

ALPHA-1 ANTITRYPIN (A1AT) GENETIC TESTING

		Patient Type		
Test Type	Test Method	Symptomatic Patient	1 st Degree Relative of Proband	Preconceptual Counseling
Initial Investigation	Serum A1AT Level	A1AT level determines need to proceed to Diagnostic test	Proceed to Diagnostic test regardless of the serum A1AT level	
Preliminary Diagnostic:	PCR based DNA testing for S and Z mutations	Stop here if the preliminary diagnostic test result agrees with the serum A1AT level (see Table of Expected Values by Presumptive Genotype).		
	Protease inhibitor Isoelectric focusing (Pi-IEF) (if indicated)	Note Pi-IEF to be performed at St Paul's hospital, on the same serum sample, for all heterozygous Z carriers to rule out F/Z		
Definitive Diagnostic	Gene Sequencing of coding region of the <i>SERPINA1</i> gene	Utilize to investigate cases in which the preliminary diagnostic test does not explain a relatively low serum A1AT level.		

Table of Expected Values by Presumptive Genotype¹

Genotype	mean	-1.28 SD (10th percentile)	+2 SD (97.5th percentile)
MM	1.47	0.91	2.35
MS	1.2	0.73	1.94
SS	0.88	0.65	1.24
MZ	0.85	0.59	1.25
SZ	0.6	NA	0.82
ZZ	0.28	N/A	0.72

Please note that the values in the table were derived from Snyder et al and verified using patient data as analyzed according to the protocol.

References:

1. Snyder MR, Katzmann JA, Butz ML, et al. Diagnosis of alpha-1-antitrypsin deficiency: An algorithm of quantification, genotyping, and phenotyping. Clin Chem. 2006;52(12):2236-2242.
2. Mattman A, Gilfix BM, Chen SX, DeMarco ML, Kyle BD, Parker ML, Agbor TA, Jung B, Selvarajah S, Barakauskas VE, Vaags AK, Estey MP, Nelson TN, Speevak MD. Alpha-1-antitrypsin molecular testing in Canada: A seven year, multi-centre comparison. Clin Biochem. 2020 Jul;81:27-33. doi: 10.1016/j.clinbiochem.2020.05.001. Epub 2020 May 6. PMID: 32387440.