ASSOCIATION OF MBL2 GENE POLYMORPHISMS WITH HIV-1 INFECTION IN MOROCCO

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BACKGROUND

Human Mannose-binding lectin (MBL) is a serum protein secreted by the liver. It is encoded by the *MBL2* gene and participates in the activation of the innate immune defense system through the lectin-complement pathway. Several studies showed that the deficiency of the *MBL2* gene is correlated to several infectious and autoimmune diseases susceptibility, including HIV-1 infection. In order to clarify the direct or indirect contribution of MBL protein in HIV-1 infection, further research are being conducted on the genetic diversity of the *MBL2* and its impact on HIV-1 infection susceptibility and disease progression.. The present study aims to investigate the impact of six *MBL2* gene polymorphisms (rs11003125, rs7096206, rs7095891, rs5030737, rs1800450, and rs1800451) located in the promoter, 5' UTR and exon 1 regions on HIV-1 infection susceptibility, AIDS development and the antiretroviral treatment response outcome among Moroccan population.

This study highlights the importance of ***MBL2*** polymorphisms in the modulation of **HIV-1 infection susceptibility** among **Moroccan** volunteers

METHODS



This case-control study involves the peripheral venous blood of 400 consenting participants, including 200 people with HIV-1 and 200 healthy controls from Moroccan population. The genomic DNA was isolated from the samples according to the standard phenol-chloroform method. The extracted DNA samples was amplified using conventional PCR. Then, the genotyping of the six *MBL2* gene polymorphisms was performed by an automated DNA sequencing adapted from the Sanger method by fluorescence. The generated sequences were analyzed using BioEdit software. The statistical analysis based on the comparison between the two groups using the Chi-square test, was performed using the R statistical software. The tests correction for statistical significance was applied by the Bonferroni adjustment (*p.adjust*) to avoid a spurious positive (type I error). A *p.adjust*-value < 0.05 was considered statistically significant.

RESULTS

The demographic characteristics of study participants showed that 200 people with HIV-1 (composed of 110 females and 90 males) with a mean age of 37.20 ± 9.21 years and 200 controls (140 females and 60 males) with a mean age of 49.92 ± 17.67 years were enrolled.

Overall, the GG genotype of rs7096206 polymorphism has a protective association with HIV-1 infection susceptibility with a *p.adjust*-value of 0.028 (OR=0.50 ; 95% CI=0.29-0.85). While the TT genotype of rs503037 and AA genotype of rs1800451 polymorphisms are associated with an increased risk of HIV-1 infection susceptibility (*p.adjust*=0.042 ;OR=3.30; 95% CI=1.21-9.00 and *p.adjust*< 0.001 OR=3.07; 95% CI=1.71-5.51, respectively).

Table. Distribution of genotype and allele frequencies of *MBL2* polymorphisms and susceptibility to HIV-1 infection.

	Polymorphisms	People with HIV-1 (%)	Healthy controls (%)	OR [95 % CI]	*p.adjust*-value
rs7096206	**Genotype frequency**				
	CC	24.00	13.50	1.00 [reference]	-
	CG	13.50	16.00	0.48 [0.24-0.95]	0.104
	GG	62.50	70.50	**0.50 [0.29-0.85]**	**0.028**
	Allele frequency				
	C	30.70	21.50	1.00 [reference]	-
	G	69.30	78.50	**0.62 [0.45-0.85]**	**0.006**
rs5030737	**Genotype frequency**				
	CC	82.00	85.43	1.00 [reference]	-
	CT	7.50	11.26	0.69 [0.33-1.44]	0.978
	TT	10.50	3.31	**3.30 [1.21-9.00]**	**0.042**
	Allele frequency				
	C	85.80	91.10	1.00 [reference]	-
	T	14.20	8.90	1.69 [1.04-2.75]	0.064
rs1800451	**Genotype frequency**				
	GG	62.00	78.15	1.00 [reference]	-
	GA	9.00	9.93	1.14 [0.55-2.37]	>0.999
	AA	29.00	11.92	**3.07 [1.71-5.51]**	**<0.001**
	Allele frequency				
	G	66.50	83.10	1.00 [reference]	-
	A	33.50	16.90	**2.48 [1.72-3.57]**	**<0.001**

Moreover, a significant association between CGA haplotype in the first exon and HIV-1 infection susceptibility was found. was observed in 19 % of people with HIV-1 and 8.61 % of healthy subjects with a *p.adjust*-value of 0.014; indicating that the haplotype CGA is associated with an increased risk of acquiring HIV-1 (OR=1.89; 95 % CI=1.27–2.82).

CONCLUSIONS

Our findings highlight the contribution of the homozygote mutated polymorphisms of the *MBL2* gene in the modulation of HIV-1 infection susceptibility.

- The genetic polymorphisms of *MBL2* are associated with an increase (rs5030737 and rs1800451) and a decrease (rs7096206) in the susceptibility to HIV-1 infection.
- The genotypic and allelic analysis of the *MBL2* gene and the progression of HIV-1 infection to the AIDS stage showed no significant difference in the frequency distributions between the AIDS and non-AIDS groups for all studied polymorphisms.
- A significant increase risk of acquiring HIV-1 only in the CGA haplotype of exon 1.
- No significant difference in the frequency distributions between all studied polymorphisms and AIDS development or antiretroviral treatment response as measured by CD4 + T levels and HIV-1 RNA viral load level was detected (*p.adjust* > 0.05).

Further studies should be performed on a lager human population with diverse ethnicities in order to have a statistical power to detect significant associations and reveal the role of MBL protein on HIV-1 infection susceptibility.

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