

Supplementary Table 3 - Sources for HLA Protein Sequence and Functional Domain Determinants

HLA locus	PDB ID/ allele for structure information	UniProt ID/ allele for domain information	IMGT/HLA Acc. #/ allele for sequence coordinates	Reference allele for Variant Type 1 definition
HLA-A ^a	1w72 / A*0101	P30443 / A*0101	HLA00001 / A*01010101	A*0101
HLA-B ^b	3bp4 / B*2705	P01889 / B*0702 ^f	HLA00132 / B*070201	B*0702
HLA-C ^c	1im9 / Cw*0401	P30504 / Cw*0401	HLA00401 / Cw*010201	Cw*0102
HLA-DRA	1fyt / DRA*0101	P01903 / DRA*0101	HLA00662 / DRA*0101	DRA*0101
HLA-DRB1 ^d	1fyt / DRB1*0101	P04229 / DRB1*0101	HLA00664 / DRB1*010101	DRB1*0101
HLA-DRB3 ^e	2q6w / DRB3*0101	P79483 / DRB3*0101	HLA00664 / DRB1*010101	DRB3*0101
HLA-DRB4 ^e	Structure not available ^g	Information not available	HLA00664 / DRB1*010101	DRB4*0101
HLA-DRB5 ^e	1h15 / DRB5*0101	Q30154 / DRB5*0101	HLA00664 / DRB1*010101	DRB5*0101
HLA-DPA1	Structure not available ^g	P20036 / DPA1*0103	HLA00499 / DPA1*010301	DPA1*0103
HLA-DPB1	Structure not available ^g	P04440 / DPB1*0401	HLA00514 / DPB1*010101	DPB1*0101
HLA-DQA1	1jk8 / DQA1*0302	P04225 / DQA1*0302	HLA00601/ DQA1*010101	DQA1*0101
HLA-DQB1	1jk8/DQB1*0302	P01920 / DQB1*0302	HLA00638/ DQB1*050101	DQB1*0501

^a Dohring, C., Scheidegger, D., Samaridis, J., Cella, M. & Colonna, M. A human killer inhibitory receptor specific for HLA-A1,2. *J Immunol* 156, 3098-3101 (1996), Gao, G.F. et al. Crystal structure of the complex between human CD8alpha(alpha) and HLA-A2. *Nature* 387, 630-634 (1997), Marsh, S.G.E., Parham, P., Barber, L.D. *The HLA Facts Book*. (Academic Press, San Diego, CA; 2000), Pende, D. et al. The natural killer cell receptor specific for HLA-A allotypes: a novel member of the p58/p70 family of inhibitory receptors that is characterized by three immunoglobulin-like domains and is expressed as a 140-kD disulphide-linked dimer. *J Exp Med* 184, 505-518 (1996), Saper, M.A., Bjorkman, P.J. & Wiley, D.C. Refined structure of the human histocompatibility antigen HLA-A2 at 2.6 Å resolution. *J Mol Biol* 219, 277-319 (1991), Thananchai, H. et al. Cutting Edge: Allele-specific and peptide-dependent interactions between KIR3DL1 and HLA-A and HLA-B. *J Immunol* 178, 33-37 (2007).

^b Barber, L.D. et al. Polymorphism in the alpha 1 helix of the HLA-B heavy chain can have an overriding influence on peptide-binding specificity. *J Immunol* 158, 1660-1669 (1997), Madden, D.R., Gorga, J.C., Strominger, J.L. & Wiley, D.C. The three-dimensional structure of HLA-B27 at 2.1 Å resolution suggests a general mechanism for tight peptide binding to MHC. *Cell* 70, 1035-1048 (1992), Roder, G. et al. Crystal structures of two peptide-HLA-B*1501 complexes; structural characterization of the HLA-B62 supertype. *Acta Crystallogr D Biol Crystallogr* 62, 1300-1310 (2006), Tynan, F.E. et al. T cell receptor recognition of a 'super-bulged' major histocompatibility complex class I-bound peptide. *Nat Immunol* 6, 1114-1122 (2005).

^c Boyington, J.C., Motyka, S.A., Schuck, P., Brooks, A.G. & Sun, P.D. Crystal structure of an NK cell immunoglobulin-like receptor in complex with its class I MHC ligand. *Nature* 405, 537-543 (2000), Fan, Q.R., Long, E.O. & Wiley, D.C. Crystal structure of the human natural killer cell inhibitory receptor KIR2DL1-HLA-Cw4 complex. *Nat Immunol* 2, 452-460 (2001), Fan, Q.R. & Wiley, D.C. Structure of human histocompatibility leukocyte antigen (HLA)-Cw4, a ligand for the KIR2D natural killer cell inhibitory receptor. *J Exp Med* 190, 113-123 (1999).

^d Brogdon, J., Eckels, D.D., Davies, C., White, S. & Doyle, C. A site for CD4 binding in the beta 1 domain of the MHC class II protein HLA-DR1. *J Immunol* 161, 5472-5480 (1998), Fleury, S. et al. HLA-DR polymorphism affects the interaction with CD4. *J Exp Med* 182, 733-741 (1995).

^e Fleury, S. et al. HLA-DR polymorphism affects the interaction with CD4. *J Exp Med* 182, 733-741 (1995).

^f Domain information is not available for B*2705 thus the domain information of the reference allele B*0702 was obtained

^gNo structures were available for these proteins in the PDB.

Supplementary Table 4 - Characteristics of the Study Cohort

Affection	Ethnicity			Total
	Caucasian	African- American	Hispanic	
Systemic Sclerosis	961	178	161	1,300
Control	579	263	198	1,000