IL7RA rs10491434 Polymorphism Is Related to Spontaneous HIV Infection Control: A Retrospective Study

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BACKGROUND

Interleukin 7 receptor (**IL7R**) is vital in the adaptive immune response against HIV. We assessed IL7RA polymorphisms (SNPs) in antiretroviral therapy (ART)-naïve HIV patients for their association with spontaneous HIV infection control.

METHODS

We conducted a retrospective cohort study comprising **667** ART-naïve people living with HIV (PLWH). The participants were categorized into four groups based on disease progression, treated as an ordinal variable: **150** rapid progressors (**RPs**), **334** moderate or typical progressors (**PMs**), **86** long-term elite controllers (**LTNP-EC**), and **97** long-term elite non-controllers (**LTNP-non-EC**). Three SNPs in the IL7RA gene were genotyped using Agena Bioscience's MassARRAY platform: rs6897932 (located in exon 6), rs987106 (located in an intronic region), and rs10491434 (located in the 3' untranslated region [3'UTR]). The association between IL7RA SNPs and spontaneous control of HIV infection was assessed through ordinal logistic regression.

Table 1. Characteristics of the study population. **Statistical analysis**: Values were expressed in absolute numbers (%) and medians (P25-P75). *P*-values were calculated with the Chi-square and Kruskal-Wallis tests.

Characteristics	RPs	MPs	LTNPs-EC	LTNPs-non-EC	*P-value*
No.	150	334	86	97	-
Male	142 (94.6)	283 (84.7)	49 (57.6)	68 (70.1)	**<0.001**
Age at study inclusion (years)	38 (33-44)	38 (33-45)	49 (47-52)	48 (46-52)	**<0.001**
Age at HIV diagnosis (years)	34 (30-38)	32 (27-38)	40 (34-43)	39 (35-44)	**<0.001**
Year at HIV diagnosis	2009 (2007-2010)	2006 (2005-2008)	1992 (1989-1996)	1993 (1991-1998)	**<0.001**
Risk group					**<0.001**
Injection drug users	7 (4.7)	29 (8.7)	63 (74.1)	67 (69.1)	-
Homosexual	126 (84)	220 (65.8)	3 (3.5)	10 (10.3)	-
Heterosexual	15 (10)	76 (22.7)	15 (17.6)	12 (12.4)	-
Others	2 (1.3)	9 (2.7)	4 (4.7)	8 (8.2)	-

RESULTS

Table 2. Allele counts for *IL7RA* SNPs and the Hardy-Weinberg equilibrium analysis in PLWH. **Statistical analysis**: *P*-values were calculated using the chi-square test. **Findings**: All *IL7RA* SNPs exhibited an allele frequency >5%, signifying their relative commonality within the studied population. Moreover, the *IL7RA* SNPs adhered to Hardy-Weinberg equilibrium, implying that the observed genotypic frequencies did not significantly deviate from the expected frequencies based on the assumption of genetic equilibrium.

rs10491434	**A**	**G**	**χ^2**	***P-value***
RP	219 (73.0%)	81 (27.0%)	0.643	0.423
MP	476 (71.3%)	192 (28.7%)	1.506	0.220
LTNP-non-EC	134 (69.1%)	60 (30.9%)	0.369	0.543
LTNP-EC	109 (63.4%)	63 (36.6%)	1.390	0.238
All PLWH	938 (70.3%)	396 (29.7%)	3.289	0.078
rs6897932	**C**	**T**	**χ^2**	***P-value***
RP	228 (76.0%)	72 (24.0%)	2.262	0.133
MP	515 (77.1%)	153 (22.9%)	1.191	0.275
LTNP-non-EC	149 (76.8%)	45 (23.2%)	0.016	0.901
LTNP-EC	132 (76.7%)	40 (23.3%)	2.014	0.156
All PLWH	1024 (76.8%)	310 (23.2%)	0.185	0.665
rs987106	**T**	**A**	**χ^2**	***P-value***
RP	152 (51.0%)	146 (49.0%)	0.164	0.686
MP	349 (52.2%)	319 (47.8%)	0.001	0.971
LTNP-non-EC	105 (54.7%)	87 (45.3%)	0.497	0.481
LTNP-EC	102 (59.3%)	70 (40.7%)	1.516	0.218
All PLWH	708 (53.2%)	622 (46.8%)	0.158	0.697

Figure 1. Distribution of *IL7RA* genotypes and spontaneous control of HIV infection. **Statistical analysis**: A linear association test was conducted in patient groups. **Findings**: A significant genetic association was observed between the G allele of rs10491434 and a greater probability of experiencing spontaneous control of HIV infection

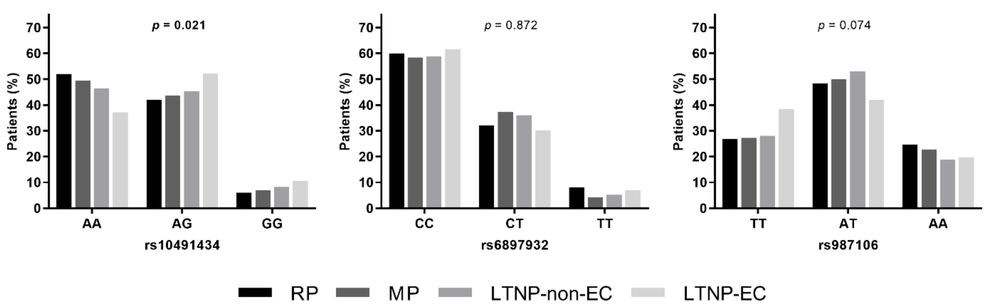


Table 3. Genetic association of *IL7RA* SNPs with spontaneous HIV control in treatment ART-naïve PLWH. **Statistical analysis**: The data underwent analysis using ordinal logistic regressions, with adjustments made for gender, age at HIV diagnosis, and injection drug uses as risk factors for HIV acquisition. The *IL7RA* haplotypes encompass the three SNPs. Significant differences are highlighted in bold. **Abbreviations**: 95%CI = 95% confidence interval; aOR = adjusted odds ratio; OR = odds ratio. **Findings**: Individuals carrying the rs10491434 G allele demonstrated a higher likelihood of experiencing spontaneous control of HIV infection (*p*=0.023). Moreover, a significant association was observed with the *IL7RA* GCT haplotype, composed of the three SNPs, concerning the control of untreated HIV infection (*p*=0.050).

		Unadjusted		Adjusted	
SNPs	**%**	**OR (95%CI)**	***P-value***	**aOR (95%CI)**	***P-value***
Alleles					
rs10491434 G	30.5	1.28 (1.02 - 1.61)	**0.032**	1.33 (1.04 - 1.69)	**0.023**
rs6897932 T	23.1	0.98 (0.77 - 1240)	0.837	0.89 (0.69 – 1.13)	0.334
rs987106 A	46.2	0.84 (0.69 - 1031)	0.095	0.89 (0.72 – 1.10)	0.279
Haplotypes					
ACA	45.9	0.91 (0.78; 1.05)	0.193	0.97 (0.73; 1.28)	0.821
ATT	23.7	0.97 (0.83; 1.13)	0.701	0.97 (0.73; 1.32)	0.887
GCT	29.0	1.23 (1.06; 1.42)	**0.006**	1.34 (1.00; 1.79)	**0.050**

CONCLUSIONS

- The presence of the G allele in the SNP rs10491434 of *IL7RA* is linked to a higher probability of spontaneous HIV control.
- The GCT haplotype of *IL7RA*, which consists of the minor allele of rs10491434 and the major alleles of rs6897932 and rs987106, exhibited a higher probability of spontaneous HIV control.
- The importance of the *IL7RA* rs10491434 G allele in HIV control is highlighted. Insights gained offer promise for novel therapeutic strategies in managing HIV by understanding its role in disease progression.

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