HLA-CW*0602 Is a Susceptibility Factor in Type I Psoriasis, and Evidence Ala-73 Is Increased in Male Type I Psoriatics

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We investigated the HLA-C locus of 87 unrelated patients with chronic plaque psoriasis by genotyping with sequence-specifc amplification primers. The HLA-Cw*0602 allele was significantly increased in male and female type I psoriatics but not significantly increased in either male or female type II psoriatics. The overall frequency of Ala-73 (present in Cw*04, Cw*0602, Cw*07, Cw*12, Cw*1503, and Cw*17) in psoriatics was 88.5% but the incidence of Ala-73 in our Caucasian controls was also high at 84.3%. Ala-73 was present in 97.2% of type I and 85.7% of type II male psoriatics ($\chi^2 = 8.43$, $p = 0.001$; $\chi^2 = 0.01$, p = nonsignificant, respectively), in contrast to 81.5% of type I and 80% of type II female psoriatics (nonsignificant). HLA-Cw*0602 appeared more discriminating in determining disease susceptibility in our population than Ala-73, in line with earlier serologic studies implicating HLA-Cw6. Thus, although the frequency of HLA-Cw*0602 decreased from 54.0% in type I to 29.2% in type II psoriatics, the overall frequency of Ala-73, present in 90.4% of type I and 83.3% of type II psoriatics, did not. (i) Thus this study confirms the strong association between psoriasis and HLA-Cw*0602 by using sequence-specific amplification primers. (ii) Results show that Ala-73 on HLA-C molecules is increased in frequency in psoriasis, but results observed show an association more subtle than previously thought, with HLA-Cw*0602 playing the major role. (iii) This report documents the differential association of HLA genes in male and female psoriatic patients. An interaction between gender and immunogenetics may influence susceptibility to psoriasis. *Key words: human leukocyte antigens/sequence-specific amplification primers/gender/immunogenetics. J Invest Dermatol 109:183–186, 1997*

It is well recognized by standard serologic typing that psoriasis is significantly associated with the human leukocyte antigens (HLA) A1, B13, B17, B37, B39, Cw*0602, Cw11, and DR7 (Tsuji *et al*, 1977; Brenner *et al*, 1978; Murray *et al*, 1980; Tiilikainen *et al*, 1980; Marcusson *et al*, 1981; Ozawa *et al*, 1981), but psoriasis is unique because of its association with certain HLA-C loci. Tight linkage between HLA-C loci and psoriasis has been demonstrated by analysis of restriction fragment length polymorphisms and pulsed-field gel electrophoresis (Ozawa *et al*, 1988). HLA-Cw*0602 is the most frequently described association and has been confirmed in other racial groups (Ozawa *et al*, 1988; Ikäheimo *et al*, 1994; Roitberg-Tambur *et al*, 1994). This indicates that there is tight linkage between the HLA-C loci and the gene controlling susceptibility to psoriasis or that amino acid residues on certain HLA-C locus products may themselves directly contribute to disease susceptibility. An association between a specific nucleotide sequence of HLA-C (Ala-73) has been shown to be strongly associated with psoriasis vulgaris in Japan (Asahina *et al*, 1992). The nucleotide sequence coding for alanine at position 73 was significantly increased in Japanese patients with psoriasis compared with healthy individuals (81 *vs.* 48%; $p < 0.0001$). Codon 73, which codes for Ala-73 instead of Thr-73, is an important component of HLA-C genes and is present in Cw*04, Cw*0602, Cw*07, Cw*12, Cw*1503, and Cw*17 alleles. This amino acid is situated on the α1 domain of the HLA-C molecule, which forms one side of the putative antigen binding cleft (Bjorkman *et al*, 1987). The residue may play an important role in determining susceptibility to the disease, perhaps through determining the conformation of the C cleft and subsequently the peptide that binds to it.

We have investigated the HLA-C locus in a group of 87 unrelated Caucasian patients with chronic plaque psoriasis to determine whether Ala-73 is a disease susceptibility factor in a United Kingdom population. Complement-mediated microcytotoxicity (serology) using human alloantiserum is the most widely used method of typing for the HLA class I products HLA-A, HLA-B, and HLA-C. Although HLA-A and HLA-B serology is reasonably accurate and reliable, serologic detection of HLA-C is poor, up to 50% of the population having only one detectable HLA-C allele (Baur *et al*, 1984; Aizawa *et al*, 1986), and many HLA-C alleles are not detected at all by serology (Bunce *et al*, 1994b). Recently, typing by polymerase chain reaction (PCR) using either sequence-specific primers (PCR-SSP; Bunce *et al*, 1994a, 1994b) or sequence-specific probes (Levine *et al*, 1994; Kennedy *et al*, 1995) has proved to be accurate and efficient in detecting HLA-C. To elucidate the role of HLA-C in psoriasis, we

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Abbreviations: MHC, major histocompatibility complex; SSP, sequence-specific primers.

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used high-resolution PCR-SSP (Bunce *et al*, 1996) supplemented with an additional PCR specifically to detect Ala-73.

MATERIALS AND METHODS

Patients and Controls Eighty-seven unrelated Caucasian patients (50 male and 37 female) with chronic stable plaque psoriasis were recruited randomly from the dermatology outpatient clinic. The overall age range was 13–81 y and the mean age of the group was 52 y. The peak age of onset in the male patients was 25–29 y (24.5% of male population) with a further peak at 60–64 y (10.2% of male population). Females had an earlier peak age of onset at 15–19 y (18.4% of female population) and a further peak at 60–64 y (13.2% of female population). There were 36 male (72%) and 27 female patients (73%) with early-onset disease (onset less than 40 y old), and these were grouped to type I psoriasis; 14 male and 10 female patients with late-onset disease (onset greater than 40 y old) were grouped to type II psoriasis. Typing was also performed on a control population of 604 random Caucasian cadaver donors composed of 366 males and 238 females (Bunce *et al*, 1996).

DNA Extraction Genomic DNA was isolated from lymphocytes obtained from ethylenediamine tetraacetic acid anti-coagulated blood. The DNA was prepared by an improved salting-out method (Bunce *et al*, 1995). Briefly, the buffy coat from 5 ml of anti-coagulated blood was lysed in a red cell lysis buffer consisting of 0.144 M NH_4Cl and 1 mM $NaHCO_3$. After centrifugation, the pellet was rinsed in red cell lysis buffer and resuspended in 3 ml of nuclei lysis buffer (0.4 M NaCl, 2 mM sodium ethylenediamine tetraacetic acid, 10 mM Tris-HCl) and 200 μl of 10% (wt/vol) sodium dodecyl sulfate in water. One hundred twenty microliters of 10 mg proteinase K per ml in PK buffer (1.5 mM sodium ethylenediamine tetraacetic acid, 1% sodium dodecyl sulfate, pH 8.2) were added, and the lysate was incubated for 12 h at 42°C with overhead rotation. After incubation, 1 ml of 6 M NaCl and 3 ml of chloroform were added, vortex-mixed, and centrifuged at 3000 rpm for 30 min. DNA aspirated from the top aqueous phase was precipitated with 95% ethanol, washed in 70% ethanol, and resuspended in distilled water.

Amplification Primers and PCR Conditions Amplification primers and primer mixes were as previously described (Bunce *et al*, 1996). Ala-73 was specifically detected with a combination of sense primer 5′-ACAA-GCGCCAGGCACAGG(HLA-C exon 2, 199–216) and the anti-sense primer 5′-GCGGCG(G/T)TCCAGGAGCG (HLA-C exon 3, 120–136), which produced a 447-bp amplicon when Ala-73 was present in an HLA-C locus allele. Amplification control primers giving rise to a 796-bp fragment from the third intron of HLA-DRB1 were included in all PCRs as previously described (Olerup *et al*, 1992). PCR conditions and parameters were as previously described (Bunce *et al*, 1995), except for the addition of creosol red (62 mg per ml) in the primer mixes as an aid to dispensing. Gel electrophoresis conditions were as previously described (Bunce *et al*, 1995).

The PCR-SSP HLA-C typing has been shown to be highly reliable in our laboratory (Bunce *et al*, 1994a, 1994b, 1995, 1996) and in other laboratories (Ando *et al*, 1996). Furthermore, PCR-SSP HLA-C typing of International Histocompatibility Workshop Cell Lines (Yang *et al*, 1987) is comparable to results obtained with PCR-sequence–specific probes HLA-C typing (Levine *et al*, 1994; Kennedy *et al*, 1995; Prasad *et al*, 1996).

Analysis Antigen frequencies were calculated by antigen counting and gene frequencies were calculated by using the formula: gene frequency = $1 - (1 - \text{antigen frequency})^{1/2}$.

Significance was calculated with χ^2 test with Yate's correction (Bradford Hill and Hill, 1991). The p values were corrected by multiplying by the number of antigens investigated.

RESULTS

The genotpye and antigen frequencies identified by PCR-SSP in the 604 controls and 87 patients with chronic plaque psoriasis are shown in **Table I**, and the significance of HLA-Cw*0602 and Ala-73 are shown in **Table II**. Some Cw alleles are not represented in the tested Caucasian population **(Table I)** and are thought to be either the result of sequence errors or found only rarely (if at all) in Caucasian populations (Bunce *et al*, 1996).

There was a strong association between chronic plaque psoriasis and HLA-Cw*0602. HLA-Cw*0602 was present in 54.0% of type I psoriatics ($\chi^2 = 23.05$; $p < 0.0001$) and was significantly increased in both male 55.6% ($\chi^2 = 25.14$; $p < 0.0001$) and female type I psoriatics 51.8% ($\chi^2 = 20.32$; $p < 0.0001$). In contrast, HLA-Cw*0602 was present overall in only 29.2% of type II psoriatics, male psoriatics made up 28.6%, and female psoriatics made up 30% (not significant).

Table I. PCR-SSP-Determined Genotype and Antigen Frequencies in Controls and Psoriatics[a]

	Random Caucasians (n = 604)		Psoriatics (n = 87)			
Allele	Genotype Frequency	Antigen Frequency	Genotype Frequency	Antigen Frequency	χ^{2b}	p value
Cw*0102	0.028	5.464	0.023	4.598	0	ns
Cw*0202	0.029	5.629	0.053	10.345	0.94	<0.5
Cw*0302	—	—	—	—		
Cw*0303	0.046	8.940	0.023	4.598	0.88	<0.5
Cw*0304	0.085	16.225	0.065	12.644	0.27	ns
Cw*0401	0.100	19.040	0.103	19.540	0.01	ns
Cw*0402	—	—	—	—		
Cw*0403	—	—	—	—		
Cw*0501	0.104	19.702	0.090	17.241	0.07	ns
Cw*0602	0.107	20.199	0.273	47.126	15.04	<0.0001
Cw*0701	0.165	30.298	0.129	24.138	0.67	<0.5
Cw*0702	0.150	27.980	0.103	19.540	1.53	<0.5
Cw*0703	—	—	—	—		
Cw*0704	0.019	3.974	0.012	2.299	0.08	ns
Cw*0801	—	—	—	—		
Cw*0802	0.038	7.450	0.012	2.299	1.87	ns
Cw*0803	—	—	—	—		
Cw*1202	0.004	0.828	0.012	2.299	0.07	ns
Cw*1203	0.032	6.457	0.041	8.046	0.03	ns
Cw*1301	—	—	—	—		
Cw*1402	0.011	2.152	—	—	0.63	<0.5
Cw*1403	—	—	—	—		
Cw*1502	0.021	4.139	0.017	3.448	0.01	ns
Cw*1503	—	—	—	—		
Cw*1504	—	—	—	—		
Cw*1505	0.002	0.331	—	—	1.32	<0.5
Cw*1601	0.041	8.113	0.035	6.897	0	ns
Cw*1602	0.002	0.331	—	—	1.32	<0.5
Cw*1701	0.004	0.828	—	—	0.04	ns
Cw*1801	—	—	—	—		

[a] Genotype and antigen frequencies identified by PCR-SSP in 604 random U.K. Caucasians and 87 psoriasis patients.

[b] χ^2 between control and psoriatics antigen frequencies calculated by using Yates correction.

Of the controls, 306 of 366 males (83.6%) were Ala-73-positive compared with 203 of 238 females (85.3%; nonsignificant). The overall frequency of Ala-73 in psoriatics was 88.5% compared with 84.3% in the control group. Ala-73, however, was present in 97.2% (35 of 36) of type I and 85.7% (12 of 14) of type II male psoriatics ($\chi^2 = 8.43$ and $p < 0.001$ *vs.* $\chi^2 = 0.01$ and p = not significant), in contrast to 81.5% (22 of 27) of type I and 80% (8 of 10) of type II female psoriatics (not significant).

Thus although the HLA-Cw*0602 frequency decreased from 54.0% in type I psoriatics to 29.2% in type II psoriatics, the overall frequency of Ala-73 did not.

DISCUSSION

Current evidence indicates there is tight linkage between HLA-C loci and the gene(s) controlling susceptibility to psoriasis. Psoriasis is associated with an increased frequency of HLA Cw6 (Cw*0602), assigned a relative risk of 14–24 in various reports (Elder *et al*, 1994). This association is unique, as no other disease is known to be primarily linked to the HLA-C locus but the association may simply be the result of linkage disequilibrium with other putative disease susceptibility genes.

Two types of psoriasis can be differentiated according to the age of onset (Henseler and Christopher, 1985). Type I manifests early in life, is HLA-Cw*0602-associated, and frequently affects other family members. Type II manifests later in life and is more likely to be sporadic and nonfamilial. Females are reported to develop psoriasis at an earlier age than males (Holgate, 1975; Henseler and

Table II. HLA-Cw*0602 Is Significantly Increased in Male and Female Type I Psoriatics and Alanine at Position 73 Is Significantly Increased in Male Type I Psoriatics Only

	Cw*0602			Alanine at Position 73		
Subject	Cw*0602, %	χ^{2a}	p value	Ala-73	χ^2	p value
All type I psoriatics (n = 63)	54	23.05	<0.0001	90.4	1.18	<0.5
Female type I psoriatics (n = 27)	51.8	20.32	<0.0001	81.5	0.51	Not significant
Male type I psoriatics (n = 36)	55.6	25.14	<0.0001	97.2	8.43	<0.001
All type II psoriatics (n = 24)	29.2	1.72	<0.5	83.3	0.15	Not significant
Female type II psoriatics (n = 10)	30.0	2.06	<0.5	80.0	0.96	Not significant
Male type II psoriatics (n = 14)	28.6	1.48	<0.5	85.7	0.01	Not significant
All psoriatics (type I and II)	47.1			88.5		
Controls (n = 604)	20.2			84.3		

[a] χ^2 with Yate's correction comparing patients to controls.

Christopher, 1985). This was the case in our cohort of patients, females with a peak age of onset at 15–19 y in contrast to males with a peak age of onset at 25–29 y.

In this study, HLA-C locus genotyping was performed with sequence-specific amplification primers. Complement-mediated microcytotoxicity (serology) using human alloantiserum is the most widely used method for typing the classical transplantation antigens, including HLA-C loci. Serology is ineffective for HLA-C typing (Bunce *et al*, 1996), however, possibly due to the fact that despite similar mRNA levels, HLA-C antigens are expressed on cell surfaces at approximately 10% of the level of either HLA-A or HLA-B (Gussow *et al*, 1987). This may be caused by inefficient assembly of HLA-C molecules with β^2-microglobulin (Neefjes and Ploegh, 1988) or rapid turnover of HLA-C mRNA (McCutcheson *et al*, 1995), or it is possible that haplotype-specific defects and differences in the regulatory complexes of HLA-C may cause differential expression of HLA-C (Cereb *et al*, 1994). The lack of efficient HLA-C cell-surface expression coupled with a relative lack of HLA-C serologic typing reagents results in a 37.2% discrepency rate between serology and PCR-SSP in United Kingdom Caucasians (Bunce *et al*, 1996). To accurately identify serologically detectable and undetectable HLA-C antigens, we used a PCR-SSP system to detect all the sequenced HLA-C alleles (Bunce *et al*, 1996) and to independently detect Ala-73.

The analysis of HLA-C PCR-SSP typing from 87 unrelated patients and 604 normal controls has shown a strong association between psoriasis and HLA-Cw*0602. HLA-Cw*0602 was significantly increased in type I psoriasis in both male and female patients. In contrast the presence of HLA-Cw*0602 in type II psoriatics did not reach statistical significance. There was a high frequency of Ala-73 in all psoriatics (88.5%), confirming the high incidence previously reported in Japan. Ala-73 was also present at high frequency in the general Caucasian population (84.3%), and there was no significant difference in Ala-73 in male and female controls. Ala-73 was carried by 97.2% of type I male psoriatics compared with 85.7% of type II male psoriatics (χ^2 = 8.43, p = 0.001), whereas Ala-73 was carried by only 81.5% of type I female psoriatics and 80% of type II female psoriatics, showing no significant difference compared to the control population. Since type I disease develops earlier in young females and appears more strongly linked to the major histocompatibility complex (MHC), one might expect female patients to have a stronger MHC association. This is not so, but our results suggest there is an interplay between gender and the MHC in susceptibility to psoriasis. Further, this study confirms the importance of Ala-73 on HLA-C molecules as a susceptibility factor to the development of psoriasis but suggests that the association is more subtle than previously thought, with HLA-Cw*0602 playing the major role.

A considerable proportion of the cellular infiltrate in psoriasis consists of activated T helper cells. A popular hypothesis is that inflammation and hyperproliferation in psoriatic lesions is the result of release of mediators from lymphocytes and associated cells during a cell-mediated immune response induced by the local presentation of as yet unidentified antigen(s) (Camp, 1992). The responses to such local antigens may be the result of cross-reactivity with foreign antigens such as streptococcal or retroviral proteins (Bos, 1988). HLA molecules bind to antigens, and the HLA-peptide complex is recognized by T lymphocytes, which become activated and initiate an immune response to that antigen. It is conceivable that certain HLA molecules act as susceptibility factors to psoriasis through the interaction between HLA molecules and local antigens, leading to an autoimmune response. Microorganisms may serve as triggering agents through molecular mimicry. Analysis of protein and DNA databases has revealed that the sigma 2 protein of type 1 reovirus contains an amino acid sequence, Gln-Ala-Gln-Ala-Asp-Arg-Val, which is identical to the disease susceptibility determinant of the HLA-C molecule (George *et al*, 1987; Asahina *et al*, 1992). Crystallographic analysis of HLA class I molecules has revealed that these molecules have a receptor-like shape with a peptide binding groove (Bjorkman *et al*, 1987; Garrett *et al*, 1989). Alteration in the amino acid composition of the groove would cause dimensional or polarity changes, leading to differential ability of the HLA molecule to bind and present antigens.

To elucidate whether Ala-73 or any other HLA-C amino acid is involved in susceptibility to psoriasis, it would be necessary to identify triggering agents and analyze T-cell clones that recognize the HLA-C molecule-antigen complex. Another potential mechanism relates to a gene designated S that has recently been identified in the class I region of the MHC and is expressed exclusively in terminally differentiated keratinocytes (Zhou and Chaplin, 1993). The gene is closely linked to the HLA-C gene, located 160 kb telomeric, and reported to be found in association with HLA-C loci. Although the function of the S protein is unknown, the restriction of its expression to the granular cell layer of the epidermis suggests that it participates in establishing the unique structure of terminally differentiated skin. One could speculate that certain alleles of the S gene may contribute to the pathogenesis of psoriasis, and these genes are in linkage disequilibrium with certain HLA-C loci.

REFERENCES

Aizawa M: Antigens and gene frequencies of ethnic groups. In: Aizawa M, Natori T, Wakisaka A, Konoeda Y (eds.). *HLA in Asia-Oceana*. Hokkaido University Press, Japan, 1986, pp 1079–1091

Ando H, Mizuki R, Ando Y: HLA-C genotyping in the Japanese population by the PCR-SSP method. *Tissue Antigens* 46:55–58, 1996

Asahina A, Nakagawa H, Akazaki S, Kuwata S, Tokunaga K, Ishibashi Y, Juji T: Major histocompatibility complex markers and molecular analysis of HLA-C genes in Japanese psoriatics. In: Ohkawara A, McGuire J, (eds.). *The Biology of the Epidermis: Molecular and Functional Aspects*. Elsevier Science Publications, New York, 1992, pp 183–191

Baur MP, Neugebauer M, Albert ED: Reference tables of two-locus haplotype frequencies for all MHC marker loci. In: Albert ED, Baur MP, Mayr WR, (eds.). *Histocompatibility Testing*. Springer-Verlag, Berlin, 1984, pp 677–755

Bjorkman PJ, Saper MA, Samraoui B, Bennett WS, Strominger JL, Wiley DC: Structure of the human class I histocompatibility antigen HLA-A2. *Nature* 329:506–12, 1987

Bos JD: The pathomechanisms of psoriasis; the skin immune system and cyclosporin. *Br J Dermatol* 118:141–55, 1988

Bradford Hill A and Hill ID: The χ^2 approximation. In: *Principles of Medical Statistics.* Edward Arnold, London, 1991, pp 132–134

Brenner W, Gschnait F, Mayr WR: HLA B13, B17, B37 and Cw6 in psoriasis vulgaris: association with the age of onset. *Arch Dermatol Res* 262:337–339, 1978

Bunce M, Barnardo MCNM, Procter J, Marsh SGE, Vilches C, Welsh KI: High resolution HLA-C typing by PCR-SSP: identification of allelic frequencies and linkage disequilibria in 604 unrelated random UK Caucasians and a comparison with serology. *Tissue Antigens* 48:680–691, 1996

Bunce M, Barnardo MCNM, Welsh KI: Improvements in HLA-C typing using sequence-specific primers (PCR-SSP) including the definition of HLA-Cw9 and Cw10 and a new allele "HLA-Cw7/8v". *Tissue Antigens* 44:200–203, 1994a

Bunce M, O'Neill CM, Barnardo MCNM, Krausa P, Browning M, Morris P, Welsh KI: Phototyping: comprehensive DNA typing for HLA-A, B, C, DRB1, DRB3, DRB4, DRB5 & DQB1 by PCR with 144 primer mixes utilising sequence-specific primers (PCR-SSP). *Tissue Antigens* 46:355–367, 1995

Bunce M, Welsh KI: Rapid DNA typing for HLA-C using sequence-specific primers (PCR-SSP): identification of serological and non-serologically defined HLA-C alleles including several new alleles. *Tissue Antigens* 43:7–17, 1994b

Camp RDR: Psoriasis—Immunological mechanisms. In: Rook AJ, Wilkinson DS, Ebling FJ (eds.). *Textbook of Dermatology.* 5th ed. Vol 2. Blackwell Scientific Publications, Oxford, United Kingdom, 1992, pp 1401–1402

Cereb N, Lee S, Maye P, Kong Y, Yang SY: Non-random allelic variation in the regulatory complex of HLA class I genes. *Hum Immunol* 41:46–51, 1994

Elder JT, Nair RP, Guo S-W, Henseler T, Christophers E, Voorhees J: The genetics of psoriasis. *Arch Dermatol* 130:216–224, 1994

George C, Crowe A, Munemitsu S, Atwater J, Samuel C: Biosynthesis of reovirus-specified polypeptides. *Biochem Biophys Res Commun* 147:1153–1161, 1987

Garrett TPJ, Saper MA, Bjorkman PJ, Strominger JL, Wiley DC: Specificity pockets for the side chains of peptide antigens in HLA-Aw68. *Nature* 342:692–696, 1989

Gussow D, Rein RS, Meijer I, de Hoog W, Seemann G, Hochstenbach F, Ploegh H: Isolation, expression and primary structure of HLA-Cw1 and HLA-Cw2 genes: evolutionary aspects. *Immunogenetics* 25:313–322, 1987

Henseler T, Christophers E: Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. *J Am Acad Dermatol* 13:450–456, 1985

Holgate MC: The age of onset of psoriasis and the relationship to parental psoriasis. *Br J Dermatol* 92:443–8, 1975

Ikäheimo I, Silvennoinen-Kassinen S, Karvonen J, Tiilikainen A: Alanine at position 73 of HLA-C is associated with psoriasis vulgaris in Finland. *Br J Dermatol* 131:257–259, 1994

Kennedy L, Poulton KV, Dyer PA, Ollier WER, Thomson W: Definition of HLA-C alleles using sequence-specific oligonucleotide probes (PCR-SSOP). *Tissue Antigens* 46:187–195, 1995

Levine JE, Yang SY: SSOP typing of the Tenth International Histocompatibility Workshop reference cell lines for HLA-C alleles. *Tissue Antigens* 44:174–183, 1994

Marcusson JA, Johannesson A, Möller E: HLA-A, B, C and DR antigens in psoriasis. *Tissue Antigens* 17:525–529, 1981

Murray C, Mann DL, Gerber LN, Barth W, Perlmann S, Decker JL: Histocompatibility alloantigens in psoriasis and psoriatic arthritis. Evidence for the influence of multiple genes in the major histocompatibility complex. *J Clin Invest* 66:670–5, 1980

McCutcheson JA, Gumperz J, Smith KD, Lutz CT, Parham P: Low HLA-C expression at cell surfaces correlates with increased turnover of heavy chain mRNA. *J Exp Med* 181:2085–2095, 1995

Neefjes JJ, Ploegh HL: Allele and locus-specific differences in cell surface expression and the association of HLA class I heavy chain with β_2-microglobulin: differential effects of inhibition of glycosylation on class I subunit association. *Eur J Immunol* 18:801–810, 1988

Olerup O, Zetterquist H: HLA-DR typing by PCR amplification with sequence-specific primers (PCR-SSP) in 2 hours: an alternative to serological DR typing in clinical practice including donor-recipient matching in cadaveric transplantation. *Tissue Antigens* 39:225–235, 1992

Ozawa A, Ohkido M, Inoko H, Ando A: Specific restriction fragment length polymorphism on the HLA-C region and susceptibility to psoriasis vulgaris. *J Invest Dermatol* 90:402–405, 1988

Ozawa A, Ohkido M, Tsuji K: Some recent advances in HLA and skin diseases. *J Am Acad Dermatol* 4:205–230, 1981

Prasad VK, Yang SY: Allele assignment for HLA-A, B and C genes to the Tenth International Histocompatibility Workshop cell lines. *Tissue Antigens* 47:538–46, 1996

Roitberg-Tambur A, Friedmann A, Tzfoni E, Battat S, Hammo R, Safirman C, Tokunaga K, Asahina A, Brautbar C: Do specific pockets of HLA-C molecules predispose Jewish patients to psoriasis vulgaris? *J Am Acad Dermatol* 31:964–968, 1994

Tiilikainen A, Lassus A, Karvonen J, Vartiainen P, Julin M: Psoriasis and HLA-Cw6. *Br J Dermatol* 102:179–184, 1980

Tsuji K, Nose Y, Hoshino K, Inouye H, Ozawa A, Ohkido M, Sasazuki T: Further study on HLA C, D and Ia antigens in psoriasis vulgaris. *Tissue Antigens* 10:202, 1977

Yang SY, Milford E, Hammerling U: Description of the reference panel of B-lymphoblastoid cell lines for factors of the HLA system: the B-cell line panel designed for the Tenth International Histocompatibility Workshop. In: Dupont B (ed.). *Immunology of HLA.* Vol 1. Springer-Verlag, New York, 1987, pp 11–19

Zhou Y, Chaplin D: Identification in the HLA class I region of a gene expressed late in keratinocyte differentiation. *Proc Natl Acad Sci USA* 90:9470–9474, 1993