

TABLE 226-6 HOST GENETIC FACTORS THAT INFLUENCE RISK OF HIV-1 ACQUISITION AND RATES OF HIV-1 DISEASE PROGRESSION

Gene ^a	Genetic Variation	Mechanisms ^b	Genetic Effect on HIV-AIDS ^c
Genes in MHC Locus			
<i>HLA-B</i>	B*27 and B*57 B*35	Presentation of specific HIV antigens Restriction of specific HIV peptide presentation	Slower progression to AIDS; lower viral load Faster progression to AIDS; higher viral load
<i>HLA class I allele</i>	HLA-Bw4	Providing ligands for activating KIR	Slower progression to AIDS
	Homozygosity of <i>HLA</i> -class I alleles	Reduced repertoire for epitope recognition	Faster progression to AIDS; increased risk of mother-to-child transmission
<i>HLA class II allele</i>	Shared donor-recipient <i>HLA</i> alleles	Preadaptation of HIV strains	Faster disease progression
	Rare <i>HLA</i> alleles	Limited adaptation of HIV strains; less frequent escape mutants	Protection against HIV infection
<i>HLA class II allele</i>	<i>HLA-DRB1</i> alleles	Influences protein specificity of CD4+ T cell responses to HIV Gag and Nef proteins	<i>HLA-DRB1*15:02</i> —lower viral load; <i>HLA-DRB1*03:01</i> —higher viral load
<i>HLA</i> extended haplotype	A1-B8-DR3-DQ2 (AH 8.1)	Increased proinflammatory responses; higher TNF- α production	Faster progression to AIDS
<i>HLA-C</i>	35 kb upstream, rs9264942-C	Increased expression of <i>HLA-C</i>	Decreased viral load set point
<i>HCP5</i>	rs2395029-G	Linkage disequilibrium with <i>HLA-B*57:01</i>	Lower viral load
<i>MICA</i>	Noncoding SNP near <i>MICA</i> , rs4418214-T	May affect <i>HLA</i> class I peptide presentation—linkage with protective <i>HLA-B</i> alleles	Enriched in HIV-1 controllers
<i>PSORS1C3</i>	rs3131018-A	May affect <i>HLA</i> class I peptide presentation	Enriched in HIV-1 controllers
<i>ZNRD1</i>	rs9261174-C	Possible interference in processing of HIV transcripts; influences <i>ZNRD1</i> expression; linkage disequilibrium with <i>HLA-A10</i>	AIDS disease retardation
Chemokine Receptors			
<i>CCR5</i>	32-bp deletion in the ORF (Δ 32), rs333	Truncated <i>CCR5</i> protein	Δ 32/ Δ 32: resistance to acquiring HIV infection Δ 32/wild type: delays AIDS onset; improves immune reconstitution during ART
<i>CCR2</i>	Promoter SNPs, haplotypes (HHA to HHG*2)	Altered <i>CCR5</i> expression, e.g., HHE allele correlates with high <i>CCR5</i> expression	HHE/HHE: increased HIV/AIDS susceptibility
	SNP in ORF (64 V \rightarrow I), rs1799864	Possibly due to linkage with polymorphism in <i>CCR5</i> promoter	64I: delayed AIDS onset
<i>CXCR6</i>	rs2234358 G \rightarrow T in the 3'UTR	Trafficking of effector T cells and activation of NK T cells Minor HIV co-receptor	Prevalence of rs2234358-T was lower in long-term nonprogressors
<i>CX3CR1</i>	SNPs in ORF (249 V \rightarrow I); and 280 T \rightarrow M, rs3732378)	280M reduces receptor expression and binding of fractalkine, the CX3CR1 ligand	249I and 280M are associated with faster AIDS onset in some Caucasian cohorts; inconsistent effects were detected in other cohorts
<i>DARC</i>	African-specific promoter SNP (-46T \rightarrow C), rs2814778	-46C/C associates with low neutrophil counts; influences circulating chemokine levels; alters HIV binding to RBCs and transfection of HIV-1	-46C/C: increased risk of acquiring HIV but slower HIV disease progression; Duffy-null-associated low neutrophil trait associated with increased HIV risk in Africans
Chemokines			
<i>CCL3L</i> , <i>CCL4L</i>	Gene copy number of <i>CCL3L</i> and <i>CCL4L</i>	High numbers of <i>CCL3L</i> and <i>CCL4L</i> gene-containing segmental duplications correlate with high <i>CCL3L</i> and <i>CCL4L</i> levels	Gene copy number lower than population median associates with increased HIV/AIDS susceptibility and reduced immune reconstitution during ART
<i>CCL5</i>	Promoter SNPs	Altered gene expression	Altered HIV-AIDS susceptibility
<i>CCL2</i>	Promoter SNP (-2578 T \rightarrow G), rs1024611	-2578G allele: increased <i>CCL2</i> expression and monocyte recruitment	-2578G/G associates with increased risk of developing HIV-1-associated dementia and a rapid AIDS onset
Cytokines			
<i>IL-6</i>	Promoter SNP (-174 G \rightarrow C), rs1800795	-174G/G associates with increased IL-6 and CRP levels	-174G/G associates with high risk of KS development and variable recovery of CD4 cells during ART
<i>IL-10</i>	Promoter SNP (-592 C \rightarrow A), rs1800872	-592A results in decreased IL-10 levels	-592A associates with increased HIV-AIDS susceptibility
Innate Immunity Genes			
<i>MBL</i>	Coding alleles (O)	Low plasma concentration and structural variation of <i>MBL</i> protein	Slow progression to AIDS in heterozygous subjects (A/O)
	X allele (promoter SNP -221)	Decreased levels of <i>MBL</i> protein	Faster progression to AIDS in homozygous X/X subjects
<i>Apobec-3G</i>	ORF SNP (186 H \rightarrow R), rs8177832	Reduced anti-HIV-1 activity	186R associates with rapid AIDS onset in African Americans
<i>TLR7</i>	ORF SNP (Gln11Leu), rs179008	Decreased expression of <i>TLR7</i> leading to lack of recognition of HIV-infected cells	The Leu-containing protein associated with higher viral load and faster progression to AIDS

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