

## **SUPPLEMENTAL MATERIALS**

### **Supplemental Tables**

Table S1. Candidate variants tested for association with CMV reactivation and disease

Table S2. Quality control of candidate variant genotyping and imputation (Excel file)

Table S3. Association of candidate variants with CMV reactivation in the discovery cohort (Excel file)

Table S4. Association of candidate variants with high-level CMV reactivation in the discovery cohort (Excel file)

Table S5. Association of candidate variants with CMV disease in the discovery cohort (Excel file)

Table S6. Association of donor and recipient variants with CMV reactivation and disease from GWAS analysis (Excel file)

Table S7. Quality Control of discovery variants that met criteria for GWAS replication testing (Excel file)

Table S8. GWAS associations with p-values  $<1 \times 10^{-6}$  in the combined discovery and replication cohorts (Excel file)

Table S9. GWAS Quality Control of variants in Table S8 (Excel file)

### **Supplemental Figure**

Figure S1. Manhattan plots showing recipient and donor SNP associations with CMV reactivation and disease in the combined discovery and replication cohorts

### **Footnotes for Tables S1-S9 (Excel files)**

Abbreviations: AIDS, acquired immunodeficiency syndrome; Chr, chromosome; CMV, cytomegalovirus; HCT, hematopoietic cell transplantation; HIV, Human Immunodeficiency virus; HR, hazard ratio; HWE, Hardy-Weinberg equilibrium; LB, lower boundary of the 95% confidence interval; MAF, minor allele frequency; SNP, single nucleotide polymorphism; SOT, solid organ transplantation; Type, genotyped (G) or imputed (I); UB, upper boundary of the 95% confidence interval.

Where beta is listed as "ND" In Tables S3, S4 and S6, a model could not be fit due to lack of observations (i.e., the recessive model with no 'aa' genotypes). Where beta is listed as "NC", a model could be fit but failed to converge due to lack of events, meaning HR = 0 but no valid s.e. or confidence interval.

**Table S1. Candidate SNPs and associated phenotypes**

Chr	Gene	SNP/Indel	Phenotypes					References	
			HSCT	SOT	Congenital/ Pediatric CMV	HIV/ AIDS	Other		
1	<i>IL10</i>	rs1800893	x					1	
1	<i>IL10</i>	rs1800896	x	x			x	x	1-4
1	<i>IL10</i>	rs1800871	x					x	1,4
1	<i>IL10</i>	rs1800872						x	4
1	<i>IL10</i>	rs3024492	x						1
1	<i>IL10</i>	rs1878672	x						1
1	<i>IKBKE</i>	rs1953090						x	5
1	<i>MTHFR</i>	rs1801133						x	6
2	<i>IL1B</i>	rs16944				x			7
2	<i>IL1B</i>	rs1143634				x		x	8,9
2	<i>PDCD1</i>	rs11568821		x					10,11
2	<i>IL1A</i>	rs1800587				x		x	8,9
2	<i>STAT4</i>	rs7574865	x						12
2	<i>SLC11A1</i>	rs17235409					x		2
2	<i>CD28</i>	rs3116496	x						13
2	<i>CTLA-4</i>	rs4553808	x	x					11,13,14
2	<i>CTLA-4</i>	rs231775		x					14
2	<i>CTLA-4</i>	rs3087243	x	x					14,15
2	<i>CTLA-4</i>	rs5742909		x					14
2	<i>CTLA-4</i>	rs11571317		x					14
2	<i>CTLA-4</i>	rs16840252		x					14
2	<i>ITGAV</i>	rs3795865						x	5
3	<i>CCR5</i>	rs1800023	x					x	1,16,17
3	<i>CCR5</i>	rs2734648	x						1
3	<i>CCR5</i>	rs17141079	x						1
3	<i>CCR5</i>	rs1799988					x		18
3	<i>CCR2</i>	rs1799864					x		18
3	<i>TLR9</i>	rs187084				x			19
3	<i>TLR9</i>	rs352139				x			19
3	<i>TLR9</i>	rs352140	x			x		x	19-25
3	<i>TLR9</i>	rs5743836	x	x					26,27
3	<i>TLR9</i>	rs5743849						x	5
3	<i>PTX3</i>	rs2305619	x						28
3	<i>PTX3</i>	rs3816527	x						28
4	<i>TLR1</i>	rs5743572						x	29
4	<i>TLR2</i>	rs1898830				x			22,30,31
4	<i>TLR2</i>	rs5743708		x		x		x	20,26,32-36
4	<i>TLR2</i>	rs121917864						x	37
4	<i>TLR2</i>	rs3804100				x			22,31
4	<i>TLR3</i>	rs3775291				x		x	36,38,39
4	<i>TLR3</i>	rs3775292						x	5
4	<i>TLR3</i>	rs3775296				x			39
4	<i>TLR10</i>	rs4513579						x	29
4	<i>IL2</i>	rs2069762						x	40
4	<i>IL2</i>	rs2069763						x	40

4	<i>NFKB1</i>	rs28362491		x					41
5	<i>IL7R</i>	rs6897932		x					42
5	<i>IL12B</i>	rs3212227		x	x	x			2,9,10,43,44
5	<i>IL4</i>	rs2243248						x	40
5	<i>IL4</i>	rs2243250						x	40
5	<i>IL4</i>	rs2070874						x	40
5	<i>microRNA</i>	rs2910164		x					45
6	<i>TNF</i>	rs1799964				x			30
6	<i>TNF</i>	rs1800629				x	x	x	9,46,47
6	<i>HLA-C</i>	rs2308557		x					48
6	<i>HLA-C</i>	rs17408553		x					48
6	<i>HLA-C</i>	rs9264942						x	49
6	<i>HLA-E</i>	rs1264457						x	50
6	<i>HLA-G</i>	rs1063320		x					51
6	<i>MICA</i>	rs2596538		x					52
6	<i>MICA</i>	rs1051792		x					53
6	<i>MICB</i>	rs2523651						x	54
6	<i>IL17A</i>	rs8193036		x					55
6	<i>HLA-G</i>	rs13675/rs1704/rs371194629		x	x			x	56-59
7	<i>LANCL2</i>	rs1568821		x					60
7	<i>NOD1</i>	rs2284358						x	29
7	<i>NOD1</i>	rs2970500						x	29
7	<i>NOD1</i>	rs10267377						x	29
7	<i>IL6</i>	rs1800795				x		x	8
7	<i>ABCB1</i>	rs1128503		x					61
7	<i>ABCB1</i>	rs2032582		x					61
7	<i>ABCB1</i>	rs1045642		x					61
7	<i>CYP3A5</i>	rs776746		x					62
8	<i>LY96</i>	rs6472812						x	29
8	<i>DEFB1</i>	rs1799946				x			63
8	<i>DEFB1</i>	rs1800972				x			63
8	<i>DEFB1</i>	rs11362				x			63
8	<i>SDC2</i>	rs1042381		x					64
9	<i>TLR4</i>	rs4986790		x	x			x	22,24,36,37,65
9	<i>TLR4</i>	rs4986791		x	x				22,24,36,65
9	<i>FCN2</i>	rs7851696		x					66
10	<i>MBL2</i>	rs11003125				x			22
10	<i>MBL2</i>	rs7096206				x			22,65,67
10	<i>MBL2</i>	rs1800450				x			22,65,67,68
10	<i>MBL2</i>	rs5030737		x					65,66,68
10	<i>MBL2</i>	rs1800451		x					65,66,68
10	<i>MAPK8</i>	rs17010454						x	5
10	<i>CXCL12</i>	rs1801157						x	18
11	<i>IL10R1</i>	rs3135932						x	69,70
11	<i>IL10R1</i>	rs2229113						x	69,70
11	<i>IL10R1</i>	rs2229114						x	70
11	<i>IL10R1</i>	rs2228055						x	70
11	<i>IL10R1</i>	rs4252279						x	70
11	<i>IL10R1</i>	rs4252314						x	70
11	<i>IL10R1</i>	rs4252286						x	70

12	<i>INFG</i>	rs2430561	x	x		71–73
12	<i>IRAK4</i>	rs1838341			x	5
12	<i>VDR</i>	rs2228570		x		74
12	<i>VDR</i>	rs1544410		x		75
12	<i>VDR</i>	rs731236		x		75
12	<i>KLRK1</i>	rs2255336			x	76
12	<i>microRNA</i>	rs11614913		x		45
14	<i>IGHG1</i>	rs1071803		x	x	77–79
17	<i>CCL2</i>	rs13900	x		x	1,7
17	<i>CCL2</i>	rs1024611	x		x	1,7
17	<i>CCL8</i>	rs3138035		x		80
19	<i>IFNL4</i>	rs12979860	x	x		26,81–84
19	<i>IFNL4</i>	rs368234815	x	x	x	83,85,86
19	<i>IFNL4</i>	rs8099917		x		87
19	<i>LILRB1</i>	rs10423364		x		88
19	<i>LILRB1</i>	rs1061680			x	2
19	<i>DC-SIGN</i>	rs735240	x	x		26,64
19	<i>DC-SIGN</i>	rs2287886	x			64
19	<i>TGFB1</i>	rs1800470			x	40
19	<i>TGFB1</i>	rs1800471			x	40
20	<i>microRNA</i>	rs3746444		x		45
22	<i>PPARA</i>	rs4253728		x		89
22	<i>EP300</i>	rs20551			x	90
X	<i>FOXP3</i>	rs3761548	x			91
X	<i>TLR7</i>	rs179009			x	5,36
X	<i>TLR7</i>	rs179008			x	5,36
X	<i>TLR7</i>	rs179018			x	5,36
X	<i>TLR7</i>	rs179013			x	5,36
X	<i>TLR8</i>	rs3764880	x			64
X	<i>TLR8</i>	rs3747414	x			64

## References

1. Loeffler J, Steffens M, Arlt E-M, et al. Polymorphisms in the genes encoding chemokine receptor 5, interleukin-10, and monocyte chemoattractant protein 1 contribute to cytomegalovirus reactivation and disease after allogeneic stem cell transplantation. *J. Clin. Microbiol.* 2006;44(5):1847–1850.
2. Affandi JS, Aghafar ZKA, Rodriguez B, et al. Can immune-related genotypes illuminate the immunopathogenesis of cytomegalovirus disease in human immunodeficiency virus-infected patients? *Hum. Immunol.* 2012;73(2):168–174.
3. Alakulppi NS, Kyllönen LE, Salo HME, et al. The impact of donor cytokine gene polymorphisms on the incidence of cytomegalovirus infection after kidney transplantation. *Transpl. Immunol.* 2006;16(3–4):258–262.
4. Hurme M, Haanpää M, Nurmikko T, et al. IL-10 gene polymorphism and herpesvirus infections. *J. Med. Virol.* 2003;70 Suppl 1:S48-50.
5. Arav-Boger R, Wojcik GL, Duggal P, et al. Polymorphisms in Toll-like receptor genes influence antibody responses to cytomegalovirus glycoprotein B vaccine. *BMC Res Notes.* 2012;5:140.
6. Fodil-Cornu N, Kozij N, Wu Q, Rozen R, Vidal SM. Methylenetetrahydrofolate reductase (MTHFR) deficiency enhances resistance against cytomegalovirus infection. *Genes Immun.* 2009;10(7):662–666.

- 
7. Kasztelewicz B, Czech-Kowalska J, Lipka B, et al. Cytokine gene polymorphism associations with congenital cytomegalovirus infection and sensorineural hearing loss. *Eur. J. Clin. Microbiol. Infect. Dis.* 2017;36(10):1811–1818.
  8. Wujcicka WI, Wilczyński JS, Nowakowska DE. Association of SNPs from IL1A, IL1B, and IL6 Genes with Human Cytomegalovirus Infection Among Pregnant Women. *Viral Immunol.* 2017;30(4):288–297.
  9. Wujcicka W, Wilczyński J, Paradowska E, Studzińska M, Nowakowska D. The role of single nucleotide polymorphisms, contained in proinflammatory cytokine genes, in the development of congenital infection with human cytomegalovirus in fetuses and neonates. *Microb. Pathog.* 2017;105:106–116.
  10. Hoffmann TW, Halimi J-M, Büchler M, et al. Association between a polymorphism in the human programmed death-1 (PD-1) gene and cytomegalovirus infection after kidney transplantation. *J. Med. Genet.* 2010;47(1):54–58.
  11. Niknam A, Karimi MH, Yaghobi R, et al. The Association Between Viral Infections and Co-stimulatory Gene Polymorphisms in Kidney Transplant Outcomes. *Jundishapur J Microbiol.* 2016;9(8):e31338.
  12. Wun CM, Piao Z, Hong KT, et al. Effect of donor STAT4 polymorphism rs7574865 on clinical outcomes of pediatric acute leukemia patients after hematopoietic stem cell transplant. *Int. Immunopharmacol.* 2017;43:62–69.
  13. Saadi MI, Yaghobi R, Karimi MH, et al. Association of the costimulatory molecule gene polymorphisms and active cytomegalovirus infection in hematopoietic stem cell transplant patients. *Mol. Biol. Rep.* 2013;40(10):5833–5842.
  14. Misra MK, Pandey SK, Kapoor R, Sharma RK, Agrawal S. Cytotoxic T-lymphocyte antigen 4 gene polymorphism influences the incidence of symptomatic human cytomegalovirus infection after renal transplantation. *Pharmacogenet. Genomics.* 2015;25(1):19–29.
  15. Xiao H, Luo Y, Lai X, et al. Genetic variations in T-cell activation and effector pathways modulate alloimmune responses after allogeneic hematopoietic stem cell transplantation in patients with hematologic malignancies. *Haematologica.* 2012;97(12):1804–1812.
  16. Corrales I, Giménez E, Solano C, et al. Incidence and dynamics of active cytomegalovirus infection in allogeneic stem cell transplant patients according to single nucleotide polymorphisms in donor and recipient CCR5, MCP-1, IL-10, and TLR9 genes. *J. Med. Virol.* 2015;87(2):248–255.
  17. Bravo D, Clari MA, Aguilar G, et al. Looking for biological factors to predict the risk of active cytomegalovirus infection in non-immunosuppressed critically ill patients. *J. Med. Virol.* 2014;86(5):827–833.
  18. Sezgin E, van Natta ML, Ahuja A, et al. Association of host genetic risk factors with the course of cytomegalovirus retinitis in patients infected with human immunodeficiency virus. *Am. J. Ophthalmol.* 2011;151(6):999-1006.e4.
  19. Paradowska E, Jabłońska A, Studzińska M, et al. TLR9 -1486T/C and 2848C/T SNPs Are Associated with Human Cytomegalovirus Infection in Infants. *PLoS ONE.* 2016;11(4):e0154100.
  20. Wujcicka W, Paradowska E, Studzińska M, Wilczyński J, Nowakowska D. TLR2 2258 G>A single nucleotide polymorphism and the risk of congenital infection with human cytomegalovirus. *Viol. J.* 2017;14(1):12.
  21. Beima-Sofie K, Wamalwa D, Maleche-Obimbo E, et al. Toll-like receptor 9 polymorphism is associated with increased Epstein-Barr virus and Cytomegalovirus acquisition in HIV-exposed infants. *AIDS.* 2018;32(2):267–270.
  22. Gelemanović A, Dobberpuhl K, Krakar G, et al. Host genetics and susceptibility to congenital and childhood cytomegalovirus infection: a systematic review. *Croat. Med. J.* 2016;57(4):321–330.
  23. Wujcicka W, Paradowska E, Studzińska M, Wilczyński J, Nowakowska D. Toll-like receptors genes polymorphisms and the occurrence of HCMV infection among pregnant women. *Viol. J.* 2017;14(1):64.
  24. Wujcicka W, Paradowska E, Studzińska M, et al. TLR9 2848 GA heterozygotic status possibly predisposes fetuses and newborns to congenital infection with human cytomegalovirus. *PLoS ONE.* 2015;10(4):e0122831.
  25. Xiao HW, Luo Y, Lai XY, et al. Donor TLR9 gene tagSNPs influence susceptibility to aGVHD and CMV reactivation in the allo-HSCT setting without polymorphisms in the TLR4 and NOD2 genes. *Bone Marrow Transplant.* 2014;49(2):241–247.

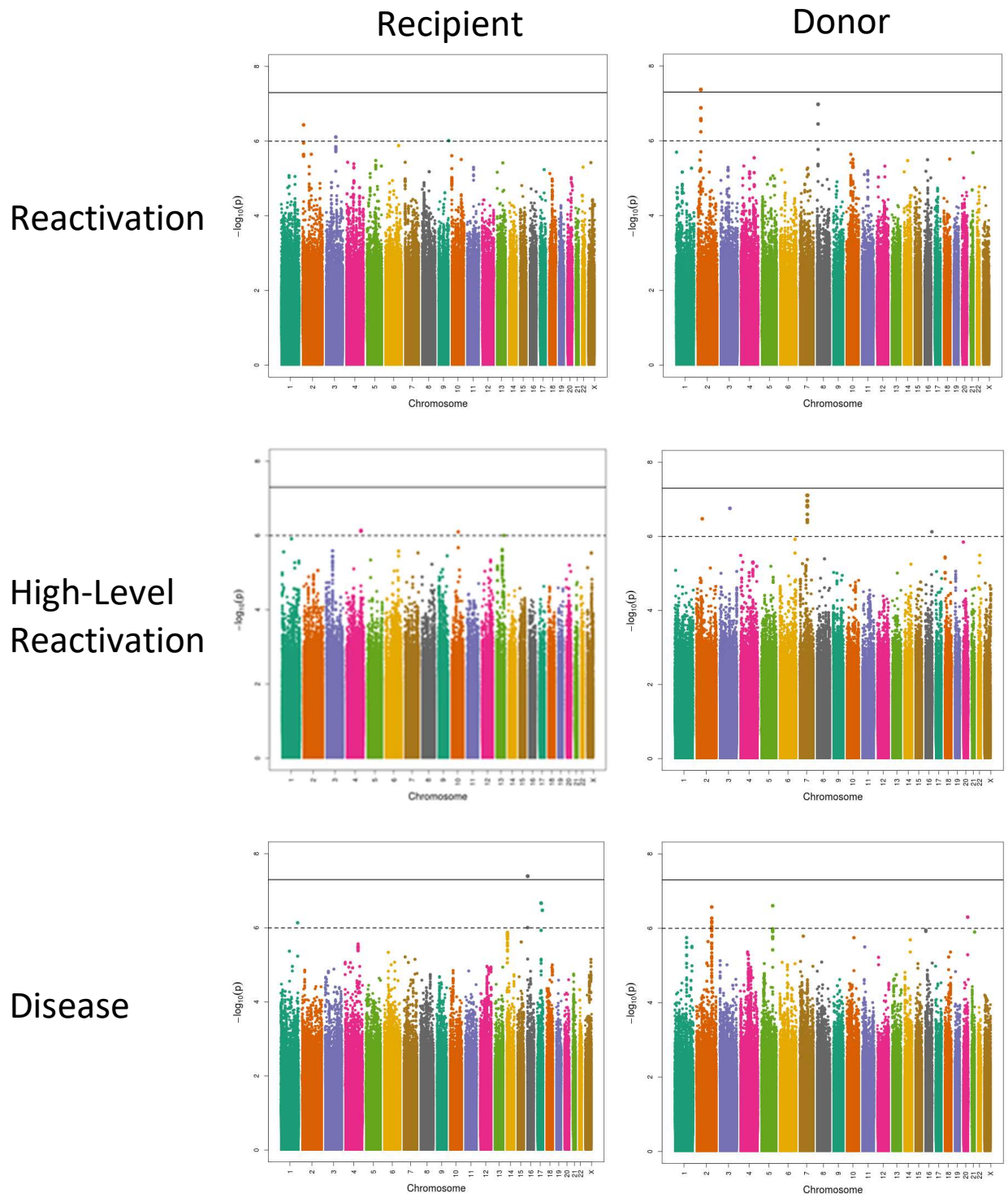
- 
26. Fernández-Ruiz M, Corrales I, Arias M, et al. Association between individual and combined SNPs in genes related to innate immunity and incidence of CMV infection in seropositive kidney transplant recipients. *Am. J. Transplant.* 2015;15(5):1323–1335.
  27. Carvalho A, Cunha C, Carotti A, et al. Polymorphisms in Toll-like receptor genes and susceptibility to infections in allogeneic stem cell transplantation. *Exp. Hematol.* 2009;37(9):1022–1029.
  28. Campos CF, Leite L, Pereira P, et al. PTX3 Polymorphisms Influence Cytomegalovirus Reactivation After Stem-Cell Transplantation. *Front Immunol.* 2019;10:88.
  29. Fan Y-H, Roy S, Mukhopadhyay R, et al. Role of nucleotide-binding oligomerization domain 1 (NOD1) and its variants in human cytomegalovirus control in vitro and in vivo. *Proc. Natl. Acad. Sci. U.S.A.* 2016;113(48):E7818–E7827.
  30. Eldar-Yedidia Y, Hillel M, Cohen A, et al. Association of toll-like receptors polymorphism and intrauterine transmission of cytomegalovirus. *PLoS ONE.* 2017;12(12):e0189921.
  31. Taniguchi R, Koyano S, Suzutani T, et al. Polymorphisms in TLR-2 are associated with congenital cytomegalovirus (CMV) infection but not with congenital CMV disease. *Int. J. Infect. Dis.* 2013;17(12):e1092-1097.
  32. Kijpittayarit S, Eid AJ, Brown RA, Paya CV, Razonable RR. Relationship between Toll-like receptor 2 polymorphism and cytomegalovirus disease after liver transplantation. *Clin. Infect. Dis.* 2007;44(10):1315–1320.
  33. Schneider M, Matiqi T, Kundi M, et al. Clinical significance of the single nucleotide polymorphism TLR2 R753Q in heart transplant recipients at risk for cytomegalovirus disease. *J. Clin. Virol.* 2016;84:64–69.
  34. Kang SH, Abdel-Massih RC, Brown RA, et al. Homozygosity for the toll-like receptor 2 R753Q single-nucleotide polymorphism is a risk factor for cytomegalovirus disease after liver transplantation. *J. Infect. Dis.* 2012;205(4):639–646.
  35. Brown RA, Gralowski JH, Razonable RR. The R753Q polymorphism abrogates toll-like receptor 2 signaling in response to human cytomegalovirus. *Clin. Infect. Dis.* 2009;49(9):e96-99.
  36. Wujcicka W, Wilczyński J, Nowakowska D. Alterations in TLRs as new molecular markers of congenital infections with Human cytomegalovirus? *Pathog Dis.* 2014;70(1):3–16.
  37. Jabłońska A, Paradowska E, Studzińska M, et al. Relationship between toll-like receptor 2 Arg677Trp and Arg753Gln and toll-like receptor 4 Asp299Gly polymorphisms and cytomegalovirus infection. *Int. J. Infect. Dis.* 2014;25:11–15.
  38. Nahum A, Dadi H, Bates A, Roifman CM. The biological significance of TLR3 variant, L412F, in conferring susceptibility to cutaneous candidiasis, CMV and autoimmunity. *Autoimmun Rev.* 2012;11(5):341–347.
  39. Studzińska M, Jabłońska A, Wiśniewska-Ligier M, et al. Association of TLR3 L412F Polymorphism with Cytomegalovirus Infection in Children. *PLoS ONE.* 2017;12(1):e0169420.
  40. Cano P, Han FS, Wang H-L, Fernandez-Vina M, Han XY. Cytokine gene polymorphisms affect reactivation of cytomegalovirus in patients with cancer. *Cytokine.* 2012;60(2):417–422.
  41. Leone F, Gigliotti P, La Russa A, et al. NFKB1 promoter polymorphism: A new predictive marker of cytomegalovirus infection after kidney transplantation. *Transpl Infect Dis.* 2019;21(1):e13027.
  42. Kielsen K, Enevold C, Heilmann C, et al. Donor Genotype in the Interleukin-7 Receptor  $\alpha$ -Chain Predicts Risk of Graft-versus-Host Disease and Cytomegalovirus Infection after Allogeneic Hematopoietic Stem Cell Transplantation. *Front Immunol.* 2018;9:109.
  43. Hoffmann TW, Halimi J-M, Büchler M, et al. Association between a polymorphism in the IL-12p40 gene and cytomegalovirus reactivation after kidney transplantation. *Transplantation.* 2008;85(10):1406–1411.
  44. Hoffmann TW, Halimi J-M, Büchler M, et al. Impact of a polymorphism in the IL-12p40 gene on the outcome of kidney transplantation. *Transplant. Proc.* 2009;41(2):654–656.
  45. Misra MK, Mishra A, Pandey SK, et al. Genetic variation in Micro-RNA genes of host genome affects clinical manifestation of symptomatic Human Cytomegalovirus infection. *Hum. Immunol.* 2015;76(10):765–769.

- 
46. Hurme M, Helminen M. Resistance to human cytomegalovirus infection may be influenced by genetic polymorphisms of the tumour necrosis factor-alpha and interleukin-1 receptor antagonist genes. *Scand. J. Infect. Dis.* 1998;30(5):447–449.
  47. Deghaide NHS, Rodrigues M de LV, Castelli EC, et al. Tumor necrosis factor region polymorphisms are associated with AIDS and with cytomegalovirus retinitis. *AIDS.* 2009;23(13):1641–1647.
  48. Wu X, He J, Wu D, et al. KIR and HLA-Cw genotypes of donor-recipient pairs influence the rate of CMV reactivation following non-T-cell deleted unrelated donor hematopoietic cell transplantation. *Am. J. Hematol.* 2009;84(11):776–777.
  49. Charoudeh HN, Schmitter K, Buser A, Gonzalez A, Stern M. A polymorphism affecting HLA-C surface expression associates with herpes simplex virus and cytomegalovirus immunoglobulin G seropositivity. *Tissue Antigens.* 2012;80(3):263–264.
  50. Gong F, Ding L, Jiang D, et al. Association of human leukocyte antigen E polymorphism with human cytomegalovirus reactivation in Chinese burn patients. *Acta Biochim. Biophys. Sin. (Shanghai).* 2013;45(11):982–984.
  51. Guberina H, Tomoya Michita R, Dolff S, et al. Recipient HLA-G +3142 CC Genotype and Concentrations of Soluble HLA-G Impact on Occurrence of CMV Infection after Living-Donor Kidney Transplantation. *Int J Mol Sci.* 2017;18(11):.
  52. Rohn H, Tomoya Michita R, Schwich E, et al. The Donor Major Histocompatibility Complex Class I Chain-Related Molecule A Allele rs2596538 G Predicts Cytomegalovirus Viremia in Kidney Transplant Recipients. *Front Immunol.* 2018;9:917.
  53. Michita RT, Chies JAB, Schramm S, et al. A Valine Mismatch at Position 129 of MICA Is an Independent Predictor of Cytomegalovirus Infection and Acute Kidney Rejection in Simultaneous Pancreas-Kidney Transplantation Recipients. *Int J Mol Sci.* 2018;19(9):.
  54. Shirts BH, Kim JJ, Reich S, et al. Polymorphisms in MICB are associated with human herpes virus seropositivity and schizophrenia risk. *Schizophr. Res.* 2007;94(1–3):342–353.
  55. Carvalho A, Cunha C, Di Ianni M, et al. Prognostic significance of genetic variants in the IL-23/Th17 pathway for the outcome of T cell-depleted allogeneic stem cell transplantation. *Bone Marrow Transplant.* 2010;45(11):1645–1652.
  56. Misra MK, Prakash S, Kapoor R, et al. Association of HLA-G promoter and 14-bp insertion-deletion variants with acute allograft rejection and end-stage renal disease. *Tissue Antigens.* 2013;82(5):317–326.
  57. Zheng X-Q, Zhu F, Shi W-W, Lin A, Yan W-H. The HLA-G 14 bp insertion/deletion polymorphism is a putative susceptible factor for active human cytomegalovirus infection in children. *Tissue Antigens.* 2009;74(4):317–321.
  58. de Almeida BS, Muniz YCN, Prompt AH, et al. Genetic association between HLA-G 14-bp polymorphism and diseases: A systematic review and meta-analysis. *Hum. Immunol.* 2018;79(10):724–735.
  59. Jin Z-K, Xu C-X, Tian P-X, et al. Impact of HLA-G 14-bp polymorphism on acute rejection and cytomegalovirus infection in kidney transplant recipients from northwestern China. *Transpl. Immunol.* 2012;27(2–3):69–74.
  60. Forconi C, Gatault P, Miquelstorena-Standley E, et al. Polymorphism in programmed cell death 1 gene is strongly associated with lung and kidney allograft survival in recipients from CMV-positive donors. *J. Heart Lung Transplant.* 2017;36(3):315–324.
  61. Cattaneo D, Ruggerenti P, Baldelli S, et al. ABCB1 genotypes predict cyclosporine-related adverse events and kidney allograft outcome. *J. Am. Soc. Nephrol.* 2009;20(6):1404–1415.
  62. Mizuno S, Nakatani K, Muraki Y, et al. Combination assays for evaluation of immune function and CYP3A5 genotype to identify the risk of infectious complications and mortality in living donor liver transplant patients. *Ann. Transplant.* 2013;18:349–357.
  63. Tesse R, Santoro N, Giordano P, et al. Association between DEFB1 gene haplotype and herpes viruses seroprevalence in children with acute lymphoblastic leukemia. *Pediatr Hematol Oncol.* 2009;26(8):573–582.
  64. Mezger M, Steffens M, Semmler C, et al. Investigation of promoter variations in dendritic cell-specific ICAM3-grabbing non-integrin (DC-SIGN) (CD209) and their relevance for human

- 
- cytomegalovirus reactivation and disease after allogeneic stem-cell transplantation. *Clin. Microbiol. Infect.* 2008;14(3):228–234.
65. Cervera C, Lozano F, Saval N, et al. The influence of innate immunity gene receptors polymorphisms in renal transplant infections. *Transplantation.* 2007;83(11):1493–1500.
  66. de Rooij B-JF, van der Beek MT, van Hoek B, et al. Mannose-binding lectin and ficolin-2 gene polymorphisms predispose to cytomegalovirus (re)infection after orthotopic liver transplantation. *J. Hepatol.* 2011;55(4):800–807.
  67. Hu Y, Wu D, Tao R, Shang S. Association between mannose-binding lectin gene polymorphism and pediatric cytomegalovirus infection. *Viral Immunol.* 2010;23(4):443–447.
  68. Cervera C, Lozano F, Linares L, et al. Influence of mannose-binding lectin gene polymorphisms on the invasiveness of cytomegalovirus disease after solid organ transplantation. *Transplant. Proc.* 2009;41(6):2259–2261.
  69. Gruber SG, Gloria Luciani M, Grundtner P, Zdanov A, Gasche C. Differential signaling of cmvIL-10 through common variants of the IL-10 receptor 1. *Eur. J. Immunol.* 2008;38(12):3365–3375.
  70. Sezgin E, Jabs DA, Hendrickson SL, et al. Effect of host genetics on the development of cytomegalovirus retinitis in patients with AIDS. *J. Infect. Dis.* 2010;202(4):606–613.
  71. Vu D, Shah T, Ansari J, et al. Interferon-gamma gene polymorphism +874 A/T is associated with an increased risk of cytomegalovirus infection among Hispanic renal transplant recipients. *Transpl Infect Dis.* 2014;16(5):724–732.
  72. Mitsani D, Nguyen MH, Girnita DM, et al. A polymorphism linked to elevated levels of interferon- $\gamma$  is associated with an increased risk of cytomegalovirus disease among Caucasian lung transplant recipients at a single center. *J. Heart Lung Transplant.* 2011;30(5):523–529.
  73. Lange A. Genetic factors predicting IFN-gamma generation potential in patients with sarcoidosis and after haematopoietic stem cell transplantation. *Int. J. Immunogenet.* 2008;35(4–5):385–388.
  74. Zhao Y-G, Shi B-Y, Xiao L, et al. Association of vitamin D receptor FokI and Apal polymorphisms with human cytomegalovirus disease in the first three months following kidney transplantation. *Chin. Med. J.* 2012;125(19):3500–3504.
  75. Falleti E, Bitetto D, Fabris C, et al. Association between vitamin D receptor genetic polymorphisms and acute cellular rejection in liver-transplanted patients. *Transpl. Int.* 2012;25(3):314–322.
  76. Taniguchi R, Koyano S, Suzutani T, et al. A Thr72Ala polymorphism in the NKG2D gene is associated with early symptomatic congenital cytomegalovirus disease. *Infection.* 2015;43(3):353–359.
  77. Simon B, Weseslindtner L, Görzer I, et al. Subclass-specific antibody responses to human cytomegalovirus in lung transplant recipients and their association with constant heavy immunoglobulin G chain polymorphism and virus replication. *J. Heart Lung Transplant.* 2016;35(3):370–377.
  78. Pandey JP, Namboodiri AM, Mohan S, Nietert PJ, Peterson L. Genetic markers of immunoglobulin G and immunity to cytomegalovirus in patients with breast cancer. *Cell. Immunol.* 2017;312:67–70.
  79. Vietzen H, Görzer I, Puchhammer-Stöckl E. Association of Human Immunoglobulin G1 Heavy Chain Variants With Neutralization Capacity and Antibody-Dependent Cellular Cytotoxicity Against Human Cytomegalovirus. *J. Infect. Dis.* 2016;214(8):1175–1179.
  80. Lisboa LF, Egli A, Fairbanks J, et al. CCL8 and the Immune Control of Cytomegalovirus in Organ Transplant Recipients. *Am. J. Transplant.* 2015;15(7):1882–1892.
  81. Bravo D, Solano C, Giménez E, et al. Effect of the IL28B Rs12979860 C/T polymorphism on the incidence and features of active cytomegalovirus infection in allogeneic stem cell transplant patients. *J. Med. Virol.* 2014;86(5):838–844.
  82. Corrales I, Solano C, Amat P, et al. IL28B genetic variation and cytomegalovirus-specific T-cell immunity in allogeneic stem cell transplant recipients. *J. Med. Virol.* 2017;89(4):685–695.
  83. Annibali O, Piccioni L, Tomarchio V, et al. Impact of IFN lambda 3/4 single nucleotide polymorphisms on the cytomegalovirus reactivation in autologous stem cell transplant patients. *PLoS ONE.* 2018;13(7):e0200221.
  84. Chmelova K, Frankova S, Jirsa M, et al. IL28B rs12979860 T allele protects against CMV disease in liver transplant recipients in the post-prophylaxis and late period. *Transpl Infect Dis.* 2019;21(4):e13124.



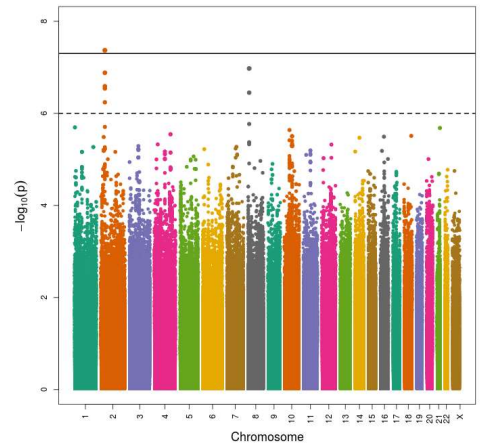
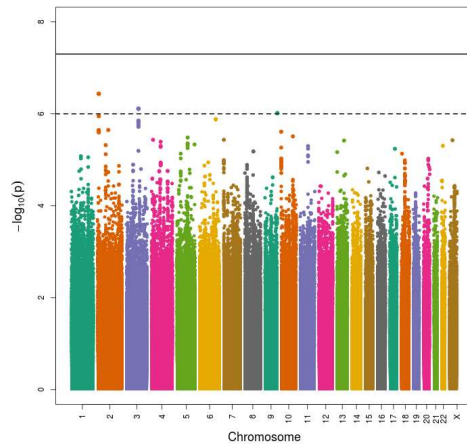
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85. Manuel O, Wójtowicz A, Bibert S, et al. Influence of IFNL3/4 polymorphisms on the incidence of cytomegalovirus infection after solid-organ transplantation. *J. Infect. Dis.* 2015;211(6):906–914.
  86. Bibert S, Wojtowicz A, Taffé P, et al. The IFNL3/4 ΔG variant increases susceptibility to cytomegalovirus retinitis among HIV-infected patients. *AIDS.* 2014;28(13):1885–1889.
  87. Egli A, Levin A, Santer DM, et al. Immunomodulatory Function of Interleukin 28B during primary infection with cytomegalovirus. *J. Infect. Dis.* 2014;210(5):717–727.
  88. Yu K, Davidson CL, Wójtowicz A, et al. LILRB1 polymorphisms influence posttransplant HCMV susceptibility and ligand interactions. *J. Clin. Invest.* 2018;128(4):1523–1537.
  89. Madsen MJ, Bergmann TK, Brøsen K, Thiesson HC. The Pharmacogenetics of Tacrolimus in Corticosteroid-Sparse Pediatric and Adult Kidney Transplant Recipients. *Drugs R D.* 2017;17(2):279–286.
  90. Martín-Antonio B, Álvarez-Laderas I, Cardesa R, et al. A constitutional variant in the transcription factor EP300 strongly influences the clinical outcome of patients submitted to allo-SCT. *Bone Marrow Transplant.* 2012;47(9):1206–1211.
  91. Piao Z, Kim HJ, Choi JY, et al. Effect of FOXP3 polymorphism on the clinical outcomes after allogeneic hematopoietic stem cell transplantation in pediatric acute leukemia patients. *Int. Immunopharmacol.* 2016;31:132–139.



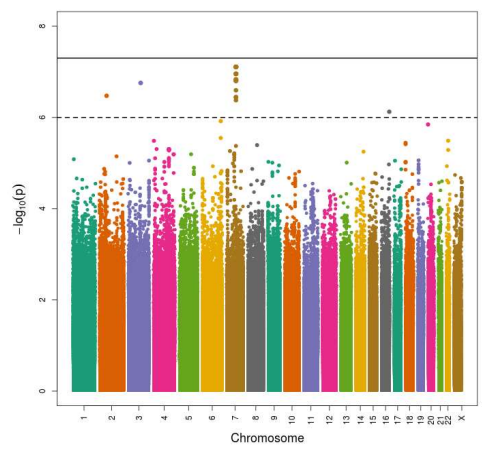
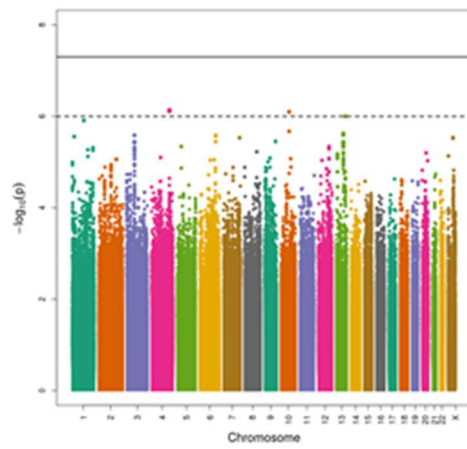
Recipient

Donor

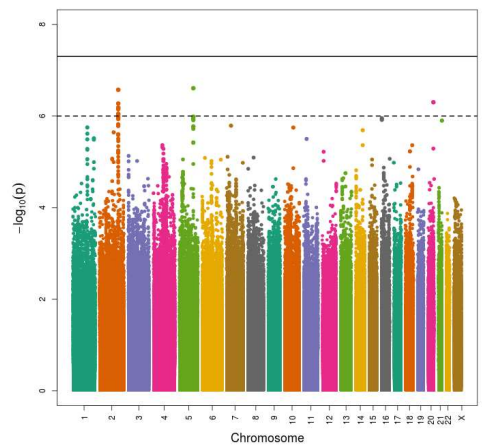
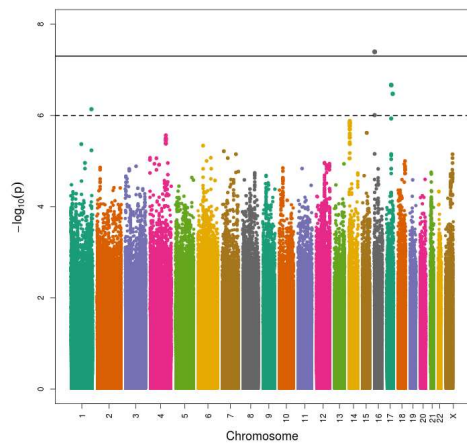
Reactivation



High-Level Reactivation



Disease



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**Figure S1. Manhattan plots show recipient and donor SNP associations with CMV reactivation and disease in the combined discovery and replication cohorts.** Each panel shows the  $-\log_{10}(\text{p-value})$  for post-QC variants with MAF > 1% for autosomes and chromosome X. The results in each panel represent  $\sim 8.7 \times 10^6$  variants. The solid line shows genome-wide significance ( $5 \times 10^{-8}$ ). The dotted line shows the threshold used to select variants for replication ( $1 \times 10^{-6}$ ). Vertically aligned associations reflect variants that are strongly correlated by linkage disequilibrium. Recipient genomic inflation values were 1.009 for CMV reactivation, 1.009 for high-level reactivation, and 1.008 for CMV disease, and donor genomic inflation values were 1.004 for CMV reactivation, 1.005 for high-level reactivation, and 1.017 for CMV disease.