

Supplementary Figures:

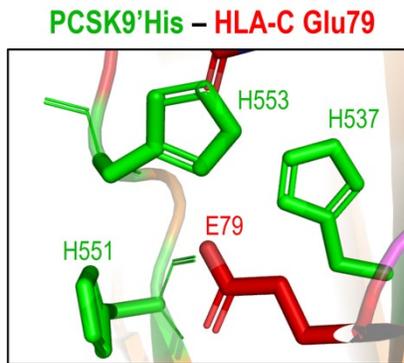
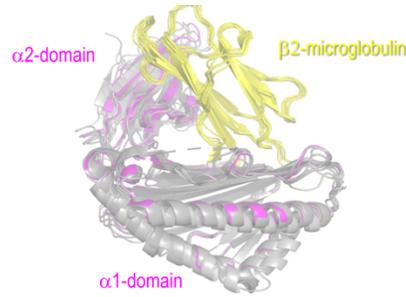


Figure S1. Graphic representation of the 3 Histidine residues in the PCSK9' CHRD (green) in contact with Glu79 of HLA-C (red).

A



Q30201 · HFE_HUMAN PDB: 1A6Z
 P10321 · HLA-C_HUMAN PDB: 6JTO
 Q53Z42 · HLA-A2_HUMAN PDB: 6TRN
 P01889 · HLA-B_HUMAN PDB: 1M05
 P30511 · HLA-F_HUMAN PDB: 5IUE
 P17693 · HLA-G_HUMAN PDB: 3KY0

B

HFE_10001	1	-----MGPRARALLLLMLLQTAVLQ-----GRLLR-----SHSLHYLFMGASEQD	41
HLA-C_10002	1	----MRVMAPRALLLLSGGLALTETWA-----CShSMRYFDtAVSRPG	40
HLA-A_10003	1	----MAVMAPRTLLLLSGALALTQTTWA-----GShSMRYFFtSVSRPG	40
HLA-B_10004	1	----MLVMAPRTVLLLLSAALALTETWA-----GShSMRYFYtSVSRPG	40
HLA-E_10005	1	--MEPS--FYSSRRPWLPPrpGrVSAgSGWKRPLpGVERGRpGGGELGEPrrEEGRADLSPSSpPGShSLKYFHTSVSRPG	78
HLA-F_10006	1	-----MAPRSLLLSGALALTDTWA-----GShSLRYFStAVSRPG	37
HLA-G_10007	1	MKTPrMVVMAPRTLFLLLSGALTLTETWA-----GShSMRYFSAAVSRPG	45
α1 domain			
HFE_10001	42	LGLSLFEALGYVDDQLFVFDYH-- ESRRVEFR TPWVSSRISQMWLQLSQSLKGDHMFtVDFWtIMENhNHSK-ESHTL	118
HLA-C_10002	41	RGEPrFISVGYVDDtQFVrFDSDAAS PRGE PrAPWVEQEG- PEYWDRE TQKYKRQAQADrVSLrNLrGYYNQSEdGSHTL	119
HLA-A_10003	41	RGEPrFIaVGYVDDtQFVrFDSDAASQRMEPrAPWIEQEG- PEYWDQET RNMKAHSQDrANLGLrGRGYYNQSEdGSHTI	119
HLA-B_10004	41	RGEPrFISVGYVDDtQFVrFDSDAASPrEPrAPWIEQEG- PEYWD RNTQIYKAQQT DR ESLrNLrGYYNQSEAGSHTL	119
HLA-E_10005	79	RGEPrFISVGYVDDtQFVrFDSDAASPrMVPrAPWMEQEG- SEYWDRE TRsARbTAQIFrVNLrTLrGRGYYNQSEAGSHTL	157
HLA-F_10006	38	RGEPrYIAVEYVDDtQFLrFDSDAAIPrMEPrEPWVEQEG- PQYEW WTtGYAKANAQDrVALrNLrLrRYYNQSEAGSHTL	116
HLA-G_10007	46	RGEPrFIAMGYVDDtQFVrFDSDSACPrMEPrAPWVEQEG- PEYWEET RNTKAHAQDrMNLQTLrGRGYYNQSEASHTL	124
α2 domain			
HFE_10001	119	QVILGCEMQEDN-STEGYWKYGDQDHLFCpDtlDwRAAEPrAWPT KL EWERhKIRARQNRAYLE RD CPAQQLLEL	197
HLA-C_10002	120	QRMSGCDLGPdGRLLrGRYDQsAYDgKDYIALNEDLrSWtAADtAAQITQRKLEAARAAEQ-LRAYLEGTcVewLrRrYLEN	198
HLA-A_10003	120	QIMYGCDVGPdGRFLrGRYRQdAYDgKDYIALNEDLrSWtAADtAAQITKRKWEAVHAAEQ-RRVYLEG RCV DGLrRrYLEN	198
HLA-B_10004	120	QSMYGCDVGPdGRLLrGRHDQYAYDgKDYIALNEDLrSWtAADtAAQITQRKWEAAREAEQ-RRAYLE GE cVewLrRrYLEN	198
HLA-E_10005	158	QWMHGCELGPdGRFLrGRYEQfAYDgKDYLTlNEDLrSWtAVDtAAQIS ER KSNdASAEH-QRAYLE DT cVewLhKYLEK	236
HLA-F_10006	117	QGMNGCDMGPdGRLLrGRYHQhAYDgKDYISLNEDLrSWtAADtVAQITQRfY EABE YABE-FRtYLEG CE LLrRrYLEN	195
HLA-G_10007	125	QWMIGCDLGSdGRLLrGRYEQYAYDgKDYIALNEDLrSWtAADtAAQIS KRK CEANVAEQ-RRAYLEGTcVewLhRrYLEN	203
HFE_10001	198	GRGVLdQQVpPLVKVtHH-VtSSVtTLrCRALNYpQNItMKWlKDKQpMDAKEFEpKdVLPNGDGtYQGWITLAVpPGE	276
HLA-C_10002	199	GKETLQRaEPPKtHvTHHPLSDHEATLrCWALGFYPAEItLTWQRdGEDQ-TQdTELvETrPAGDGTfQKWAAVVpSGQ	277
HLA-A_10003	199	GKETLQRtDPPKtHmTHHPISDHEATLrCWALGFYPAEItLTWQRdGEDQ-TQdTELvETrPAGDGTfQKWAAVVpSGE	277
HLA-B_10004	199	GKDKLERADPPKtHvTHHPISDHEATLrCWALGFYPAEItLTWQRdGEDQ-TQdTELvETrPAGDRtFQKWAAVVpSGE	277
HLA-E_10005	237	GKETLLHLEPPKtHvTHHPISDHEATLrCWALGFYPAEItLTWQRdGEGH-TQdTELvETrPAGDGTfQKWAAVVpSGE	315
HLA-F_10006	196	GKETLQRADPPKAHVHHPISDHEATLrCWALGFYPAEItLTWQRdGEEQ-TQdTELvETrPAGDGTfQKWAAVVpPGE	274
HLA-G_10007	204	GKEMLQRADPPKtHvTHHPVFDYEAATLrCWALGFYPAEItLTWQRdGEDQ-TQdVELvETrPAGDGTfQKWAAVVpSGE	282
HFE_10001	277	EQRyTcQVEHPLdQPLIVIEpSPSGTL-VIG VIS CIaV FVVI-LF IGIL F ILrKRQSGrGAMGHYVLAERE-----	348
HLA-C_10002	278	EQRyTcHMQHEGLQEPtLrSwEPSSQPTIPIMG IV AGLAVLVVLAVLGAVV TAMMC RRKSSGGKGGs CS QAAC S NSAqGS	357
HLA-A_10003	278	EQRyTcHVQHEGLPKPLtLrWELSSQPTIPiV II AGLVLLGAV-VTGAVVA AVMW RRKSSDRKGGsYtQAASDSAqGS	356
HLA-B_10004	278	EQRyTcHVQHEGLPKPLtLrWEPSSQSTVPiV IV AGLAVLAVV-VIGAVVA AVMC RRKSSGGKGGsYSQA ACS DSAqGS	356
HLA-E_10005	316	EQRyTcHVQHEGLPEPvTLrWKPASQPTIPiV II AGLVLLGSV-VSGAVVA AVIW RRKSSGGKGGsYSKA EW SDSAqGS	394
HLA-F_10006	275	EQRyTcHVQHEGLPQPLiLrWEQSPQPTIPiV IV AGLVLLGAV-VTGAVVA AVMW RRKSSDRNRGSGsYQA AA YSVVSGN	353
HLA-G_10007	283	EQRyTcHVQHEGLPEPLrWkQSSLPtIPiM IV AGLVVLA AV-VTGA VVA AVLW RRKSSD-----	343
HFE_10001	358	-----D ESL LT TK A-----	366
HLA-C_10002	357	-----DVSLT AK V-----	365
HLA-B_10004	357	-----DVSLT A -----	362
HLA-E_10005	395	-----ESHSL-----	399
HLA-F_10006	354	-----LMI T WSSSL F LLGVL F QGYL G CLrShSVLGRrKvGD M WIL F FLW L WtS F NT A FL A L Q SL R FG F GRrGR S FL L R S WH H LM	433
HLA-G_10007	354	-----	
HFE_10001	434	-----KRVQIKIFD	442
HLA-C_10002		-----	
HLA-A_10003		-----	
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HLA-E_10005		-----	
HLA-F_10006		-----	
HLA-G_10007		-----	

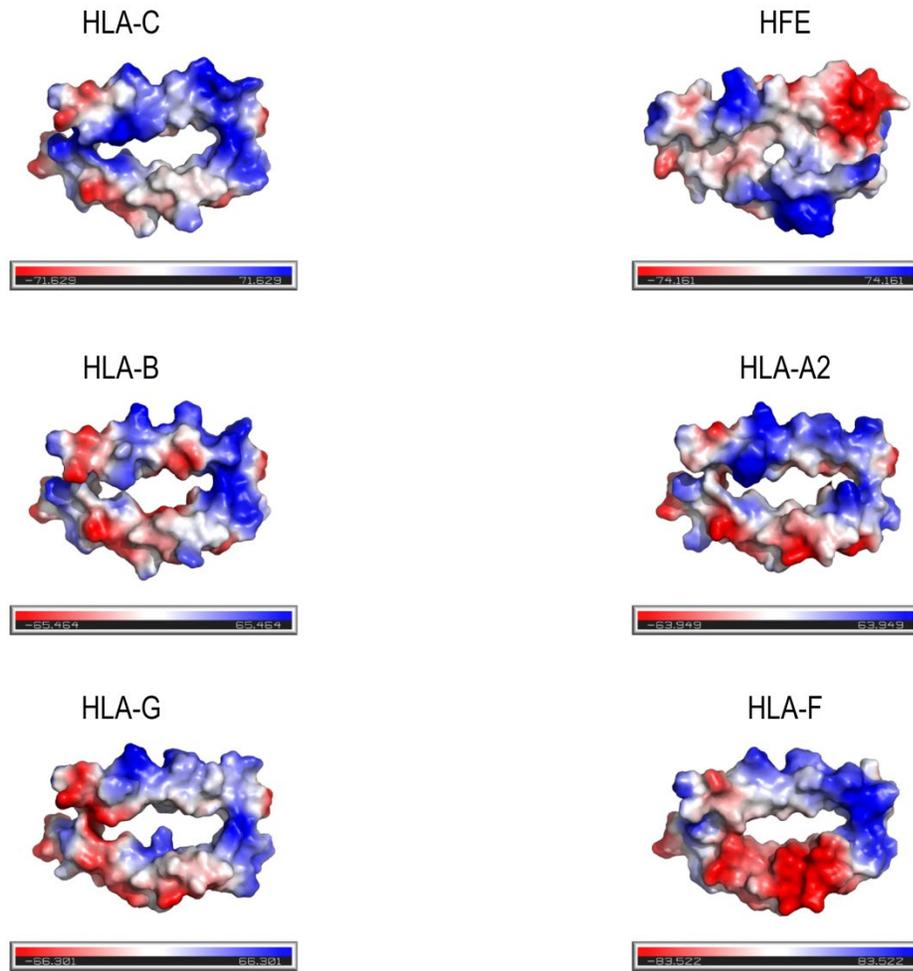
C

Figure S2. Structure and interaction sites of all MHC-I molecules. (A) Superimpose of the structures of the different MHC-I molecules: HFE PBD:1a6z; HLA-C PDB: 6jto (pink); HLA-A2 PBD: 6trn; HLA-B PDB: 1m05; HLA-F PDB: 5iue; HLA-G PDB: 3kyo. (B) Sequence alignment of MHC-I molecules and visualization of basic residues (highlighted in blue) and acidic residues (highlighted in red) of the antigenic pocket of MHC-I molecules. Notice the unique residues underlined or boxed in black. (C) Electrostatic potential of the antigenic pocket of MHC-I molecules.