AVB-CG
CENTRE DE RÉFÉRENCE
ATRÉSIE DES VOIES BILIAIRES
ET CHOLESTASES GÉNÉTIQUES

Mutation sequence analysis			
Contributed by : CHU Lille			
HGVS nomenclature (NM_000295.4)			
Nomenclarure including the signal peptide			
c.227_229delTCT			
Type of variation	Mutation Location	Genetic background	ACMG classification
AAT variant	Exon 2	M2	Pathogenic
Comments			
The Pi Mmalton variant was first discovered by Cox in 1976.			

AAT variant and Q0 alleles			
Variant name	Also Known as	Pathogenicity	HGVS nomenclature protéine
M_{malton}		Deficient Precipitating	p.Phe76del

3D position of aa affected	Mobility on polyacrylamide gel	Mobility on agarose gel
		M

AATserum level (g/L)		Anti-elastolytic activity (IU/L)	
Heterozygous	**Homozygous**	**Heterozygous**	**Homozygous**
0.69	0.12		
Comments			
Slightly more cathodal mobility than M2 on IEF gels. At the heterozygous state, it thus may be confounded with an M protein.			
Occurrence			
Ethnic background without frequency range :			

Ethnic background and frequency			
Frequency range		**Group tested**	
from (%)	To (%)	Size	Description (who was tested)
	0.04		

Occurrence comments

from gnomAD (2.1). However, the Pi Mmalton variant is not so rare in Spain, Sardinia and Maghreb countries.

Overall comments

Occurrence comments

This variant was identified at a homozygous status in a 47-year old man presenting with pulmonary emphysema. This variant was also identified at a homozygous status in a 48-year old man presenting with pulmonary emphysema and treated by substitution therapy (picture 2). Some associations with the Pi Z allele have been described (see Ref. 2): - a 41-year-old man of french caucasian origin with severe dyspnea (AAT = 0.33 g/L) - a 37-year-old woman with asthma and bronchiectasis (AAT = 0.22 g/L)

References n°1

Medline ID	Authors	Title
2788166	Curiel DT,Holmes MD,Okayama H,Brantly ML,Vogelmeier C,Travis WD,Stier LE,Perks WH,Crystal RG	Molecular basis of the liver and lung disease associated with the alpha 1-antitrypsin deficiency allele Mmalton.

Journal	Year	Volume	Num	Pp
The Journal of biological chemistry	1989	264	23	13938-45

References n°2

Medline ID	Authors	Title
26446624	Joly P,Guillaud O,Hervieu V,Francina A,Mornex JF,Chapuis-Cellier C	Clinical heterogeneity and potential high pathogenicity of the Mmalton Alpha 1 antitrypsin allele at the homozygous, compound heterozygous and heterozygous states.

Journal	Year	Volume	Num	Pp
Orphanet journal of rare diseases	2015	10		130

Last Update

First publication : 07-21-2020 11:47 Last update : 09-05-2020 21:39 by Pr Joly Philippe