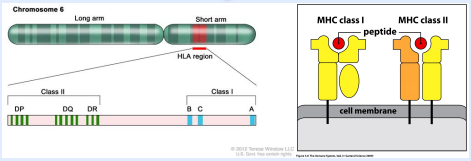
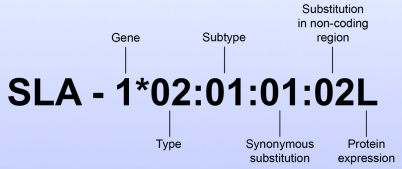
The Swine Leukocyte Antigen (SLA) Nomenclature System of the International Society for Animal Genetics (ISAG) and the International Union of Immunological Societies (IUIS): Update 2016

by the SLA Nomenclature Committee

Human vs. porcine MHC



SLA Nomenclature System



Definition of SLA Haplotypes

Background & Objectives

A systematic nomenclature for the genes, alleles and haplotypes of the swine MHC is critical to the research in swine genetic diversity, immunology, health, vaccinology, and organ or cell transplantation. The Swine Leukocyte Antigen (SLA) system is among the most well characterized MHC systems in non-human animal species. To date, there are 223 class I and 212 class II alleles officially designated, together with 60 class I (1-2-3) and 49 class II (DRB1-DQB1) haplotypes at the high-resolution (allele) level.

Recent evidence has suggested certain loci in the SLA system previously recognized as pseudogenes (e.g. SLA-9, SLA-11, DQB2 and DOB2) may be expressed at transcript level for some haplotypes. Continuous efforts on characterizing SLA alleles and haplotypes and exploring their diversity in various pig populations will deepen our understanding of the architecture and polymorphism of the SLA system and their role in disease, vaccine and allo- or xenograft responses.

SLA alleles and haplotypes

SLA Nomenclature Committee

- Acts as a gatekeeper for maintaining high quality standards of accepted sequences
- Periodically updates of the IPD-MHC SLA Database
- Works with journal editors to make official nomenclature as a requirement for non-human MHC sequences

Authors' Information

Funding: VIC IUIS and National Research Foundation of Korea (JHL). IPD Website: Anthony Nolan Research Institute (HLA Informatics Group) and EBI.

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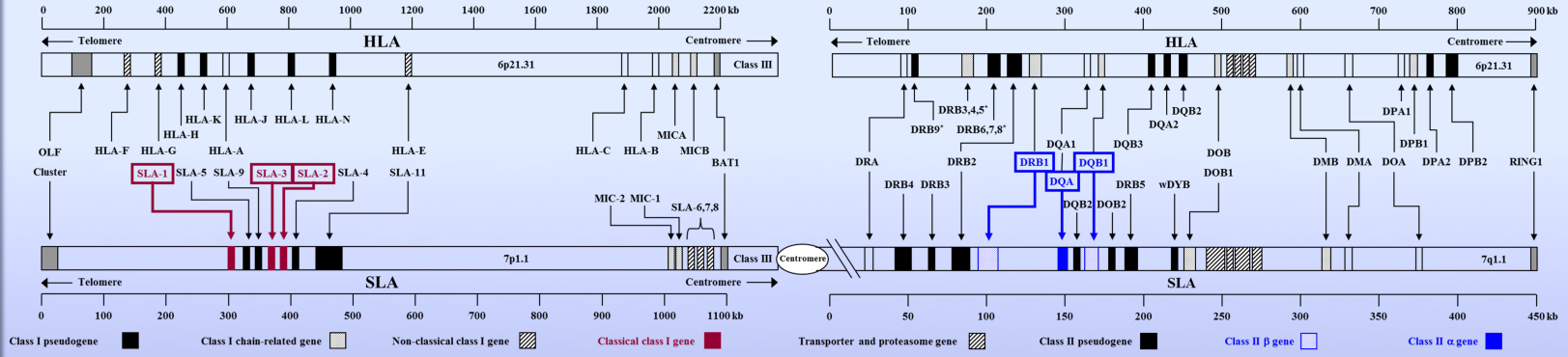

Genomic organization of the MHC class I and class II region of the human leukocyte antigen (HLA) and swine leukocyte antigen (SLA) complex. Not all genes are shown and scale is approximate. Typical SLA class I and SLA class II genes most researchers are interested in typing for are indicated in red and blue, respectively.

Modified after Lunney et al. Dev. Comp. Immunol. 33 (2009) 362-374.

Notes

- SLA complex is a gene-dense region in the swine genome
- 3 major gene clusters
  - SLA class I (1.1 Mb)
  - SLA class III (0.7 Mb)
  - SLA class II (0.5 Mb)
- So far the only mammalian MHC spanning the centromere.

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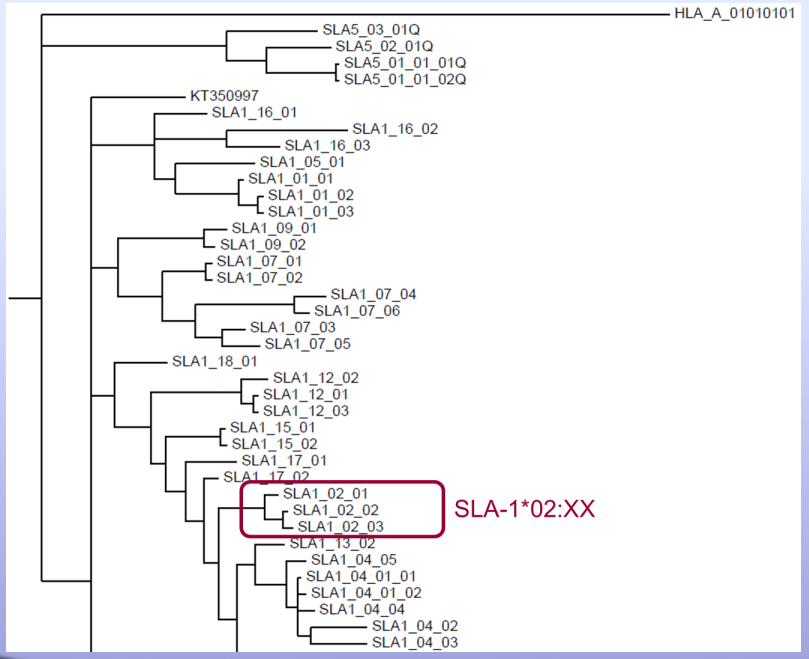
SLA Nomenclature System



Designation	Indication
SLA-1	A particular SLA locus
SLA-1a, SLA-1b, SLA-1c	a = the most centromeric b = telomeric to a c = telomeric to b……etc
SLA-1*02	**A group of alleles (by phylogeny and/or sequence motif)**
SLA-1*02:01	A confirmed allele
SLA-1*02:01:01	A confirmed allele which differs by synonymous nucleotide substitution
SLA-1*02:01N	Null allele
SLA-1*02:01Q	Questionable expression
SLA-1*02:01L	Low expression

Notes

- SLA peptide-binding domains interact with receptors of immune cells (e.g., TCR)
- Polymorphic domains are mainly encoded by exon 2 and 3
- Allelic group assignments are based on "group-specific" polymorphic sequence motifs

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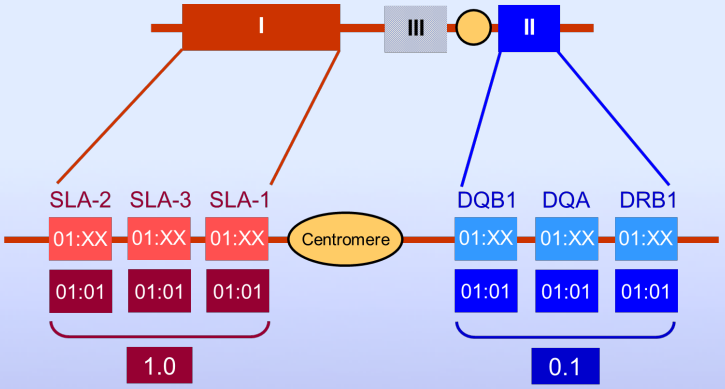
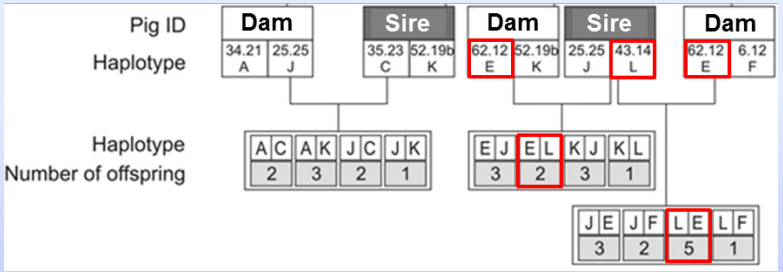
Definition of SLA haplotypes





Low-resolution (Lr) haplotypes are identified by a PCR-based typing assay and define the MHC background of an animal on allele-group level → e.g., SLA-1*01:XX; DRB1*01:XX. High-resolution (Hr) haplotypes are defined on allele level by sequence-based typing methods → e.g., SLA-1*01:01; DRB1*01:01. Ho et al. Tissue Antigens 73 (2009) 307-315.

The figure shows the pedigree and SLA genotypes of selected German Landrace pigs. The linked low-resolution haplotypes lead to 29 genotypes of which the genotype Lr-43.14/62.12 appeared at the highest frequency of 9.2%. Gimsa, Ho, Hammer, Immunogenetics (2016), revised manuscript.

Notes

- In pigs, strong linkage disequilibrium of the SLA loci
- Haplotype (Hp) = a specific combination of alleles of genes on same chromosome
- Some Hp: duplicated SLA-1 locus, some loci not expressed
- 60 SLA class I (1-2-3) and 49 (DRB1-DQB1) class II haplotypes

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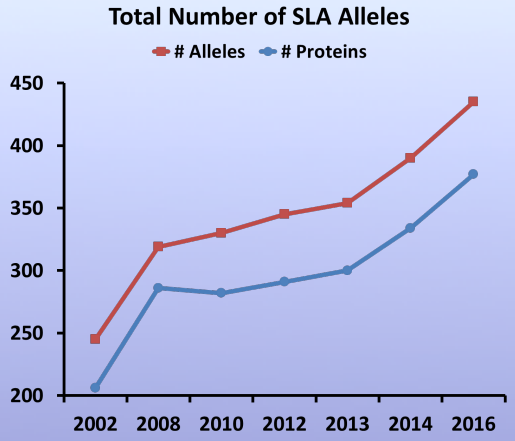
SLA alleles, proteins and haplotypes

	Description	Locus	# Alleles	# Proteins
SLA class I	Classical	SLA-1	70	68
	(Ia α-chain)	SLA-2	87	84
		SLA-3	36	33
	Non-classical	SLA-6	9	9
	(Ib α-chain)	SLA-7	3	3
		SLA-8	5	5
	Other	SLA-12	6	6
	Pseudogenes		7	0
	Total number		223	208



	Description	Locus	# Alleles	# Proteins
SLA class II	α-chain	DRA	14	6
	β-chain	DRB1	89	84
	α-chain	DQA	22	21
	β-chain	DQB1	52	47
	α-chain	DMA	7	5
	β-chain	DMB	1	1
	α-chain	DOA	2	2
	β-chain	DOB1	3	3
	Pseudogenes		22	0
	Total number		212	169

Notes

Number of alleles:
- 223 SLA class I
- 212 SLA class II

High-Resolution Haplotypes:
- 60 SLA class I (1-2-3)
- 49 SLA class II (DRB1-DQB1)

SLA region remains largely unknown in many haplotypes and in outbred pigs

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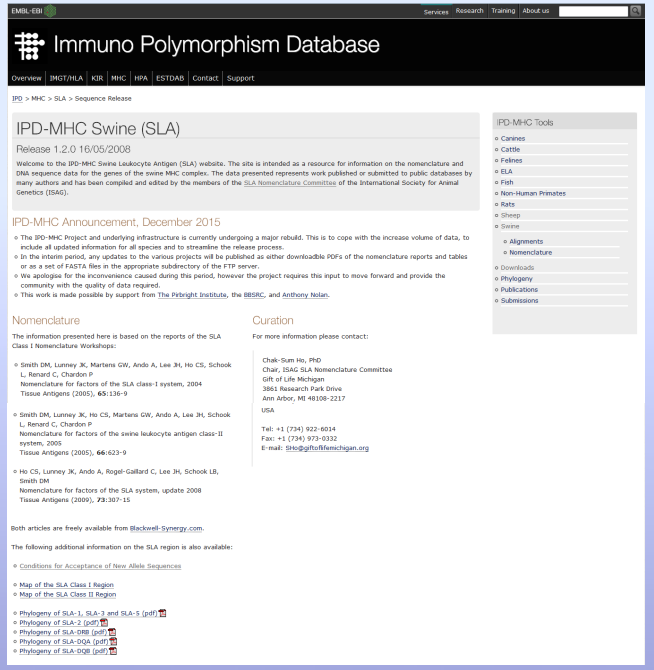
SLA Nomenclature Committee

The SLA Nomenclature Committee was established in 2002 at the 28th International Society of Animal Genetics (ISAG) Conference in Göttingen, Germany. It subsequently became affiliated with the Veterinary Immunology Committee of the International Union of Immunological Societies (VIC IUIS). It is now a standing committee of both, ISAG and VIC IUIS and comprises eight members representing North American, Asian and European research institutions.

Objectives & Responsibilities of the Committee

- To validate newly identified SLA sequences according to the guidelines established for maintaining high quality standards of the accepted sequences.
- To assign appropriate nomenclatures for new alleles as they are validated.
- To serve as a curator of the IPD-MHC SLA Database and the repository of SLA sequences and haplotypes.
- Work with journal editors to make official nomenclature as a requirement for non-human MHC sequences.



Notes

- Validation of new sequences = tedious & time consuming
- Phylogeny has limited capacity for allele-group assignment as number of alleles increases
- The SLA system is among the most well characterized MHC systems

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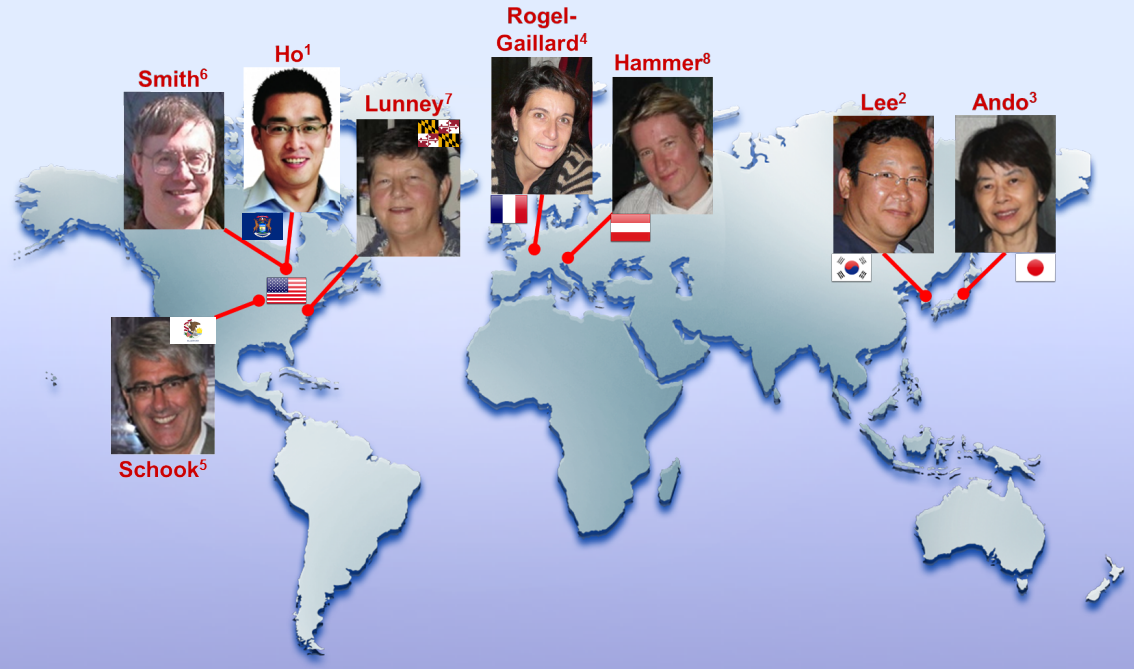

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