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*****Example Report*****

Patient Age/Gender: Unknown Female
Printed: 28-Jun-19 10:40:31

Procedure	Result	Units	Ref Interval	Accession	Collected	Received	Reported/ Verified
Ashkenazi Jewish Diseases, Specimen	Whole Blood			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02
Ashkenazi Jewish Diseases, Panel Results	**Positive** *			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02
Ashkenazi Jewish Diseases, Gene 1	**IKBKAP** *			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02
AJP Gene 1, Allele 1	**c.2204+6T>C** *			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02
AJP Gene 1, Allele 2	Negative			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02
Ashkenazi Jewish Diseases, Gene 2	**GBA** *			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02
AJP Gene 2, Allele 1	**c.1448T>C** *			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02
AJP Gene 2, Allele 2	Negative			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02
Ashkenazi Jewish Diseases Carrier Status	Yes			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02
Ashkenazi Jewish Diseases, Interp	See Note f			19-164-900063	13-Jun-19 11:51:00	13-Jun-19 11:51:00	13-Jun-19 14:00:02

13-Jun-19 11:51:00 Ashkenazi Jewish Diseases, Interp:

Section 79-1 of New York State Civil Rights Law requires informed consent be obtained from patients (or their legal guardians) prior to pursuing genetic testing. These forms must be kept on file by the ordering physician. Consent forms for genetic testing are available at www.aruplab.com. Incidental findings are not reported unless clinically significant but are available upon request.

Indication for testing: Carrier screening for genetic disorders common in Ashkenazi Jewish individuals.

Positive: Two pathogenic variants were detected, c.2204+6T>C in the IKBKAP gene and c.1448T>C in the GBA gene. Therefore, this individual is a carrier of both Familial dysautonomia and Gaucher disease. Genetic counseling is recommended. This individual's reproductive partner should be offered screening for the disorder. At-risk family members should be offered testing to determine carrier status for the identified variants. None of the other targeted variants associated with the 16 common Ashkenazi Jewish disorders screened by this panel were identified. If this individual is of Ashkenazi Jewish descent, he/she may use the table below to review the residual carrier risk for the other disorders. If this individual has a positive family history of a disorder covered by this panel, the figures for that disorder do not apply.

Familial dysautonomia is a debilitating disease caused by abnormal development and survival of sensory, sympathetic and parasympathetic neurons. Symptoms include gastrointestinal dysfunction, vomiting and autonomic crises, recurrent pneumonia, altered sensitivity to pain and temperature, scoliosis, and cardiovascular instability. Other characteristics include infantile hypotonia, deteriorating wide-based ataxic gait that deteriorates, and decreased life expectancy.

Gaucher disease affects lysosomal storage and has extreme symptom variability, ranging from perinatal lethality to asymptomatic individuals. Three Gaucher subtypes have been identified based on symptom characteristics. Individuals affected with Gaucher disease type 1 may be asymptomatic. Symptomatic individuals may have bone disease, hepatosplenomegaly, anemia, thrombocytopenia, and lung disease. Affected individuals with at least one copy of the p.N409S variant do not develop primary neurologic disease associated with this disorder.

This result has been reviewed and approved by Rong Mao, M.D.

13-Jun-19 11:51:00 Ashkenazi Jewish Diseases, Interp:
BACKGROUND INFORMATION: Ashkenazi Jewish Diseases, 16 Genes

OVERVIEW: This targeted panel detects 51 variants common in the Ashkenazi Jewish population associated with 16 disorders, including ABCC8-related hyperinsulinism, Bloom syndrome, Canavan disease, familial dysautonomia, Fanconi anemia group C, Gaucher disease, glycogen storage disease 1A, Joubert syndrome type 2, lipoamide dehydrogenase deficiency, maple syrup urine disease type 1B, mucolipidosis type IV, NEB-related nemaline myopathy, Niemann-Pick disease type C, Tay-Sachs disease, Usher syndrome type 1F and type 3.
INHERITANCE: Autosomal recessive.
CLINICAL SENSITIVITY: Among Ashkenazi Jewish individuals:

- 99 percent for Canavan disease, lipoamide dehydrogenase deficiency, familial dysautonomia, Fanconi anemia group C, glycogen storage disease type 1A, Joubert syndrome type 2, maple syrup urine disease type 1B, and NEB-related nemaline myopathy
- 98 percent for Usher syndrome type 3
- 97 percent for ABCC8-related hyperinsulinism and Bloom syndrome
- 95 percent for mucolipidosis type IV
- 94 percent for Tay-Sachs disease
- 90 percent for Gaucher disease and Niemann-Pick disease type A
- 62 percent for Usher syndrome type 1F

METHODOLOGY: Polymerase chain reaction (PCR) and fluorescence monitoring. See table below for specific variants tested.
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
LIMITATIONS: Variants other than those tested on this panel will not be detected. Diagnostic errors can occur due to rare sequence variations.

DISEASE (GENE)	VARIANTS TESTED	ASHKENAZI DISEASE INCIDENCE	ASHKENAZI PRETEST CARRIER RISK	ASHKENAZI CARRIER RISK AFTER NEG RESULT
ABCC8-related hyper-insulin-ism (ABCC8)	p.F1388del (c.4163_4165del) p.V187D (c.560T>A) c.3992-9G>A	1/7,800	1/52	1/1,700
Bloom Syndrome (BLM)	p.Y736Lfs (c.2207_2212delins TAGATTC)	1/40,000	1/100	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)	1/10,000	1/50	1/4,900
Familial Dys-autonomia (IKBKAP)	p.R696P (c.2087G>C) c.2204+6T>C	1/3,600	1/32	1/3,100
Fanconi Anemia Group C (FANCC)	p.D23Ifs (c.67delG) c.456+4A>T	1/32,000	1/89	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)	1/900	1/15	1/141

	p.R535H (c.1604G>A)			
Glycogen Storage Disease Type 1A (G6PC)	p.Q27Rfs (c.79delC) p.R83H (c.248G>A) p.R83C (c.247C>T) p.Y128Tfs (c.379_380dupTA) 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)	1/20,000	1/71	1/7,000
Joubert Syndrome Type 2 (TMEM216)	p.R73L (c.218G>T)	1/34,000	1/92	1/9,100
Lipoamide Dehydro-genase Deficiency (DLD)	p.Y35X (c.104dupA) p.G229C (c.685G>T)	1/35,000	1/94	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)	1/50,000	1/113	1/11,200
Mucolip-idosis IV	c.406-2A>G g.511_6943del	1/63,000	1/127	1/2,500
NEB-related Nemaline Myopathy (NEB)	exon 55 del (p.R2478_D2512del)	1/47,000	1/108	1/10,700
Niemann-Pick Type-A Disease (SMPD1)	p.L304P (c.911T>C) p.F333Sfs (c.996delC) p.R498L (c.1493G>T) p.R610del (c.1829_1831delGCC)	1/32,000	1/90	1/890
Tay-Sachs Disease (HEXA)	7.6 kb del p.G269S (c.805G>A) c.1073+1G>A p.Y427Ifs (c.1274_1277dupTATC) c.1421+1G>C Pseudodeficiency	1/3,000	1/30	1/480

	alleles: p.R247W (c.739C>T) p.R249W (c.745C>T)			
Usher Syndrome Type 1F (PCDH15)	p.R245X (c.733C>T)	1/20,500	1/72	1/190
Usher Syndrome Type 3 (CLRN1)	p.N48K (c.144T>G)	1/82,000	1/143	1/7,100

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS