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Identification of a Novel DPA1 Allele, DPA1*010602 in an East African Population

Trevor A. Peterson^{1,2}, Ma Luo^{1,2,*}, Xiaojuan Mao¹, Robert C. Brunham³, and Francis A. Plummer^{1,2}

¹ Department of Medical Microbiology, University of Manitoba, 730 William Avenue, Winnipeg, Manitoba, Canada

² National Microbiology Laboratory, Winnipeg, Manitoba, Canada

³ University of British Columbia Centre of Disease Control, Vancouver, BC, Canada

Abstract

We report here a novel DPA1 allele, DPA1*010602, which was identified from an East African population during sequence-based HLA-DPA1 typing. Through cloning and sequencing multiple clones we confirmed that the new allele is identical to DPA1*010301 at exon 2 except for 2 nucleotide substitutions (ATG to CAG) at codon 31. The substitutions changed the amino acid at codon 31 from Methionine (Met) to Glutamine (Gln). The WHO nomenclature committee has named this new allele, DPA1*010602.

Keywords

DPA1*010602; DPA1; TBSA

HLA-DP consists of variable alpha (DPA1) and beta chains (DPB1) that form membrane-anchored heterodimers and present antigens to CD4+ T cells [2]. The combinations of DPA1 and DPB1 determine the DP molecule's specificity for antigen presentation. DPA1 is one of the less polymorphic genes of the Major Histocompatibility Complex with only 26 alleles in the current database [3]. HLA-DPA1 is expressed on antigen presenting cells, such as dendritic cells, B-cells and macrophages. The expression of DPA1 was also detected on intestinal epithelial cells of noninflamed small and to a lesser extent large bowel[4]. Studies have shown that HLA-DPA1 alleles play an important role in several autoimmune diseases like Crohn's disease[4] and parasitic infections such as hepatosplenic schistosomiasis japonica[5]. During sequence-based genotyping of HLA-DPA1 of an East African female sexworker cohort to study the role of DPA1 in HIV-1 infection and disease progression, we identified a new allele, DPA1*010602 from a Kenyan woman. Here we describe the identification of this novel DPA1 allele.

*Address Correspondence to: Dr. Ma Luo, Department of Medical Microbiology, University of Manitoba, 730 William Avenue, Winnipeg, Manitoba, Canada R3E 0W3, E-mail: mluo@cc.umanitoba.ca, Fax: (204) 789-2018.

#The name DPA1*010602 has been officially assigned by the WHO Nomenclature Committee. This follows the agreed policy that, subject to the conditions stated in the most recent Nomenclature Report [1], 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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Genomic DNA was isolated from blood samples using a BioRobot EZ1 (QIAGEN Inc. Mississauga, ON). The DPA1 locus (exon 2) was amplified using primers (forward: 5'-ACATTTTGTGTCGTGTTTTCTCT-3'; reverse: 5'-CTCTCATCCCTTCCAGTTG-3') from 13th IWHG [6] by polymerase chain reaction. The PCR product was purified using Amicon Microcon-PCR Centrifugal filter device (MILLIPORE, Bedford, MA, USA). The purified products were sequenced with sequencing primers (forward sequencing primer: 5'-GGCGGACCATGTGTCAACTTAT-3'; reverse sequencing primer: 5'-GCCTGAGTGTGGTTGGAACG-3') using ABI PRISM BigDye Terminator Cycle Sequencing Ready Reaction Kits (Applied Biosystems, Foster City, CA, USA). The sequence was analyzed with AB3100 Genetic Analyser (Applied Biosystems, Foster City, CA, USA) and genotyped with CodonExpress, a computer software developed based on a Taxonomy-based Sequence analysis [7,8].

The allele, DPA*010602 was identified from a Kenyan woman. The sample was typed as DPA*010301 with a heterozygous sequence combination ATG/CAG at codon 31 when the sequence was analysed using Codon Express™ [7,8]. The extra new sequence, CAG, at codon 31 indicates a potential new DPA1 allele (Figure 1) To confirm the new sequence, the sample was reamplified and the PCR products were cloned using a TOPO TA cloning Kit (Invitrogen Co. Carlsbad, CA, USA). The sequences were then analysed by using Sequencher 4.8 (Gene Codes Co. Ann Arbor, MI, USA) to see if the clones contained the new allele. Of 80 Clones that were sequenced, 40 clones were typed as DPA1*010301, 40 clones were typed as the DPA1*010301 except with a new sequence "CAG" at codon 31. The two-nucleotide differences change the amino acid from Methionine to Glutamine. The new DPA1 allele was designated as DPA1*010602 by the WHO Nomenclature Committee [1]. The other class I and class II alleles for this patient are: A*6601, A*6802, B*530101, B*8101/02, Cw*06020101, Cw*1801/02, DPB1*010101, DPB1*020102, DQB1*050101, DQB*0602, DRB1*01 and DRB1*15/16, DRB5*01/02.

The new allele, DPA1*010602 was identified among 547 individuals in this population and is a rare DPA1 allele. The identification of this new allele suggests that there is a great genetic diversity in the East African population and sequence-based HLA typing of large populations will be able to identify novel and rare alleles.

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		5		10		15										
DPA1*010301	CG	GAC	CAT	GTG	TCA	ACT	TAT	GCC	GCG	TTT	GTA	CAG	ACG	CAT	AGA	
DPA1*010602	--	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
		20		25		30										
DPA1*010301	CCA	ACA	GGG	GAG	TTT	ATG	TTT	GAA	TTT	GAT	GAA	GAT	GAG	ATG	TTC	
DPA1*010602	---	---	---	---	---	---	---	---	---	---	---	---	---	CA-	---	---
		35		40		45										
DPA1*010301	TAT	GTG	GAT	CTG	GAC	AAG	AAG	GAG	ACC	GTC	TGG	CAT	CTG	GAG	GAG	
DPA1*010602	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
		50		55		60										
DPA1*010301	TTT	GGC	CAA	GCC	TTT	TCC	TTT	GAG	GCT	CAG	GGC	GGG	CTG	GCT	AAC	
DPA1*010602	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
		65		70		75										
DPA1*010301	ATT	GCT	ATA	TTG	AAC	AAC	AAC	TTG	AAT	ACC	TTG	ATC	CAG	CGT	TCC	
DPA1*010602	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
		80		85												
DPA1*010301	AAC	CAC	ACT	CAG	GCC	ACC	AAC	G								
DPA1*010602	---	---	---	---	---	---	---	-								

Figure 1. Alignment of the exon 2 nucleotide sequences of the new DPA1 allele DPA1*010602 with DPA1*010301

The Genbank Accession number for the new allele is EU729350. A dash indicates identity between sequences. Codons are numbered according to Marsh et al [1].