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

Mutation sequence analysis			
Contributed by : CHU Lyon			
HGVS nomenclature (NM_000295.4)			
Nomenclarure including the signal peptide			
c.272G>A			
Type of variation	Mutation Location	Genetic background	ACMG classification
AAT variant	Exon 2	M1 Val	Pathogenic
Comments			
rs28931568 This mutation creates a polymorphism for the restriction endonuclease AvaII.			

AAT variant and Q0 alleles			
Variant name	Also Known as	Pathogenicity	HGVS nomenclature protéine
$M_{mineral\ springs}$		Deficient Dysfunctional	p.Gly91Glu

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

AATserum level (g/L)		Anti-elastolytic activity (IU/L)	
Heterozygous	**Homozygous**	**Heterozygous**	**Homozygous**
0.5 à 0.8			
Comments			
The alpha 1AT Mmineral springs migrates cathodal to the normal M2 allele.			
Occurrence			
Ethnic background without frequency range :			
Ethnic background and frequency			

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

Occurrence comments

The Mmineral springs allele was first observed in a black family.

Overall comments

Occurrence comments

- Cytoplasmic blot analysis of blood monocytes of the Mmineral springs homozygote demonstrated levels of alpha 1AT mRNA transcripts comparable to those in cells of a normal M1 control. - Evaluation of in vitro translation of Mmineral springs alpha 1AT mRNA transcript demonstrated a normal capacity to direct the translation of alpha 1AT. - However, a reduced alpha 1AT secretion on the basis of aberrant post-translational alpha 1AT biosynthesis was demonstrated for the Mmineral springs allele. - Furthermore, for alpha 1AT protein that does reach the circulation, the causing mutation markedly affects the ability of the molecule to neutrophil elastase.

References

Medline ID	Authors	Title
1967187	Curiel DT,Vogelmeier C,Hubbard RC,Stier LE,Crystal RG	Molecular basis of alpha 1-antitrypsin deficiency and emphysema associated with the alpha 1-antitrypsin Mmineral springs allele.

Journal	Year	Volume	Num	Pp
Molecular and cellular biology	1990	10	1	47-56

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