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.194T>C			
Type of variation	Mutation Location	Genetic background	ACMG classification
AAT variant	Exon 2		Pathogenic
Comments			
rs28931569			

AAT variant and Q0 alleles			
Variant name	Also Known as	Pathogenicity	HGVS nomenclature protéine
$M_{procida}$		Deficient	p.Leu65Pro

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**
0.71		9963	
Comments			
Associated with a M2 allele. Evaluation of the crystallographic structure of alAT suggests the "Leu to Pro“ mutation may disrupt ?-helix A in the region of Pro21-Ser45,suggesting the possibility that the a1AT Mprocida molecule is unstable and degraded intracellularly prior to secretion. No liver accumulation. The Leu-Pro substitution involves two uncharged amino acids, a fact that is consistent with the observation of a very small difference in electrophoretic mobility between Mprocida and the common normal M1(Val213)			

Occurrence

Ethnic background without frequency range :

Ethnic background and frequency

Frequency range		Group tested	
from (%)	To (%)	Size	Description (who was tested)
0.01	0.03		

Occurrence comments

From gnomAD

Overall comments

Occurrence comments

This variant was identified at a heterozygous status in a 22-year old man presenting with alpha-1 antitrypsin deficiency. It was also identified at a heterozygous status with a M1 variant in a 43-year old man presenting with COPD and in a 75-year old man presenting with pulmonary emphysema and with a I variant in a 66-year old man presenting with pulmonary emphysema. Evaluation of the crystallographic structure of alAT suggests the "Leu to Pro“ mutation may disrupt ?-helix A in the region of Pro21-Ser45,suggesting the possibility that the a1AT Mprocida molecule is unstable and degraded intracellularly prior to secretion. No liver accumulation.

References

Medline ID	Authors	Title
3262617	Takahashi H,Nukiwa T,Satoh K,Ogushi F,Brantly M,Fells G,Stier L,Courtney M,Crystal RG	Characterization of the gene and protein of the alpha 1-antitrypsin "deficiency" allele Mprocida.

Journal	Year	Volume	Num	Pp
The Journal of biological chemistry	1988	263	30	15528-34

Last Update

First publication : 08-25-2020 09:42 Last update : 10-22-2020 17:03 by Pr Joly Philippe