by bi-directional sequence analysis of exons 2,3, and 4 of the TNFRSF1A gene.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood, buccal swab
8. Methodology: Analysis of the entire coding region: Sequence analysis, Targeted mutation analysis, Sequence analysis of select exons, Mutation scanning of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-14-06):
 - a) "Familial Hibernian fever" or "TRAPS" = 1168 citations
 - b) "TNFRSF1A" = 1119 citations
 - c) "a" and "TNFRSF1A" = 56 citations (limit to human)

1. Gene Symbol: CYP11B1 Chromosomal Locus: 8q21; Gene Symbol: CYP11B2 Chromosomal Locus: 8q21
2. Protein Name: Cytochrome P450 11B1
3. Disease: Familial hyperaldosteronism type 1; Aldosteronism; Sensitive to Dexamethasone; Glucocorticoid-Remediable Aldosteronism; Glucocorticoid-Suppressible Hyperaldosteronism
4. Description: This gene encodes a member of the cytochrome P450 superfamily of enzymes. The cytochrome P450 proteins are monooxygenases which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids. This protein localizes to the mitochondrial inner membrane and is involved in the conversion of progesterone to cortisol in the adrenal cortex. Mutations in this gene cause congenital adrenal hyperplasia due to 11-beta-hydroxylase deficiency. Transcript variants encoding different isoforms have been noted for this gene.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; deletion/duplication analysis; mutation scanning; sequence analysis of select exons; targeted analysis; enzyme assay; protein analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (11-11-06)
 - a) "hyperaldosteronism" = 6424 citations
 - b) "CYP11B1" = 242 citations
 - c) a and b = 45 citations (limit to human)

1. Gene Symbol: LDLR Chromosomal Locus: 19p13.2
2. Protein Name: Low-density lipoprotein receptor
3. Disease: Familial hypercholesteremia; Familial Hypercholesterolemia; Hyperlipoproteinemia Type IIA
4. Description: The low density lipoprotein receptor (LDLR) gene family consists of cell surface proteins involved in receptor-mediated endocytosis of specific ligands. Low density lipoprotein (LDL) is normally bound at the cell membrane and taken into the cell ending up in lysosomes where the protein is degraded and the cholesterol is made available for repression of microsomal enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, the rate-limiting step in cholesterol synthesis. At the same time, a reciprocal stimulation of cholesterol ester synthesis takes place. Mutations in this gene cause the autosomal dominant disorder, familial hypercholesterolemia.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; mutation scanning, deletion/duplication analysis; sequence analysis; targeted mutations analysis; sequence analysis of select exons.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful for diagnostic purposes
11. Source of Information: Genetests.org; UpToDate Online
12. Exploratory Medline Search: (November 16, 2006)
 - a) "Familial hypercholesteremia" = 26 citations
 - b) "LDLR" = 5261 citations
 - c) a and b = 2 citations

1. Gene Symbol: ABCC8; Chromosomal Locus: 11p15.1
2. Protein Name: ATP-binding cassette transporter sub-family C member 8
3. Disease: Familial hyperinsulinism; ABCC8-Related Hyperinsulinism
4. Description: Familial hyperinsulinism (FHI) is defined as hypoglycemia in the newborn or infant, associated with inappropriately elevated serum concentration of insulin and metabolic evidence of increased insulin action. The latter may include inappropriately low serum ketone bodies, increased glucose response to glucagon administration, and a glucose requirement to prevent hypoglycemia that is greater than the obligate glucose needs of the appropriate age group. Five genes are known to be associated with FHI. Approximately 45% of affected individuals have mutations in *ABCC8* (*SURI*)
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood and urine
8. Methodology: Analysis of the entire coding region; sequence analysis; mutations scanning, targeted mutation analysis; deletion/duplication analysis; linkage analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 16, 2006)
 - a) "Familial hyperinsulinism" = 27 citations
 - b) "ABCC8" = 33020 citations
 - c) a and b = 24 citations

1. Gene Symbol: GCK; Chromosomal Locus: 7p15-p13
2. Protein Name: Glucokinase
3. Disease: Familial hyperinsulinism; GCK-Related Hyperinsulinism
4. Description: Familial hyperinsulinism (FHI) is defined as hypoglycemia in the newborn or infant, associated with inappropriately elevated serum concentration of insulin and metabolic evidence of increased insulin action. The latter may include inappropriately low serum ketone bodies, increased glucose response to glucagon administration, and a glucose requirement to prevent hypoglycemia that is greater than the obligate glucose needs of the appropriate age group. Five genes are known to be associated with FHI. Rarely, individuals have activating mutation in GCK, the gene encoding the enzyme glucokinase.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 16, 2006)
 - a) "Familial hyperinsulinism" = 27 citations
 - b) "GCK" = 598 citations
 - c) a and b = 1 citations

1. Gene Symbol: GLUD1; Chromosomal Locus: 10q23.3
2. Protein Name: Glutamate dehydrogenase 1
3. Disease: Familial hyperinsulinism; GLUD1-Related Hyperinsulinism; Hyperinsulinism-Hyperammonemia Syndrome
4. Description: Familial hyperinsulinism (FHI) is defined as hypoglycemia in the newborn or infant, associated with inappropriately elevated serum concentration of insulin and metabolic evidence of increased insulin action. The latter may include inappropriately low serum ketone bodies, increased glucose response to glucagon administration, and a glucose requirement to prevent hypoglycemia that is greater than the obligate glucose needs of the appropriate age group. Five genes are known to be associated with FHI. Approximately 5% of individuals have activating mutation in GLUD1, the gene encoding the enzyme glutamine dehydrogenase (GDH).
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutations scanning; deletion/duplication analysis; linkage analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 16, 2006)
 - a) "Familial hyperinsulinism" = 29 citations
 - b) "GLUD1" = 1029 citations
 - c) a and b = 0 citations

1. Gene Symbol: HADHSC (SCHAD) Chromosomal Locus: 4q22-q26
2. Protein Name: Short chain 3-hydroxyacyl-CoA dehydrogenase
3. Disease: Familial hyperinsulinism; HADHSC-Related Hyperinsulinism
4. Description: Familial hyperinsulinism (FHI) is defined as hypoglycemia in the newborn or infant, associated with inappropriately elevated serum concentration of insulin and metabolic evidence of increased insulin action. The latter may include inappropriately low serum ketone bodies, increased glucose response to glucagon administration, and a glucose requirement to prevent hypoglycemia that is greater than the obligate glucose needs of the appropriate age group. Five genes are known to be associated with FHI. Rarely, individuals have recessive, inactivation mutations in HADHSC (alias SCHAD), the gene encoding the enzyme L-3-hydroxyacyl-coenzyme A dehydrogenase, short chain.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis; (Additional Testing Offered: Preimplantation genetic diagnosis. Comments: Preimplantation genetic diagnosis only. Available for families with known mutations or previously established linkage.)
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 16, 2006)
 - a) "Familial hyperinsulinism" = 27 citations
 - b) "HADHSC" = 22781 citations
 - c) a and b = 21 citations

1. Gene Symbol: KCNJ11; Chromosomal Locus: 11p15.1
2. Protein Name: ATP-sensitive inward rectifier potassium channel 11
3. Disease: Familial hyperinsulinism; KCNJ11-Related Hyperinsulinism
4. Description: Familial hyperinsulinism (FHI) is defined as hypoglycemia in the newborn or infant, associated with inappropriately elevated serum concentration of insulin and metabolic evidence of increased insulin action. The latter may include inappropriately low serum ketone bodies, increased glucose response to glucagon administration, and a glucose requirement to prevent hypoglycemia that is greater than the obligate glucose needs of the appropriate age group. Five genes are known to be associated with FHI. Approximately 5 % of individuals have mutations in KCNJ11. (The proteins encoded by ABCC8 and KCNJ11 make up the beta KATP channel, which regulates insulin secretion.)
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; mutation scanning, targeted mutation analysis; deletion/duplication analysis; linkage analysis.
9. Other Diseases: Type 2 diabetes mellitus
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 16, 2006)
 - a) "Familial hyperinsulinism" = 27 citations
 - b) "KCNJ11" = 7173 citations
 - c) a and b = 13 citations

1. Gene Symbol: MYH7, TNNT2, TPM1, MYBPC3, TNNI3, MYL, MYL2, ACTC
Chromosomal Locus: 14q12, 1q32, 15q22.1, 11p11.2, 19q13.4, 3p, 12q23-q24.3, 15q14.
2. Protein Name: Myosin heavy chain, cardiac muscle beta isoform; Troponin T, cardiac muscle isoforms; Tropomyosin 1 alpha chain; Myosin-binding protein C, cardiac-type; Troponin I, cardiac muscle; Myosin regulatory light chain 2, ventricular/cardiac muscle isoform; Actin, alpha cardiac.
3. Disease: Familial Hypertrophic Cardiomyopathy (CMH)
4. Description: Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere, caused by mutations in one of several genes that encode different components of the contractile apparatus. It has an autosomal dominant pattern of inheritance and is characterized by hypertrophy of the left ventricle, with markedly variable clinical manifestations and morphologic and hemodynamic abnormalities]. In a subset of patients, the site and extent of cardiac hypertrophy results in obstruction to left ventricular outflow.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutation scanning.
9. Other Diseases: Unclear
10. Clinical use(s) for the Medicare population: Unclear (early onset type) may be useful for diagnostic purposes
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-20-06):
 - a) "Familial Hypertrophic Cardiomyopathy" = 556 citations
 - b) "MYH7" or TNNT2" or TPM1" or MYBPC3" or TNNI3" or MYL" or MYL2" or ACTC" = 52 citations
 - c) "a" and "b" = 51 citations (limit to human)

1. Gene Symbol: ACTC; Chromosomal Locus: 15q14
2. Protein Name: Actin, alpha cardiac
3. Disease: Familial Hypertrophic Cardiomyopathy; HCM
4. Description: Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere, caused by mutations in one of several genes that encode different components of the contractile apparatus. It has an autosomal dominant pattern of inheritance and is characterized by hypertrophy of the left ventricle, with markedly variable clinical manifestations and morphologic and hemodynamic abnormalities]. In a subset of patients, the site and extent of cardiac hypertrophy results in obstruction to left ventricular outflow
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutation scanning.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search:
 - a) "Familial Hypertrophic Cardiomyopathy" = 5878 citations
 - b) "Actin" = 12358 citations
 - c) a and b = 67 citations

1. Gene Symbol: MYBPC3; Locus Name: CMH4; Chromosomal Locus: 11p11.2
2. Protein Name: Myosin-binding protein C, cardiac-type
3. Disease: Familial Hypertrophic Cardiomyopathy; CMH
4. Description: Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere, caused by mutations in one of several genes that encode different components of the contractile apparatus. It has an autosomal dominant pattern of inheritance and is characterized by hypertrophy of the left ventricle, with markedly variable clinical manifestations and morphologic and hemodynamic abnormalities]. In a subset of patients, the site and extent of cardiac hypertrophy results in obstruction to left ventricular outflow
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutation scanning.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Familial Hypertrophic Cardiomyopathy" = 5878 citations
 - b) "Myosin-binding protein C" = 5002 citations
 - c) a and b = 337 citations

1. Gene Symbol: MYH7; Locus Name: CMH1; Chromosomal Locus: 14q12
2. Protein Name: Myosin heavy chain, cardiac muscle beta isoform.
3. Disease: Familial Hypertrophic Cardiomyopathy; HCM
4. Description: Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere, caused by mutations in one of several genes that encode different components of the contractile apparatus. It has an autosomal dominant pattern of inheritance and is characterized by hypertrophy of the left ventricle, with markedly variable clinical manifestations and morphologic and hemodynamic abnormalities]. In a subset of patients, the site and extent of cardiac hypertrophy results in obstruction to left ventricular outflow
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutation scanning.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Familial Hypertrophic Cardiomyopathy" = 5878 citations
 - b) "Myosin heavy chain" = 1162 citations
 - c) a and b = 155 citations

1. Gene Symbol: MYL2; Locus Name: CMH10; Chromosomal Locus: 12q23-q24.3
2. Protein Name: Myosin regulatory light chain 2, ventricular/cardiac muscle isoform
3. Disease: Familial Hypertrophic Cardiomyopathy; HCM
4. Description: Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere, caused by mutations in one of several genes that encode different components of the contractile apparatus. It has an autosomal dominant pattern of inheritance and is characterized by hypertrophy of the left ventricle, with markedly variable clinical manifestations and morphologic and hemodynamic abnormalities]. In a subset of patients, the site and extent of cardiac hypertrophy results in obstruction to left ventricular outflow
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutation scanning.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search:
 - a) "Familial Hypertrophic Cardiomyopathy" = 5878 citations
 - b) "Myosin regulatory light chain 2" = 472 citations
 - c) a and b = 35 citations

1. Gene Symbol: MYL3 Chromosomal Locus: 3p Locus Name: CMH8
2. Protein Name: Myosin light polypeptide 3
3. Disease: Familial Hypertrophic Cardiomyopathy; CMH
4. Description: Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere, caused by mutations in one of several genes that encode different components of the contractile apparatus. It has an autosomal dominant pattern of inheritance and is characterized by hypertrophy of the left ventricle, with markedly variable clinical manifestations and morphologic and hemodynamic abnormalities]. In a subset of patients, the site and extent of cardiac hypertrophy results in obstruction to left ventricular outflow
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutation scanning.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Hypertrophic Cardiomyopathy" = 5878 citations
 - b) "Myosin light polypeptide 3" = 472 citations
 - c) a and b = 173 citations

1. Gene Symbol: TNNI3 Chromosomal Locus: 19q13.4 Locus Name: CMH7
2. Protein Name: Troponin I, cardiac muscle
3. Disease: Familial Hypertrophic Cardiomyopathy; CMH
4. Description: Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere, caused by mutations in one of several genes that encode different components of the contractile apparatus. It has an autosomal dominant pattern of inheritance and is characterized by hypertrophy of the left ventricle, with markedly variable clinical manifestations and morphologic and hemodynamic abnormalities]. In a subset of patients, the site and extent of cardiac hypertrophy results in obstruction to left ventricular outflow
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutation scanning.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Familial Hypertrophic Cardiomyopathy" = 5878 citations
 - b) "Troponin I" = 1997 citations
 - c) a and b = 67 citations

1. Gene Symbol: TNNT2; Locus Name: CMH2; Chromosomal Locus: 1q32
2. Protein Name: Troponin T, cardiac muscle isoforms.
3. Disease: Familial Hypertrophic Cardiomyopathy; CMH
4. Description: Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere, caused by mutations in one of several genes that encode different components of the contractile apparatus. It has an autosomal dominant pattern of inheritance and is characterized by hypertrophy of the left ventricle, with markedly variable clinical manifestations and morphologic and hemodynamic abnormalities]. In a subset of patients, the site and extent of cardiac hypertrophy results in obstruction to left ventricular outflow
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutation scanning.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Familial Hypertrophic Cardiomyopathy" = 5878 citations
 - b) "Troponin T" = 1833 citations
 - c) a and b = 126 citations

1. Gene Symbol: TPM1; Locus Name: CMH3; Chromosomal Locus: 15q22.1
2. Protein Name: Tropomyosin 1 alpha chain
3. Disease: Familial Hypertrophic Cardiomyopathy; CMH
4. Description: Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere, caused by mutations in one of several genes that encode different components of the contractile apparatus. It has an autosomal dominant pattern of inheritance and is characterized by hypertrophy of the left ventricle, with markedly variable clinical manifestations and morphologic and hemodynamic abnormalities]. In a subset of patients, the site and extent of cardiac hypertrophy results in obstruction to left ventricular outflow
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons; mutation scanning.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Familial Hypertrophic Cardiomyopathy" = 5878 citations
 - b) "Tropomyosin 1 alpha chain" = 749 citations
 - c) a and b = 73 citations

1. Gene Symbol: CYP11B2; Chromosomal Locus: 8q21
2. Protein Name: Cytochrome P450 11B2, mitochondrial
3. Disease: Familial Hypoaldosteronism Type 2
4. Description: This gene encodes a member of the cytochrome P450 superfamily of enzymes. The cytochrome P450 proteins are monooxygenases which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids. This protein localizes to the mitochondrial inner membrane. The enzyme has steroid 18-hydroxylase activity to synthesize aldosterone and 18-oxocortisol as well as steroid 11 beta-hydroxylase activity. Mutations in this gene cause corticosterone methyl oxidase deficiency.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; targeted mutation analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (11-15-06)
 - a) "Familial Hypoaldosteronism Type 2" = 20 citations
 - b) "exp Aldosterone Synthase" = 385 citations
 - c) a and b = 1 citations

1. Gene Symbol: TAZ, DTNA; Chromosomal Locus: Xq28, 18q12.1-q12.2
2. Protein Name: Tafazzin; Dystrobrevin alpha
3. Disease: Familial Isolated Noncompaction of Left Ventricular Myocardium (INVM)
4. Description: The official name of this gene is “tafazzin (cardiomyopathy, dilated 3A (X-linked); endocardial fibroelastosis 2; Barth syndrome).” The TAZ gene provides instructions for producing a group of proteins called tafazzins. Tafazzins seem to have two distinct functions in cells and tissues. First, tafazzins play a role in the maintenance of the inner membrane of energy-producing centers inside of cells (the mitochondria). Specifically, these proteins are involved in maintaining levels of a specific type of fat (lipid) called cardiolipin. Adequate levels of cardiolipin are essential for energy production in the mitochondria. Tafazzins also promote the differentiation and maturation of cells that build bones (osteoblasts), while preventing cells that store fat (adipocytes) from maturing.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; targeted mutation analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) “Isolated Noncompaction of Left Ventricular Myocardium” = 4 citations
 - b) “TAZ” = 158 citations
 - c) a and b = 1 citations

1. Gene Symbol: LPL; Chromosomal Locus: 8p22
2. Protein Name: Lipoprotein lipase
3. Disease: Familial Lipoprotein Lipase Deficiency; Familial LPL deficiency; Type I Hyperlipoproteinemia
4. Description: Familial lipoprotein lipase deficiency is an inherited condition that disrupts the normal breakdown of fats in the body. The condition is characterized by inflammation of the pancreas (pancreatitis), abdominal pain, enlargement of the liver and spleen (hepatosplenomegaly) and small yellow skin lesions called eruptive xanthomas.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; targeted mutation analysis.
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Unclear (early onset type) may be useful for diagnostic purposes
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Familial Lipoprotein Lipase Deficiency" = 37 citations
 - b) "lipoprotein lipase" = 4760 citations
 - c) a and b = 37 citations

1. Gene Symbol: MEFV; Chromosomal Locus: 16p13
2. Protein Name: Pyrin
3. Disease: Familial Mediterranean Fever; Recurrent Polyserositis; Familial Mediterranean Fever Type 1; Familial Mediterranean Fever Type 2
4. Description: Familial Mediterranean fever (FMF) type 1 is characterized by recurrent short episodes of inflammation and serositis including fever, peritonitis, synovitis, pleuritis, and, rarely, pericarditis and meningitis. The symptoms and severity vary among affected individuals, sometimes even among members of the same family. Amyloidosis, which can lead to renal failure, is the most severe complication. FMF type 2 is characterized by amyloidosis as the first clinical manifestation of FMF in an otherwise asymptomatic individual.
Diagnosis/testing. The diagnosis of FMF is clinical and is suspected in individuals with recurrent episodes of fever associated with abdominal pain (peritonitis) and/or pleuritic pain and/or arthritis (ankle/knee) usually lasting two to three days. Blood tests reveal a high erythrocyte sedimentation rate, leukocytosis, and a high fibrinogen level. *MEFV* is the only gene currently known to be associated with FMF. Molecular genetic testing is also used for carrier detection.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis of select exons; sequence analysis; targeted mutation analysis; linkage analysis; deletion/duplication analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear, maybe be useful for diagnostic purposes
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Familial Mediterranean Fever" = 1927 citations
 - b) "Pyrin" = 160 citations
 - c) a and b = 78 citations

1. Gene Symbol: UMOD; Chromosomal Locus: 16p12.3
2. Protein Name: Uromodulin
3. Disease: Familial Nephropathy with gout; UMOD-Related Kidney Disease; Uromodulin Associated Kidney Disease; Uromodulin Storage Disease; Medullary Cystic Kidney Disease 2 Kidney Disease 2; Medullary Cystic.
4. Description: This gene encodes uromodulin, the most abundant protein in normal urine. Its excretion in urine follows proteolytic cleavage of the ectodomain of its glycosyl phosphatidylinositol-anchored counterpart that is situated on the luminal cell surface of the loop of Henle. Uromodulin may act as a constitutive inhibitor of calcium crystallization in renal fluids. Excretion of uromodulin in urine may provide defense against urinary tract infections caused by uropathogenic bacteria. Defects in this gene are associated with the autosomal dominant renal disorders medullary cystic kidney disease-2 (MCKD2) and familial juvenile hyperuricemic nephropathy (FJHN). These disorders are characterized by juvenile onset of hyperuricemia, gout, and progressive renal failure. While several transcript variants may exist for this gene, the full-length natures of only two have been described to date. These two represent the major variants of this gene and encode the same isoform.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: sequence analysis; sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a. "Familial Nephropathy with gout" = 9 citations
 - b. "Uromodulin" = 98 citations
 - c. a and b = 1 citations

1. Gene Symbol: LMNA; Chromosomal Locus: 1q21.2
2. Protein Name: Lamin-A/C
3. Disease: Familial Partial Lipodystrophy, Dunnigan Type
4. Description: The LMNA gene provides instructions for making several slightly different proteins. The two major proteins, lamin A and lamin C, are produced in most of the body's cells. These proteins have a nearly identical sequence of protein building blocks (amino acids). The small difference in the sequence makes lamin A longer than lamin C.

Lamins A and C are a type of structural protein called an intermediate filament protein. Intermediate filaments provide stability and strength to cells. Lamins A and C are essential scaffolding (supporting) components of the nuclear envelope, which is a structure that surrounds the nucleus in cells. Specifically, these proteins are located in the nuclear lamina, a mesh-like layer of intermediate filaments that is attached to the inner membrane of the nuclear envelope. The nuclear envelope regulates the movement of molecules into and out of the nucleus, and researchers believe it may play a role in regulating the activity of certain genes.

The lamin A protein must be processed within the cell before becoming part of the lamina. Its initial form, called prelamin A, undergoes a complex series of steps that are necessary for the protein to be inserted into the lamina. Lamin C does not have to undergo this processing before becoming part of the lamina.

5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; sequence analysis of select exons.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear, generally early onset
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Familial Partial Lipodystrophy, Dunnigan Type" = 52 citations
 - b) "LMNA" = 211 citations

1. Gene Symbol: Unknown Chromosomal Locus: Unknown
2. Protein Name: ND
3. Disease: Familial Pulmonary Fibrosis; Adult Familial Cryptogenic Fibrosing Alveolitis
4. Description: Familial pulmonary fibrosis (termed FPF in this *GeneReview*) is characterized by two or more cases of idiopathic interstitial pneumonia (IIP) in two or more first degree relatives (parent, sib, or offspring). The clinical findings of IIP are bibasilar reticular abnormalities, ground glass opacities, or diffuse nodular lesions on high resolution computed tomography and abnormal pulmonary function studies that include evidence of restriction (reduced VC with an increase in FEV1/FVC ratio) and/or impaired gas exchange (increased $P_{(A-a)}O_2$ with rest or exercise or decreased diffusion capacity of the lung for carbon monoxide). Like IPF, FPF may be complicated by lung cancer. Alveolar cell carcinoma, small cell carcinoma, and adenocarcinoma have been described [Beaumont et al 1981, McDonnell et al 1982].

Although the genes associated with familial pulmonary fibrosis are not known, the following is known: Mutations in the gene encoding surfactant protein-C are associated with the development of an inflammatory form of IIP in one family and what appears to be either idiopathic pulmonary fibrosis (IPF) or NSIP in another large family]. Polymorphisms of various cytokines (IL-1RA, TNF- α , and IL-6) have been reported to be associated with the development of IPF]. Loci associated with familial pulmonary fibrosis are not known. However, several loci have been associated with the development of familial sarcoidosis

5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: NA
8. Methodology: ND
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (November 15, 2006)
 - a) "Familial pulmonary fibrosis = 13 citations

1. Gene Symbol: BRCA2; Chromosomal Locus: 13q12.3
2. Protein Name: Breast cancer type 2 susceptibility protein
3. Disease: Fanconi Anemia (BRCA2-Related Fanconi Anemia)
4. Description: Researchers have identified more than 450 mutations in the BRCA2 gene, many of which cause an increased risk of breast cancer. Many of these mutations are insertions or deletions of a small number of DNA building blocks (base pairs) in the BRCA2 gene. Most of these mutations disrupt protein production, resulting in an abnormally small, nonfunctional version of the BRCA2 protein. Other mutations change one of the protein building blocks (amino acids) used to make the BRCA2 protein. Researchers believe that the defective BRCA2 protein is unable to help fix damaged DNA. As a result, mutations build up and can cause cells to divide in an uncontrolled way and form a tumor.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Chromosome breakage studies, Preimplantation genetic diagnosis
9. Other Diseases: Breast ovarian, and prostate cancer
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-14-06):
 - a) "Fanconi Anemia" = 1898 citations
 - b) "BRCA2" = 3035 citations
 - c) "Fanconi Anemia" and "BRCA2" = 85 citations (limit to human)

1. Gene Symbol: FANCA; Chromosomal Locus: 16q24.3
2. Protein Name: Fanconi anemia group A protein
3. Disease: Fanconi Anemia (FANCA-Related Fanconi Anemia)
4. Description: The Fanconi anemia complementation group (FANC) currently includes FANCA, FANCB, FANCC, FANCD1 (also called BRCA2), FANCD2, FANCE, FANCF, FANCG, and FANCL. The previously defined group FANCH is the same as FANCA. Fanconi anemia is a genetically heterogeneous recessive disorder characterized by cytogenetic instability, hypersensitivity to DNA crosslinking agents, increased chromosomal breakage, and defective DNA repair. The members of the Fanconi anemia complementation group do not share sequence similarity; they are related by their assembly into a common nuclear protein complex. This gene encodes the protein for complementation group A. Alternative splicing results in multiple transcript variants encoding different isoforms. Mutations in this gene are the most common cause of Fanconi anemia.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; mutation scanning; deletion/duplication analysis; linkage analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-14-06):
 - a) "Fanconi Anemia" = 1898 citations
 - b) "FANCA" = 138 citations
 - c) "Fanconi Anemia" and "FANCA" = 136 citations (limit to human)

1. Gene Symbol: FANCC; Chromosomal Locus: 9q22.3
2. Protein Name: Fanconi anemia group C protein
3. Disease: Fanconi Anemia; FANCC-Related Fanconi Anemia
4. Description: The Fanconi anemia complementation group (FANC) currently includes FANCA, FANCB, FANCC, FANCD1 (also called BRCA2), FANCD2, FANCE, FANCF, FANCG, and FANCL. The previously defined group FANCH is the same as FANCA. Fanconi anemia is a genetically heterogeneous recessive disorder characterized by cytogenetic instability, hypersensitivity to DNA crosslinking agents, increased chromosomal breakage, and defective DNA repair. The members of the Fanconi anemia complementation group do not share sequence similarity; they are related by their assembly into a common nuclear protein complex. This gene encodes the protein for complementation group A. Alternative splicing results in multiple transcript variants encoding different isoforms. Mutations in this gene are the most common cause of Fanconi anemia.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons; targeted mutation analysis.
9. Other Diseases: Unclear
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-14-06):
 - a) "Fanconi Anemia" = 1898 citations
 - b) "FANCC" = 160 citations
 - c) "Fanconi Anemia" and "FANCC" = 160 citations (limit to human)

1. Gene Symbol: FANCG; Chromosomal Locus: 9p13
2. Protein Name: Fanconi anemia group G protein
3. Disease: Fanconi Anemia; FANCG-Related Fanconi Anemia
4. Description: The Fanconi anemia complementation group (FANC) currently includes FANCA, FANCB, FANCC, FANCD1 (also called BRCA2), FANCD2, FANCE, FANCF, FANCG, and FANCL. The previously defined group FANCH is the same as FANCA. Fanconi anemia is a genetically heterogeneous recessive disorder characterized by cytogenetic instability, hypersensitivity to DNA crosslinking agents, increased chromosomal breakage, and defective DNA repair. The members of the Fanconi anemia complementation group do not share sequence similarity; they are related by their assembly into a common nuclear protein complex. This gene encodes the protein for complementation group A. Alternative splicing results in multiple transcript variants encoding different isoforms. Mutations in this gene are the most common cause of Fanconi anemia.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis; analysis of the entire coding region, mutation scanning.
9. Other Diseases: Unclear
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-14-06):
 - a) "Fanconi Anemia" = 1898 citations
 - b) "FANCG" = 103 citations
 - c) "Fanconi Anemia" and "FANCG" = 99 citations (limit to human)

1. Protein Name: Fanconi anemia group J protein
2. Gene Symbol: BRIP1; Chromosomal Locus: 17q22
3. Disease: Fanconi Anemia; FANCI-Related Fanconi Anemia
4. Description: Fanconi anemia (FA) is an autosomal recessive disorder characterized by several congenital anomalies, progressive bone marrow failure, and an increased incidence of malignancies
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Direct DNA methods may include mutation analysis, mutation scanning, sequence analysis, or other means of molecular genetic testing to detect a genetic alteration associated with Fanconi anemia
9. Other Diseases: Breast and ovarian cancer
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search (11-20-06):
 - a) Fanconi anemia = 2135 citations
 - b) BRIP1 = 23 citations
 - c) a and b combined = 13 citations (limit to humans)

1. Gene Symbol: ND; Chromosomal Locus: ND
2. Protein Name: ND
3. Disease: Fatty Acid Oxidation Disorders (FAOD)
4. Description: Mitochondrial trifunctional protein deficiency is a rare condition that prevents the body from converting certain fats to energy, particularly during periods without food (fasting). Normally, through a process called fatty acid oxidation, several enzymes work in a step-wise fashion to break down (metabolize) fats and convert them to energy. People with mitochondrial trifunctional protein deficiency have inadequate levels of an enzyme required for three steps that metabolize a group of fats called long-chain fatty acids.

Onset of mitochondrial trifunctional protein deficiency may begin during infancy or later in life. Signs and symptoms that occur during infancy include feeding difficulties, lack of energy (lethargy), low blood sugar (hypoglycemia), muscle weakness (hypotonia), and liver problems. Infants with this disorder are also at high risk for complications such as life-threatening heart and breathing problems, coma, and sudden unexpected death. Characteristic features of mitochondrial trifunctional protein deficiency that begins after infancy include hypotonia, muscle pain, a breakdown of muscle tissue, and abnormalities in the nervous system that affect arms and legs (peripheral neuropathy).

Problems related to mitochondrial trifunctional protein deficiency can be triggered by periods of fasting or by illnesses such as viral infections. This disorder is sometimes mistaken for Reye syndrome, a severe disorder that may develop in children while they appear to be recovering from viral infections such as chicken pox or flu. Most cases of Reye syndrome are associated with the use of aspirin during these viral infections.

5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analyte; enzyme assay
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search: NA

1. Gene Symbol: AFF2 (FRAXE); Chromosomal Locus: Xq28
2. Protein Name: AF4/FMR2 family member 2 (Fragile X mental retardation 2 protein)
3. Disease: FRAXE Syndrome; Fragile X (E); Fragile X Mental Retardation 2
4. Description: Fragile X syndrome is a genetic condition that causes a range of developmental problems including learning disabilities and mental retardation. Usually males are more severely affected by this disorder than females. In addition to learning difficulties, affected males tend to be restless, fidgety, and inattentive. About one-third of males with fragile X also have autism, a developmental disorder that affects communication and social interaction. Most males with fragile X have characteristic physical features that become more apparent with age. These features include a long and narrow face, large ears, prominent jaw and forehead, unusually flexible fingers, and enlarged testicles (macroorchidism) after puberty.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Methylation analysis; targeted mutations analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org
12. Exploratory Medline Search:
 - a) FRAXE syndrome or Fragile X = 3413 citations
 - b) Fragile X mental retardation 2 protein = 7429 citations
 - c) a and b combined = 846 citations (limit to humans)

1. Gene Symbol: MYH3; Chromosomal Locus: 17p13.1
2. Protein Name: Myosin heavy chain, fast skeletal muscle, embryonic
3. Disease: Freeman-Sheldon Syndrome; Craniocarpotarsal Dysplasia; Distal Arthrogryposis Type 2A
4. Description: Myosin is a major contractile protein which converts chemical energy into mechanical energy through the hydrolysis of ATP. Myosin is a hexameric protein composed of a pair of myosin heavy chains (MYH) and two pairs of nonidentical light chains. This gene is a member of the MYH family and encodes a protein with an IQ domain and a myosin head-like domain. Mutations in this gene have been associated with two congenital contracture (arthrogryposis) syndromes, Freeman-Sheldon syndrome and Sheldon-Hall syndrome.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis; linkage analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ND
11. Source of Information: Genetests.org, Entrez Gene
12. Exploratory Medline Search (11/10/06):
 - a) "Freeman-Sheldon Syndrome" = 81024 citations
 - b) "MYH3" = 59928 citations
 - c) a and b combined = 1328 citations (limit to humans)

1. Gene Symbol: GALK1 Chromosomal Locus: 17q24
2. Protein Name: Galactokinase
3. Disease: Galactokinase deficiency
4. Description: Galactokinase converts galactose to galactose-1-phosphate. The deficiency results in the accumulation of galactose and urine galactitol. Adults with the condition may have cataracts, elevated red cell galactose, galactosuria, or elevated urinary galactitol and normal GALT enzyme activity.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analyte, Enzyme assay
9. Other Diseases: n/d
10. Clinical use(s): n/d
11. Source of Information: GeneTests.org, Academic Medical Centre, University of Amsterdam
Laboratory Genetic Metabolic Diseases
12. Exploratory Medline Search (11/8/2006):
 - a) "galactosemia.mp. or exp Galactosemias/"=1864
 - b) "Galactokinase.mp. or exp Galactokinase/ or GLAK1.mp"=976
 - c) a and b = 137

1. Gene Symbol: GALE Chromosomal Locus: 1p36-p35
2. Protein Name: UDP-glucose 4-epimerase
3. Disease: Galactose epimerase deficiency, Galactosemia
4. Description: A cause of galactosemia. The enzyme converts UDPgalactose to UDPglucose. In most patients with epimerase deficiency, the defect is localized to red blood cells. These individuals typically have normal growth and development.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Enzyme assay
9. Other Diseases: n/d
10. Clinical use(s): May be applicable to the Medicare population.
11. Source of Information: GeneTests.org, Emory University
Emory Biochemical Genetics Laboratory
12. Exploratory Medline Search (11/8/2006) :
 - a) "galactosemia.mp. or exp Galactosemias/"=1864
 - b) "UDP-glucose 4-epimerase.mp. or exp UDPglucose 4-Epimerase/"=391
 - c) a and b = 56

1. Gene Symbol: PPGB, Carboxypeptidase C
2. Protein Name: Lysosomal Protective Protein (Cathepsin A)
3. Disease: Galactosialidosis
4. Description: Galactosialidosis is one of seven identified Glycoprotein storage diseases (these are lysosomal storage diseases). The lysosomal Protective Protein/Cathepsin A (PPCA) is absent. It participates in oligosaccharide catabolism along with beta-Galactosidase and Neuraminidase and also protects the latter from being broken down in the lysosome. Thus, when PPCA is absent, it also leads to the absence of B-Galactosidase and Neuraminidase. The clinical phenotype includes coarse facial features, abnormal bone formation in multiple bones, and cherry red spots on ophthalmology evaluation.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analyte, Enzyme assay
9. Other Diseases: n/d
10. Clinical use(s): Unclear (early onset)
11. Source of Information: GeneTests.org, Greenwood Genetics Center
Metabolic Laboratory
12. Exploratory Medline Search (11/8/2006):
 - a) "galactosialidosis.mp."=182
 - b) "cathepsin A.mp. or exp Carboxypeptidase C/"=501
 - c) a and b = 67

1. Gene Symbol: GLI3 Chromosomal Locus: 7p13
2. Protein Name: Zinc finger protein GLI3
3. Disease: GLI3-related disorders: Greig cephalopolysyndactyly syndrome or Cephalopolysyndactyly Syndrome
4. Description: The clinical phenotype may include polydactyly, true ocular hypertelorism, and macrocephaly. Individuals with the mild form of the syndrome may have subtle craniofacial findings, while people with severe disease may have seizures, hydrocephalus, and mental retardation. GLI3 is the only gene known to be associated with the condition.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; FISH-metaphase
9. Other Diseases: n/d
10. Clinical use(s): Unclear use in the Medicare population.
11. Source of Information: GeneTests.org, Georgetown University Medical Center
Clinical Molecular Diagnostic Laboratory
12. Exploratory Medline Search (11/09/2006)
 - a) "Cephalopolysyndactyly Syndrome.mp."=
 - b) "GLI3.mp."=322
 - c) a and b = 37

1. Gene Symbol: G6PD
2. Protein Name: Glucose-6-phosphate 1-dehydrogenase
3. Disease: Glucose-6-phosphate dehydrogenase deficiency
4. Description: Perhaps the most common genetic deficiency in man. G6PD protects the body from oxidative insults, and rrythrocytes are especially sensitive to them. G6PD deficiency can result in hemolysis and in life threatening reactions to several medications, foods and infections.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Enzyme assay
9. Other Diseases: n/d
10. Clinical use(s): Unclear (early onset)
11. Source of Information: GeneTests.org, Pediatrix Screening, Inc.
12. Exploratory Medline Search (11/08/2006):
 - a) "exp Glucosephosphate Dehydrogenase Deficiency/ or Glucose-6-phosphate dehydrogenase deficiency.mp. or exp Favism/"=3797
 - b) "G6PD.mp"=2562
 - c) a and b = 1013

1. Gene Symbol: GAA Chromosomal Locus: 17q25.2-q25.3
2. Protein Name: Lysosomal alpha-glucosidase
3. Disease: Glycogen Storage Disease Type II or Acid Maltase Deficiency or Pompe Disease
4. Description: As in the other glycogen storage diseases, deficiency of the enzyme leads to accumulation of glycogen in lysosomes and cytoplasm, resulting in tissue destruction. In the adult form, the primary clinical finding is skeletal myopathy, with a more protracted course leading to respiratory failure. The heart and the liver are spared and the onset may be at any age. The clinical evolution is variable.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories (outside the USA)
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Targeted mutation analysis; Analyte, Enzyme assay, Protein analysis
9. Other Diseases: n/d
10. Clinical use(s): Potentially useful in the Medicare population.
11. Source of Information: GeneTests.org, Adelaide Women's and Children's Hospital
National Referral Laboratory
12. Exploratory Medline Search (11/08/2006):
 - a) "Glycogen Storage Disease Type II.mp. or exp Glycogen Storage Disease Type II/"=712
 - b) "exp Glucan 1,4-alpha-Glucosidase/"=1352
 - c) a and b = 162

1. Gene Symbol: LAMP2 Chromosomal Locus: Xq24
2. Protein Name: Lysosome-associated membrane glycoprotein 2
3. Disease: Glycogen Storage Disease Type IIb or Danon Disease or GSDIIb or X-Linked Vacuolar Cardiomyopathy and Myopathy
4. Description: As in the other glucogen storage diseases, deficiency of the enzyme leads to accumulation of glycogen in lysosomes and cytoplasm, resulting in tissue destruction. The clinical phenotype is characterized by cardiomyopathy, skeletal myopathy, and variable mental retardation. The age of onset ranges from infancy to adulthood and female carriers have a later onset of disease. The cardiomyopathy may be the presenting manifestation.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories (outside the USA)
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: n/d
10. Clinical use(s): Probably not relevant for the Medicare population.
11. Source of Information: GeneTests.org, Academic Medical Center
DNA Diagnostics Laboratory
12. Exploratory Medline Search (11/08/2006):
 - a) "Danon disease.mp. or exp Glycogen Storage Disease Type IIb/"=27
 - b) "LAMP2.mp"=63
 - c) a and b = 10

1. Gene Symbol: AGL Chromosomal Locus: 1p21
2. Protein Name: Glycogen debranching enzyme
3. Disease: Glycogen Storage Disease Type III, or Cori Disease or Debrancher Deficiency or Forbe Disease or GSDIII
4. Description: As in the other glucogen storage diseases, deficiency of the enzyme leads to accumulation of glycogen in lysosomes and cytoplasm, resulting in tissue destruction. Both liver and muscle involvement characterize the disease in the majority of patients. The onset is during the childhood, early adulthood.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Enzyme assay
9. Other Diseases: n/d
10. Clinical use(s): Probably not applicable to the Medicare population.
11. Source of Information: GeneTests.org, Athena Diagnostics Inc, Reference Lab
12. Exploratory Medline Search (11/08/2006):
 - a) "Cori disease.mp. or exp Glycogen Storage Disease Type III"=238
 - b) "Glycogen debranching enzyme.mp. or exp Glycogen Debranching Enzyme System"=257
 - c) a and b=52

1. Protein Name: Glycogen branching enzyme
2. Gene Symbol: GBE1 Chromosomal Locus: 3p12
3. Disease: Glycogen Storage Disease Type IV or Brancher Deficiency or GSDIV or Andersen disease
4. Description: As in the other glucogen storage diseases, deficiency of the enzyme leads to accumulation of glycogen in lysosomes and cytoplasm, resulting in tissue destruction. Here of interest is the adult form that can present as an isolated myopathy, or as adult polyglucosan body disease, a multisystem disorder. These patients have symptoms and signs of upper and lower motor neuron involvement. Progressive dementia may also be found.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Enzyme assay
9. Other Diseases: n/d
10. Clinical use(s): Probably not applicable to the Medicare population.
11. Source of Information: GeneTests.org, Athena Diagnostics Inc, Reference Lab
12. Exploratory Medline Search (11/08/2006):
 - a) "exp Glycogen Storage Disease Type IV/"=130
 - b) "Glycogen branching enzyme"=263
 - c) a and b=31

1. Gene Symbol: PYGM Chromosomal Locus: 11q13
2. Protein Name: Glycogen phosphorylase, muscle form
3. Disease: Glycogen Storage Disease Type V or GSDV or Glycogenosis Type V or McArdle Disease or Muscle Glycogen Phosphorylase Deficiency or Myophosphorylase Deficiency
4. Description: As in the other glucogen storage diseases, deficiency of the enzyme leads to accumulation of glycogen in lysosomes and cytoplasm, resulting in tissue destruction. The disease has onset in adolescence or early adulthood with exercise intolerance, fatigue, myalgia, cramps, myoglobinuria, poor endurance, muscle swelling, and fixed weakness. Stiffness or weakness of exercising muscles can be induced by either brief periods of intense isometric exercise or by less intense but sustained dynamic exercise.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Enzyme assay
9. Other Diseases: n/d
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org, Athena Diagnostics Inc, Reference Lab; UpToDate
12. Exploratory Medline Search (11/08/2006)
 - a) "exp Glycogen Storage Disease Type V/"=424
 - b) "exp Glycogen phosphorylase, muscle form/"=59
 - c) a and b = 25

1. Gene Symbol: PYGL Chromosomal Locus: 14q21-q22
2. Protein Name: Glycogen phosphorylase, liver form
3. Disease: Glycogen Storage Disease Type VI or GSDVI or HERS Disease
4. Description: As in the other glucogen storage diseases, deficiency of the enzyme leads to accumulation of glycogen in lysosomes and cytoplasm, resulting in tissue destruction. Patients typically present in early childhood with the characteristic features of growth retardation and prominent hepatomegaly. Skeletal and cardiac muscle are not affected. The disease improves with age, and hepatomegaly resolves in most cases. The disease has a benign course.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Enzyme assay
9. Other Diseases: n/d
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org, Duke University Medical Center, Glycogen Storage Disease Laboratory
12. Exploratory Medline Search (11/08/2006):
 - a) "exp Glycogen Storage Disease Type VI/"=36
 - b) "exp Glycogen Phosphorylase, Liver Form/ or PYGL.mp"=11
 - c) a and b=3

1. Gene Symbol: PFKM Chromosomal Locus: 12q13
2. Protein Name: 6-phosphofructokinase, muscle type
3. Disease: Glycogen Storage Disease Type VII or GSDVII or PFK Deficiency or Phosphofructokinase Deficiency or Tarui Disease
4. Description: As in the other glycogen storage diseases, deficiency of the enzyme leads to accumulation of glycogen in lysosomes and cytoplasm, resulting in tissue destruction. The disease typically presents in childhood with fatigue, muscle cramps, and exercise intolerance. A high carbohydrate meal or administration of glucose prior to exercise aggravates symptoms. Presentation sometimes occurs in middle age to late adulthood with fixed muscle weakness and progressive atrophy.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Enzyme assay
9. Other Diseases: n/d
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org; Athena Diagnostics Inc; UptoDate
12. Exploratory Medline Search (11/08/2006)
 - a) "exp Glycogen Storage Disease Type VII"=82
 - b) "exp Phosphofructokinase-1, Muscle Type/ or pfk.m.p"=42
 - c) a and b=7

1. Gene Symbol: GNE Chromosomal Locus: 9p12-p11
2. Protein Name: Bifunctional UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase
3. Disease: GNE-related myopathies (Inclusion body myopathy2 – Nonaka myopathy)
4. Description: This is an adult-onset, autosomal recessive disorder, characterized by slow progression of muscle weakness, both distal and proximal, but with the unusual feature of relative sparing of the quadriceps even in the advanced stages of the disease.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: Nonaka Myopathy
10. Clinical use(s): The disease is adult onset but rare. Probably not applicable to the Medicare population.
11. Source of Information: GeneTests.org, GeneDx, Inc
12. Exploratory Medline Search (11/08/2006)
 - a) “inclusion body myopathy.mp.”=124
 - b) “N-acetylmannosamine kinase.mp.”=59
 - c) a and b = 28

1. Gene Symbol: TGFBI Chromosomal Locus: 5q31
2. Protein Name: Transforming growth factor-beta-induced protein ig-h3
3. Disease: Granular corneal dystrophy or Groenouw Corneal Dystrophy Type I or Reis-Bucklers Corneal Dystrophy
4. Description: In this condition, there are opacities consisting of grayish white granules with sharp borders mainly in a disc-shaped area in the center of the cornea. The peripheral cornea is usually clear and the cornea between granules is clear. Although the onset may be as early as in the first 10 years, visual acuity during childhood is usually good. The clinical course is variable.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories (outside the USA)
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Linkage analysis, Sequence analysis of select exons, Targeted mutation analysis
9. Other Diseases: n/d
10. Clinical use(s): Probably not applicable to the Medicare population.
11. Source of Information: GeneTests.org, Institute of Research in Ophthalmology, Laboratory of Molecular Ophthalmology
12. Exploratory Medline Search (11/08/2006)
 - a) "exp Corneal Dystrophies, Hereditary/"=2205
 - b) "TGFBI.mp."=69
 - c) a and b = 47

1. Gene Symbol: PHKA2 Chromosomal Locus: Xp22.2-p22.1
2. Protein Name: Phosphorylase B kinase alpha regulatory chain, liver isoform
3. Disease: PHKA2-Related Glycogen Storage Disease Type IX or GSDIXa or GSDVIII or Glycogen Storage Disease Type IX, X-Linked or Glycogen Storage Disease Type IXa or Glycogen Storage Disease Type VIII, X-Linked or Phosphorylase Kinase Deficiency of Liver, X-Linked
4. Description: This is an X-linked disorder. There is confusion over the “Glycogen storage disease” classification of phosphorylase b kinase deficiency as both numbers VIII and IX have been assigned. The disease is mild. There is a normal liver response to glucagon (contrary to other liver-affecting glycogen storage diseases). Most adults are asymptomatic.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: n/d
10. Clinical use(s): Probably of little applicability in the Medicare population
11. Source of Information: GeneTests.org; UptoDate
12. Exploratory Medline Search (11/08/2006)
 - a) “exp glycogen storage disease type viii/”=13
 - b) “PHKA2”=25
 - c) a and b =0

1. Gene Symbol: HOXA13 Chromosomal Locus: 7p15-p14.2
2. Protein Name: Homeobox protein Hox-A13
3. Disease: Hand-foot-genital (uterus) syndrome
4. Description: The clinical features include small feet with unusually short great toes and abnormal thumbs. Clinodactyly is present. The condition is rare. Females with the disorder have duplication of the genital tract, including longitudinal vaginal septum. Because males also have the condition the correct naming is Hand-Foor-Genitsl syndrome. Most cases are probably due to mutations in HOXA13, but other (homeobox) genes may play a role.
5. Purpose: Diagnostics
6. Availability: clinical laboratory
7. Specimen: ND
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: No
10. Clinical use(s): Probably not widely applicable to the Medicare population.
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search 10/20/2006:
 - a) "exp Hand Deformities, Congenital/ or exp Foot Deformities, Congenital/ or Hand-foot-uterus.mp."=5954 citations
 - b) "exp Genes, Homeobox/ or Homeobox protein HoxA13.mp."=5685 citations
 - c) a and b limit to humans = 19 citations

1. Gene Symbol: HPD Chromosomal Locus: 12q24-qter
2. Protein Name: 4-hydroxyphenylpyruvate dioxygenase
3. Disease: Hawkinsinuria or 4-Hydroxyphenylpyruvate Hydroxylase Deficiency
4. Description: Hawkinsinuria is an autosomal dominant inborn error of metabolism (4-hydroxyphenylpyruvate hydroxylase deficiency). Metabolic acidosis and tyrosinemia are transient, and symptoms improve within the first year of life. Patients continue to excrete the hawkinsin metabolite in their urine throughout life.
5. Purpose: Diagnostics
6. Availability: Clinical laboratories
7. Specimen: Plasma, serum, CSF; or urine
8. Methodology: Analyte (aminoacid analysis and measurement of hawkinsin)
9. Other Diseases: no
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search: (10/20/2006)
 - a) "exp Amino Acid Metabolism, Inborn Errors/ or hawkinsinuria.mp"= 17,658 citations
 - b) "exp 4-Hydroxyphenylpyruvate Dioxygenase/ or HDP.mp."= 531 citations
 - c) a and b limited to humans = 55 citations

1. Gene Symbol: HBA2 Chromosomal Locus: 16pter-p13.3
2. Protein Name: Hemoglobin alpha chain
3. Disease: Hemoglobin constant spring
4. Description: The most common nondeletional alpha-thalassemic mutation, an important cause of HbH-like disease. It is caused by a mutation in the stop codon of the alpha 2 -globin gene that results in poor output an alpha-globin.
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: Blood sample
8. Methodology: Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s): Probably not applicable to the Medicare population - The condition is relatively rare.
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search:
 - a) "exp alpha-Thalassemia/ or exp Hemoglobinopathies/ or exp Hemoglobins, Abnormal/ or Hemoglobin constant spring.mp. or exp Thalassemia/ or exp Hemoglobin H/"=31,049 citations
 - b) "HbA2.mp. or exp Hemoglobin A2/"=537 citations
 - c) a and b limited to humas = 535 citations

1. Gene Symbol: F8 Chromosomal Locus: Xq28
2. Protein Name: Coagulation factor VIII
3. Disease: Hemophilia A
4. Description: Hypocoagulility and bleeding tendency of various degrees because of mutations in the factor VIII gene (Hemophilia A). Individuals with mild hemophilia A are often not diagnosed until later in life.
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis; Linkage analysis; Deletion/duplication analysis;
9. Other Diseases: no
10. Clinical use(s): May be applicable to the Medicare population Differentiate hypocoagulable states, many people with mild disease are diagnosed only late in life
11. Source of Information: GeneTests.org;
12. Exploratory Medline Search (20/10/2006):
 - a) "Hemophilia A"=13100 citations
 - b) "Coagulation factor VIII"= 11952 citations
 - c) a and b limit to humans = 5165 citations

1. Gene Symbol: F9 Chromosomal Locus: Xq27.1-q27.2
2. Protein Name: Coagulation factor IX
3. Disease: Hemophilia B
4. Description: Hypocoagulability and bleeding tendency of various degrees because of mutations in the factor factor IX gene (Hemophilia B). Individuals with mild hemophilia B are often not diagnosed until later in life.
5. Purpose: Diagnostics.
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis; Linkage analysis; Deletion/duplication analysis;
9. Other Diseases: no
10. Clinical use(s): May be applicable to the Medicare population - Differentiate hypocoagulable states, many people with mild disease are diagnosed only late in life
11. Source of Information: GeneTests.org;
12. Exploratory Medline Search:
 - a) "Hemophilia B" = 2925 citations
 - b) "Coagulation factor IX"=4157 citations
 - c) a and b limit in humans = 1384 citations

1. Gene Symbol: *SERPING1* Chromosomal Locus: 11q11-q13.1
2. Protein Name: Plasma protease C1 inhibitor
3. Disease: Hereditary Angioneurotic Edema
4. Description: Hereditary angioneurotic edema is an autosomal dominant disorder that results from an inherited deficiency of C1 (the activated first component of complement)-inhibitor function. It is characterized by episodic local subcutaneous edema and submucosal edema involving the upper respiratory and gastrointestinal tracts. There are two types of the disorder. In type I (the majority of these patients) serum levels of C1 inhibitor are low. In type II, the levels of C1 inhibitor are normal or elevated, but the protein is nonfunctional. The two types are clinically indistinguishable.
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen:
8. Methodology: Analysis of the entire coding region: Mutation scanning, Analysis of the entire coding region: Sequence analysis, Linkage analysis; Enzyme assay, Protein analysis. Sequence analysis of select exons.
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search (09/10/2006):
 - a) "Hereditary Angioneurotic Edema" = 271 citations
 - b) "Plasma protease C1 inhibitor" = 69 citations
 - c) "Hereditary Angioneurotic Edema" and "Plasma protease C1 inhibitor" = 2 (limit to humans) citations

1. Gene symbol: CPO Chromosomal Locus: 3q12
2. Protein Name: Coproporphyrinogen III Oxidase
3. Disease: Hereditary Coproporphyrin
4. Description: This is an hepatic form of porphyria, characterized by massive excretion of coproporphyrin III in the urine and the feces. The disorder is dominantly inherited. Cases may be asymptomatic, but may suffer attacks resembling those of acute intermittent porphyria, perhaps precipitated by drugs.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratory
7. Specimen: [Coproporphyrin III in the urine]
8. Methodology: Analyte
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search:
 - a) "Hereditary Coproporphyrin" = 187 citations
 - b) "Coproporphyrinogen III Oxidase" = 218 citations
 - c) "Hereditary Coproporphyrin" and "Coproporphyrinogen III Oxidase" = 5 (limit to humans) citations

1. Gene Symbol: ALDOB Chromosomal Locus: 9q22.3
2. Protein Name: Fructose-bisphosphate aldolase B
3. Disease: Hereditary Fructose Intolerance
4. Description: This is an autosomal recessive disorder of fructose metabolism due to a deficiency of fructose-1-phosphate aldolase activity. The disease is different from fructose intolerance. The accumulated fructose-1-phosphate inhibits glycogen breakdown and glucose synthesis, thereby causing severe hypoglycemia following ingestion of fructose. Patients develop a strong distaste for sweet food, and can avoid a recurrence of symptoms during the chronic course of the disease by remaining on a fructose- and sucrose-free diet.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons. Deletion / duplication analysis, Targeted mutation analysis: Enzyme assay
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search (10/9/2006):
 - a) "Hereditary Fructose Intolerance" = 246 citations
 - b) "Fructose-bisphosphate aldolase B" = 2 citations
 - c) "Hereditary Fructose Intolerance" and "Fructose-bisphosphate aldolase B" = 0 (limit to humans) citations

1. Gene Symbol: POU3F4 Chromosomal Locus: Xq21.1
2. Protein Name: POU domain, class 3, transcription factor 4
3. Disease: DFN3 Nonsyndromic Hearing Loss and Deafness
4. Description: X-Linked recessive manner of inheritance of a mixed conductive-sensorineural hearing loss, the conductive component of which is caused by stapedial fixation. Concurrent anomalies preclude surgical correction. May progress to profound loss.
5. Purpose: verify clinical diagnosis of hereditary hearing loss
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Targeted mutation analysis
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: 11/04/2006
 - a) "exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.mp" =31288 citations
 - b) "POU3F4" =52 citations
 - c) a and b = 23 citations

1. Gene Symbol: COCH Chromosomal Locus: 14q12-q13
2. Protein Name: Cochlin
3. Disease: Hereditary hearing loss and deafness (non-syndromic), DFNA-9
4. Description: The COCH (cochlin) gene has been associated with a post-lingual onset (usually at the 2nd decade) progressive impairment of high frequencies.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis
9. Other Diseases: no
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org ; UptoDate
12. Exploratory Medline Search: 04/11/2006
 - a) "exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.mp" =31288 citations
 - b) "cochlin or COCH.mp" =111 citations
 - c) a and b = 53 citations

1. Gene Symbol: SLC26A4 Chromosomal Locus: 7q31
2. Protein Name: Pendrin
3. Disease: Hereditary hearing loss and deafness (non-syndromic), DFNB4 (Pendred syndrome)
4. Description: Pendred syndrome is characterized by severe to profound bilateral sensorineural hearing impairment that is usually congenital and non-progressive, vestibular dysfunction, and temporal bone abnormalities.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: 11/04/2006
 - a) "exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.mp" =31236 citations
 - b) "SLC26A4.mp or pendrin.mp" =280 citations
 - c) a and b = 99 citations

1. Gene Symbol: GJB2 Chromosomal Locus: 13q11-q12
2. Protein Name: Gap junction beta-2 protein (Connexin 26)
3. Disease: Hereditary hearing loss and deafness (non-syndromic), GJB2-Related DFNA 3
Nonsyndromic Hearing Loss and Deafness
4. Description: Many genes have been associated with hearing loss and deafness, conductive and sensorineural. The GJB2 gene has been associated with a non-syndromic form with onset after the 2nd decade.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis
9. Other Diseases: Palmoplantar keratoderma, Keratitis-ichthyosis-deafness (KID) syndrome, Hystrix-like ichthyosis-deafness (HID) syndrome, Vohwinkel syndrome
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org ; UptoDate
12. Exploratory Medline Search: 20/10/2006
 - a) “exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.m” =31236 citations
 - b) “exp Connexins/ or GJB2.mp” =4915 citations
 - c) a and b = 419 citations

1. Gene Symbol: GJB2 Chromosomal Locus: 13q11-q12
2. Protein Name: Gap junction beta-2 protein (Connexin 26)
3. Disease: Hereditary hearing loss and deafness (non-syndromic), DFNB1
4. Description: DFNB1 is characterized by congenital, non-progressive mild-to-profound sensorineural hearing impairment. This is an autosomal recessive trait.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis, Linkage analysis
9. Other Diseases: no
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: 20/10/2006
 - a) "exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.mp" =31236 citations
 - b) "exp Connexins/ or GJB2.mp" =4915 citations
 - c) a and b = 419 citations

1. Gene Symbol: GJB6 Chromosomal Locus: 13q12
2. Protein Name: Gap junction beta-2 protein (Connexin 30)
3. Disease: Hereditary hearing loss and deafness (non-syndromic); GJB6-Related DFNA 3
Nonsyndromic Hearing Loss and Deafness
4. Description: Many genes have been associated with hearing loss and deafness, conductive and sensorineural. The GJB6 gene has been associated with a non-syndromic form with onset both early and after the 2nd decade.
5. Purpose: diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis
9. Other Diseases: Clouston syndrome
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org ; UptoDate
12. Exploratory Medline Search: 20/10/2006
 - a) “exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.mp” =31236 citations
 - b) “exp Connexins/ or GJB6.mp” =4890 citations
 - c) a and b = 419 citations

1. Gene Symbol: GJB6 Chromosomal Locus: 13q12
2. Protein Name: Gap junction beta-6 protein (Connexin 30)
3. Disease: Hereditary hearing loss and deafness (non-syndromic), DFNB1
4. Description: The GJB6 gene has been associated with DFNB1, a congenital, non-progressive mild-to-profound sensorineural hearing impairment. No other associated medical findings are present
5. Purpose: verify clinical diagnosis of hereditary hearing loss
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis
9. Other Diseases: Clouston syndrome
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: 20/10/2006
 - a) “exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.mp” =31236 citations
 - b) “exp Connexins/ or GJB6.mp” =4890 citations
 - c) a and b = 419 citations

1. Gene Symbol: KCNQ4 (DFNA2)
2. Protein Name: Potassium voltage-gated channel subfamily KQT member 4
3. Disease: Hereditary hearing loss and deafness
4. Description: Many genes have been associated with hearing loss and deafness, conductive and sensorineural. The KCNQ4 gene has been associated with a non-syndromic form with onset after the 2nd decade.
5. Purpose: verify clinical diagnosis of hereditary hearing loss
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis of selected exons
9. Other Diseases: no
10. Clinical use(s) to the Medicare population: Unclear (early onset)
11. Source of Information: GeneTests.org ; UptoDate
12. Exploratory Medline Search:
 - a) “exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.m” =31236 citations
 - b) “KCNQ4” =622 citations
 - c) a and b =36 citations

1. Gene Symbol: MT-RNR1 Chromosomal Locus: Mitochondrial
2. Protein Name: Mitochondrial 12S ribosomal RNA
3. Disease: MTRNR1-Related Hearing Loss and Deafness; Aminoglycoside Ototoxicity (MTRNR1-related)
4. Description: Nonsyndromic mitochondrial hearing loss is characterized by moderate-to-profound hearing loss, no other systemic findings on history or physical examination, and a mutation in either the MTRNR1 gene or the MTTS1 gene. Associated with ototoxicity after any dose of aminoglycosides.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Targeted mutation analysis
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: 11/04/2006
 - a) “exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.mp” =31628 citations
 - b) “exp RNA, Ribosomal/ or Mitochondrial 12S ribosomal RNA.mp” =31683 citations
 - c) a and b = 79 citations

1. Gene Symbol: MT-TS1 Chromosomal Locus: Mitochondrial
2. Protein Name: Mitochondrial tRNA serine 1
3. Disease: MTTS1-Related Hearing Loss and Deafness; Aminoglycoside Ototoxicity (MTTS1-related)
4. Description: Nonsyndromic mitochondrial hearing loss is characterized by moderate-to-profound hearing loss, no other systemic findings on history or physical examination, and a mutation in the MTTS1 gene (encodes the t-RNA for Serine). Associated with ototoxicity after any dose of aminoglycosides.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Targeted mutation analysis
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: 11/04/2006
 - a) "exp Hearing Loss, Sensorineural/ or exp Deafness/ or Hereditary Hearing Loss.mp" =31628 citations
 - b) "Mitochondrial tRNA serine 1.mp. or MTTS1.mp or exp RNA, Transfer, Ser/" =350 citations
 - c) a and b = 79 citations

1. Gene Symbol: EXT1 Chromosomal Locus: 8q24.11-q24.13
Gene Symbol: EXT2 Chromosomal Locus: 11p12-p11
2. Protein Name: Exostosin-1; Exostosin-2 genes
3. Disease: Hereditary Multiple Exostoses, Types I and II
4. Description: Multiple hereditary exostoses (EXT) is an autosomal dominant disorder characterized by multiple projections of bone capped by cartilage, most numerous in the metaphyses of long bones, but also occurring on the diaphyses of long bones. Flat bones, vertebrae, and the ribs may also be affected, but the skull is usually not involved. Symptoms arise from mass effects (pressure on adjacent structures). The mutations in the exostosin genes 1 and 2 are causal for the conditions in the majority of cases.
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Array Genomic Hybridization, FISH-metaphase, Analysis of the entire coding region: Sequence analysis, Linkage analysis. Deletion / duplication analysis. FISH-interphase
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search (10/9/2006):
 - a) "exp Exostoses, Multiple Hereditary/" = 784 citations
 - b) "Exostosin" = 16 citations
 - c) "exp Exostoses, Multiple Hereditary/" and "Exostosin" = 3 (limit to humans) citations

1. Gene Symbol: WT1 Chromosomal Locus: 11p13
2. Protein Name: Wilms' tumor protein
3. Disease: Hereditary nephrotic syndromes, WT1-Related Disorders
4. Description: WT1 is a locus associated with Wilms Tumor and other diseases, like Denys-Drash Syndrome, Frasier Syndrome, Isolated Diffuse Mesangial Sclerosis
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: ns
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; FISH-metaphase; Array Genomic Hybridization
9. Other Diseases: Denys-Drash Syndrome | Familial Wilms Tumor | Frasier Syndrome | Isolated Diffuse Mesangial Sclerosis
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: geneTests.org; OMIM
12. Exploratory Medline Search:
 - a) "Denys-Drash Syndrome or Familial Wilms Tumor or Frasier Syndrome or Isolated Diffuse Mesangial Sclerosis"=7369 citations
 - b) "exp WT1 Proteins/ or wt1.mp"=1605 citations
 - c) a and b = 769 citations

1. Gene Symbol: PMP22 Chromosomal Locus: 17p11.2
2. Protein Name: Peripheral myelin protein 22
3. Disease: Hereditary Pressure Sensitive Neuropathy or Tomaculous Neuropathy or NHPP
4. Description: The disorder is characterized by repeated focal pressure neuropathies such as carpal tunnel syndrome and peroneal palsy with foot drop. The first attack usually occurs in the second or third decade. Recovery from acute neuropathy is often complete (otherwise mild).
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis; Linkage analysis; FISH-metaphase; FISH-interphase
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search:
 - a) "exp "Hereditary Motor and Sensory Neuropathies"/ or NHPP.mp or Tomaculous Neuropathy.mp"=3597 citations
 - b) "Peripheral myelin protein 22.mp or PMP22.mp"=678 citations
 - c) a and b=447 citations

1. Gene Symbol: HSN2 Chromosomal Locus: 12p13.33
2. Protein Name: HSN2 protein
3. Disease: Hereditary Sensory and Autonomic Neuropathy Type II, HSN2
4. Description: A recessive form of congenital sensory neuropathy. Most reported cases had childhood onset.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: sequence analysis
9. Other Diseases: No
10. Clinical use(s) to the Medicare population: Unclear (early onset)
11. Source of Information: geneTests.org; OMIM
12. Exploratory Medline Search:
 - a) "exp "Hereditary Sensory and Autonomic Neuropathies"/"=4 92 citations
 - b) "HSN2.mp"= 6 citations
 - c) a and b = 6 citations

1. Gene Symbol: SPG7; Locus Name: SPG7; Chromosomal Locus: 16q24.3
2. Protein Name: Paraplegin
3. Disease: Hereditary Spastic Paraplegia, Paraplegin Type (spastic paraplegia 7)
4. Description: Many genes have been associated with the disorder. SPG7, the paraplegin gene, follows an autosomal recessive trait. Progressive, may start at all ages, usually in adulthood.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; Sequence analysis of RNA
9. Other Diseases: No
10. Clinical use(s): Disease may have very late onset, so it may be directly applicable to the Medicare population.
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search (11/06/2006):
 - a) "exp Spastic Paraplegia, Hereditary/"=440 citations
 - b) "paraplegin.mp or spg7.mp"=53 citations
 - c) a and b = 35 citations

1. Gene Symbol: SPAST Chromosomal Locus: 2p22-p21
2. Protein Name: spastin
3. Disease: Hereditary Spastic Paraplegia, Spastin Type (spastic paraplegia 4)
4. Description: Many genes have been associated with the disorder. SPG4, the spastin gene, follows an autosomal dominant trait. Progressive, may start at all ages, usually in young adulthood.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; Targeted Mutation analysis
9. Other Diseases: No
10. Clinical use(s) to the Medicare population: Unclear (mostly early onset)
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search (11/06/2006):
 - a) "exp Spastic Paraplegia, Hereditary/"=440 citations
 - b) "spastin.mp or spg4.mp"=160 citations
 - c) a and b = 111 citations

1. Gene Symbol: DPYD Chromosomal Locus: 1p22
2. Protein Name: Dihydropyrimidine dehydrogenase [NADP+]
3. Disease: Hereditary Thymine-Uraciluria or DPD Deficiency or Familial Pyrimidinemia
4. Description: Innate metabolism error with high phenotypic variability. The manner of inheritance is autosomal recessive.
5. Purpose: Diagnostic.
6. Availability: Clinical Laboratory
7. Specimen: blood, urine
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis; Analyte; Enzyme assay
9. Other Diseases: No
10. Clinical use(s): Probably not applicable to the Medicare population
11. Source of Information: GeneTests.org
12. Exploratory Medline Search:
 - a) "DPD Deficiency.mp."=87 citations
 - b) "exp "Dihydrouracil Dehydrogenase (NADP)"/"=733 citations
 - c) a and b = 80 citations

1. Gene Symbol: PRSS1 Chromosomal Locus: 7q35
2. Protein Name: Trypsin I
3. Disease: Hereditary pancreatitis, calcific pancreatitis
4. Description: The trypsin precursor in the pancreatic juice (trypsinogen) may be activated in the pancreas. Various mutations (dominant and recessive) in the PRSS1 gene may ruin a fail-safe mechanism to prevent trypsin from damaging the pancreas.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis
9. Other Diseases: No
10. Clinical use(s) in the medicare population: Unclear (early onset)
11. Source of Information: genetests.org
12. Exploratory Medline Search:
 - a) "Hereditary pancreatitis.mp"=326 citations
 - b) "PRSS1.mp"=109 citations
 - c) a and b =47 citations

1. Gene Symbol: SPINK1 Chromosomal Locus: 5q32
2. Protein Name: Pancreatic secretory trypsin inhibitor
3. Disease: Hereditary pancreatitis, calcific pancreatitis
4. Description: Pancreatic secretory trypsin inhibitor is secreted from pancreatic acinar cells into pancreatic juice. Its physiologic role has been thought to be the prevention of trypsin-catalyzed premature activation of zymogens within the pancreas and the pancreatic duct.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis
9. Other Diseases: No
10. Clinical use(s): May be useful in the medicare population
11. Source of Information: geneTests.org
12. Exploratory Medline Search:
 - a) "Hereditary pancreatitis.mp"=326 citations
 - b) "SPINK1.mp"=241 citations
 - c) a and b =36 citations

1. Gene Symbol: HPS1; Locus Name: HPS1 Chromosomal Locus: 10q23.1
2. Protein Name: Hermansky-Pudlak syndrome 1 protein
3. Disease: Hermansky-Pudlak Syndrome 1 (HPS1)
4. Description: This is a multisystemic disorder with oculocutaneous albinism, bleeding diathesis and pulmonary or gastrointestinal complications, and is an autosomal recessive trait. Detection of HPS1, mainly for individuals from Eastern Puerto Rico. Test used for differential diagnosis of albinism or platelet disorders.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood, buccal swabs
8. Methodology: Targeted Mutation analysis
9. Other Diseases: No
10. Clinical use(s): Probably not useful; Note that clinical use is limited to individuals from Eastern Puerto Rico.
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search (11/04/2006):
 - a) "exp Hermanski-Pudlak Syndrome/"=151 citations
 - b) "hps1.mp."=80 citations
 - c) a and b = 50 citations

1. Gene Symbol: HPS3; Locus Name: HPS3; Chromosomal Locus: 3q24
2. Protein Name: Hermansky-Pudlak syndrome 3 protein
3. Disease: Hermansky-Pudlak Syndrome 3 (HPS3)
4. Description: This is a multisystemic disorder with oculocutaneous albinism, bleeding diathesis and pulmonary or gastrointestinal complications, and is an autosomal recessive trait. Detection of HPS1, mainly for individuals from eastern Puerto Rico or of Ashkenazi Jewish origin. Test used for differential diagnosis of albinism or platelet disorders.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood, buccal swabs
8. Methodology: Targeted Mutation analysis
9. Other Diseases: No
10. Clinical use(s): Probably no use in the Medicare population. Note that clinical testing is limited to those with Puerto-Rican ancestry and Ashkenazi Jews ancestry.
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search (11/04/2006):
 - a) "exp Hermanski-Pudlak Syndrome/"=151 citations
 - b) "hps3.mp."=23 citations
 - c) a and b = 20 citations

1. Gene Symbol: CBS Chromosomal Locus: 21q22.3
2. Protein Name: Cystathionine beta-synthase
3. Disease: Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency or Homocystinuria, Cystathionine Beta-Synthase Deficiency
4. Description: The condition is characterized by developmental delay/mental retardation, ectopia lentis and/or severe myopia, skeletal abnormalities (excessive height and length of the limbs) and thromboembolism. Expressivity is variable for all of the clinical signs. Two phenotypes, responsive and non-responsive disease are recognized. Thromboembolism may result in early deaths.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratory
7. Specimen: Blood, plasma, urine
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Targeted mutation analysis; Analyte; Enzyme assay
9. Other Diseases: NA
10. Clinical use(s): Might be useful in the Medicare population.
11. Source of Information: genetests.org; OMIM
12. Exploratory Medline Search (11/06/2006):
 - a) "exp Homocystinuria/ or Cystathionine Beta-Synthase Deficiency.mp."=1325 citations
 - b) "Cystathionine Beta-Synthase.mp. or exp Cystathionine beta-Synthase/"=867 citations
 - c) a and b=276 citations

1. Gene Symbol: GLRA1 Chromosomal Locus: 5q32
2. Protein Name: Glycine receptor alpha-1 chain
3. Disease: Hyperekplexia, GLRA1-related, or familial startle disease
4. Description: The gene encodes the beta subunit of the inhibitory glycine receptor that mediates postsynaptic inhibition in the spinal cord and other regions of the central nervous system. Receptor malfunction may result in exaggerated startle responses and pronounced head-retraction jerks (reflecting a disinhibition of vestigial brainstem reflexes.)
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: ND
8. Methodology: Sequence analysis of select exons; Targeted mutation analysis
9. Other Diseases: No
10. Clinical use(s): Probably no use in the Medicare population
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (11/06/2006):
 - a) "Hyperekplexia.mp. or familial startle disease.mp." = 177 citations
 - b) "Glycine receptor alpha-1 chain.mp. or exp Receptors, Glycine/ or GLRA1.mp."=1581 citations
 - c) a and b = 78 citations

1. Gene Symbol: MVK Chromosomal Locus: 12q24
2. Protein Name: Mevalonate kinase
3. Disease: Hyper IgD Syndrome or Hyperimmunoglobulinemia D and Periodic Fever Syndrome or Periodic Fever, Dutch Type
4. Description: This is an autosomal recessive disorder characterized by recurrent episodes of fever associated with lymphadenopathy, arthralgia, gastrointestinal disturbance, and skin rash. The diagnostic hallmark of HIDS is a constitutively elevated level of serum immunoglobulin D (IgD), although patients have been reported with normal IgD levels. The metabolism of isoprenoids (which is related to the mevalonate kinase) was found affected during the fever episodes rather than between them. Usually presents in early childhood.
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analyte; Enzyme assay
9. Other Diseases: NA
10. Clinical use(s): Probably not relevant to the Medicare population
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search:
 - a) "hyper IgD syndrome.mp. or HIDS.mp"=106 citations
 - b) "Mevalonate kinase.mp or MVK.mp"=265 citations
 - c) a and b = 44 citations

1. Gene Symbol: SCN4A Chromosomal Locus: 17q23.1-q25.3
2. Protein Name: Sodium channel protein type 4 subunit alpha
3. Disease: Hyperkalemic Periodic Paralysis Type 1
4. Description: Episodic flaccid generalized weakness (rather than paralysis), due to malfunctioning Na channel (the voltage-gated skeletal muscle sodium channel.). Onset is usually before the age of 20. Many older individuals may develop chronic myopathy.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons; Targeted mutation analysis
9. Other Diseases: Hypokalemic periodic paralysis and Paramyotonia congenita
10. Clinical use(s): May not be directly applicable to the Medicare population
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search:
 - a) "Hyperkalemic Periodic Paralysis.mp. or exp Paralysis, Hyperkalemic Periodic/"= 232 citations
 - b) "SCN4A"=126 citations
 - c) a and b = 50 citations

1. Gene Symbol: AGXT Chromosomal Locus: 2q36-q37
2. Protein Name: Serine-pyruvate aminotransferase
3. Disease: Hyperoxaluria (primary, type 1), Alanine-Glyoxylate Aminotransferase Deficiency or Glycolic Aciduria or Peroxisomal Alanine:Glyoxylate Aminotransferase Deficiency
4. Description: The condition is caused by a deficiency of the liver peroxisomal enzyme alanine:glyoxylate aminotransferase (AGT), which catalyzes the conversion of glyoxylate to glycine. When AGT activity is absent, glyoxylate is converted to oxalate, which forms insoluble calcium salts that accumulate in the kidney and other organs. The disease may progress to end-stage renal disease (ESRD) with a history of renal stones or calcinosis. Age at onset of symptoms typically ranges from one to 25 years.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Targeted mutation analysis; Linkage analysis; Analyte; Enzyme assay
9. Other Diseases: NA
10. Clinical use(s): Probably not applicable to the Medicare population. The age of onset is early and the diagnosis typically set before the ages typically applicable to Medicare population.
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search (11/08/2006):
 - a) "primary hyperoxaluria type 1.mp. or exp Hyperoxaluria, Primary/"=471 citations
 - b) "Serine-pyruvate aminotransferase.mp. or AGXT.mp"=129 citations
 - c) a and b = 46 citations

1. Gene Symbol: FGFR3 Chromosomal Locus: 4p16.3
2. Protein Name: Fibroblast growth factor receptor 3
3. Disease: Hypochondroplasia
4. Description: Hypochondroplasia is a skeletal dysplasia that results in a phenotype of short stature, stocky build, disproportionately short arms and legs, broad and short hands and feet, mild joint laxity, and macrocephaly. The skeletal features are very similar to achondroplasia but tend to be milder. The manner of inheritance is autosomal dominant. 70% of affected people have FGFR3 mutations, but genetic heterogeneity exists.
5. Purpose: Diagnosis
6. Availability: Clinical Laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s): Probably of little use for the Medicare population.
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search (11/08/2006):
 - a) "Hypochondroplasia.mp." = 165 citations
 - b) "Fibroblast growth factor receptor 3.mp. or exp Receptor, Fibroblast Growth Factor, Type 3/" = 647 citations
 - c) a and b = 65 citations

1. Gene Symbol: KAL1 Chromosomal Locus: Xp22.3
2. Protein Name: Anosmin-1
3. Disease: Hypogonadotrophic hypogonadism (X-linked), Kallman Syndrome 1 or Hypogonadotrophic hypogonadism with anosmia
4. Description: This is an X-linked disorder. The features of X-linked Kallmann syndrome primarily include hypogonadotropic hypogonadism and anosmia, however the phenotype is variable. Some males have large deletions of Xp22.3 and manifest several clinical features including Kallmann syndrome and ichthyosis (steroid sulfatase deficiency).
5. Purpose: Diagnostics
6. Availability: Clinical Laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; FISH-metaphase; FISH-interphase; Array Genomic Hybridization
9. Other Diseases: NA
10. Clinical use(s): May be applicable in the Medicare population.
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search (11/08/2006):
 - a) "Hypogonadotrophic hypogonadism.mp or exp Kallmann Syndrome/"=628 citations
 - b) "anosmin 1.mp. or KAL1.mp."=113 citations
 - c) a and b = 89 citations

1. Gene Symbol: ALPL Chromosomal Locus: 1p36.1-p34
2. Protein Name: Alkaline phosphatase, tissue-nonspecific isozyme
3. Disease: Hypophosphatasia or Phosphoethanolaminuria
4. Description: The patients present with demineralization, bone pain, fractures, and have little or no measurable alkaline phosphatase
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Targeted mutation analysis; Linkage analysis
9. Other Diseases: NA
10. Clinical use(s): Probably applicable to the Medicare population
11. Source of Information: genetests.org; PubMed; OMIM
12. Exploratory Medline Search:
 - a) "Hypophosphatasia.mp. or exp Hypophosphatasia/"= 612 citations
 - b) "exp Alkaline Phosphatase/ or ALPL.mp."= 40017 citations
 - c) a and b = 281 citations

1. Gene Symbol: KRT2; Chromosomal Locus: 12q11-q13
2. Protein Name: Keratin, type II cytoskeletal 2 epidermal
3. Disease: Ichthyosis Bullosa of Siemens
4. Description: Any of several generalized skin disorders characterized by dryness, roughness, and scaliness, due to hypertrophy of the stratum corneum epidermis. Most are genetic, but some are acquired, developing in association with other systemic disease or genetic syndrome.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not directly applicable to the Medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (11-16-06)
 - a) "Ichthyosis Bullosa of Siemens" = 4014
 - b) "KRT2" = 13135
 - c) a and b = 162

1. Gene Symbol: GJB2; Chromosomal Locus: 13q11-q12
2. Protein Name: Gap junction beta-2 protein (Connexin 26)
3. Disease: Ichthyosis, Hystrix-like, with Deafness
4. Description: Gap junctions were first characterized by electron microscopy as regionally specialized structures on plasma membranes of contacting adherent cells. These structures were shown to consist of cell-to-cell channels. Proteins, called connexins, purified from fractions of enriched gap junctions from different tissues differ. The connexins are designated by their molecular mass. Another system of nomenclature divides gap junction proteins into 2 categories, alpha and beta, according to sequence similarities at the nucleotide and amino acid levels. For example, CX43 (MIM 121014) is designated alpha-1 gap junction protein, whereas CX32 (GJB1; MIM 304040) and CX26 are called beta-1 and beta-2 gap junction proteins, respectively. This nomenclature emphasizes that CX32 and CX26 are more homologous to each other than either of them is to CX43.[supplied by OMIM]
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region; sequence analysis.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not directly applicable to the Medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (11-16-06)
 - a) "Ichthyosis, Hystrix-like" = 4
 - b) "GJB2" = 1736
 - c) a and b = 2

1. Gene Symbol: STS; Chromosomal Locus: Xp22.32
2. Protein Name: Steryl-sulfatase
3. Disease: Ichthyosis, X-Linked; Placental Steroid Sulfatase Deficiency; Steroid Sulfatase Deficiency
4. Description: The protein encoded by this gene catalyzes the conversion of sulfated steroid precursors to estrogens during pregnancy. The encoded protein is found in the endoplasmic reticulum, where it acts as a homodimer. Mutations in this gene are known to cause X-linked ichthyosis (XLI).
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Enzyme assay, FISH-metaphase, FISH-interphase.
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not directly applicable to the Medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (11-16-06)
 - a) "Ichthyosis, X-Linked" = 445
 - b) "STS" = 2703
 - c) a and b = 85

1. Gene Symbol: PDB1, PDB2; Chromosomal Locus: 6p21, 18q21-q2
2. Protein Name: ND
3. Disease: Inclusion Body Myopathy with Paget Disease and Frontotemporal Dementia
4. Description: Paget's disease of bone causes bones to grow larger and weaker than normal. The disease may affect one or more bones but does not spread from affected bones to other bones in the body. You can have Paget's disease in any bone in your body, but most people have it in their pelvis, skull, spine, or leg bones. These bones may become misshapen, and they can break more easily because they are weaker than normal bones. Some people with Paget's disease feel pain in these bones, too. Inclusion body myopathy associated with Paget disease of the bone (PDB) and frontotemporal dementia (FTD), or IBMPFD, reported in a few families with autosomal dominant inheritance (MIM 605382).
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: ND
8. Methodology: Linkage analysis, targeted mutation analysis.
- 9.
10. Other Diseases: NA
11. Clinical use(s) for the Medicare population: Rare: probably not directly applicable to the Medicare population
12. Source of Information: Genetests.org
13. Exploratory Medline Search: (11-16-06)
 - a) "Inclusion Body Myopathy with Paget Disease and Frontotemporal Dementia" =
 - b) "PDB"1 or "PDB2" =
 - c) a and b =

1. Gene Symbol: KCNQ1 Chromosomal Locus: 11p15.5
2. Protein Name: Potassium voltage-gated channel subfamily KQT member 1
3. Disease: Jervell and Lange-Neilsen Syndrome, LQT1
4. Description: The syndrome presents with congenital sensorineural deafness without DFNB1 (no deleterious mutations in the GJB1 - connexin 26 gene) and personal history of syncope or seizure or a family history of sudden death before age 40 years. There is a long QT interval in the ECG predisposing to arrhythmias.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Mutation scanning; Deletion/duplication analysis; Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably of little use for the Medicare population
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/31/06):
 - a) "Jervell and Lange-Neilsen Syndrome" or "Jervell Syndrome" or "Lange-Neilsen Syndrome" or "JLNS"
= 26 citations
 - b) "KCNQ1" = 501 citations
 - c) a and b = 15 citations (limit to humans)

1. Gene Symbol: KCNE1 Chromosomal Locus: 21q22.1-q22.2
2. Protein Name: Potassium voltage-gated channel subfamily E member 1
3. Disease: Jervell and Lange-Neilsen Syndrome, LQT5
4. Description: The syndrome presents with congenital sensorineural deafness without DFNB1 (no deleterious mutations in the GJB1 - connexin 26 gene) and personal history of syncope or seizure or a family history of sudden death before age 40 years. There is a long QT interval in the ECG predisposing to arrhythmias.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Mutation scanning; Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not applicable to the Medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/31/06):
 - a) "Jervell and Lange-Neilsen Syndrome" or "Jervell Syndrome" or "Lange-Neilsen Syndrome" or "JLNS"
= 26 citations
 - b) "KCNE1" = 217 citations
 - c) "a" and "KCNE1" = 10 citations (limit to humans)

1. Gene Symbol: GJB2 (Chromosomal Locus: 13q11-q12)
2. Protein Name: Gap junction beta-2 protein (Connexin 26)
3. Disease: Keratitis-Ichthyosis-Deafness Syndrome
4. Description: The disease is a rare ectodermal dysplasia affecting the skin, hearing and vision with variable clinical presentation. Sensorineural hearing loss is often congenital, bilateral and severe. The syndrome is inherited in an autosomal dominant fashion but the majority (over 90%) of cases due to de novo mutation in the GJB2 gene.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood, buccal swab
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: Hereditary Sensorineural hearing loss and deafness
10. Clinical use(s) for the Medicare population: Probably not applicable.
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/31/06):
 - a) "Keratitis-Ichthyosis-Deafness Syndrome" or "KID syndrome" = 85 citations
 - b) "GJB2" = 345 citations
 - c) "a" and "GJB2" = 15 citations (limit to humans)

1. Gene Symbol: C20orf42 Chromosomal Locus: 20p13
2. Protein Name: Unc-112 related protein 1
3. Disease: Kindler Syndrome or hereditary acrokeratotic poikiloderma
4. Description: The condition entails skin alterations and lesions that develop early. The clinical phenotype is variable, but includes vesicopustule formations confined to the hands and feet, eczematoid dermatitis (widespread), gradual appearance of diffuse poikiloderma (with striate and reticulate atrophy which spares the head and persists into adulthood), and development of keratotic papules on the hands, feet, elbows, and knees.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not applicable
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/31/06):
 - a) "Kindler Syndrome" or "Acrokeratotic Poikiloderma" = 62 citations
 - b) "C20orf42" = 13 citations
 - c) "a" and "C20orf42" = 12 citations (limit to humans)

1. Gene Symbol: KEL Chromosomal Locus: 7q33
2. Protein Name: Kell blood group glycoprotein
3. Disease: NA
4. Description: Anti-K is capable of causing severe HTRs and HDN. In fact, anti-K, along with anti-c and anti-E, currently make up the great majority of cases of clinically significant HDN
5. Purpose: Prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: NA
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset).
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/16/06):
 - a) "Red cell antigen\$" = 393 citations
 - b) "Kell" = 916 citations
 - c) "KEL" = 374 citations
 - d) ("Red cell antigen\$" or "Kell") and "KEL" = 40 citations (limit to humans)

1. Gene Symbol: LDHA Chromosomal Locus: 11p15;
Gene Symbol: LDHB Chromosomal Locus: 12p12;
Gene Symbol: LDHC Chromosomal Locus: 11p15
2. Protein Name: L-Lactate Dehydrogenase M Chain; L-Lactate Dehydrogenase H Chain; L-Lactate Dehydrogenase X Chain
3. Disease: Lactate Dehydrogenase Deficiency
4. Description: The condition belongs to the glycogen storage diseases. Deficiency of the M isoform of LDH, caused by mutations in the LDHA gene, results in childhood-onset myopathy (exercise intolerance, muscle stiffness, and myoglobinuria), which has an autosomal recessive inheritance. Deficiency of the H isoform is caused by mutations in the LDHB gene and appears to have no clinical consequences.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Enzyme assay
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (age of onset childhood to adulthood)
11. Source of Information: Genetests.org; UpToDate
12. Exploratory Medline Search (11/08/06):
 - a) "LDH deficiency.mp. or exp Glycogen Storage Disease/" = 3646 citations
 - b) "LDHA" or "LDHB" or "LDHC" = 164 citations
 - c) "a" and "b" = 0 citations

1. Gene Symbol: Critical Region: LGCR Chromosomal Locus: 8q24.11-q24.13
2. Protein Name: ND
3. Disease: Langer-Giedion Syndrome or Tricho-rhino-phalangeal Syndrome Type II
4. Description: The disease is associated with loss of functional copies of the TRPS1 and EXT1 genes. The clinical phenotype is multiple exostoses, bulbous nose, peculiar facies, and sparse scalp hair.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Array genomic hybridization; FISH-metaphase; FISH-interphase
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not applicable to the Medicare population
11. Source of Information: Genetests.org; OMIM; UptoDate
12. Exploratory Medline Search (8/30/06):
 - a) "Langer-Giedion Syndrome" = 96 citations
 - b) "LGCR" = 6 citations
 - c) "Langer-Giedion Syndrome" and "LGCR" = 5 citations

1. Gene Symbol: TGFBI Chromosomal Locus: 5q31
2. Protein Name: Transforming growth factor-beta-induced protein ig-h3
3. Disease: Lattice Corneal Dystrophy Type 1
4. Description: The condition is characterized by corneal dystrophic lesions. The cornea between the lesions is clear. Optic acuity is normal in early ages. Manifestation is early (by the 2nd decade).
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; Sequence analysis of select exons; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably of little use in the Medicare population, onset is early.
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/30/06):
 - a) "Corneal Dystroph\$" = 2424 citations
 - b) "TGFBI" = 69 citations
 - c) "Corneal Dystroph\$" and "TGFBI" = 54 citations (limit to humans)

1. Gene Symbol: PTPN11 Chromosomal Locus: 12q24.1
2. Protein Name: Tyrosine-protein phosphatase non-receptor type 11
3. Disease: LEOPARD Syndrome (Cardiomyopathic Lentiginosis)
4. Description: LEOPARD stands for: multiple lentigines, ECG abnormalities, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, growth retardation, and sensorineural deafness. Darkly-pigmented multiple lentigines are a hallmark feature of LEOPARD syndrome. Congenital heart defects, usually pulmonic stenosis or subvalvular aortic stenosis, are a major feature.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Mutation scanning of select exons; linkage analysis; Analysis of the entire coding region: Mutation scanning
9. Other Diseases: Noonan Syndrome
10. Clinical use(s) for the Medicare population: Probably not applicable to the Medicare population
11. Source of Information: Genetests.org; OMIM; PubMed
12. Exploratory Medline Search (8/30/06:
 - a) "exp LEOPARD Syndrome" or "exp Lentigo" or "lentig\$" = 3036 citations
 - b) "PTPN11" = 120 citations
 - c) "a" and "PTPN11" = 17 citations (limit to humans)

1. Gene Symbol: LMNA Chromosomal Locus: 1q21.2
2. Protein Name: Lamin-A/C
3. Disease: Lipoatrophy with Diabetes, Hepatic Steatosis, Hypertrophic Cardiomyopathy and Leukomelanodermic Papules
4. Description: The name of the condition is its description: Lipoatrophy with Diabetes, Hepatic Steatosis, Hypertrophic Cardiomyopathy and Leukomelanodermic Papules. The condition is rare. It is associated with progeria (premature aging).
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood, buccal swabs, tissue
8. Methodology: Analysis of the entire coding region: Sequence analysis; linkage analysis
9. Other Diseases: Emery-Dreifuss Muscular Dystrophy; Dilated Cardiomyopathy; Cardiomyopathy with Conduction Defects; Partial Lipodystrophy; Charcot-Marie-Tooth; Mandibuloacral Dysplasia; Hutchinson-Gilford Progeria Syndrome
10. Clinical use(s) for the Medicare population: The disease is not common: probably not widely applicable to the Medicare population
11. Source of Information: Genetests.org; OMIM; PubMed
12. Exploratory Medline Search (8/30/06):
 - a) "Lipoatrophy" or "Lipoatrophy" = 2980 citations
 - b) "LMNA" = 223 citations
 - c) "a" and "LMNA" = 83 citations (limit to humans)

1. Gene Symbol: TGFBR1 Chromosomal Locus: 9q33-q34;
Gene Symbol: TGFBR2 Chromosomal Locus: 3p22
2. Protein Name: TGF-beta receptor type I; TGF-beta receptor type-2
3. Disease: Loeys-Dietz Aortic Aneurysm Syndrome
4. Description: The condition is characterized by aortic aneurysms hypertelorism, bifid uvula and/or cleft palate, and generalized arterial tortuosity with ascending aortic aneurysm and dissection. The syndrome shows variable clinical expression. The manner of inheritance is autosomal dominant. Some similarity (clinical) to Marfan syndrome.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not applicable to the Medicare population.
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/29/06):
 - a) "Loeys-Dietz Aortic Aneurysm Syndrome" = 2 citations
 - b) "TGFBR1" or "TGFBR2" = 120 citations
 - c) "Loeys-Dietz Aortic Aneurysm Syndrome" and "b" = 2 citations (limit to humans)

1. Gene Symbol: SH2D1A Chromosomal Locus: Xq25
2. Protein Name: SH2 domain protein 1A
3. Disease: Lymphoproliferative Disease, X-linked
4. Description: The disease has three phenotypes, namely an inappropriate immune response to Epstein-Barr virus infection resulting in unusually severe and often fatal infectious mononucleosis (up to 90% mortality if untreated), dysgammaglobulinemia, and/or lymphoproliferative disorders typically of B-cell origin. X-linked, affects males with variable clinical course even in the same family. May be associated with Lymphomas or other lymphoproliferative disease.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; protein analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/29/06):
 - a) "Lymphoproliferative Disorders" or "Lymphoproliferative Disease" = 246753 citations
 - b) "SH2D1A" = 176 citations
 - c) "a" and "SH2D1A" = 123 citations

1. Protein Name: Collagen alpha 1(XI) chain
2. Gene Symbol: COL11A1 Chromosomal Locus: 1p21
3. Disease: Marshall Syndrome
4. Description: Marshall syndrome is associated with COL11A1 mutations and has clinical features that include a craniofacial appearance characterized by a flat midface, depressed nasal bridge, short nose, and anteverted nares. Patients have ocular abnormalities (eg, cataracts, myopia), sensorineural hearing loss, and spondyloepiphyseal abnormalities
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (disease complications extend until 4th decade of life)
11. Source of Information: Genetests.org; Uptodate online
12. Exploratory Medline Search (8/29/06):
 - a) "Marshall Syndrome" = 35 citations
 - b) "COL11A1" = 62 citations
 - c) "Marshall Syndrome" and "COL11A1" = 9 citations (limit to humans)

1. Gene Symbol: ACADM Chromosomal Locus: 1p31
2. Protein Name: Medium-chain acyl-CoA dehydrogenase (MCAD)
3. Disease: Medium Chain Acyl-Coenzyme A Dehydrogenase Deficiency
4. Description: MCAD deficiency is inherited autosomal recessive and is associated with mutations in the *ACADM* gene. The medium chain acyl-CoA dehydrogenase (MCAD) deficiency is the most common enzyme deficiency in fatty acid oxidation. Patients with MCAD deficiency may present clinically as an acute encephalopathy. Apparent life threatening events (ALTEs) have also been reported. During symptomatic episodes, patients may have hypoketotic hypoglycemia. Symptoms are commonly precipitated by metabolic stress such as fasting or infection
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood; tissue
8. Methodology: Targeted mutation analysis; Analysis of the entire coding region: Sequence analysis; Analyte, Enzyme assay; Sequence analysis of select exons; Protein analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Diagnostic as presentation in later life is possible
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/29/06:
 - a) (“Acyl-Coenzyme A Dehydrogenase Deficiency” and “Medium chain”) or “MCAD deficiency” = 206 citations
 - b) “ACADM” = 13 citations
 - c) “a” and “ACADM” = 3 citations (limit to humans)

1. Gene Symbol: GNAS (GNAS1) Chromosomal Locus: 20q13.2
2. Protein Name: Guanine nucleotide-binding protein G(s), alpha subunit
3. Disease: McCune-Albright Syndrome
4. Description: McCune-Albright Syndrome (MAS) is a rare disorder defined as the triad of peripheral precocious puberty, café-au-lait skin pigmentation, and fibrous dysplasia of bone. Patients with MAS have a mutation of the alpha subunit of the G3 protein that activities adenylate cyclase
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Tissue or blood
8. Methodology: Targeted mutation analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (early onset)
11. Source of Information: Genetests.org; Uptodate
12. Exploratory Medline Search (8/29/06):
 - a) “McCune-Albright Syndrome” or “Polyostotic Fibrous Dysplasia” or “MAS” = 4885 citations
 - b) “GNAS” or “GNAS1” = 271 citations
 - c) “a” or “b” = 69 citations (limit to humans)

1. Gene Symbol: MT-TK Chromosomal Locus: Mitochondrial
2. Protein Name: Mitochondrial tRNA lysine
3. Disease: Mitochondrial Disorders, MERRF
4. Description: MERRF (**M**yoclonic **E**pilepsy associated with **R**agged **R**ed **F**ibers) is a multisystem disorder characterized by myoclonus, which is often the first symptom, followed by generalized epilepsy, ataxia, weakness, and dementia. Other common clinical features include hearing loss, short stature, optic atrophy, and cardiomyopathy with Wolff-Parkinson-White (WPW) syndrome. MERRF is caused by mutations in mtDNA and is transmitted by maternal inheritance.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; Enzyme assay, Protein analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/28/06):
 - a. "Mitochondrial Encephalomyopath\$" or "MERRF" = 1849 citations
 - b. "MT-TK" = 2 citations
 - c. "a" and "MT-ND5" = 0 citations

1. Gene Symbol: MLS Chromosomal Locus: Xp22.3
2. Protein Name: MLS syndrome FISH analysis
3. Disease: Microphthalmia with Linear Skin Defects
4. Description: MLS is an X-linked dominant disorder characterized primarily by linear skin defects on the face and neck and eye abnormalities (microphthalmia/sclerocornea). The phenotype is variable, with some affected individuals having brain abnormalities, some degree of mental retardation and cardiac defects.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Array genomic hybridization; FISH-metaphase; FISH-interphase
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/29/06):
 - a. "Microphthalmia with Linear Skin Defects" = 30 citations
 - b. "MLS" = 1805 citations
 - c. "Microphthalmia with Linear Skin Defects" and "MLS" = 30 citations (limit to humans)

1. Gene Symbol: MT-RNR1 Chromosomal Locus: Mitochondrial
2. Protein Name: Mitochondrial 12S ribosomal RNA
3. Disease: Mitochondrial Disorders, MTRNR1-Related Hearing Loss and Deafness
4. Description: Mutations in *MTRNR1* can be associated with predisposition to aminoglycoside ototoxicity and/or late-onset sensorineural hearing loss. Nonsyndromic mitochondrial hearing loss is caused by mutations in mtDNA and is transmitted by maternal inheritance. The median age of onset of sensorineural hearing loss in individuals who have a mutation in *MTRNR1*, but are not exposed to aminoglycosides, is around age 20 years
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons
9. Other Diseases: other phenotypes associated with mutations in mitochondrial DNA
10. Clinical use(s) for the Medicare population: Unclear applicability
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/28/06:
 - a) “(Mitochondrial or Nonsyndromic) and (Hearing Loss or Deafness))” or “Aminoglycoside Ototoxicity” = 7896 citations
 - b) “*MTRNR1*” = 6 citations
 - c) “a” and “b” = 6 citations (limit to humans)

1. Gene Symbol: MT-TS1 Chromosomal Locus: Mitochondrial
2. Test Name: Mitochondrial tRNA serine 1
3. Disease: Mitochondrial Disorders, MTRNR1-Related Hearing Loss and Deafness
4. Description: Mutations in *MTTS1* are usually associated with onset of sensorineural hearing loss in childhood and can be associated with predisposition to aminoglycoside ototoxicity and/or late-onset sensorineural hearing loss. Nonsyndromic mitochondrial hearing loss is caused by mutations in mtDNA and is transmitted by maternal inheritance.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons
9. Other Diseases: other phenotypes associated with mutations in mitochondrial DNA
10. Clinical use(s) for the Medicare population: Unclear applicability
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/28/06:
 - a) "MT-TS1" or "MTTS1" = 1 citation

1. Gene Symbol: MT-TL1 Chromosomal Locus: Mitochondrial
2. Protein Name: Mitochondrial tRNA leucine 1
3. Disease: Mitochondrial Disorders, Diabetes and Hearing Loss
4. Description: The A3243G point mutation may cause CPEO, diabetes mellitus and deafness, or a severe encephalopathy with recurrent strokes and epilepsy. The most common mtDNA mutations responsible for non-syndromic maternally inherited sensorineural hearing loss localize to two regions of the mitochondrial genome: the 12S rRNA and the tRNA ser(UCN) genes.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Deletion/duplication analysis; Analysis of the entire coding region: Mutation scanning; Analysis of the entire coding region: Sequence analysis
9. Other Diseases: other mitochondrial deletion syndromes
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) "Mitochondrial Disorders" = 6926 citations
 - b) "diabet\$" or "hearing loss" = 298465 citations
 - c) "a" and "b" = 551 citations
 - d) "MT-TL1" = 0 citations
 - e) "c" and "MT-TL1" = 0 citations

1. Gene Symbol: MT-CYB Chromosomal Locus: Mitochondrial
2. Protein Name: Cytochrome b; NADH-ubiquinone oxidoreductase chain 1; NADH-ubiquinone oxidoreductase chain 2; NADH-ubiquinone oxidoreductase chain 4; NADH-ubiquinone oxidoreductase chain 5; NADH-ubiquinone oxidoreductase chain 6
3. Disease: Mitochondrial Disorders, Leber Hereditary Optic Neuropathy
4. Description: Leber's optic neuropathy (LON) is a maternally inherited late-onset optic atrophy. LON usually presents with acute or subacute, painless loss of central visual acuity that occurs between 12 and 30 years of age. The typical ophthalmoscopic features include circumpapillary telangiectatic microangiopathy and swelling of the nerve fiber layer around the optic disc. Mutations in the mitochondrial genes *MTND1*, *MTND2*, *MTND4*, *MTND5*, and *MTND6* are known to be associated with Leber hereditary optic neuropathy.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; Enzyme assay, Protein analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/28/06):
 - a) "Mitochondrial Diseases" or "Leber's" = 7298 citations
 - b) "MT-CYB or MT-ND1 or MT-ND2 or MT-ND4 or MT-ND5 or MT-ND6" = 8 citations
 - c) "a" and "b" = 0 citations

1. Gene Symbol: MT-ND5 Chromosomal Locus: Mitochondrial; Gene Symbol: MT-TL1 Chromosomal Locus: Mitochondrial
2. Protein Name: NADH-ubiquinone oxidoreductase chain 5; Mitochondrial tRNA leucine 1
3. Disease: Mitochondrial Encephalomyopathy, Lactic Acidosis, and Strokelike Episodes
4. Description: MELAS is a multisystem disease caused by mutations in mitochondrial DNA. The most common mutation that accounts for 80% of the MELAS cases is 3243A>G in the *MTTL1* gene. Early psychomotor development is usually normal, but short stature is common. First onset of symptoms is frequently between the ages of two and ten years. The most common initial symptoms are generalized tonic-clonic seizures, recurrent headaches, anorexia, and recurrent vomiting. Exercise intolerance or proximal limb weakness can be the initial manifestation. Seizures are often associated with stroke-like episodes of transient hemiparesis or cortical blindness. Stroke-like episodes, typically before age 40 years.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; Enzyme assay, Protein analysis; Sequence analysis of select exons
9. Other Diseases: Other mitochondrial deletion disorders
10. Clinical use(s) for the Medicare population: Unclear (symptom onset early)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/28/06):
 - a) "Mitochondrial Encephalomyopath\$" or "MELAS" = 2062 citations
 - b) "MT-TL1" = 0 citations
 - c) "MT-ND5" = 1 citations
 - d) "a" and "MT-ND5" = 0 citations

1. Test Name: Mitochondrial DNA deletion analysis
2. Protein Names: ND
3. Disease: Kearns-Sayre syndrome (KSS)
4. Description: Kearns-Sayre syndrome (KSS) is caused by large deletions of mitochondrial DNA. Patients with KSS usually exhibit signs and symptoms before the third decade of life, with ophthalmoplegia, ptosis, pigmentary retinopathy, and one of the following: cardiac conduction defect, cerebellar dysfunction, or elevated CSF protein (>100 mg/dl). Patients may also have heterogeneous multisystemic disorders. The mutant mitochondrial DNA is usually detectable in muscle but not in blood
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Muscle (Freshly frozen)
8. Methodology: Southern analysis
9. Other Diseases: Other phenotypes of mitochondrial deletions
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (9/15/06)
 - a. "Mitochondrial DNA deletion"=5471
 - b. "Kearns-Sayre syndrome "=236
 - c. a and b (humans)=108

1. Gene Symbol: ECGF1 Chromosomal Locus: 22q13.3-qter
2. Protein Name: Thymidine phosphorylase
3. Disease: Mitochondrial Neurogastrointestinal Encephalopathy Disease
4. Description: The clinical diagnosis of MNGIE disease is based on the presence of severe gastrointestinal dysmotility, cachexia, ptosis, external ophthalmoplegia, sensorimotor neuropathy, asymptomatic leukoencephalopathy. Molecular genetic testing of *ECGF1* sequence alterations detects approximately 100% of affected individuals.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; Analyzte; Enzyme assay
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06:
 - a) “exp MELAS Syndrome/” or “Thymidine Phosphorylase Deficiency” or “Neurogastrointestinal Encephalopathy” or “Myoneurogastrointestinal Encephalopathy” = 730 citations
 - b) “ECGF1” = 7 citations
 - c) “a” and “ECGF1” = 0 citations

1. Test Name: Mitochondrial DNA deletion analysis
2. Protein Name: ND
3. Disease: Progressive external ophthalmoplegia (PEO)
4. Description: Progressive external ophthalmoplegia (PEO) is a mitochondrial myopathy with drooping of the eyelids (ptosis), paralysis of the extraocular muscles (ophthalmoplegia), and variably severe proximal limb weakness. Mitochondrial DNA deletion syndromes are caused by deletion of mtDNA and, when inherited, are transmitted by maternal inheritance.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Muscle (Freshly frozen)
8. Methodology: Southern blot analysis
9. Other Diseases: Other phenotypes of mitochondrial deletions
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (9/15/06)
 - a. "mitochondrial DNA deletion"=5419
 - b. "Progressive external ophthalmoplegia"=496
 - c. a and b (limit to humans)=241

1. Gene Symbol: BCS1L Chromosomal Locus: 2q33;
Gene Symbol: MT-ND1 to MT-ND6
2. Protein Name: NADH-ubiquinone oxidoreductase chain 1 to 6
3. Disease: Mitochondrial Respiratory Chain Complex I Deficiency, mitochondrial genes
4. Description: Mitochondrial Respiratory Chain Complex I Deficiency causes multisystemic disorders involving neuromuscular system
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Muscle or skin biopsy
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; enzyme assay;
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) “respiratory complex\$” or “Respiratory Chain Complex\$” or exp Electron Transport Complex III/ = 2436 citations
 - b) “MT-ND1” or “MT-ND2” or “MT-ND3” or “MT-ND4” or “MT-ND4L” or MT-ND5” or MT-ND6” = 7 citations
 - c) “a” and “b” = 0 citations

1. Gene Symbol: NDUFS1 Chromosomal Locus: 2q33-q34;
Gene Symbol: NDUFS4 Chromosomal Locus: 5q11.1;
Gene Symbol: NDUFV1 Chromosomal Locus: 11q13
2. Protein Name: NADH-ubiquinone oxidoreductase 75 kDa subunit;
NADH-ubiquinone oxidoreductase 18 kDa subunit;
NADH-ubiquinone oxidoreductase 51 kDa subunit
3. Disease: Mitochondrial Respiratory Chain Complex I Deficiency, nuclear genes
4. Description: Mitochondrial Respiratory Chain Complex I Deficiency causes multisystemic disorders involving neuromuscular system
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Muscle or skin biopsy
8. Methodology: Analysis of the entire coding region: Sequence analysis; enzyme assay
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) “respiratory complex\$” or “Respiratory Chain Complex\$” or exp Electron Transport Complex III/ = 2436 citations
 - b) “NDUFS1” or “NDUFS4” or “NDUFV1” = 59 citations
 - c) “a” and “b” = 13 citations (limited to humans)

1. Gene Symbol: BCS1L Chromosomal Locus: 2q33
2. Protein Name: Mitochondrial chaperone BCS1
3. Disease: Mitochondrial Respiratory Chain Complex III Deficiency, BCS1L-Related
4. Description: Mitochondrial Respiratory Chain Complex III Deficiency causes multisystemic disorders involving neuromuscular system
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Muscle or skin biopsy
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Mutation scanning; enzyme assay;
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) “respiratory complex\$” or “Respiratory Chain Complex\$” or exp Electron Transport Complex III/ = 2436 citations
 - b) “BCS1L” = 7 citations
 - c) “a” and “BCSIL” = 6 citations (limited to humans)

1. Gene Symbol: UQCRB Chromosomal Locus: Ch. 8
2. Protein Name: Ubiquinol-cytochrome C reductase complex 14 kDa
3. Disease: Mitochondrial Respiratory Chain Complex III Deficiency, UQCRB-Related
4. Description: Mitochondrial Respiratory Chain Complex III Deficiency causes multisystemic disorders involving neuromuscular system
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Muscle or skin biopsy
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) “respiratory complex\$” or “Respiratory Chain Complex\$” or exp Electron Transport Complex III/ = 2436 citations
 - b) “UQCRB” = 4 citations
 - c) “a” and “UQCRB” = 2 citations (limited to humans)

1. Gene Symbol: HNF4A Chromosomal Locus: 20q12-q13.1
2. Protein Name: Hepatocyte nuclear factor-4-alpha
3. Disease: MODY Types I (Maturity onset diabetes of the young)
4. Description: Mutations in the (HNF-4-alpha) gene on chromosome 20 cause the condition formerly called MODY1. HNF-4-alpha is expressed both in the liver and in pancreatic beta cells
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; linkage analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/29/06):
 - a) "Diabetes Mellitus, Type 2" or "MODY type 1" or "MODY1" or "Maturity-Onset Diabet\$" = 41462 citations
 - b) "HNF4A" = 225 citations
 - c) "a" and "HNF4A" = 97 citations (limit to humans)

1. Gene Symbol: GCK Chromosomal Locus: 7p15-p13
2. Protein Name: Glucokinase
3. Disease: MODY Types II (Maturity onset diabetes of the young)
4. Description: Mutations in the glucokinase gene on chromosome 7 have been described, and were formerly called MODY II. Defects in the expression of glucokinase, which phosphorylates glucose to glucose-6-phosphate and probably acts as a glucose sensor, result in deficient insulin secretion. On occasion, the expressed enzyme functions but is unstable, again leading to an insulin secretory deficit
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Linkage analysis; Deletion/duplication analysis; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org; UptoDate
12. Exploratory Medline Search (8/29/06):
 - a) "Diabetes Mellitus, Type 2" or "MODY type 2" or "MODY2" or "Maturity-Onset Diabet\$" = 41464 citations
 - b) "GCK" = 139 citations
 - c) "a" and "GCK" = 49 citations (limit to humans)

1. Gene Symbol: TCF1 Chromosomal Locus: 12q24.2
2. Protein Name: Hepatocyte nuclear factor 1- alpha
3. Disease: MODY Types III (Maturity onset diabetes of the young)
4. Description: One of several mutations in the HNF-1-alpha gene on chromosome 12 was formerly called MODY III. Patients with HNF-1-alpha diabetes have increased insulin sensitivity and marked sensitivity to the hypoglycemic effects of sulfonylureas compared to metformin
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons;; Analysis of the entire coding region: Mutation scanning; Linkage analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ??
11. Source of Information: Genetests.org; UptoDate
12. Exploratory Medline Search (8/29/06):
 - a) "Diabetes Mellitus, Type 2" or "MODY type 3" or "MODY3" or "Maturity-Onset Diabet\$" = 41470 citations
 - b) "TCF1" = 766 citations
 - c) "a" and "TCF1" = 236 citations (limit to humans)

1. Gene Symbol: IPF1 Chromosomal Locus: 13q12.1
2. Protein Name: Insulin promotor factor-1
3. Disease: MODY Types IV (Maturity onset diabetes of the young)
4. Description: Mutations in the insulin promoter factor 1 (IPF-1) gene can lead to what was called MODY4 by reduced binding of the protein to the insulin gene promoter. Less severe mutations in IPF-1 may predispose to late onset type 2 diabetes
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Linkage analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: ??
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/29/06):
 - a) “Diabetes Mellitus, Type 4” or “MODY type 4” or “MODY4” or “Maturity-Onset Diabet\$” = 41466 citations
 - b) “IPF1” = 68 citations
 - c) “a” and “IPF1” = 18 citations (limit to humans)

1. Gene Symbol: TCF2 (HNF1 Beta) Chromosomal Locus: 17cen q21.3
2. Protein Name: Hepatocyte nuclear factor 1- beta (Transcription factor 2)
3. Disease: MODY Types V (Maturity onset diabetes of the young)
4. Description: Mutations in the HNF-1-beta gene produce a syndrome that was formerly called MODY V. Affected patients can develop a variety of manifestations in addition to early onset diabetes. These include pancreatic atrophy (on CT scan), abnormal renal development (renal dysplasia that can be detected on ultrasonography in the fetus, single or multiple renal cysts, glomerulocystic disease, oligomeganephronia), slowly progressive renal insufficiency, elevated serum aminotransferases, and genital abnormalities (epididymal cysts, atresia of vas deferens, and bicornuate uterus)
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Linkage analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org; UptoDate
12. Exploratory Medline Search (8/29/06):
 - a) "Diabetes Mellitus, Type 5" or "MODY type 5" or "MODY5" or "Maturity-Onset Diabet\$" = 41463 citations
 - b) "TCF2" or "HNF1 Beta" = 650 citations
 - c) "a" and "b" = 229 citations (limit to humans)

1. Gene Symbol: NEUROD1 Chromosomal Locus: 2q32
2. Protein Name: Neurogenic differentiation factor 1
3. Disease: MODY Types VI (Maturity onset diabetes of the young)
4. Description: Mutations in the gene for neurogenic differentiation factor-1 (also called NEUROD1 or BETA2) can lead to what was called MODY6. NEUROD1 normally functions as a regulatory switch for endocrine pancreatic development.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Linkage analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/29/06):
 - a) "Diabetes Mellitus, Type 5" or "MODY type 5" or "MODY5" or "Maturity-Onset Diabet\$" = 41462 citations
 - b) "NEUROD1" = 158 citations
 - c) "a" and "NEUROD1" = 30 citations (limit to humans)

1. Gene Symbol: CIAS1 Chromosomal Locus: 1q44
2. Protein Name: Cold autoinflammatory syndrome 1
3. Disease: Muckle Wells Syndrome
4. Description: The Muckle-Wells syndrome is a rare, periodic urticarial syndrome associated with mutations in cryopyrin. It has a similar phenotype to familial cold autoinflammatory syndrome except for lack of cold sensitivity and frequent sensorineural hearing loss
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis: Sequence analysis of select exons
9. Other Diseases: Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/29/06:
 - a) "Muckle Wells" or "periodic fever" = 346 citations
 - b) "CIAS1" = 83 citations
 - c) "a" and "CIAS1" = 37 citations

1. Gene Symbol: NOG (SYNS1) Chromosomal Locus: 17q22
2. Protein Name: Noggin
3. Disease: Multiple Synostoses Syndrome
4. Description: Multiple synostoses syndrome (SYNS1) is due to mutations in the gene encoding noggin (NOG) on chromosome 17q
5. Purpose: Diagnostic
6. Availability: Clinical laboratory (Only outside US)
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) "Multiple Synostoses" or "Synostosis" or "Facioaudiosymphalangism" or "Symphalangism-Brachydactyly Syndrome" = 5507 citations
 - b) "NOG" = 709 citations
 - c) "a" and "NOG" = 7 citations (limited to humans)

1. Gene Symbol: LMX1B Chromosomal Locus: 9q34.1
2. Protein Name: LIM homeobox transcription factor 1 beta
3. Disease: Nail-Patella Syndrome
4. Description: *LMX1B* is the only gene known to be associated with Nail-patella syndrome (NPS) an autosomal dominant disorder that involves a classic clinical tetrad of changes in the nails, knees, and elbows, and the presence of iliac horns. Renal involvement, first manifest as proteinuria with or without hematuria, occurs in 30-50% of affected individuals; renal failure occurs in about 5% of affected individuals. Primary open-angle glaucoma and ocular hypertension also occur at increased frequency and at a younger age than in the general population.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) "Nail-Patella Syndrome" or "Fong disease" or "Hood disease" or "Osteo-Onychodysplasia" = 395 citations
 - b) "LMX1B" = 99 citations
 - c) "a" and "LMX1B" = 39 citations

1. Gene Symbol: HLA-DQB1*0602 and HLA-DQA1*0102 haplotype
2. Test Name: **Narcolepsy EvaluatR™**
3. Disease: Narcolepsy
4. Description: This test detects the HLA-DQB1*0602 and HLA-DQA1*0102 haplotype that is found in 85-95% of patients with narcolepsy.
5. Purpose: Prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: DNA sequencing
- 9.
10. Other Diseases:
11. Clinical use(s) for the Medicare population: Unclear
 - a) Prognostication
12. Source of Information: Specialty Labs
13. Exploratory Medline Search:
 - a. "Narcolepsy.mp. or exp Narcolepsy"= 1127
 - b. "HLA-DQ.mp. or exp HLA-DQ Antigens" = 2585
 - c. a and b (limit to humans) = 71

1. Gene Symbol: PANK2 Chromosomal Locus: 20p13-p12.3
2. Protein Name: Pantothenate kinase 2
3. Disease: Neurodegeneration with Brain Iron Accumulation
4. Description: Pantothenate kinase-associated neurodegeneration (PKAN) is a form of neurodegeneration with brain iron accumulation, or NBIA (formerly called Hallervorden-Spatz syndrome). PKAN is characterized by progressive dystonia and basal ganglia iron deposition with onset that usually occurs before age ten years. NBIA inherited autosomal recessive have identifiable mutations in the *PANK2* gene.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis; Mutation scanning; Sequence analysis of select exons; deletion/duplication analysis
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) “neurodegenerat\$” or Nerve Degeneration = 16813 citations
 - b) “Pantothenate Kinase-Associated Neurodegeneration” = 36 citations
 - c) “Hallervorden-Spatz” = 342 citations
 - d) “a” or “b” or “c” = 36652 citations
 - e) “PANK2” = 38 citations
 - f) “d” and “PANK2” = 36 citations (limited to humans)

1. Gene Symbol: NF1 Chromosomal Locus: 17q11.2
2. Protein Name: Neurofibromin
3. Disease: Neurofibromatosis 1
4. Description: Heterozygous mutations of the *NF1* gene are responsible for the vast majority of cases of neurofibromatosis. Homozygosity for a mutation of one of the genes associated with hereditary non-polyposis colon cancer can produce neurofibromatosis 1 in rare cases. Multiple café au lait spots, axillary and inguinal freckling, multiple discrete dermal neurofibromas, and iris Lisch nodules characterize NF1. Learning disabilities are frequent.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis of RNA; Array genomic hybridization; FISH-metaphase; FISH-interphase; linkage analysis; Deletion/duplication analysis; Mutation scanning; Sequence analysis of select exons; Protein truncation testing (PTT); Sequence analysis; Array genomic hybridization
9. Other Diseases: Mutations of NF1 have been present in multiple spinal neurofibromas, optic glioma, and encephalocraniocutaneous lipomatosis
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) "Neurofibromatosis" = 9034 citations
 - b) "NF1" = 1948 citations
 - c) "Neurofibromatosis" and "NF1" = 1238 citations (limit to humans)

1. Gene Symbol: AVP Chromosomal Locus: 20p13
2. Protein Name: Vasopressin-neurophysin 2-copeptin
3. Disease: Neurohypophyseal Diabetes Insipidus
4. Description: Familial Neurohypophyseal Diabetes Insipidus is much more rare, usually being transmitted as an autosomal dominant trait. Most cases are associated with a point mutation in the gene controlling the synthesis of the ADH precursor preprovasopressin-neurophysin II; multiple mutations in this gene have been identified. Development of marked polyuria even though only one of the two hormone producing genes is defective.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory (Outside US)
7. Specimen: Blood
8. Methodology: Sequence analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) "Diabetes Insipidus" and "Neurohypophyseal" = 109 citations
 - b) "Neurohypophyseal Diabetes Insipidus" = 63 citations
 - c) "a" or "b" = 111 citations
 - d) "AVP" = 7015 citations
 - e) "c" and "AVP" = 47 citations (limit to humans)

1. Test Name: Neutrophil Antigen Genotyping
2. Gene Symbol: FCGR3A Chromosomal Locus: 1q23
3. Disease: None
4. Description: Neutrophil antigen genotyping detects transfusion related acute lung injury (TRALI), neonatal alloimmune neutropenia, drug-induced and autoimmune neutropenia.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: ND
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) "Neutrophil Antigen" = 75 citations
 - b) "FCGR3A" = 49 citations
 - c) "Neutrophil Antigen" and "FCGR3A" = 1 citations (limit to humans)

1. Gene Symbol: SMPD1 Chromosomal Locus: 11p15.4-p15.1
2. Protein Name: Sphingomyelin phosphodiesterase
3. Disease: Niemann-Pick Disease due to Sphingomyelinase Deficiency (Type B or 1S)
4. Description: Formerly designated as type B, type 1S is a chronic non-neuronopathic form. It is characterized by the onset of hepatosplenomegaly during infancy or childhood and has a good prognosis for survival into adulthood. Other clinical manifestations include short stature with delayed skeletal maturation and ocular abnormalities (macular halos and cherry red maculae. Type 1S is associated with milder mutations of the acid sphingomyelinase gene, which cause residual activity of the enzyme
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: white blood cells or cultured fibroblasts
8. Methodology: Analyte; Enzyme assay; Sequence analysis; target mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a. "Niemann-Pick Diseases" = 1365 citations
 - b. "Sphingomyelinase" = 2105 citations
 - c. "SMPD1" = 17 citations
 - d. ("Niemann-Pick Diseases" and "Sphingomyelinase") and "SMPD1" = 11 citations (limit to humans)

1. Gene Symbol: KRT1 Chromosomal Locus: 12q11-q13;
Gene Symbol: KRT16 Chromosomal Locus: 17q12-q21
2. Protein Name: Keratin, type II cytoskeletal 1; Keratin, type I cytoskeletal 16
3. Disease: Nonepidermolytic Palmoplantar Hyperkeratosis
4. Description: Nonepidermolytic palmoplantar keratoderma shows a characteristic phenotype of focal palmoplantar keratoderma with oral, genital, and follicular lesions. NEPPK is associated with mutation in the keratin 1 gene and occasionally with mutation in the keratin 16 gene.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Buccal swab
8. Methodology: Sequence analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) "Keratoderma, Palmoplantar" = 1493 citations
 - b) "KRT1" or "KRT16" = 131 citations
 - c) "Keratoderma, Palmoplantar" and ("KRT1" or "KRT16") = 12 citations (limit to humans)

1. Gene Symbol: WFS1 Chromosomal Locus: 4p16.1
2. Protein Name: Wolframin
3. Description: Mutations in *WFS1* cause deafness at the DFNA 6/14 locus. This type of deafness is characterized by an audioprofile that shows familial low-frequency hearing loss.
4. Purpose: Diagnostic
5. Availability: Clinical laboratory
6. Specimen: Blood
7. Methodology: Sequence analysis of select exons; Mutation scanning
8. Disease: Nonsyndromic Low-Frequency Sensorineural Hearing Loss
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
 - a) "Sensorineural Hearing Loss" = 14063 citations
 - b) "WFS1" = 137 citations
 - c) "Sensorineural Hearing Loss" and "WFS1" = 30 citations

1. Gene Symbol: KRAS Chromosomal Locus: 12p12.1;
Gene Symbol: PTPN11 Chromosomal Locus: 12q24.1
2. Protein Name: GTPase Kras; Tyrosine-protein phosphatase non-receptor type 11
3. Disease: Noonan Syndrome (KRAS-Related, PTPN11-Related)
4. Description: Noonan syndrome (NS) is characterized by short stature; congenital heart defect; broad or webbed neck; unusual chest shape with superior pectus carinatum, inferior pectus excavatum, and apparently low-set nipples; developmental delay of variable degree; cryptorchidism; and characteristic facies. Two genes are associated with Noonan syndrome PTPN11 (50%) and KRAS gene in 5 to 10%
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis;
9. Other Diseases: LEOPARD syndrome; Leukemia and solid tumors; Noonan-like/multiple giant-cell lesion syndrome
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06:
 - a) "Noonan Syndrome" = 929 citations
 - b) "KRAS" = 295 citations
 - c) "PTPN11" = 120 citations
 - d) "Noonan Syndrome" and ("KRAS" or "PTPN11") = 71 citations (limit to humans)

1. Gene Symbol: ADRB2 Chromosomal Locus: 5q32-q34;
Gene Symbol: MC4R Chromosomal Locus: 18q22
2. Protein Name: Beta-2 adrenergic receptor; Melanocortin receptor 4
3. Disease: Obesity
4. Description: Severe obesity with onset at or before 5 years and is associated with mutations in MC4R gene and polymorphisms in the ADRB2 gene
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset obesity)
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/24/06):
 - a) "Obesity" or "obes\$" = 97459 citations
 - b) "ADRB2" = 92 citations
 - c) "MC4R" = 280 citations
 - d) "ADRB2" or "MC4R" = 370 citations
 - e) "a" and "d" = 129 citations

1. Gene Symbol: GPR143 Chromosomal Locus: Xp22.3
2. Protein Name: G-protein coupled receptor 143
3. Disease: Ocular Albinism, X-linked
4. Description: X-linked ocular albinism (XLOA) is a disorder of melanosome biogenesis leading to congenital and persistent visual impairment in affected males. GPR143 (OA1) is the only gene known to be associated with X-linked ocular albinism
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis; Targeted mutation analysis; Deletion/duplication analysis
9. Other Diseases: Continuous gene syndrome
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/24/06):
 - a) "Ocular Albinism" or "XLOA" or "OA1" = 335 citations
 - b) "GPR143" = 36 citations
 - c) "a" and "GPR143" = 30 citations

1. Gene Symbol: TYR Chromosomal Locus: 11q14-q21
2. Protein Name: Tyrosinase
3. Disease: Oculocutaneous Albinism, Type 1 (Type 1A, Type 1B)
4. Description: Oculocutaneous albinism type 1 (OCA1) is characterized by reduced synthesis of melanin in the skin, hair, and eyes, associated with ocular findings of nystagmus, reduced iris pigment with iris translucency, reduced retinal pigment, foveal hypoplasia with significantly reduced visual acuity usually in the range of 20/100 to 20/400, and misrouting of the optic nerves resulting in alternating strabismus and reduced stereoscopic vision. *TYR* is the only gene known to be associated with oculocutaneous albinism type 1
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; linkage analysis; Sequence analysis of select exons; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/24/06):
 - a) "Oculocutaneous Albinism" or "OCA1" or "Tyrosinase-Related OCA" = 748 citations
 - b) "TYR" = 18526 citations
 - c) "a" and "TYR" = 40 citations

1. Gene Symbol: OCA2 Chromosomal Locus: 15q11.2-q12
2. Protein Name: P protein
3. Disease: Oculocutaneous Albinism, Type 2
4. Description: The gene *OCA2* (previously called the *P* gene) is the only gene known to be associated with oculocutaneous albinism type 2 that has the following features: hypopigmentation of the skin and hair and the characteristic ocular changes found in all types of albinism, including nystagmus; reduced iris pigment with iris translucency; reduced retinal pigment with visualization of the choroidal blood vessels on ophthalmoscopic examination; foveal hypoplasia associated with reduction in visual acuity; and misrouting of the optic nerves at the chiasm associated with alternating strabismus, reduced stereoscopic vision, and an altered visual evoked potential (VEP).
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/24/06):
 - a) "Oculocutaneous Albinism" = 741 citations
 - b) "OCA2" = 106 citations
 - c) "Oculocutaneous Albinism"" and "OCA2" = 62 citations

1. Gene Symbol: SCN4A Chromosomal Locus: 17q23.1-q25.3
2. Protein Name: Sodium channel protein type 4 subunit alpha
3. Disease: Paramyotonia Congenita
4. Description: One of the sodium channelopathies. The disease has paradoxical myotonia (the myotonia increases with exercise). The inheritance is autosomal dominant and the symptoms usually begin in the first decade.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Sequence analysis of select exons
9. Other Diseases: Hyperkalemic periodic paralysis and Hypokalemic periodic paralysis.
10. Clinical use(s) for the Medicare population: Probably not applicable to the Medicare population
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/23/06):
 - a) "Paramyotonia Congenita" = 194 citations
 - b) "SCN4A" = 125 citations
 - c) "Paramyotonia Congenita" and "SCN4A" = 35 citations

1. Gene Symbol: SLC26A4 Chromosomal Locus: 7q31
2. Protein name: Pendrin
3. Disease: Pendred syndrome / DFNB4
4. Description: The SLC26A4 gene is associated with Pendred syndrome. However, mutations are not invariably found in this gene, making it likely that Pendred syndrome is a heterogenous disease. Pendred syndrome is also known as Autosomal Recessive Sensorineural Hearing Impairment and Goiter. Pendred syndrome is characterized by severe to profound bilateral sensorineural hearing impairment that is usually congenital and non-progressive, vestibular dysfunction, temporal bone abnormalities, and development of euthyroid goiter in late childhood to early adulthood.
5. Purpose: Prognostic, Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Mutation analysis, DNA sequencing
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Unclear (early onset)
 - a) To identify the potential for abnormal thyroid function and risk of goiter
 - b) Confirmation of diagnosis
11. Source of Information: GeneTests.org, Center for Genetic Testing at Saint Francis
12. Exploratory Medline Search:
 - a. "Pendred syndrome.mp." = 111
 - b. "SLC26A4.mp." = 213
 - c. a and b (limit to humans) = 64

1. Gene Symbol: PGK1 Chromosomal Locus: Xq13
2. Protein Name: Phosphoglycerate Kinase 1
3. Disease: Phosphoglycerate kinase deficiency (PGK Deficiency)
4. Description: Deficiency of phosphoglycerate kinase results in two different clinical presentations: Central nervous system dysfunction with seizures and mental retardation that is associated with nonspherocytic hemolytic anemia; and a myopathy with exercise intolerance, myoglobinuria, cramps, and slowly progressive weakness. The myopathic form typically presents in childhood and is difficult to distinguish clinically from Glycogen storage disease V and VII without muscle biopsy and biochemical determinations.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Enzyme assay
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population
11. Source of Information: Genetests.org; Uptodate
12. Exploratory Medline Search (8/23/06):
 - a) "Phosphoglycerate kinase deficiency" or "PGK Deficiency" = 59 citations
 - b) "PGK1" = 264 citations
 - c) "a" and "b" = 2 citations (limit to humans)

1. Protein Name: Phosphoglycerate mutase 2
2. Gene Symbol: PGAM2 Chromosomal Locus: 7p13-p12.3
3. Disease: Phosphoglycerate mutase deficiency
4. Description: The disease may is characterized by exercise intolerance, muscle aches, cramps, and myoglobinuria following intense physical activity. Symptoms may begin in childhood or adolescence.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Enzyme assay
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population
11. Source of Information: Genetests.org; Uptodate
12. Exploratory Medline Search (8/23/06):
 - a) "Phosphoglycerate mutase deficiency" or "PGAM Deficiency" = 19 citations
 - b) "PGAM2" = 7 citations
 - c) ("Phosphoglycerate mutase deficiency" or "PGAM Deficiency") and "PGAM2" = 0 citations

1. Gene Symbol: PRNP Chromosomal Locus: 20pter-p12
2. Protein Name: Major Prion Protein (PrP)
3. Disease: Prion diseases
4. Description: Group of neurodegenerative diseases that have long incubation periods and progress inexorably once clinical symptoms appear.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: ND
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: These are rare. From this perspective not useful for the Medicare population.
11. Source of Information: Genetests.org; UptoDate
12. Exploratory Medline Search (8/22/06):
 - a) "Prion diseases" = 9199 citations
 - b) "Transmissible Spongiform Encephalopathies" = 1017 citations
 - c) "Familial Creutzfeldt-Jakob Disease" = 100 citations
 - d) "Fatal Familial Insomnia" = 220 citations
 - e) "Gerstmann-Straussler-Scheinker Disease" = 338 citations
 - f) "PRNP" = 454 citations
 - g) ("Prion diseases" or "Transmissible Spongiform Encephalopathies" or "Familial Creutzfeldt-Jakob Disease" or "Fatal Familial Insomnia" or "Gerstmann-Straussler-Scheinker Disease") and "PRNP" = 262 citations (limit to humans)

1. Gene Symbol: PFC Chromosomal Locus: Xp11.4-p11.23
2. Protein Name: Properdin
3. Disease: Properdin Deficiency, X-Linked
4. Description: Properdin (factor P) is a plasma protein that is active in the alternative complement pathway of the innate immune system. It is a positive regulatory factor that binds to many microbial surfaces to stabilize the C3b,Bb convertase. Deficiency of properdin is associated in particular with a heightened susceptibility to Neisseria species.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Mutation scanning
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Might be applicable to the Medicare population. However the disease is not common: thus: probably not applicable to the medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/21/06):
 - a) "Properdin Deficiency" = 51 citations
 - b) "PFC" = 3946 citations
 - c) "Properdin Deficiency" and "PFC" = 2 citations (limit to humans)

1. Gene Symbol: SCNN1B Chromosomal Locus: 16p13-p12; Gene Symbol: SCNN1G Chromosomal Locus: 16p13-p12
2. Protein Name: Amiloride-sensitive sodium channel beta-subunit; Amiloride-sensitive sodium channel gamma-subunit
3. Disease: Pseudohypoaldosteronism or Liddle syndrome
4. Description: Liddle's syndrome is a rare autosomal dominant condition in which there is a primary increase in collecting tubule sodium reabsorption and, in most cases, potassium secretion. Liddle's syndrome classically presents with the concurrent triad of hypertension, hypokalemia, and metabolic alkalosis in a relatively young patient.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: The disease is rare. Probably not applicable to the Medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/21/06):
 - a) "Pseudoaldosteronism" = 54 citations
 - b) "SCNN1B" = 13 citations
 - c) "SCNN1G" = 13 citations
 - d) "Pseudoaldosteronism" and ("SCNN1B" or "SCNN1G") = 2 citations (limit to humans)

1. Gene Symbol: TIMP3 Chromosomal Locus: 22q12.1-q13.2
2. Protein Name: Metalloproteinase inhibitor 3 (Tissue inhibitor of metalloproteinase 3)
3. Disease: Pseudoinflammatory fundus dystrophy or Sorsby Fundus Dystrophy or Sorsby Syndrome
4. Description: The disease is a rare autosomal dominant disorder that results in degeneration of the macular region of the retina, with onset usually in the fourth to fifth decade of life. It leads to the rapid loss of central vision, often followed by further loss of peripheral vision. SFD shares several pathological features commonly found in the 'wet' or exudative form of age-related macular degeneration, the most common cause of blindness in the elderly in developed countries.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Mutation scanning; Sequence analysis of select exons; Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: The disease is rare, thus not directly applicable to the Medicare population.
11. Source of Information: Genetests.org;
12. Exploratory Medline Search (8/21/06):
 - a) "Pseudoinflammatory fundus dystrophy" = 2 citations
 - b) "Sorsby Fundus Dystrophy" = 27 citations
 - c) "Sorsby Syndrome" = 4 citations
 - d) "TIMP3" = 176 citations
 - e) ("Pseudoinflammatory fundus dystrophy" or "Sorsby Fundus Dystrophy" or "Sorsby Syndrome") and "TIMP3" = 11 citations (limit to humans)

1. Gene Symbol: ATP1A3 Chromosomal Locus: 9q12-q13.2
2. Protein Name: Sodium/potassium-transporting ATPase alpha-3 chain
3. Disease: Rapid-onset dystonia parkinsonism
4. Description: Parkinson-like neurodegenerative disorder with rapid onset and rapid progression.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not widely applicable to the Medicare population. The age of onset is younger than the Medicare population.
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/21/06):
 - a) "Rapid-onset dystonia parkinsonism" = 24 citations
 - b) "ATP1A3" = 19 citations
 - c) "Rapid-onset dystonia parkinsonism" and "ATP1A3" = 5 citations (limit to humans)

1. Gene Symbol: SLC5A2 Chromosomal Locus: 16p11.2
2. Protein Name: Sodium/glucose cotransporter 2
3. Disease: Renal glucosuria
4. Description: Autosomal recessive renal glucosuria can be attributed to mutation in the sodium/glucose cotransporter SGLT2 encoded by the SLC5A2 gene. The clinical picture is loss of 50 to 60 g of glucose in the urine daily despite a normal glucose tolerance test.
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not widely applicable to the Medicare population
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/16/06):
 - a) "renal glucosuria" = 59 citations
 - b) "SLC5A2" = 23
 - c) "renal glucosuria" and "SLC5A2" = 7 citations (limit to humans)

1. Gene Symbol: CA2 Chromosomal Locus: 8q22
2. Protein Name: Carbonic anhydrase II
3. Disease: Renal Tubular Acidosis with Osteopetrosis
4. Description: Renal tubular acidosis secondary to a carbonic anhydrase II mutation. Mutations in carbonic anhydrase II (CA2) cause an autosomal recessive form of osteopetrosis characterized by failure to thrive, developmental delay and renal tubular acidosis. These patients do not usually have fractures but may be blind due to optic nerve compression. Carbonic anhydrase II catalyzes the formation of protons in the cytoplasm of osteoclasts
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably not widely applicable to the Medicare population (early onset)
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/16/06):
 - a) "Renal Tubular Acidosis" = 2478 citations
 - b) "Osteo" = 215230 citations
 - c) "CA2" = 105691 citations
 - d) "Renal Tubular Acidosis" and "Osteo" and "CA2" = 4 citations (limit to humans)

1. Gene Symbol: SLC4A4 Chromosomal Locus: 4q21
2. Protein Name: Solute carrier family 4, sodium bicarbonate cotransporter, member 4
3. Disease: Proximal Renal Tubular Acidosis with Ocular Abnormalities
4. Description: This is an autosomal recessive proximal renal tubular acidosis with ocular abnormalities and it is caused by mutation in the SLC4A4 gene.
5. Purpose: Diagnostics
6. Availability: Clinical laboratory (Outside US)
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably of limited applicability in the Medicare population
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/21/06):
 - a) "Renal Tubular Acidosis" = 2130 citations
 - b) "SLC4A4" = 56 citations
 - c) "Renal Tubular Acidosis" and "SLC4A4" = 13 citations (limit to humans)

1. Gene Symbol: ATP6V1B1 Chromosomal Locus: 2cen-q13
2. Protein Name: Vacuolar ATP synthase subunit B, kidney isoform
3. Disease: Renal tubular acidosis with progressive nerve deafness
4. Description: There is evidence that renal tubular acidosis (RTA) with progressive sensorineural deafness is caused by mutation in the ATP6V1B1 (ATP6B1) gene
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory (Outside US)
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Probably of limited applicability to the Medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Searc(8/16/06):
 - a) "Renal tubular acidosis" = 2478 citations
 - b) "ATP6V1B1" = 12 citations
 - c) "Renal tubular acidosis" and "ATP6V1B1" = 8 citations (limit to humans)

1. Gene Symbol: FOXC1 Chromosomal Locus: 6p25; Gene Symbol: PITX2 Chromosomal Locus: 4q25-q26
2. Protein Name: Forkhead box protein C1; Pituitary homeobox 2
3. Disease: Rieger syndrome or Axenfeld Syndrome or Axenfeld-Rieger Syndrome or Iridogoniodysgenesis with Somatic Anomalies
4. Description: Rieger syndrome represents a spectrum of diseases that involve congenital anomalies of the anterior segment of the eyes. In addition, about 50% of patients will develop glaucoma, leading to decline of vision and potential blindness. Non-ocular findings include dental hypoplasia, craniofacial dysmorphism, redundant umbilical skin, cardiac defects, limb anomalies, pituitary abnormalities, sensory hearing loss and/or mental defects. The condition is rare.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; FISH-metaphase; Array Genomic Hybridization; Mutation scanning of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Rare condition, probably without wide applicability to the Medicare population.
11. Source of Information: Genetests.org; GeneDx website; OMIM
12. Exploratory Medline Search (8/15/06):
 - a) "Rieger syndrome" or "Axenfeld Syndrome" or "Iridogoniodysgenesis with Somatic Anomalies" = 146 citations
 - b) "FOXC1" or "PITX2" = 354 citations
 - c) "a" and "b" = 58 citations (limit to humans)

1. Gene Symbol*: HEXA Chromosomal Locus: 15q23-q24
Gene Symbol*: HEXB Chromosomal Locus: 5q 13
2. Protein Name: Beta-hexosaminidase alpha chain; Beta-hexosaminidase beta chain
3. Disease: Sandhoff Disease (GM2 Gangliosidosis)
4. Description: Sandhoff disease is a rare inherited disorder that causes progressive destruction of nerve cells in the brain and spinal cord (the central nervous system). Mutations in the HEXB gene cause Sandhoff disease. The HEXB gene provides instructions for making a protein that is part of two critical enzymes in the nervous system, beta-hexosaminidase A and beta-hexosaminidase B
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood; tissue
8. Methodology: enzyme assay; analyte
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (most common form is in childhood).
11. Source of Information: Genetests.org; genetics home reference (NLM)
12. Exploratory Medline Search (8/15/06):
 - a) "Sandhoff Disease" or "GM2 Gangliosidoses" = 1261 citations
 - b) "HEXA" or "HEXB" = 1565 citations
 - c) "a" or "b" = 132 citations (limit to humans)

1. Gene Symbol: NAGA Chromosomal Locus: 22q11
2. Protein Name: Alpha-N-acetylgalactosaminidase
3. Disease: Schindler Disease
4. Description: Schindler disease is associated with NAGA gene and there is a deficiency or absence of the enzyme alpha-N-acetylgalactosidase. This leads to a build up of a compound called glycosphingolipids in different tissues of the body and causes the symptoms of the disorder. There are two forms of this disorder one where symptoms appear during infancy, type I and one where they begin during adolescence or early adulthood, type II.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood; tissue
8. Methodology: Analysis of the entire coding region: Sequence analysis; analyte; enzyme assay
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (may be for adult onset disease)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/15/06):
 - a) "Schindler Disease " or "N-Acetyl-alpha-D-Galactosaminidase Deficiency" or "Neuroaxonal Dystrophy" = 315 citations
 - b) "NAGA" = 219 citations
 - c) "a" and "NAGA" = 22 citations (limit to humans)

1. Gene Symbol: SBDS Chromosomal Locus: 7q11
2. Protein Name: Direct mutation analysis by sequencing of SBDS gene
3. Disease: Shwachman-diamond syndrome
4. Description: Shwachman-Diamond syndrome is characterized primarily by exocrine pancreatic insufficiency, hematologic abnormalities, including increased risk of malignant transformation, and skeletal abnormalities. Shwachman-Bodian-Diamond syndrome is caused by mutations in the SBDS gene.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Buccal tissue; Blood (only among those without bone marrow transplant)
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/15/06):
 - a) "Shwachman-diamond syndrome" or "SDS" = 44968 citations
 - b) "SBDS" = 50 citations
 - c) "a" and "SBDS" = 19 citations (limit to humans)

1. Gene Symbol: ABCB7 Chromosomal Locus: Xq13.1-q13.3
2. Protein Name: ATP-binding cassette, sub-family B, member 7
3. Disease: X-Linked Sideroblastic Anemia and Ataxia
4. Description: Sideroblastic anemia and ataxia (XLSA/A) is an X-linked inherited disease characterized by moderate anemia and early-onset spinocerebellar syndrome in males manifesting primarily as ataxia, dysmetria, and dysdiadochokinesis. *ABCB7* is the only gene known to be associated with X-linked sideroblastic anemia and ataxia.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (age of onset 2nd or 3rd decade)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/15/06):
 - a) "Sideroblastic Anemia" or "Ataxia" = citations
 - b) "ABCB7" = 9 citations
 - c) "a" and "ABCB7" = 6 citations (limit to humans)

1. Gene Symbol: GPC3 Chromosomal Locus: Xq26
2. Protein Name: Glypican-3
3. Disease: Simpson-Golabi-Behmel Syndrome
4. Description: SGBS is a rare, X-linked overgrowth syndrome involving deletions of GPC3 coding regions in male patients with SGBS. Suspected diagnosis of a congenital overgrowth syndrome with any or all of the following symptoms present: macrosomia at birth (weight > 90th% corrected for gestational age); macroglossia; macrocephaly; polydactyly or syndactyly; supernumerary nipples; abdominal wall defects; neonatal hypoglycemia
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Analysis of the entire coding region: Sequence analysis: Deletion/duplication analysis; Analysis of the entire coding region: Mutation scanning
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/15/06):
 - a) "Simpson-Golabi-Behmel" or "SGBS" = 116 citations
 - b) "GPC3" = 106 citations
 - c) "a" and "GPC3" = 38 citations (limit to humans)

1. Gene Symbol: ALDH3A2 Chromosomal Locus: 17p11.2
2. Protein Name: Fatty aldehyde dehydrogenase
3. Description: FALDH deficiency results in Sjogren-Larsson syndrome (SLS), a rare skin disease, which is inherited in an autosomal recessive manner. Other characteristic features are delayed motor development due to spastic diplegia or tetraplegia, mental retardation, speech delay, short stature, and seizures. "Glistening white dots" on the retina and pigmentary retinal degeneration are found in about one-third of patients.
4. Purpose: Diagnostic
5. Availability: Clinical laboratories
6. Specimen: Blood, buccal cheek swabs
7. Methodology: Sequence analysis
8. Disease: SLS
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: GeneDx
12. Exploratory Medline Search: (10/26/06)
 - a. "Sjogren-Larsson syndrome"=243
 - b. "ALDH3A2"= 14
 - c. a and b (limit to humans) = 10

1. Gene Symbol: TBX4 Chromosomal Locus: 17q21-q22
2. Protein Name: T-Box transcription factor TBX4
3. Disease: Small Patella Syndrome
4. Description: small patella syndrome can be caused by mutations in the TBX4 gene and is an autosomal dominant inheritance with affected individuals was found to have small or absent patellas.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory (outside US)
7. Specimen: Blood
8. Methodology: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/15/06):
 - a) "Small Patella Syndrome" = 10 citations
 - b) "TBX4" = 47 citations
 - c) "Small Patella Syndrome" and "TBX4" = 1 citations (limit to humans)

1. Gene Symbol: NIPA1 Chromosomal Locus: 15q11.1
2. Protein Name: Non-imprinted in Prader-Willi/Angelman syndrome region protein 1
3. Disease: Spastic Paraplegia 6
4. Description: Spastic Paraplegia 6 is a slowly progressive lower extremity weakness and spasticity, autosomal Dominant Hereditary Spastic Paraplegia with mutations in the *NIPA1* gene
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/15/06):
 - a) "Spastic Paraplegia" or "SPG6" = 984 citations
 - b) "NIPA1" = 8 citations
 - c) "a" and "NIPA1" = 5 citations (limit to humans)

1. Gene Symbol: HSPD1 Chromosomal Locus: 2q33.1
2. Protein Name: 60 kDa heat shock protein
3. Disease: Spastic Paraplegia 13
4. Description: The hereditary spastic paraplegias (SPGs) comprise a group of clinically and genetically heterogeneous disorders causing progressive spasticity and weakness of the lower limbs. Spastic paraplegia 13 can be caused by mutation in the mitochondrial chaperonin HSP60
5. Purpose: Diagnostic
6. Availability: Clinical laboratory (outside US)
7. Specimen: Blood
8. Methodology: Mutation scanning; Targeted mutation analysis; Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/15/06):
 - a) "Spastic Paraplegia" or "SPG13" = 983 citations
 - b) "HSPD1" = 11 citations
 - c) "a" and "HSPD1" = 1 citations (limit to humans)

1. Gene Symbol: TRAPPC2 (SEDL) Chromosomal Locus: Xp22.2-p22.1
2. Protein Name: Trafficking protein particle complex protein 2
3. Disease: Spondyloepiphyseal Dysplasia Tarda, X-linked (SED Tarda, X-Linked)
4. Description: In adults, X-linked spondyloepiphyseal dysplasia tarda (X-linked SEDT) associated with mutations in *TRAPPC2* (*SEDL*) is characterized by disproportionately short stature with short trunk and arm span significantly greater than height. At birth, affected males are normal in length and have normal body proportions. Affected males exhibit retarded linear growth beginning around six to eight years of age.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/14/06):
 - a) "Spondyloepiphyseal Dysplasia Tarda" or "X-Linked SED" = 115 citations
 - b) "TRAPPC2" = 29 citations
 - c) "a" and "TRAPPC2" = 22 citations

1. Test Name: Collagen alpha 1(XI) chain
2. Gene Symbol: COL11A1 Chromosomal Locus: 1p21
3. Disease: Stickler Syndrome Type II
4. Description: Stickler syndrome is a connective tissue disorder that can include ocular findings of myopia, cataract, and retinal detachment; hearing loss that is both conductive and sensorineural; midfacial underdevelopment and cleft palate (either alone or as part of the Robin sequence); and mild spondyloepiphyseal dysplasia and/or precocious arthritis. Mutations in three genes, *COL2A1*, *COL11A1*, and *COL11A2*, have been associated with the Stickler syndrome, termed Stickler syndrome type I, II, and III respectively.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons; Mutation scanning; Sequence analysis
9. Other Diseases: Achondrogenesis type II; Hypochondrogenesis; Spondyloepiphyseal dysplasia congenita (SED congenita); etc..
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/14/06):
 - a) "Stickler Syndrome" = 179 citations
 - b) "COL11A1" = 61 citations
 - c) "Stickler Syndrome" and "COL11A1" = 24 citations (limit to humans)

1. Gene Symbol: COL11A2 Chromosomal Locus: 6p21.3
2. Protein Name: Collagen alpha 2(XI) chain
3. Disease: Stickler Syndrome Type III
4. Description: Stickler syndrome is a connective tissue disorder that can include ocular findings of myopia, cataract, and retinal detachment; hearing loss that is both conductive and sensorineural; midfacial underdevelopment and cleft palate (either alone or as part of the Robin sequence); and mild spondyloepiphyseal dysplasia and/or precocious arthritis. Mutations in three genes, *COL2A1*, *COL11A1*, and *COL11A2*, have been associated with the Stickler syndrome, termed Stickler syndrome type I, II, and III respectively.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/14/06):
 - a) "Stickler Syndrome" = 179 citations
 - b) "COL11A2" = 144 citations
 - c) "Stickler Syndrome" and "COL11A2" = 20 citations (limit to humans)

1. Gene Symbol: TFR2 Chromosomal Locus: 7q22
2. Protein Name: Transferrin receptor protein 2
3. Disease: TFR2-related hereditary hemochromatosis
4. Description: *TFR2*-related hereditary hemochromatosis (*TFR2*-HHC) is characterized by deregulated, increased intestinal iron absorption resulting in iron accumulation in the liver, heart, pancreas, and endocrine organs. Typically, individuals present with abdominal pain, fatigue, arthralgia, decreased libido, or, most frequently, with biochemical evidence of iron overload. Age of onset is early.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/14/06):
 - a) "Hemochromatosis" = 5846 citations
 - b) "TFR2" or "Type 3" = 9217 citations
 - c) "Hemochromatosis" and "b" = 128 citations (limit to humans)

1. Gene Symbol: F2 Chromosomal Locus: 11p11-q12
2. Protein Name: Prothrombin
3. Disease: Thrombophilia
4. Description: Elevated plasma prothrombin levels, which is associated with the 20210 G-A mutation in the prothrombin (Factor II) gene leads to increased risk of venous thrombosis. Heterozygote carriers of this mutation have an estimated 3 to 8 fold increased risk for venous thrombosis, with a further increased risk for homozygotes. The prothrombin 20210 G-A mutation has an overall prevalence of approximately 2% in the Caucasian population
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Prothrombin"=8184
 - b) "20210 G-A mutation"=17
 - c) a and b (humans)=5

1. Gene Symbol: SERPINE1 Chromosomal Locus: 7q21.3-q22
2. Protein Name: Plasminogen activator inhibitor-1
3. Disease: Thrombosis risk
4. Description: Homozygosity or heterozygosity for the 4G PAI-1 allele is associated with thrombotic risk.
5. Purpose: Prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood; tissue
8. Methodology: Sequence analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Unclear. Mostly early onset and frequent in pregnant women. Detects individuals who at risk for thrombosis
11. Source of Information: Specialty Labs
12. Exploratory Medline Search: (10/26/06)
 - a. "Thrombosis risk" = 22901
 - b. "SERPINE1"=4952
 - c. a and b (limit to humans) = 232

1. Gene Symbol: THRB Chromosomal Locus: 3p24.3
2. Protein Name: Thyroid hormone receptor beta-1
3. Disease: Thyroid hormone resistance
4. Description: Mutations in the Thyroid hormone receptor beta-1 gene associated with thyroid hormone resistance that is a rare syndrome in which thyroid hormone levels are increased and thyroid stimulating hormone level is not suppressed.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Thyroid Hormone Resistance" or "RTH" = 503 citations
 - b) "THRB" = 138 citations
 - c) "a" and "THRB" = 6 citations (limit to humans)

1. Gene Symbol: *MSX1* Chromosomal Locus: 4p16.1
2. Protein Name: Homeobox protein *MSX-1*
3. Disease: Tooth and nail syndrome
4. Description: Witkop syndrome, also known as tooth and nail syndrome (TNS), is a rare autosomal dominant disorder. Affected individuals have nail dysplasia and several congenitally missing teeth. a nonsense mutation in *MSX1* causes TNS and that *Msx1* is critical for both tooth and nail development.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory outside United States
7. Specimen: Blood, buccal tissue
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Tooth and nail syndrome" or "Witkop('s) syndrome" = 12 citations
 - b) "MSX1" or "msh-like 1" = 417 citations
 - c) "a" and "b" = 1 citations

1. Gene Symbol: TP73L Chromosomal Locus: 3q27
2. Protein Name: Tumor protein p73-like
3. Disease: TP63-related disorders
4. Description: Mutations in the *p63* gene are found in a number of human syndromes, including ectrodactyly-ectodermal dysplasia-cleft lip/palate (EEC) syndrome, limb-mammary syndrome (LMS), Hay–Wells syndrome and in non-syndromic split-hand/split-foot malformation (SHFM).
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Not useful (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) “adult syndrome” = 19 citations
 - b) “Ankyloblepharon-Ectodermal Defect” = 15 citations
 - c) “Cleft Lip” = 9363 citations
 - d) “Ectodermal Dysplasia” = 2714 citations
 - e) “Clefting Syndrome” = 60 citations
 - f) “Limb-Mammary Syndrome” = 9 citations
 - g) Split-Hand or Foot Malformation = 165 citations
 - h) “a-g” and “TP73L” = 44 citations (limit to humans)

1. Gene Symbol: ABHD5 Chromosomal Locus: 3p21
2. Protein Name: CGI58 protein
3. Disease: Triglyceride storage disease with impaired long chain fatty acid oxidation
4. Description: Triglyceride storage disease with impaired long-chain fatty acid oxidation, a rare form of nonbullous congenital ichthyosiform erythroderma has been caused by mutation in the CGI58 gene.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood, tissue
8. Methodology: Analysis of the entire coding region: Sequence analysis; analyte
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Triglyceride Storage Disease" = 16 citations
 - b) "Chanarin-Dorfman Syndrome" = 14 citations
 - c) "Neutral Lipid Storage Disease" = 32 citations
 - d) "ABHD5" = 9 citations
 - e) "a-c" and "ABHD5" = 6 citations

1. Gene Symbol: FMO3 Chromosomal Locus: 1q23-q25
2. Protein Name: Hepatic Flavin-Containing Monooxygenase 3 (Dimethylaniline Monooxygenase (N-Oxide Forming) 3)
3. Disease: Trimethylaminuria
4. Description: Trimethylaminuria is usually inherited autosomal dominant disease. Most of the mutations are nonsense mutations in the region of chromosome 1, where the gene that codes for flavin-containing monooxygenase 3 (FMO3) resides. FMO3 is the enzyme involved in breaking down trimethylamine (the compound responsible for the fish odor in the secretions).
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analyte
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Trimethylaminuria" = 78 citations
 - b) "Flavin-containing monooxygenase 3" or "FMO3" = 140 citations
 - c) "Trimethylaminuria" and "b" = 25 citations (limit to humans)

1. Gene Symbol: ARG1 Chromosomal Locus: 6q23
2. Protein Name: Arginase-1
3. Disease: Arginase Deficiency (Urea cycle disorders)
4. Description: Arginase deficiency is an autosomal recessive inborn error of metabolism caused by a defect in the final step in the urea cycle, the hydrolysis of arginine to urea and ornithine.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: red blood cell lysates and liver
8. Methodology: Enzyme assay, analyte, targeted mutational analysis
9. Other Diseases: Urea Cycle Disorder
10. Clinical use(s) for the Medicare population: Unclear applicability (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Arginase Deficiency" = 60 citations
 - b) "arginase I" or "ARGI" = 600 citations
 - c) "Arginase Deficiency" and "b" = 2 citations (limit to humans)

1. Gene Symbol: ASL Chromosomal Locus: 7cen-q11.2
2. Protein Name: Argininosuccinate lyase
3. Disease: Argininosuccinicaciduria (Urea cycle disorders)
4. Description: Argininosuccinic aciduria is an autosomal recessive disorder of the urea cycle. Urea cycle disorders are characterized by the triad of hyperammonemia, encephalopathy, and respiratory alkalosis. Five disorders involving different defects in the biosynthesis of the enzymes of the urea cycle have been described: ornithine transcarbamylase deficiency, carbamyl phosphate synthetase deficiency, argininosuccinate synthetase deficiency, or citrullinemia, argininosuccinate lyase deficiency, and arginase deficiency.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood, urine, CSF
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analyte, Enzyme assay; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (early onset)
11. Source of Information:
12. Exploratory Medline Search (8/11/06):
 - a) "Argininosuccinic aciduria" = 114 citations
 - b) "Argininosuccinate Lyase" or "ASL" = 1183 citations
 - c) "Argininosuccinic aciduria" and "b" = 44 citations (limit to humans)

1. Gene Symbol: CPS1 Chromosomal Locus: 2q35
2. Protein Name: Carbamoyl-phosphate synthase [ammonia]
3. Disease: Carbamoylphosphate Synthetase I Deficiency (Urea cycle disorders)
4. Description: A urea cycle disorder manifesting in infancy as lethargy, emesis, seizures, alterations of muscle tone, abnormal eye movements, and an elevation of serum ammonia. The disorder is caused by a reduction in the activity of hepatic mitochondrial carbamoyl-phosphate synthase [ammonia]
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Liver tissue
8. Methodology: Enzyme assay, analyte, linkage analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 “Carbamoylphosphate Synthetase I Deficiency” or “CPSI deficiency” = 6 citations

1. Gene Symbol: ASS Chromosomal Locus: 9q34
2. Protein Name: Argininosuccinate synthase
3. Disease: Citrullinemia Type I (Urea Cycle Disorders)
4. Description: A group of diseases related to a deficiency of the enzyme ARGININOSUCCINATE SYNTHASE which causes an elevation of serum levels of CITRULLINE. In neonates, clinical manifestations include lethargy, hypotonia, and seizures. Milder forms also occur. Childhood and adult forms may present with recurrent episodes of intermittent weakness, lethargy, ataxia, behavioral changes, and dysarthria.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood, CSF, urine
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analyte; Linkage analysis; Enzyme assay
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable to adult onset type
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Citrullinemia" = 94 citations
 - b) "Argininosuccinate synthase" or "ass" = 1189 citations
 - c) "Citrullinemia" and "Argininosuccinate synthase" = 26 citations (limit to humans)

1. Gene Symbol: PPOX Chromosomal Locus: 1q22
2. Protein Name: Protoporphyrinogen oxidase
3. Disease: Variegate porphyria
4. Description: An autosomal dominant porphyria that is due to a deficiency of protoporphyrinogen oxidase (EC 1.3.3.4) in the LIVER, the seventh enzyme in the 8-enzyme biosynthetic pathway of HEME. Clinical features include both neurological symptoms and cutaneous lesions. Patients excrete increased levels of porphyrin precursors, COPROPORPHYRINS and protoporphyrinogen.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Analyte
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Variegate Porphyria" = 247 citations
 - b) "PPOX" or "Protoporphyrinogen oxidase" = 214 citations
 - c) "Variegate Porphyria" and "b" = 65 citations (limit to humans)

1. Gene Symbol: ACADVL Chromosomal Locus: 17p13
2. Protein Name: Very-long-chain specific acyl-CoA dehydrogenase
3. Disease: Very long chain acyl-CoA dehydrogenase deficiency
4. Description: Inborn errors of mitochondrial fatty acid beta-oxidation include medium-chain acyl-CoA dehydrogenase deficiency, long-chain acyl-CoA dehydrogenase deficiency, short-chain acyl-CoA dehydrogenase deficiency, and very long-chain acyl-CoA dehydrogenase deficiency.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Analyte; Enzyme assay
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (very early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Long chain acyl-CoA dehydrogenase" = 90 citations (limit to humans)

1. Gene Symbol: GJB2 Chromosomal Locus: 13q11-q12
2. Protein Name: Gap junction beta-2 protein (Connexin 26)
3. Disease: Vohwinkel syndrome
4. Description: Mutations in connexin 26 can lead to Vohwinkel syndrome, a disease that belongs to the group of palmoplantar keratodermas. *GJB2* mutation screening is appropriate in all persons with congenital hearing impairment and a negative family history.
5. Purpose: Diagnostic, Counseling
6. Availability: Clinical laboratories
7. Specimen: Buccal swabs
8. Methodology: DNA Sequence analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: GeneDx
12. Exploratory Medline Search: (10/26/06)
 - a. "Vohwinkel syndrome" = 1663
 - b. "GJB2" = 351
 - c. a and b (limit to humans) = 18

1. Gene Symbol: VWF Chromosomal Locus: 12p13.3
2. Protein Name: Von Willebrand factor
3. Disease: Von willebrand disease
4. Description: Group of hemorrhagic disorders in which the von Willebrand factor (Factor VIII-related antigen) is either quantitatively or qualitatively abnormal. They are usually inherited as an autosomal dominant trait though rare kindreds are autosomal recessive. Symptoms vary depending on severity and disease type but may include prolonged bleeding time, deficiency of factor VIII, and impaired platelet adhesion.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons; Linkage analysis; Analysis of the entire coding region: Sequence analysis; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear applicability (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Von willebrand disease" = 3851 citations
 - b) "Von Willebrand factor" or "VWF" = 11294 citations
 - c) "Von willebrand disease" and "b" = 1606 citations (limit to humans)

1. Gene Symbol: PAX3 Chromosomal Locus: 2q35
2. Protein Name: Paired box protein Pax-3
3. Disease: Waardenburg Syndrome Type I
4. Description: Rare, autosomal dominant disease with variable penetrance and several known clinical types. Characteristics may include depigmentation of the hair and skin, congenital deafness, heterochromia iridis, medial eyebrow hyperplasia, hypertrophy of the nasal root, and especially dystopia canthorum. The underlying cause may be defective development of the neural crest (neurocristopathy). Waardenburg's syndrome may be closely related to piebaldism. Klein-Waardenburg Syndrome refers to a disorder that also includes upper limb abnormalities.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; FISH-interphase, FISH-metaphase; Analysis of the entire coding region: Mutation scanning
9. Other Diseases:
10. Clinical use(s) for the Medicare population: Unclear applicability (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Waardenburg's Syndrome" = 549 citations
 - b) "PAX3" = 654 citations
 - c) "Waardenburg Syndrome" and "PAX3" = 84 citations (limit to humans)

1. Gene Symbol: MITF Chromosomal Locus: 3p14.1-p12.3
2. Protein Name: Microphthalmia-associated transcription factor
3. Disease: Waardenburg Syndrome Type IIa
4. Description: Rare, autosomal dominant disease with variable penetrance and several known clinical types. Characteristics may include depigmentation of the hair and skin, congenital deafness, heterochromia iridis, medial eyebrow hyperplasia, hypertrophy of the nasal root, and especially dystopia canthorum. The underlying cause may be defective development of the neural crest (neurocristopathy). Waardenburg's syndrome may be closely related to piebaldism. Klein-Waardenburg Syndrome refers to a disorder that also includes upper limb abnormalities.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: ??
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Waardenburg's Syndrome" = 546 citations
 - b) "MITF" = 610 citations
 - c) "Waardenburg Syndrome" and "MITF" = 56 citations (limit to humans)

1. Gene Symbol: PAX3 Chromosomal Locus: 2q35
2. Protein Name: Paired box protein Pax-3
3. Disease: Waardenburg Syndrome Type III
4. Description: Rare, autosomal dominant disease with variable penetrance and several known clinical types. Characteristics may include depigmentation of the hair and skin, congenital deafness, heterochromia iridis, medial eyebrow hyperplasia, hypertrophy of the nasal root, and especially dystopia canthorum. The underlying cause may be defective development of the neural crest (neurocristopathy). Waardenburg's syndrome may be closely related to piebaldism. Klein-Waardenburg Syndrome refers to a disorder that also includes upper limb abnormalities.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; FISH-interphase, FISH-metaphase
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Unclear applicability (age of onset early)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "Waardenburg's Syndrome" = 554 citations
 - b) "PAX3" = 654 citations
 - c) "Waardenburg Syndrome" and "PAX3" = 83 citations (limit to humans)

1. Gene Symbol: KRT13 Chromosomal Locus: 17q21-q22;
Gene Symbol: KRT4 Chromosomal Locus: 12q13
2. Protein Name: Keratin, type I cytoskeletal 13; Keratin, type II cytoskeletal 4
3. Disease: White Sponge Nevus of Cannon Hereditary Mucosal Leukokeratosis
4. Description: This disorder is manifested by thickened spongy-fold mucosa with a white opalescent tint in the mouth. The vagina, rectum, and nasal cavity may be similarly involved. It is differentiated from benign intraepithelial dyskeratosis by the presence of vaginal and anal lesions and the absence of conjunctival involvement and the characteristic cell-within-cell histologic change.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood and buccal brushes
8. Methodology: Analysis of the entire coding region: Sequence analysis, Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (no data on age of onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
 - a) "White Sponge Nevus of Cannon" = 0 citations
 - b) "Hereditary Mucosal Leukokeratosis" = 5 citations

1. Gene Symbol: ELN Chromosomal Locus: 7q11.2
2. Protein Name: Elastin
3. Disease: Williams Syndrome
4. Description: A contiguous gene syndrome associated with a heterozygous microdeletion in the chromosomal region 7q11.23, encompassing the ELASTIN gene. Clinical manifestations include supravalvular aortic stenosis (AORTIC STENOSIS, SUPRAVALVULAR), MENTAL RETARDATION, elfin facies, impaired visuospatial constructive abilities, and transient hypercalcemia in infancy. The condition affects both sexes, with onset at birth or in early infancy.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: FISH-metaphase; Heterozygosity testing, Targeted mutation analysis; Array Genomic Hybridization, FISH-interphase, Deletion/duplication analysis; Linkage analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/10/06):
 - a) "Williams Syndrome" = 941 citations
 - b) "ELN" = 104 citations
 - c) "Elastin" = 4953 citations
 - d) "Williams Syndrome" and "ELN" and "Elastin" = 76 citations (limit to humans)

1. Gene Symbol: ATP7B Chromosomal Locus: 13q14.3-q21.1
2. Protein Name: Copper-transporting ATPase 2
3. Disease: Wilson disease
4. Description: Wilson disease is an autosomal recessive disorder characterized by dramatic build-up of intracellular hepatic copper with subsequent hepatic and neurologic abnormalities. The overload of copper inevitably leads to progressive liver and neurological dysfunction such as LIVER CIRRHOSIS; TREMOR; ATAXIA and intellectual deterioration. Hepatic dysfunction may precede neurologic dysfunction by several years.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: ND
8. Methodology: Analysis of the entire coding region: Mutation scanning; Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Targeted mutation analysis; Deletion/duplication analysis; Linkage analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: (3-60 years)
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/10/06):
 - a) "Wilson disease" = 816 citations
 - b) "ATP7B" = 298 citations
 - c) "Wilson disease" and "ATP7B" = 214 citations (limit to humans)

1. Gene Symbol: PRKAG2 Chromosomal Locus: 7q36
2. Protein Name: 5'-AMP-activated protein kinase, gamma-2 subunit
3. Disease: Wolff-Parkinson-White Syndrome
4. Description: A form of pre-excitation characterized by a short PR interval and a long QRS interval with a delta wave. About 80 percent of people with symptoms first have them between the ages of 11 and 50.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory (Available outside US in Amsterdam, Netherlands)
7. Specimen: ND
8. Methodology: Analysis of the entire coding region: Mutation scanning
9. Other Diseases: Preexcitation Syndrome
10. Clinical use(s) for the Medicare population: Late onset WPW may be applicable.
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/10/06):
 - a) "Wolff-Parkinson-White Syndrome" = 1809 citations
 - b) "PRKAG2" = 26 citations
 - c) Wolff-Parkinson-White Syndrome and PRKAG2 = 13 citations (limit to humans)

1. Gene Symbol: WFS1 Chromosomal Locus: 4p16.1
2. Protein Name: Wolframin
3. Disease: Wolfram syndrome
4. Description: DNA sequencing conducted to screen the entire coding region of the WFS1 gene. Mutations in gene WFS1 encoding wolframin, a 100-kDa transmembrane protein has been found to cause Wolfram syndrome.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratories (Outside US, in Netherlands and Belgium)
7. Specimen: Serum
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Death common before age 50
11. Source of Information: GeneTests.org, OVID
12. Exploratory Medline Search (8/22/06):
 - a) "Wolfram Syndrome" = 317 citations
 - b) "WFS1" = 136 citations
 - c) "Wolfram Syndrome" and "WFS1" = 119 (limit to humans)