Natural history modifiers – version 11

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New publications in this version :

HLA-B/HCP5, ZNRD1	*Limou et al, JID, 2009*
PPIA	*Rits et al, PLoS One, 2008*
HLA-B/HCP5	*Dalmasso et al, PLoS One, 2008*
DARC	*Walley et al – Julg et al – Winkler et al – Horne et al, Cell Host Microbe, 2009*
CCL3L1	*Urban et al – Bhattacharya et al – Field et al – He et al, Nat Med, 2009*
APOBEC3B	*An et al, JID, 2009*
HLA-C, HLA-B/HCP5	*Van Manen, AIDS, 2009*
HLA-C	*Thomas et al, Nat Gen, 2009*
HLA-B/HCP5, HLA-C, ZNRD1, CCR5	*Fellay et al, PLoS Genetics, 2009*
PROX1	*Herbeck et al, JID, 2010*
*HLA-B*5703*	*Pelak et al, JID 2010*

Chemokine receptors

Gene	Protein	Allele (SNP)	RefSNP	Genetic consequence	Effect on natural history	Confirmation	References
CCR5	Chemokine (C-C motif) receptor 5	554_585del32	rs333	CCR5 Δ32, Truncated protein	CCR5 deletion restricts both HIV-1 infection and progression to AIDS. It acts in a recessive way against HIV infection and in a dominant way for delaying disease progression (Dean 1996, Samson 1996, Huang 1996). The effect on HIV control is the first non-HLA association confirmed in a GWAS (Fellay 2009).	**YES**	*Dean et al, Science, 1996* *Samson et al, Nature, 1996* *Huang et al, Nat Med 1996* *Fellay et al. PloS Gen 2009*
		59029G>A (P1 haplotype), included in HHE haplotype	rs1799987	Promoter polymorphism; Increased gene transcription rate	In the absence of the protective alleles CCR5Δ32 and CCR2 64I, homozygosity AA is associated with accelerated progression to AIDS. A thorough analysis of the haplotypic structure of the CCR2/CCR5 gene cluster indentifies an haplotype HHE that carries the original promoter polymorphism. Genotyping should preferably characterize HHE (McDermott 1998,Martin 1998, Mummidi 1998, Gonzalez 1999).	**YES**	*McDermott et al, Lancet, 1998* *Martin et al, Science, 1998* *Mummidi et alNat med 1998* *Gonzalez et al, PNAS 1999*
		m303 (303T>A)	rs1800560	Stop codon at amino acid 101 ; truncated protein	Unfrequent. When present with CCR5Δ32, the rare allele confers resistance to HIV infection (Quillent 1998, Carrington 1997, Ometto 1999).	**YES**	*Quillent et al, Lancet, 1998* *Carrington et al. Am J Med Genet. 1997*

							Ometto et al. AIDS 1999
CCR2	Chemokine (C-C motif) receptor 2	190G>A	rs1799864	V64I	Dominant effect of the allele. Delays progression to AIDS.	**YES**	*Smith et al, Science, 1997*
CX3CR1	Chemokine (C-X3-C motif) receptor 1	839C>T always occurs on a 745A (249I) bearing haplotype	rs3732378	T280M	Recessive effect of the allele. 249I_280M homozygosity may increase susceptibility to HIV infection and accelerates disease progression in Caucasians. No effect of 249I without 280M on disease progression (Faure 2000, Faure 2003). Only 249I homozygosity (and not 280M) leads to more rapid disease progression in american children (Singh 2005). No influence on susceptibility and progression (Mc Dermott 2000, Hendel 2001, Kwa 2003). Increased frequency of 249I among long term non-progressors (Vidal 2005).	Controversial	*Faure et al, Science, 2000* *Faure et al, J Acquir Immune Defic Syndr, 2003* *Singh et al, JID, 2005* *McDermott et al, Science, 2000* *Hendel et al, J Acquir Immune Defic Syndr, 2001* *Kwa et al, AIDS 2003* *Vidal et al, JAIDS 2005*
IL8RA (CXCR1)	Interleukin 8 receptor, alpha	92T>G, 1003C>T	rs16858811 rs16858808	M31R R335C	An haplotype carrying 31R and 335C is protective for disease progression probably through modulation of CD4 and CXCR4 expression.	NO	*Vasilescu et al. PNAS 2007*
CXCR6	Chemokine (C-X-C motif) receptor 6	1469G>A	rs2234355	E3K	Increased survival time after PCP diagnosis among African-Americans.	NO	*Duggal et al, Genes Immun., 2003*
DARC	Duffy antigen receptor for chemokines	-46T>C	rs2814778	Disrupts the binding site of an erythroid-specific transcription factor: results in selective loss of DARC expression on RBCs	Homozygosity for the null allele increases susceptibility to infection, but associates with slower disease progression if infection does occur (He 2008). However, 4 independent groups could not replicate any of the associations.	NO	*He et al, Cell Host Microbe, 2008* *Walley et al. Cell Host Microbe 2009* *Julg et al. Cell Host Microbe 2009* *Winkler et al. Cell Host Microbe 2009* *Horne et al. Cell Host Microbe 2009*

Chemokines

Gene	Protein	Allele (SNP)	RefSNP	Genetic consequence	Effect on natural history	Confirmation	References
CCL2-*CCL7*-*CCL11*	Chemokine (C-C motif) ligand 2 -Chemokine (C-C motif) ligand 7 - Chemokine (C-C motif) ligand	Haplotype 7 (-2136T,767G, -1385A) (Modi et al) -2578A>G(or –2518A>G) -2136A>T	rs1024610 (-2136A>T) rs2857657 (767C>G) rs4795895 (-1385G>A) -2578A>G	-2136: promoter CCL2 (Higher promoter activity) -767: intron 1 CCL2 -1385:promoter CCL11 -2578: promoter CCL2 increase in CCL2 protein expression, due to	Decreased susceptibility to HIV-1 infection in Caucasians (Modi 2003). Reduced risk of acquiring HIV-1. However, accelerated disease progression once infection is established (Gonzalez 2002). Associated with AIDS dementia. Reported not to be associated with disease progression in children (Singh	**YES**	*Modi et al, AIDS, 2003* *Gonzalez et al, PNAS, 2002* *Singh et al. AIDS, 2006,* *Shiramizu et al J Investig Med 2006* *Mummidi et al, Genes & Immunity 2008*

	11	Haplotype GA (Gonzalez et al)	(not available)	differential binding of the transcription factor IRF-1 to the polymorphic region	2006).		
CCL3 (MIP1α)	Chemokine, CC Motif, Ligand 3	459C>T complete linkage disequilibrium with 113>T 1342G>T -891T>C	rs1719134 rs35511254 rs34171309 rs36048177	Intron 1 Exon 3 (E78D) Promoter	Disease accelerating effect of CT/CT haplotype pair (113C, 459T) in European Americans. In African Americans, TT haplotype associates with lower risk of acquiring HIV (Gonzalez 2001). 3 SNPs (rs35511254, rs3417109 and rs36048177) associated with protection against HIV-1 infection (Modi 2006).	**YES**	*Gonzalez et al, PNAS, 2001* *Modi et al, Am J Hum Genet, 2006*
CCL3L1 (MIP1αP)	CC chemokine ligand 3-like 1	Variable gene copy number	Not applicable	Gene dose effect	CCL3L1 copy number lower than the population average was originally found to be associated with increased HIV susceptibility and higher risk of disease progression (Gonzalez 2005). The same group also reported that higher CCL3L1 copy number associates with higher CD4 T cell response to gag and better treatment responses. Many groups have failed to replicate those results and the issue remains controversial.	Controversial	*Gonzalez et al, Science, 2005*, *Dolan et al Nat Immunol 2007* *Bugeja et al, AIDS, 2004* *Nakajima et al, Immunogenetics, 2007* *Kuhn et al, AIDS, 2007* *Shalekoff, AIDS, 2008* *Urban et al. Nat Med 2009* *Field et al. Nat Med 2009* *Bhattacharya et al. Nat Med 2009* *He et al. Nat Med 2009*
CCL4L (SCYA4L)	Chemokine, CC Motif, Ligand 4-like	R22H CCL4L2 variant: C>T at *Msp*I restriction site	Not available rs1049811	Non-synonymous R22H in CCR5-interacting region Intron 2; Homozygotes L2/L2 express half the level of CCL4L compared to common allele.	Dominant effect. Worse survival in Caucasians (Capoulade-Metay 2005). Higher frequency of L2 allele in HIV+ Caucasians.	NO NO	*Capoulade-Metay et al, AIDS, 2005* *Colobran et al, J. Immunol., 2005*
CCL5 (RANTES)	Chemokine, CC Motif, Ligand 5	-403G>A and -28C>G; Described haplotypes I:-403G/-28C II:-403A/-28C III: -403A/-28G	rs2107538 (-403) rs2280788 (-28)	Promoter polymorphism; elevated promoter activity	Haplotype III reduced CD4+ lymphocyte depletion rates in Japanese and associated with delay in HIV-1 disease progression (Liu 1999). Haplotype II increases susceptibility to infection, but delays progression to AIDS in infected Caucasian (McDermott 2000). Haplotype II is associated with increased susceptibility and more rapid progression to AIDS in European Americans (Gonzalez 2001). No effect of haplotype II on HIV-1 susceptibility in Caucasians (Fernandez 2003, Liu 2004).	General evidence for the various haplotype effects	*Liu et al, PNAS, 1999* *McDermott et al, AIDS, 2000* *Gonzalez et al, PNAS, 2001* *Fernandez et al, AIDS Res Hum Retroviruses, 2003* *Liu et al, JID, 2004*

		In1.1 (T>C) Described haplotypes with -403G>A, -28C>G, In1.1T>C -222T>C R1: GCTT R2: ACTT R3: ACCT R4: ACCC R5: AGCT	rs2280789	Intron 1; downregulates transcription	In1.1C associates with increased risk of HIV infection in European and African Americans. Haplotype R3 accelerates disease progression in European and African Americans. Proposed to improve the haplotype definitions based on -403G>A/-28C>G INT1.1C allele is associated with protection from death in Ugandan population		*An et al, PNAS, 2002*, *Duggal et al, JAIDS, 2005* *Wichukchinda et al, AIDS, 2006* *Cooke et al, JID, 2006*
CCL18(DC-CK1-/PARC/AMAC-1) *CCL3 (MIP1α)* *CCL4 (MIP1B)*	Chemokine C-C motif ligand 18 Chemokine, CC Motif, Ligand 3 Chemokine C-C motif ligand 4	Extensive SNP analysis	NA	Promoter, intron, exon or 3'UTR	7 highly correlated SNPs spanning 36 kb containing all three genes were associated with more rapid disease progression.	NO	*Modi et al, Am J Hum Genet, 2006*
CXCL12 (SDF-1)	Chemokine (C-X-C motif) ligand 12	SDF1-3'A (801G>A)	rs1801157	3'UTR	Accelerated progression to AIDS (Van Rij 1998, Mummidi 1998, Geskus 2005, Brambilla 2000, Tresoldi 2002, Bleiber 2005, Petersen 2005, Daar 2005). Recessive effect of the allele. Homozygosity delays onset of AIDS in all ethnicities (Winkler 1998). No effect on progression to disease and death (Hendel 1998, Magierowska 1999, Meyer 1999, Balotta 1999, Mangano 2000, Ioannidis 2001, Soriano 2002, Vidal 2005, Reiche 2006). Haplotype analysis separates the effects of rs754618 (increased risk of infection), while rs1801157 (=SDF1-3'A) was associated with protection against infection (Modi 2005).	Controversial	*Van Rij et al, AIDS, 1998*, *Mummidi et al, Nat. Med. 1998*, *Geskus et al. J Acquir Immune Defic Syndr. 2005* *Brambilla et al, JID, 2000*, *Tresoldi, JID, 2002*, *Bleiber et al, J Virol 2005*, *Petersen et al, JAIDS 2005*, *Daar et al. JID 2005* *Winkler et al, Science, 1998* *Hendel et al, J Acquir Immune Defic Syndr Hum Retrovirol, 1998*; *Magierowska et al, Blood, 1999*; *Meyer et al, AIDS, 1999*; *Balotta et al, JID, 1999*; *Mangano et al, J Acquir Immune Defic Syndr., 2000*; *Ioannidis et al, Ann Intern Med, 2001*; *Soriano et al, JID, 2002*,

							Vidal et al, JAIDS 2005, Reiche et al, Int J Immunogenet, 2006 Modi et al. Genes Immun., 2005

Cytokines

Gene	Protein	Allele (SNP)	RefSNP	Genetic consequence	Effect on natural history	Confirmation	References
IL1α, IL1β	Interleukin 1 alpha, interleukin 1 beta	Multiple SNPs	Multiple SNPs	Multiple SNPs	Exhaustive genotyping did not identify relevant associatrion with disease progression	No	*Do et al, J Infect Dis 2006*
IL-4	Interleukin 4	-589C>T	rs2243250	Promoter polymorphism; increased transcription.	-589T associates with acquisition of the syncytium (SI) inducing phenotype in Japanese. Trend for accelerated disease progression (Nakayama 2000). -589T protects against HIV-1 disease progression in Caucasians by reducing viral load and in Thai patients (Nakayama 2002, Vasilescu 2003, Wichukchinda 2006). No association with SI inducing phenotype and protection against progression in European and African Americans (Modi 2003). No effect on disease progression, but delayed acquisition of X4 HIV-1 in Caucasians (Kwa 2003).	Controversial	*Nakayama et al, J.Virol., 2000* *Nakayama et al, JID, 2002* *Vasilescu et al, Genes Immun, 2003* *Wichukchinda et al, AIDS, 2006* *Modi et al, Immunogenetics, 2003* *Kwa et al, AIDS, 2003*
IL-10	Interleukin 10	-592C>A	rs1800872	Promoter polymorphism; diminished IL-10 production.	Dominant effect of the allele. Carriers are at increased risk for HIV-1 infection, and they progress more rapidly to AIDS.	NO	*Shin et al, PNAS, 2000*
IL-12B	interleukin 12B	*IL12Bpro2*, a 4 nucleotide promoter deletion	not available	Associated with higher IL-12 secretion	IL-12 increases cell surface expression of CCR5. The paper proposes an epistatic interaction between IL12Bpro2 and CCR5 common genotype and high viral load.	NO	*Gabutero et al. AIDS 2007*
IL-18	Interleukin 18 (interferon-gamma-inducing factor)	-656G>T -607A>C -137G>C +113T>G +127C>T	rs1946519 rs1946518 rs187238 rs360718 rs360717	5'UTR and non coding-exon 1	No clear association between IL18 genotypes and viral load and CD4+T cell count. -607C associated with an increased risk of HIV-1 infection	NO	*Song et al, Clin Exp Immunol, 2006* *Segat et al, Immunogenetics, 2006*
IFNG	Interferon gamma	-179G>T	not available	Promoter polymorphism; rare allele inducible by TNF-α, increasing INF-χ production.	Accelerated rate of CD4 depletion in African Americans.	NO	*An et al, JID, 2003*

IRF1	Interferon regulatory factor-1	619A>C, 6516G>T, microsatellite 179 (=12 GT repeats in intron 7)	rs17848395 rs17848424	Protective alleles associated with low basal *IRF-1* expression and reduced responsiveness to exogenous IFN-γ stimulation	619A and 6516G and the microsatellite 179 are associated with HIV resistance. Not associated with disease progression.	NO	*Blake Ball et al, AIDS 2007*
LTA (TNFβ)	Lymphotoxin alpha	c2 microsatellite allele; in haplotypic association with HLA-Cw*03	not available	Intron 1 variant	More frequent in slow progressors in Caucasians.	NO	*Khoo et al, AIDS, 1997*
DEFB1	*β-defensin 1*	-44C>G -52G>A -20G>A	rs1800972 rs1799946 rs11362	5'UTR variant	Associated in two studies (Caucasian, brazilian populations) with increased risk of infection in children. -52GG genotype associates with lower HIV RNA level in breast milk but not in plasma.	YES?	*Braida et al, AIDS, 2004* *Milanese et al, AIDS, 2006* *Baroncelli et al, AIDS, 2008*

Cytokine receptors

Gene	Protein	Allele (SNP)	Ref seq.	Genetic consequence	Effect on natural history	Confirmation	References
IL1RN (IL1Ra) IL1R1	interleukin 1 receptor antagonist, interleukin 1 receptor, type I	Multiple SNPs *IL1RN*_2134T>G	rs2232354	*IL1RN* Intron 2 variant	*IL1RN* variant Associated with slow disease progression. No definitive association with genetic variants in IL1R1	No	*Do et al, J Infect Dis 2006*
IL4R	Interleukin 4 receptor alpha chain	not available	not available	I50V Haplotype or SNPs associated with :E375A and/or C406R and/or S411L and/or S478P and/or Q551R and/or V554I	V50 homozygosity is associated with slow progression. Some haplotypes may be associated with differential susceptibility to infection.	NO	*Soriano et al., Immunogenetics, 2005*
IL2Rα IL4Rα IL10Rα IFNγR1	Interleukin 2 receptor alpha chain Interleukin 4 receptor alpha chain	104 single nucleotide polymorphisms and four insertions/ deletions with a	NA		Weak associations for 13 polymorphisms with differential susceptibility to disease progression	NO	*Do et al. Immunogenetics, 2005*

	Interleukin 10 receptor alpha Interferon gamma, receptor 1	minor allelic >1%					
IFNAR1	Interferon alpha receptor 1	19 SNP with a minor allelic >1% +18339G>C +30127C>T	 rs2257167 rs2254315	 Val168Leu Intron	Putative associations with AIDS disease development for 4 SNP and 3 haplotypes. Associationof the 2 indicated SNPs with AIDS progression	NO	*Diop et al. Biomed. Pharmacother, 2006*

HLA/KIR

Gene	Protein	Allele (SNP)	Ref seq.	Genetic consequence	Effect on natural history	Confirmation	References
HLA-A *HLA-B* *HLA-C*	Major histocompatibility complex, class I,	Homozygosity at A or B or C loci	HLA-sequences	NA	Accelerated disease progression. Certain ancestral haplotypes are associated with disease progression, possibly including indirect effects due to linkage disequilibrium in the region (Carrington 1999, Flores-Villanueva 2003).	**YES**	*Carrington et al, Science, 1999* *Flores-Villanueva, J Immunol, 2003*
HLA-A	Major histocompatibility complex, class I, A	NA	HLA-A sequences	NA	Of described HLA-A alleles (HLA-A sequences), only few have been consistent with regard to HIV disease: Supertype A2 has been associated with dicreased susceptibility to HIV infection in Caucasians and Africans. HLA-A*23 associates with fast progression to AIDS in Caucasians and Africans.	**YES**	*MacDonald et al, JID, 2001* *Liu et al, JID, 2003* *Kaslow et al, Nat.Med, 1996* *Tang et al, J.Virol, 2002*
HLA-B	Major histocompatibility complex, class I, B	NA	HLA-B sequences	NA	HLA-B*5701 has been shown in multiple GWAS to be the strongest determinant of HIV control in Caucasians (association observed for a tagging SNP located in the HCP5 gene). B*5703 is the strongest protective genetic factor in a GWAS in African Americans Supertype B7, HLA-B*08, Haplotype A*01 B*08 DR3, B22 (B*54 B*55, B*56) are associated with accelerated progression to AIDS in Caucasians HLA-B*35 and HLA-B*35-Px (=B*3502, B*3503, B*3504, B*5301 in Caucasians and Africans B*27, and B*51 are associated with slow progression to AIDS in Caucasians, and B*57 with all ethnicities. Bw4 is associated with decreased risk of transmission.	**YES**	*Trachtenberg et al, Nat.Med, 2003* *Steel et al, Lancet, 1988* *Dorak et al, JID, 2003* *Kaslow et al, Nat.Med, 1996* *Scorza-Smeraldi et al, Lancet, 1986* *Itescu et al, J Acquir Immune Defic Syndr. 1992* *Carrington et al, Science, 1999* *Gao et al, NEJM, 2001* *Welzel et al AIDS 2007* *Fellay et al. Science 2007*

							Limou et al. JID 2009 *Dalmasso et al. PLoS One 2008* *Fellay et al. PLoS Gen 2009* *Pelak et al. JID 2010*
HLA-C	Major histocompatibility complex, class I, C	-35kbT>C	rs9264942	Association with HLA-C expression.	Minor allele C associates both with better HIV control (lower HIV viral load and slower progression) and higher expression of HLA-C protein. In high LD with HLA-C 4-digit alleles (Thomas 2009).	**YES**	*Fellay et al, Science, 2007* *Dalmasso et al. PLoS One 2008* *Van Manen et al. AIDS 2009* *Fellay et al. PLoS Gen 2009* *Thomas et al. Nat Gen 2009*
HLA-DRB1	Major histocompatibility complex, class II, DRB1	NA	HLA-DRB1 sequences	NA	Reports on HLA-II alleles influencing HIV disease are not consistent. However, several studies suggest the following associations for HLA-DRB1: Haplotype DR3 (DRB1*0301-DQA1*0501-DQB1*0201) and Supertype DR11and accelerated progression in Caucasians and Africans. Supertype DR13 and haplotype DRB1*13-DQB1*06 and low rate of disease progression in mixed ethnicity populations.	Under debate	*Just et al, J.Pediatr, 1995* *Brettle et al, AIDS, 1996* *Hendel et al, J. Immunol, 1999* *Itescu et al, PNAS, 1994* *Malhotra et al, J.Clin.Invest., 2001* *Lacap et al, AIDS, 2008*
HLA-G	HLA-G histocompatibility antigen, class I, G	Multiple variants analysed. 3'UTR 3743C>T, del 14bp, 3777G>C, 5'URR. Exon 2 1154G>A	HLA-G sequences	Proposed instability of mRNA, synonymous variant	Two mechanisms discussed: HLA compatibility, or functional consequences of the polymorphisms. Controversial role of the exon 2 variant	NO	*Aikhionbare et al. AIDS Res Ther 2006*, *Aikhionbare et al. AIDS 2001*, *Matte et al, AIDS 2002*,
KIR	Killer immuoglobulin-like receptors	KIR3DS1/3DL1 epistatic with HLABw4 –80Ile KIR3DS1	KIR3DS1/3DL1 databank	NA	Delayed progression in Caucasians and African Americans. In the absence of HLABw4-80Ile, the KIR allele is associated with rapid progression. Additonal KIR/HLA-B/-C combinations have been investigated by Gaudieri et al. Functional evidence of the KIR3DS1/HLABw4-80I combined influence on the effectiveness of anti-HIV NK cell activity (Alter 2007). Both KIR3DS1 homozygosity and the combination of	**YES** NO	*Martin et al, Nat.Genet., 2002* *Lopez-Vazquez et al, Hum. Immunology, 2005* *Gaudieri et al. Mol Immunol 2005*, *Gaudieri et al, Genes Immun 2005* *Martin et al Nat Genet 2007* *Alter et al, JEM, 2007*

		homozygosity			KIR3DL1/HLA-B*57 associated with a reduced risk of infection (Boulet 2008).		Boulet et al (1), AIDS, 2008 Boulet et al (2), AIDS, 2008

Other

Gene	Protein	Allele (SNP)	RefSNP	Genetic consequence	Effect on natural history	Confirmation	References
TSG101	Tumor susceptibility gene 101	–183T>C +181A>C	rs2292179 rs1395319	Promoter variant Intron	Possibly influencing CD4 depletion (Bleiber 2005). Haplotype –183T/+181C is associated with slower disease progression (Bashivora 2006). Haplotype –183C/+181C is associated with rapid AIDS progression (Bashivora 2006).	**YES**	Bleiber et al, J Virol 2005 Bashirova et al, J Virol, 2006
PPIA	Peptidylprolyl isomerase A (cyclophilin A)	1575C>G 1604C>G 1650A>G	NA rs8177826 rs6850	Promoter variants. Differential nuclear protein binding efficiency in gel shift assay (1575C>G 1604C>G)	Influencing CD4 depletion and disease progression and possibly susceptibility to infection.	**YES**	Bleiber et al, J Virol 2005 An et al, PloS Pathogen 2007 Rits et al. PLoS One 2008
PML (TRMI19)	Promyelocytic leukemia (TRMI19)	–225C>T	rs2301273	Promoter variant	Possibly influencing CD4 depletion as regressive trait	NO	Bleiber et al, J Virol 2005
TRIM5α	Tripartite motif-containing 5	127C>T 34G>T 407G>A 12468G>A 15142C>T	rs3740996 rs11601507 rs10838525 rs11038628 rs28381981	H43Y V112F R136Q G249D H419Y	Impaired TRIM5α restriction of N-MLV in vitro (Sawyer 2006, Speelmon 2006, Goldschmidt 2006, Javanbakht 2006). Common human variants of TRIM5α have no effect or modest effect on HIV-1 disease progression. Accelerated disease progression in patients homozygous for 43Y (van Manen 2008).	YES (N-MLV) Controversial (HIV-1)	Sawyer et al. Current Biology 2006 Speelmon et al. J. Virol. 2006, Goldschmidt et al, Retrovirology, 2006 Javanbakht et al, Virology, 2006 Nakayama et al, Immunogenetics 2007 van Manen et al, PloS Pathogens, 2008
PTPRC	Protein tyrosine phosphatase, receptor type, C (CD45)	77C>G	rs17612648	Synonymous P57P; Abnormal CD45 splicing.	Increased susceptibility to infection in Caucasians.	NO	Tchilian et al, AIDS, 2001
CD209 (DC-SIGN)	DC-SIGN: Dendritic cell-specific intracellular adhesion molecule-3-	Allele 6/7 (common allele: 7/7 = 7 repeats) -336T>C	NA rs4804803	Deletion of one 69 bp-repeat in DC-SIGN repeat region Promoter	Allele 6/7 associates with decreased susceptibility to HIV-infection (Liu 2004). No association (Wichukchinda 2007). Increased risk for HIV infection in Caucasians, but only when perinatally acquired, NOT mucosally (Martin	NO	Liu et al, JID, 2004 Martin et al, J. Virol, 2004 Koizumi et al AIDs Res Hum Retrovir 2007, Wichukchinda et al AIDS Res Hum Retrovir 2007

	grabbing non-integrin	-139T>C Multiple variants in Neck domain	rs2287886 NA	Promoter Neck domain variants	2004). No effect (Koizumi 2007, Wichukchinda 2007) Associated with accelerated progression to AIDS (Koizumi 2007). No effect (Wichukchinda 2007) Neck-region alleles with <5 repeats units associate with resistance to HIV-1 infection in Chinese (Zhang 2008). Multiple allelic variants and splicing isoforms influence presence and stability of DC-SIGN multimers on cell surface (Serano-Gomez 2008).		*Zhang et al, JID, 2008* *Serrano-Gomez et al, J Biol Chem, 2008*
CLEC4M (DC-SIGNR)	C-type lectin domain family 4, member M	Five, six, nine sequence repeats in the neck domain (seven in common allele)	NA	Neck domain variants.	Do not exhibit defects in pathogen capture (Gramberg 2006). Homozygote 7/7 is associated with an increased risk of HIV-1 infection (Liu 2006). Heterozygote 7/5 and 9/5 are correlated with resistance to HIV-1 infection (Liu 2006, Wichukchinda 2007). Gender-specificity? Homozygote 5/5 is associated with resistance to infection (Rathore 2008)	Controversial	*Gramberg et al. Virology, 2006* *Liu et al. JID 2006,* *Barreiro et al, J Infect Dis 2006* *Wichukchinda et al AIDS Res Hum Retrovir 2007* *Rathore et al, J Clin Immunol, 2008*
SLC11A1 (NRAMP1)	Solute carrier family 11 (proton-coupled divalent metal ion transporter), member 1	Allele 3: $T(GT)_5AC(GT)_5$ $AC(GT)_9$ (in linkage disequilibrium with 274C>T and 469+14G>T)	NA	GT repeat in 5'UTR/promoterincreased expression	Allele is more frequent in HIV negative Hispanics than in HIV positives (Marquet 1999). No association observed in Africans (Donninger 2004).	NO	*Marquet et al, JID, 1999* *Donninger et al, J Med Genet, 2004*
VDR	Vitamin D receptor	C>T, *Bsm*-I site, B allele=T T>C, *Fok*I site, F allele=C	rs1544410 rs2228570	Intron 8 variant Non-synonymous M1T; Elimination of first translation start codon. Shorter protein.	BB homozygosity is a risk factor for progression to AIDS in Caucasians (Barber 2001, Nieto 2004). Heterozygosity associates with faster progression to AIDS in Caucasians (Nieto 2004).	NO NO	*Barber et al, J. Infect. Dis., 2001* *Nieto et al, J. Steroid Biochemistry&Molecular Biology, 2004*
APOBEC3G	Apolipoprotein B mRNA-editing enzyme, catalytic polypeptide-like 3G	557A>G 40693C>T	rs8177832 NA	H186R Intron 4	186R allele associates with decline in CD4 T cells and accelerated progression to AIDS in African Americans. Intron variant associated with an increased risk of HIV-1 infection	NO	*An et al, J.Virol. 2004*, *Do et al, JID, 2005* *Valcke et al, AIDS, 2006*
APOBEC3	Apolipoprotein	29.5-kb deletion	NA	NA	Homozygous deletion was associated with HIV-1	NO	*An et al. JID 2009*

B	B mRNA-editing enzyme, catalytic polypeptide-like 3B	removing the entire gene			acquisition, faster progression to AIDS, and higher viral set point. No effect of hemizygous genotype.		
APOE	Apoliporotein E	Apo E4 isoform	NA	NA	Homozygosity for apoE4 genotype associates with an accelerated disease course; also shown to enhance HIV cell entry in vitro.	NO	*Burt et al, PNAS, 2008*
CUL5	Cullin 5	Multilpe haplotypes	Multiple haplotypes	Multiple haplotypes	Various haplotype clusters result in opposing influences on CD4 loss. Effects may be attributable to differential nuclear protein binding efficiency. There may be an additive effect with APOBEC3g H186R	NO	*An et al, PloS Genet 2007*
MBL2	Mannose-binding lectin	Variant alleles B, C, D -550C>G (C=allele L; G=allele H) ; L-allele is in LD with -328del (AAAGAG)	rs5030737 (R52C) rs1800450 (G54D) rs1800451 (G57E) -550G: not available (-328del) rs10556764	B (G54D) C (G57E) D (R52C) reduced amount of functional MBL Promoter; higher expression levels	Homozygous carriers of alleles are at increased risk of HIV infection and have shorter survival time after AIDS diagnosis in Caucasians (Garred 1997, Pastinen 1998, Boniotto 2003, Mangano 2008). Weak association of the variant alleles with slower progression to AIDS, no association with survival time after diagnosis (Maas 1998). No effect of 54D on HIV-infection in Caucasian but increased risk for rapid progression to AIDS (Amoroso 1999). No effect on HIV-infection in Hispanics (Malik 2003). Association of variant MBL*B with higher plasma viral load levels (Vallinoto 2005). Higher levels of MBL may associate with resistance to infection. Homozygotes for the H allele may progress more rapidly to AIDS in Caucasians (Boniotto 2000). No association with susceptibility to infection; slower progression in presence of heterozygosity for coding mutations (Catano 2008).	Controversial NO	*Garred et al, Lancet, 1997* *Pastinen et al, AIDS Res Hum Retroviruses, 1998* *Boniotto et al, AIDS, 2003* *Maas et al, AIDS, 1998* *Amoroso et al, AIDS, 1999* *Malik et al, Immunogenetics ,2003* *Vallinoto et al, Mol Immunol, 2005* *Boniotto et al, Genes&Immunity, 2000* *Catano et al, JID, 2008* *Mangano et al, JID, 2008*
ABCB1 (MDR1)	ATP-binding cassette, sub-family B, member 1	3435C>T In linkage disequilibrium with *ABCB1* 1236C>T and 2677G>T	rs1045642	Synonymous I1145I.	No difference in host susceptibility to HIV infection in Caucasians (Ifergan 2002). No effect on disease progression in Caucasians (Bleiber 2004). Reduction of HIV-1 infectivity in P-gp-over-expressing cells (Lee 2000). P-gp activity exerts an inhibitory effect on viral replication (Hulgan 2003).	Controversial	*Ifergan et al, AIDS, 2002* *Bleiber et al, JID, 2004* *Lee CG et al. FASEB J. 2000* *Hulgan T et al. J Acquir Immune Defic Syndr. 2003*
TNFRSF1	Tumor	36A>G,	rs4149621	Promoter, and intron	Weak positive signals of association with disease	NO	*Diop G et al, Biomed*

A	necrosis factor receptor superfamily, member 1A	11511T>C	rs12426675	SNPs			*Pharmacother 2005*
PRF1	Perforin 1 (pore forming protein)	1012C>T	ss46531523	Upstream promoter region	No effect on disease progression although 1012T genotype appears to influence perforin expression	NO	*McIlroy et al, Int J Immunogenet, 2006*
CTLA4	Cytotoxic-T-lymphocyte associated antigen 4	-1147C>T -318C>T	rs16840252 rs5742909	Promoter	Association of CTLA4 genotypes with clinical and virological outcomes following HIV-1 infection appeared to vary with time and among the cohorts.	Non conclusive	*Shao et al, AIDS, 2006*
TLR8	Toll-like receptor 8	1A>G	rs3764880	Non-synonymous, alters start codon and reduces NF-kappaB activation	Association with slower progression	NO	*Oh et al, JID, 2008*
TLR9	Toll-like receptor 9	1174G>A 1635A>G	rs352139 rs352140	SNPs in linkage disequilibrium, intron and P545P.	The 1635 G allele associates with rapid progressor status (Bochud 2007), but the genotype AA associates with higher VL and faster progression (Soriano-Sarabia 2008).	NO	*Bochud et al. AIDS 2007* *Soriano-Sarabia et al, JAIDS 2008*
ZNRD1 / RNF39	zinc ribbon domain containing 1 / ring finger protein 39	Several SNPs in perfect LD in and near these genes	rs9261174 rs3869068 rs2074480 rs7758512 rs9261129 rs2301753 rs2074479	Possible association with ZNRD1 expression; 2 non-synonymous coding SNPs in RNF39	Associated with disease progression in several genome-wide association studies. Effect partially attributable to HLA group A10 alleles that are in LD with the variants (Catano 2008).	NO	*Fellay et al, Science, 2007* *Catano et al. PloS One, 2008* *Limou et al. JID 2009* *Fellay et al. PLoS Gen 2009*
FcγRIIa	Fc fragment of IgG, low affinity IIa, receptor (CD32A)	494T>C		H131R	Faster progression to <200 CD4 in patients with RR genotype, which is less efficiently phagocytic and unable to bind IgG2.	NO	*Forthal et al, J immunol, 2007*
FUT2	Alpha(1,2) fucosyl-transferase	428G>A	rs601338	Nonsense mutation, leading to non-secretor blood group status	Enrichment of the mutation in a small population of long-term non-progressors.	NO	*Kindberg et al, AIDS, 2006*
MYH9	nonmuscle myosin heavy chain IIA	Multiple SNPs and haplotypes	NA	NA	An admixture-mapping LD scan identified variants that recessively associate with focal segmental glomerulo-sclerosis and explain to a large extent the increased burden of HIV-associated renal disease in Africans.	NO	*Kopp et al, Nat Gen, 2008*
MTDNA		Multiple DNA haplogroups	NA	NA	Haplogroups J and U5a associate with accelerated progression to AIDS and death. Haplogroups Uk, H3, and IWX associate with slower progression.	NO	*Hendrickson et al, AIDS, 2008*
PROX1	Prospero homeobox 1	3 SNPs in the upstream region	rs17762192 rs1367951 rs17762150	NA	A GWAS identified a locus 36kb upstream of PROX1 that associates with delayed progression to AIDS	NO	*Herbeck et al, JID, 2010*