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Identification of HLA-DPA1*01:03:01:57 and HLA-DPA1*02:01:01:29 from a case-control study of Atopic Dermatitis

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Abstract

DPA1*01:03:01:57 and DPA1*02:01:01:29 differ by a single nucleotide from their closest references, DPA1*01:03:01:02 and DPA1*02:01:01:06.

Keywords

HLA-DPA1; novel allele; atopic dermatitis

We report the description of two HLA-DPA1 alleles observed among four Caucasian individuals who participated in a case-control study of atopic dermatitis. The primary source of subjects for this study was the *Genetics of Atopic Dermatitis* (GAD) cohort[1]. All subjects or legal guardians provided written informed consent or, if appropriate, assent approved by their appropriate Institutional Review Board.

DNA was collected using Oragene DNA collection kits (DNA Genotek, Ottawa, Canada), following procedures previously reported[2]. Eleven HLA genes (HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1) were sequenced using a targeted,

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Author Contributions:

D.J.M and D.S.M were involved in the design of the case-control study on atopic dermatitis. G.D., I.P. and J.L.D. were involved in the genotyping and consensus sequence generation for the novel alleles. G.D., J.L.D, and D.S.M wrote the manuscript. All authors approved of the manuscript.

Conflict of Interest:

J.L.D. and D.S.M. receive royalties from Omixon. D.S.M. is also the Chair of the Scientific Advisory Board of Omixon and owns option in Omixon. D.J.M. is or recently has been a consultant for Pfizer, Leo, and Sanofi with respect to studies of atopic dermatitis and served on an advisory board for the National Eczema Association.

amplicon-based NGS approach with the Omixon Holotype HLA™ V2 kits (Budapest, Hungary). Each gene was amplified independently using Qiagen LR PCR kits (Germantown, MD, USA) on a Veriti thermal cycler (ThermoFisher, Waltham, MA, USA). Amplicons from each gene per subject were pooled together to create barcoded libraries following the Holotype V2 protocol. Pooled libraries were sequenced on an Illumina MiSeq (San Diego, CA, USA) using paired-end 2 × 150 V2 chemistry. Fastq files, containing demultiplexed reads, were analyzed using both Omixon Twin™ (7,000 pairs of reads/locus, v. 2.5.1) and GenDx NGSengine® (Utrecht, Netherlands, 300,000 pairs of reads/sample) using the IPD-IMGT/HLA database version 3.42[3]. Results from each program were compared to produce a final genotype. All heterozygous positions were physically phased throughout the length of the amplicon. Each novel allele was observed in two different individuals, where amplification and sequencing occurred independently.

HLA-DPA1*01:03:01:57 (GenBank: MZ603797; IPD-IMGT/HLA Database submission number HWS10060784) differentiates from DPA1*01:03:01:02, the closest reference allele, by a single nucleotide substitution in the 3 untranslated region (UTR), whereby a Cytosine (C) is changed to a Thymine (T) 567 bases downstream from the end of the exon 4 in the 3' UTR (Figure 1*). This allele was observed in two individuals, both of whom are Caucasian males in the control group, who share the following alleles along with this new DPA1 allele and likely define a haplotype for the novel allele: A*24:02:01, B*35:02:01, C*04:01:01, DRB1*11:04:01, DRB3*02:02:01, DQA1*05:05:01, DQB1*03:01:01, DPA1*01:03:01:57, DPB1*04:01:01.

HLA-DPA1*02:01:01:29 (GenBank: MZ603798; IPD-IMGT/HLA Database submission number HWS10060786) has a single nucleotide difference in intron 1, 215 bases upstream of exon 2, where a T is changed to a C, in comparison to the closest full-length allele DPA1*02:01:01:06 (Figure 1‡). Additionally, the DPA1*02:01:01:29 allele extends 134 nucleotides beyond the existing 3' end of the UTR defined for the DPA1*02:01:01:06 reference allele. This allele was observed in two individuals, one a Caucasian male in the control group and the other a Caucasian female with atopic dermatitis, who share the same set of Class II alleles, likely defining a partial haplotype for the novel allele: DRB1*15:02:01G, DRB5*01:02, DQA1*01:03:01, DQB1*06:01:01, DPA1*02:01:01:29, and DPB1*13:01:01G.

The names DPA1*01:03:01:57 and DPA1*02:01:01:29 have been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in March 2022. This follows the agreed policy that, subject to the conditions stated in the most recent Nomenclature Report[4], names will be assigned to new sequences as they are identified. Lists of such new names will be published in the following WHO Nomenclature Report.

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References:

1. Margolis DJ, Mitra N, Duke JL, et al. Human leukocyte antigen class-I variation is associated with atopic dermatitis: A case-control study. Hum Immunol. 2021;82(8):593–599. [PubMed: 33875297]
2. Margolis DJ, Apter AJ, Gupta J, et al. The persistence of atopic dermatitis and filaggrin (FLG) mutations in a US longitudinal cohort. J Allergy Clin Immunol. 2012;130(4):912–917. [PubMed: 22951058]
3. Robinson J, Barker DJ, Georgiou X, Cooper MA, Flicek P, Marsh SGE. IPD-IMGT/HLA Database. Nucleic Acids Res. 2020;48(D1):D948–D955. [PubMed: 31667505]
4. Marsh SGE, Albert ED, Bodmer WF, et al. Nomenclature for factors of the HLA system, 2010. Tissue Antigens. 2010;75(4):291–455. [PubMed: 20356336]

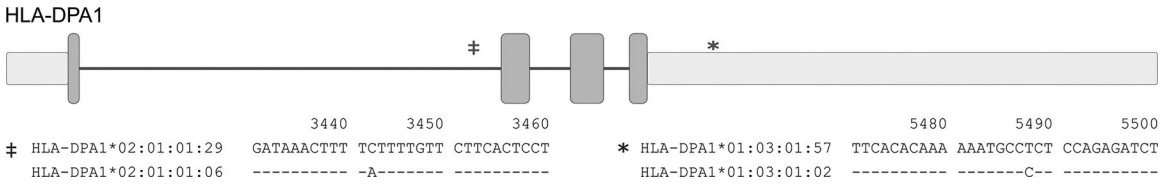

Figure 1.

Location and sequence alignments of HLA-DPA1 novelties. The DPA1 gene is represented with the exons as tall dark grey rectangles, the untranslated regions as short light grey rectangles and the introns with a line. The novel position for DPA1*01:03:01:57 is represented with a star (*) in the top panel, and the novel position for DPA1*02:01:01:29 is represented with a double cross (‡). The region surrounding the novel position for each allele is shown below the gene diagram together with the most similar reference allele.