MALDI-TOF MS GENOTYPING OF 37,234 SWISS PROVES TWO NEW LUTHERAN ALLELES, BOTH POSITIVE FOR AUB

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Background: The Basal Cell Adhesion Molecule (BCAM) gene, encodes all Lutheran blood group antigens as exemplified by the antithetic Lua/b, LU8/14, Aua/b antigens and the high-prevalence antigen LU13. The antigens are encoded at certain genetic locations of the gene, and by either one of the two specific nucleotides, defining the respective SNPs. In theory, and looking at the 4 exemplary SNPs, 16 different combinatory haplotypes were to be expected. However, only 5 of them are currently reported and accepted by the ISBT terminology committee.

Aim of the project: LU genotyping by MALDI-TOF MS based SNP-detection delivered interesting new evidences with respect to the genetic polymorphism of the Lutheran blood group system in Swiss Caucasians.

Methods

Genotyping relied on SNP-detection at coding nucleotides 230(G/A), 611(T/A), and 1615 for LU*01/02, LU*02/02.14 and LU*02/02.19, on 37'234 Swiss blood donors, respectively. For LU13, detection of SNP at coding nucleotide 1340(C/T) was tested using PCR-SSP on 336 individuals with selected genotypes.

Results: Among the 37,234 Swiss donors investigated, LU*01, LU*02, LU*02.14 and LU*02.19 alleles were observed, in all homozygous and heterozygous combinations. However, there were also 6 Lu(a+b-) subjects and 1 Lu(a-b+) donor all typed as Au(a-b+), indicating homozygous presence of two theoretically expectable LU haplotypes, proving them as new LU alleles. Both new alleles were unambiguously identified in a variety of heterozygous genotypes. Testing 336 genotypically selected DNAs for LU*02-13, positive signals were neither encountered in 42 Lu(a+b-), nor among 132 Au(a-b+), but in 16 of 96 Lu(a-b+), Au(a+b-) homozygotes. Applying LU*02.-13 PCR-SSP to all other genotypes of the 336 sample group confirmed this finding. Allele frequencies were calculated (Figure 1).

Summary: The MALDI-TOF MS project not only identified 42 Lu(a+b-) and 7 LU:-8,14 homozygous blood donors, but also delivered new genetic insights into the Lutheran blood group system. The existence of LU alleles, e.g. LU*01.19 and LU*02.19 with simultaneous genetic positivity for LU14 is new. LU*-13 may be expected homozygously once among 371 Swiss individuals.

Figure 1

The newly observed alleles of the Lutheran blood group system are boxed. Their antigen positivity and suggested allele-names are given in bold. Allele-frequencies were calculated from 37,234 Swiss donor data sets. For *LU*02-13*, frequencies were calculated from 336 genotype-selected donors.

current ISBT allelename	simultaneous antigen positivity (exemplary)				new alleles (suggested names)	allele-frequency (Switzerland)
*LU*01*	Lu^a	Au^a	Lu8	Lu13		0.0237
	Lu^a	**Au^b**	Lu8	Lu13	***LU*01.19***	0.0141
*LU*02*	Lu^b	Au^a	Lu8	Lu13		0.6152
*LU*02.14*	Lu^b	Au^a	Lu14	Lu13		0.0092
*LU*02.19*	Lu^b	Au^b	Lu8	Lu13		0.2812
	Lu^b	**Au^b**	**Lu14**	Lu13	***LU*02.19.14***	0.0053
*LU*02.-13*	Lu^b	Au^a	Lu8	**Lu-13**		0.0519
						1.0006