



**MDL Ashkenazi Jewish Carrier Screening**

**Indication:** Per the recommendations of the American College of Obstetricians and Gynecologists (ACOG), carrier screening in the preconception or prenatal period should be offered to individuals of Ashkenazi Jewish ancestry for the following four conditions: Tay-Sachs Disease, Canavan disease, Cystic Fibrosis, and Familial Dysautonomia. Furthermore, ACOG states that couples of Ashkenazi Jewish background may wish to obtain information and be tested for carrier status for the following additional diseases: Mucopolipidosis Type IV, Niemann-Pick Disease Type A, Fanconi Anemia Type C, Bloom Syndrome, and Gaucher Disease.

**Methods:** MDL has developed Bio-Plex assays capable of detecting 30 different mutations in genes ASPA, BLM, IKBKAP, HEXA, MCOLN1, GBA, FANCC, and SMPD1 responsible for Canavan Disease, Bloom Syndrome, Familial Dysautonomia, Tay–Sachs Disease, Mucopolipidosis Type IV, Gaucher Disease, Fanconi Anemia Type C, and Niemann-Pick Disease Type A, respectively. Genes specified were tested for the presence of specific mutations listed in the table below by Polymerase Chain Reactions (PCR), oligonucleotide single base extension reactions, and liquid micro-array sorting and detection.

**MDL Ashkenazi Jewish Genetic Core Panel Detection Rates**

Individual Test #	Test 1213 *	Test 1214**	Disease	Gene Symbol	Mutation(s) Screened	Detection in Ashkenazi Jewish	Detection in Non-Ashkenazi Jewish
1209	X	X	Canavan Disease	ASPA	E285A, A305E, Y231X, IVS2-2A>G	99%	55%
1207		X	Bloom Syndrome	BLM	2281del6/ins7	95%	Unknown
1210	X	X	Familial Dysautonomia	IKBKAP	IVS20+6T>C, R696P	99%	Unknown
1208	X	X	Tay–Sachs Disease	HEXA	del7.6kb, R247W, R249W, G269S, IVS9+1G>A, 1278insTATC, IVS12+1G>C	92%	Unknown
1212		X	Mucopolipidosis Type IV	MCOLN1	del6.4kb, IVS3-2A>G	95%	Unknown
1211		X	Gaucher Disease	GBA	84insG, IVS2+1G>A, N370S, del55bp, V394L, D409H, L444P, R496H	90%	55%
1205		X	Fanconi Anemia Type C	FANCC	322delG, IVS4+4A>T	99%	Unknown
1206		X	Niemann-Pick Disease Type A	SMPD1	L302P, R496L, delP330fs, delR608	95%	Unknown
1201	X	X	Cystic Fibrosis	For Cystic Fibrosis interpretative criteria, please refer to the Cystic Fibrosis Screening Interpretation Guidelines.			

\* Test #1213: Ashkenazi Jewish Carrier Screening Panel by Bio-Plex Analysis

\*\*Test #1214: Ashkenazi Jewish Carrier Screening Expanded Panel by Bio-Plex Analysis

**Result: One or more mutations detected.**

**Interpretation:** If Test #1214 was performed using the methods described, this individual tested positive for one or more of the 30 mutations listed above for Canavan Disease, Bloom Syndrome, Familial Dysautonomia, Tay–Sachs Disease, Mucopolipidosis Type IV, Gaucher Disease, Fanconi Anemia Type C, and/or Niemann-Pick Disease Type A indicating that this individual is a carrier for one or more of the syndromes listed above. If Test #1213 or individual Ashkenazi Jewish Carrier Screening Tests were performed, this individual tested positive for one or more of the mutations for the corresponding diseases in the table above indicating that this individual is a carrier for one or more of the corresponding syndromes. This interpretation is based on the assumption that this individual is not clinically affected with any of the listed syndromes. It is recommended that carrier testing by mutation analysis be offered to relatives and reproductive partners of mutation carriers along with appropriate genetic counseling.

**Reference:** ACOG Committee on Genetics. ACOG Committee Opinion. Number 298, August 2004. Prenatal and preconceptional carrier screening for genetic diseases in individuals of Eastern European Jewish descent. *Obstet Gynecol.* 2004;104:425-428.

This test was developed and its performance characteristics determined by this laboratory. It has not been cleared or approved by the Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. The laboratory is regulated by the Clinical Laboratory Improvement Act of 1988.

General Disclaimer: DNA studies do not constitute a definitive carrier test for Canavan Disease, Bloom Syndrome, Familial Dysautonomia, Tay–Sachs Disease, Mucopolipidosis Type IV, Gaucher Disease, Fanconi Anemia Type C, or Niemann-Pick Disease Type A in all individuals. Thus, interpretation is given as a probability. Accurate risk calculation requires accurate family history information. Inaccurate reporting for family history of syndromes listed will lead to errors in residual risk assessment.