

Identification of Four Novel HLA-A Alleles from an East African Population by High-Resolution Sequence-Based Typing

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ABSTRACT: We report here four novel human leukocyte antigen (HLA)–A alleles identified among an East African population during sequence-based HLA-A typing. The novel alleles were confirmed by sequencing two separate polymerase chain reaction products and by molecular cloning and sequencing multiple clones. The new allele A*9202 is identical to A*0202 at exon 2 and exon

The names listed for the sequences have 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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Human leukocyte antigen (HLA) is the most polymorphic genetic system known in humans. Among HLA loci, HLA-A is the second most polymorphic locus with 429 HLA-A alleles reported in the latest ImMunoGeneTics (IMGT)/HLA database [1]. As the "origin of humanity," Africa is the most genetically diverse region of the world. A large number of HLA alleles have been identified, and many novel alleles have been reported in the African population [2, 3]. During sequence-based HLA-A typing of an East African population, we identified four novel HLA-A alleles. In this study, we describe the identification, cloning, and sequencing of these four novel alleles.

Genomic DNA was prepared from peripheral blood mononuclear cells (PBMCs) using a QIAamp DNA Mini Kit (QIAGEN Inc., Mississauga, Ontario, Canada). Exon 2, intron 2, and exon 3 were amplified for HLA-A genes 3 except for a single nucleotide difference at codon 43 $(CGG \rightarrow CAG)$, resulting in a coding change from Arginine to Glutamine. The second new allele has a synonymous change at codon 139 (GCA-GCG), that differentiates it from A*680101. The new allele has been named by the World Health Organization nomenclature committee as A*680105. The novel allele A*2630 is identical to A*2603 at exon 2 and exon 3 except for a nonsynonymous change at codon 90 (GAC→GCC), changed from Aspartic acid to Alanine. The fourth new allele is identical to A*290201 except for a single nucleotide difference at codon 138 (ATG \rightarrow GTG), resulting in a coding change from Methionine to Valine. The new allele has been named by the World Health Organization nomenclature committee as A*2915. Identification of these novel HLA-A alleles reflects the genetic diversity of this East African population. Human Immunology 67, 833–838 (2006). © American Society for Histocompatibility and Immunogenetics, 2006. Published by Elsevier Inc.

KEYWORDS: A*2630; A*2915; A*680105; A*9202; SBT; TBSA; HLA-A

using primers from Cereb *et al.* [4, 5] by polymerase chain reaction (PCR). The resulting PCR product was purified using Amicon Microcon-PCR Centrifugal filter device (Millipore, Bedford, MA). The purified PCR products were sequenced with gene-specific primers [3] using ABI PRISM BigDye Terminator Cycle Sequencing Ready Reaction Kits (Applied Biosystems, Foster City, CA). The sequence was analyzed with ABI3100 Genetic Analyzer (Applied Biosystems). HLA-A alleles were typed with computer software, CodonExpress, developed based on a taxonomy-based sequence analysis [6, 7].

The A*9202 allele was identified in a woman from Bukoba, Tanzania. The patient was typed as A*0202 and A*new for a nucleotide difference at codon 43(CGG \rightarrow CAG), resulting in a coding change from Arginine to Glutamine (Figure 1). HLA-A was ream-

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7				Taga			tron										
A*9202 A*9202		GGCC(CTCC:				GCGC	AGGA	CCCG	JGAA(GCCG	CGCC	GGGA	GAG	G'I'C	GGGC	GGG'I'	CTCAGC
11 9202	0110		1001		5					10					15		
A*0202	GC	TCT	CAC	TCC	ATG	AGG	TAT	TTC	TTC	ACA	TCC	GTG	TCC	CGG	CCC	GGC	CGC
A*9202																	
7 4 0 0 0 0	000	a a	20		mma	3 00 0	001	25			000	a 7 a	30		010	mma	000
A*0202 A*9202	GGG 	GAG		CGC	TTC	ATC	GCA	GTG	GGC	TAC	GTG	GAC	GAC	ACG	CAG	TTC	GTG
11 9202	35										45					50	
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A*9202 A*9202	GAC	GGGC	CAGG	 FCGC(CCAC	- G' Agtc'	IGAG' ICCG	TGAC(GGTC(CCCG CGAG2	GCCC(ATCC(GGGG(GCCC(CGCA(CGAA(GCCG	CGGG	ACCC	CGAG	
A*9202 A*9202	GACO	GGGC(GGGA(CAGG GAGG	FCGCO CCCAO	CCAC	- G AGTC CCTT	IGAG ICCG IACC	TGAC(GGTC(CGGT)	CCCG CGAG2 FTCA	GCCC(ATCC(ITTT(GGGG(GCCC(CAGT!	CGCA CGAA ITAG	GCCG(GCCA)	CGGG	ACCC	CGAG	ACCCTTGC
A*9202 A*9202 A*9202	GACO	GGGC(GGGA(CAGG GAGG	FCGCO CCCAO	CCACZ GGCG(ICGG(- G AGTC CCTT	TGAG TCCG TACC CCGG	TGAC GGTC CGGT GCTG	CCCG CGAG ITCA ACCG	GCCC(ATCC) ITTT(CGGG(GGGG(GCCC(CAGT!	CGCA CGAA ITAG	GCCG(GCCA)	CGGGZ AAAA'	ACCC(ICCC(CGAG	ACCCTTGC
A*9202 A*9202 A*9202 A*9202	GACO CCCO GGGO	GGGC(GGGA(GCGG(CAGG GAGG GGCG	TCGCO CCCAO GGGC	CCACZ GGCG ICGG 95	- G' AGTC CCTT GGGA	IGAG ICCG IACC CCGG	TGAC(GGTC(CGGT GCTG	CCCG CGAG ITCA ACCG	GCCC ATCC ITTT CGGG 100	GGGG GCCC CAGT GTCC	CGCA(CGAA(ITAG(GGGC(GCCG(GCCA) CAG	CGGGI AAAA'	ACCC(ICCC(105	CGAG CCCA	ACCCTTGC GGTTGGTC
A*9202 A*9202 A*9202	GACO CCCO GGGO GT	GGGC(GGGA(GCGG(TCT	CAGG GAGG GGCG CAC	ICGCO CCCAC GGGC ACC	CCACZ GGCGG ICGGG 95 CTC	– G' AGTC' CCTT' GGGA(CAG	IGAG' ICCG IACC CCGG AGG	TGACO GGTCO CGGT GCTGZ ATG	CCCG CGAG2 ITCA ACCG TAT	GCCC ATCC ITTT CGGG 100 GGC	GGGGG GCCCC CAGT GTCCC TGC	CGCA CGAA TTAG GGGC GAC	GCCG(GCCA) CAG GTG	CGGG AAAA' GGG	ACCCO ICCCO 105 TCG	CGAG CCCA GAC	ACCCTTGC GGTTGGTC TGG
A*9202 A*9202 A*9202 A*9202 A*9202 A*9202	GACO GCCO GGGO GT	GGGGC GGGA GCGGG TCT	CAGG GAGG CAC 110	ACC	2CACA GGCG(ICGG(95 CTC	- G' AGTC' CCTT' GGGA CAG	IGAG' ICCG(IACC(CCGG(AGG	IGACO GGTCO CGGT GCTGA ATG 115	CCCG(CGAG) ITCA ACCG(TAT	GCCC(ATCC) ITTT(CGGG(100 GGC	GGGGG GCCC(CAGT GTCC(TGC	CGCA(CGAA(ITAG(GGGC(GAC	GCCGO GCCAR CAG GTG 120	CGGG AAAA GGG 	ACCCO ICCCO 105 TCG 	CGAG CCCA GAC	ACCCTTGC GGTTGGTC TGG
A*9202 A*9202 A*9202 A*9202 A*9202 A*0202 A*0202	GACC GGGG GT CGC	GGGCC GGGAC GCGGC TCT TTC	CAGG GAGG CAC 110 CTC	ACC	GGGG	- G' AGTC' CCTT' GGGA CAG TAC	IGAG' ICCG(IACC) CCGG(AGG CAC	IGACO GGTCO CGGT GCTGA ATG 115 CAG	CCCG CGAG ITCA ACCG TAT TAC	GCCC ATCC ITTT CGGG 100 GGC GCC	GGGGG GCCCC CAGT GTCCC TGC TAC	CGCA(CGAA) ITAG(GGGC(GAC GAC	GCCG GCCAJ CAG GTG 120 GGC	CGGG AAAA' GGG AAG	ACCCO ICCCO 105 TCG GAT	CGAG CCCA GAC TAC	ACCCTTGC GGTTGGTC TGG ATC
A*9202 A*9202 A*9202 A*9202 A*9202 A*9202	GACC CCCC GGGC GT CGC	GGGCC GGGAC GCGGC TCT TTC	CAGG GAGG CAC 110 CTC	ACC	GGGG	- G' AGTC' CCTT' GGGA CAG TAC	IGAG' ICCG(IACC) CCGG(AGG CAC	IGACO GGTCO CGGT GCTGA ATG 115 CAG	CCCG CGAG ITCA ACCG TAT TAC	GCCC ATCC ITTT CGGG 100 GGC GCC	GGGGG GCCCC CAGT GTCCC TGC TGC TAC	CGCA(CGAA) ITAG(GGGC(GAC GAC	GCCG GCCAJ CAG GTG 120 GGC	CGGG AAAA' GGG AAG	ACCCO ICCCO 105 TCG GAT	GAC GAC TAC	ACCCTTGC GGTTGGTC TGG ATC
A*9202 A*9202 A*9202 A*9202 A*9202 A*9202 A*9202 A*0202 A*9202	GACO CCCO GGGO GT CGC 125	GGGCC GGGAC GCGGC TCT TTC 	CAGG GAGG GGCG CAC 110 CTC 	ICGCC CCCAC GGGC ACC CGC	GGGG 95 GGGG 95 GTC GGG	- G' AGTC' CCTT' GGGA CAG TAC 130	IGAG' ICCG IACC CCGG AGG CAC 	IGACC GGTCC CGGT GCTGA ATG 115 CAG 	CCCG CGAG TTCA ACCG TAT TAC 	GCCC(ATCC) ITTT(CGGG(100 GGC GCC 	GGGGG GCCCC CAGT GTCCC TGC TAC 135	CGCA(CGAA) ITAG GGGC GAC GAC GAC	GCCGG GCCAA CAG GTG 120 GGC 	GGGG GGG AAAA' AAAG 	ACCCO ICCCO 105 TCG GAT	GAC GAC TAC 140	ACCCTTGC GGTTGGTC TGG ATC
A*9202 A*9202 A*9202 A*9202 A*9202 A*0202 A*0202	GACC GGGG GGG GT CGC 125 GCC	GGGCC GGGAC GCGGC TCT TTC CTG	CAGG GAGGG CAC 110 CTC AAA	ACC CGCC ACC CGC GGC GAG	GGGG GGGG GGGG GGG GGG GAC	- G' AGTC' CCTT' GGGA CAG TAC 130 CTG	IGAG' ICCG(IACC) CCGG(AGG CAC CGC	IGACC GGTC CGGT GCTG ATG 115 CAG TCT	CCCGC CGAGZ TTCAT ACCGC TAT TAC TGG	GCCCC ATCCC TTTTC CGGG 100 GGC GCC ACC	GGGGG GCCCC CAGT GTCCC TGC TAC 135 GCG	CGCA CGAA TTAG GGGC GAC GAC GAC GCG	GCCGG GCCAA CAG GTG 120 GGC GAC	GGGG AAAA GGG AAG ATG	ACCCO ICCCO 105 TCG GAT GCA	GAC GAC TAC 140 GCT	ACCCTTGC GGTTGGTC TGG ATC CAG
A*9202 A*9202 A*9202 A*9202 A*0202 A*9202 A*0202 A*9202 A*0202 A*9202	GAC0 GGG0 GT CGC 125 GCC 	GGGCG GGGAG TCT TTC TTC CTG	CAGG GGCGG CAC 110 CTC AAA	ACC CGCC ACC CGC GGC GAG	GGGG GGGG GGGG GGGG GAC	- G' AGTC' CCTT' GGGA CAG TAC 130 CTG 	IGAG' ICCGG IACCO CCGGG AGG CAC CGC 	IGACO GGTCC CGGT GCTGJ ATG 115 CAG TCT 	CCCG CGAGJ ITCA ACCG TAT TAC TAC TAC TAC	GCCCC ATCCC ITTTC CGGGG 100 GGC GCC ACC 	GGGGG GCCCC CAGT GTCCC TGC TAC 135 GCG 	CGCAC CGAAC ITAGO GGCC GAC GAC GCG 	GCCGG GCCAI CAG GTG 120 GGC GAC 	GGGG AAAAA GGG AAAG AAG ATG	ACCCO ICCCO ICCCO ICCCO ICCCO ICCCO ICCCO GAT GCA	GAC TAC 140 GCT 	ACCCTTGC GGTTGGTC TGG ATC CAG
A*9202 A*9202 A*9202 A*9202 A*9202 A*0202 A*9202 A*0202 A*9202 A*0202 A*0202 A*0202	GACC GGGG GT 125 GCC ACC	GGGCG GGGAG GCGGG TCT TTC CTG ACC	CAC GGCGG CAC 110 CTC AAA AAA	ACC CGCCAC ACC CGC GGC GAG CAC	GGCGG 95 CTC GGGG GGG GAC AAG	- G' AGTC' CCTT' GGGA(CAG TAC 130 CTG TGG	IGAG' ICCGG IACCO CCGGG AGG CAC CGC GAG	IGACO GGTCC CGGT GCTGJ ATG 115 CAG TCT GCG	CCCGC CGAGJ ITCAT ACCGC TAT TAC TAC TAC CCG TAG GCC	GCCCC ATCCC ITTTC CGGGG 100 GGC GCC ACC CAT	GGGGG GCCCC CAGT GTCCC TGC 135 GCG GTG	CGCAC CGAAC ITAGO GGCC GAC GAC GCG 	GCCGG GCCAI CAG GTG 120 GGC GAC 	GGGG AAAAA GGG AAAG AAG ATG	ACCCO ICCCO ICCCO ICCCO ICCCO ICCCO ICCCO GAT GCA	GAC TAC 140 GCT 	ACCCTTGC GGTTGGTC TGG ATC CAG
A*9202 A*9202 A*9202 A*9202 A*0202 A*9202 A*0202 A*9202 A*0202 A*9202	GACC GGGG GT 125 GCC ACC	GGGCG GGGAG GCGGG TCT TTC CTG ACC	CAC GGCGG CAC 110 CTC AAA AAA	ACC CGCCAC ACC CGC GGC GAG CAC	GGCGG 95 CTC GGGG GGG GAC AAG	- G' AGTC' CCTT' GGGA(CAG TAC 130 CTG TGG	IGAG' ICCGG IACCO CCGGG AGG CAC CGC GAG	IGACO GGTCC CGGT GCTGJ ATG 115 CAG TCT GCG	CCCGC CGAGJ ITCAT ACCGC TAT TAC TAC TAC CCG TAG GCC	GCCCC ATCCC ITTTC CGGGG 100 GGC GCC ACC CAT	GGGGG GCCCC CAGT GTCCC TGC 135 GCG GTG	CGCAC CGAAC ITAGO GGCC GAC GAC GCG 	GCCGG GCCAI CAG GTG 120 GGC GAC 	GGGG AAAAA GGG AAAG AAG ATG	ACCCO ICCCO ICCCO ICCCO ICCCO ICCCO ICCCO GAT GCA	GAC TAC 140 GCT 	ACCCTTGC GGTTGGTC TGG ATC CAG

A*0202 AAG GAG ACG CTG CAG CGC ACG G Intron 3 A*9202 --- --- --- --- --- --- --- GTACCAGGGGCCACGGGGCGCCTCCCTGATCGCCTGTA A*9202 GATCTCCCGGGCTGGCCTCCCACAAG

FIGURE 1 Alignment of nucleotide sequences of the new HLA-A allele, A*9202, with A*0202. The Genbank accession number for the new allele is DQ494174. A dash indicates identity between sequences. Codons are numbered according to Marsh *et al.* [1].

plified, and the PCR products were cloned with TOPO TA cloning Kit (Invitrogen Co. Carlsbad, CA). Among 38 clones sequenced, 21 clones were typed as A*0202 and 17 clones were typed as A*new with a new sequence of CAG at codon 43 (Figure 1). The new HLA-A allele was designated as A*9202 by the World Health Organization (WHO) Nomenclature Commit-

A*9202 --- ---

tee (see footnote). The HLA-B alleles of this individual are B*1516 and B*5802, and the HLA-C alleles are Cw*0602 and Cw*140201. The class II alleles of this woman are: DRB1*080401, DRB1*130201, DRB3*030101, DPA1*0301, DPA1*010301, DPB1*020102, DPB1*0402, DQA1*020101, DQA1*040101, DQB1*0401, and DQB1*060401. Download English Version:

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