Ashkenazi Jewish Genetic Diseases Panel

Individuals of Ashkenazi Jewish descent are at an increased risk for certain autosomal recessive genetic disorders. An estimated one in every four or five individuals of Ashkenazi Jewish descent is a carrier for one of these disorders.[1] In combination, the Ashkenazi Jewish Disease Panel and Cystic Fibrosis 165 Pathogenic Variants tests screen for all of the disorders that the American College of Medical Genetics and Genomics (ACMG) and the American College of Obstetrics and Gynecology (ACOG) recommend testing for in individuals of Ashkenazi Jewish descent.

Tests to Consider

Ashkenazi Jewish Diseases, 16 Genes 0051415

Method: Polymerase Chain Reaction/Fluorescence Monitoring

- Preferred gene panel for carrier screening for individuals of Ashkenazi Jewish descent considering pregnancy or currently pregnant
- Detect 51 variants associated with 16 disorders common in individuals of Ashkenazi Jewish descent

Cystic Fibrosis (CFTR) 165 Pathogenic Variants 2013661

Method: Polymerase Chain Reaction/Fluorescence Monitoring

- Carrier screening for expectant individuals and those planning a pregnancy AND diagnostic testing for individuals with symptoms of classic CF
- Not included in prenatal screening panel for individuals of Ashkenazi Jewish descent

Disease Overview

Screening

- Routine preconception or prenatal carrier screening for genetic diseases common in individuals of Ashkenazi Jewish descent is recommended by:
  - ACOG[2]
    - *ABCC8*-related hyperinsulinemia
    - Bloom syndrome
    - Canavan disease
    - Cystic fibrosis
    - Fanconi anemia group C
    - Familial dysautonomia
    - Gaucher disease
    - Glycogen storage disease type 1A
    - Joubert syndrome type 2
    - Maple syrup urine disease type 1B
    - Mucolipidosis type IV
    - Niemann-Pick type A
    - Tay-Sachs disease
    - Usher syndrome (type 1F and type 3)
  - ACMG for nine of the disorders described in the ACOG guidelines[3]
- Screening for a specific disorder may be offered to individuals not of Ashkenazi Jewish descent, including:
  - Relatives who carry one or more variants included in the test
  - Reproductive partners who are carriers of one of the panel disorders, although detection rates for non-Ashkenazi individuals is variable by disorder and largely unknown

For additional clinical information and the carrier frequency of diseases included on the Ashkenazi Jewish Diseases, 16 Genes panel, see the Ashkenazi Jewish Genetic Diseases Consult topic.

Genetics

Inheritance

Autosomal recessive

Genes/Variants

See Clinical Sensitivity table

Test Interpretation

Analytical sensitivity/specificity: 99%

Clinical Sensitivity for Individuals of Ashkenazi Jewish Descent					
Disease (and Associated Gene)	Variants Tested (HGVS Nomenclature)	Variants Tested (Legacy Nomenclature)	Clinical Sensitivity in Individuals of Ashkenazi Jewish Descent	Clinical Sensitivity in non-Ashkenazi Jewish Individuals	Carrier Risk After Negative Test for Ashkenazi Jewish Individuals
ABCC8-related hyperinsulinism (*ABCC8*)	p.F1388del (c.4163_4165del) p.V187D (c.560T>A) c.3992-9G>A	n/a	97%[4]	Unknown	1/1,700
Bloom syndrome (*BLM*)	p.Y736Lfs (c.2207_2212delinsTAGATTC)	2281del6/ins7	97%[5]	~3%	1/3,300
Canavan disease (*ASPA*)	c.433-2A>G p.Y231X (c.693C>A) p.E285A (c.854A>C) p.A305E (c.914C>A)	n/a	99%[6]	55%	1/4,900
Familial dysautonomia (*IKBKAP*)	p.R696P (c.2087G>C) c.2204+6T>C	 IVS20+6T>C	99%[3]	Unknown	1/3,100
Fanconi anemia group C (*FANCC*)	p.D23Ifs (c.67delG) c.456+4A>T	322delG IVS4+4A>T	99%[3]	Unknown	1/8,800
Gaucher disease (*GBA*)	p.L29Afs (c.84dupG) c.115+1G>A p.N409S (c.1226A>G) c.1263_1317del55 p.V433L (c.1297G>T) p.D448H (c.1342G>C) p.L483P (c.1448T>C) p.R535H (c.1604G>A)	84G>GG IVS2+1G>A N370S del55bp V394L D409H L444P R496H	90%[7]	55%	1/140
Glycogen storage disease type 1A (*G6PC*)	p.Q27Rfs (c.79delC) p.Y128Tfs (c.379_380dupTA) p.R83H (c.248G>A) p.R83C (c.247C>T) p.G188R (c.562G>C) p.Q242X (c.724C>T) p.Q347X (c.1039C>T) p.G270V (c.809G>T) p.F327del (c.979_981delTTC)	n/a	99%[8]	Varies by ethnicity	1/7,000
Joubert syndrome type 2 (*TMEM216*)	p.R73L (c.218G>T)	n/a	99%[9]	Unknown	1/9,100
Lipoamide dehydrogenase deficiency (*DLD*)	p.Y35X (c.104dupA) p.G229C (c.685G>T)	n/a	99%[10]	Unknown	1/9,300
Maple syrup urine disease type 1B (*BCKDHB*)	p.R183P (c.548G>C) p.G278S (c.832G>A) p.E372X (c.1114G>T)	n/a	99%[11]	Unknown	1/11,000

[a]For specific Tay-Sachs disease testing, see the Tay-Sachs Disease Testing fact sheet

n/a, not applicable

Disease (and Associated Gene)	Variants Tested (HGVS Nomenclature)	Variants Tested (Legacy Nomenclature)	Clinical Sensitivity in Individuals of Ashkenazi Jewish Descent	Clinical Sensitivity in non-Ashkenazi Jewish Individuals	Carrier Risk After Negative Test for Ashkenazi Jewish Individuals
Mucolipidosis type IV (*MCOLN1*)	c.406-2A>G g.511_6943del	IVS3-2A>G del6.4kb	95%[12]	6-10%	1/2,500
NEB-related nemaline myopathy (*NEB*)	exon 55 del (p.R2478_D2512del)	n/a	99%[13]	Unknown	1/10,700
Niemann-Pick disease type A (*SMPD1*)	p.L304P (c.911T>C) p.F333Sfs (c.996delC) p.R498L (c.1493G>T) p.R610del (c.1829_1831delGCC)	L302P fsP330 R496L R608del	90%[14]	Varies by ethnicity	1/900
Tay-Sachs disease (*HEXA*)[a]	7.6 kb del p.G269S (c.805G>A) c.1073+1G>A p.Y427Ifs (c.1274_1277dup TATC) c.1421+1G>C Pseudodeficiency alleles: p.R247W (c.739C>T) p.R249W (c.745C>T)	IVS9+1G>A 1278dupTATC IVS12+1G>C	94%[15]	59%	1/480
Usher syndrome type 1F (*PCDH15*)	p.R245X (c.733C>T)	n/a	62%[16]	Unknown	1/190
Usher syndrome type 3 (*CLRN1*)	p.N48K (c.144T>G)	n/a	98%[17,18]	Unknown	1/7,000

[a]For specific Tay-Sachs disease testing, see the Tay-Sachs Disease Testing fact sheet

n/a, not applicable

Results

- Positive: one pathogenic variant detected
  - Individual is a carrier of the associated disease
  - Screening for that disease should be offered to the individual's reproductive partner
  - Genetic counseling is recommended
- Negative: no targeted pathogenic variants identified
  - For residual carrier risk estimates, see the Clinical Sensitivity table

Limitations

- Variants other than those tested on this panel will not be detected
- Diagnostic errors can occur due to rare sequence variations

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Related Information

Ashkenazi Jewish Genetic Diseases
Ashkenazi Jewish Genetic Diseases Carrier Screening Algorithm
Cystic Fibrosis

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Content Review August 2019 | Last Update June 2020