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Organization, complexity and allelic diversity of the porcine (Sus scrofa domestica) immunoglobulin lambda locus

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Abstract

We have characterized the organization, complexity, and expression of the porcine (Sus scrofa domestica) immunoglobulin lambda (IGL) light chain locus, which accounts for about half of antibody light chain usage in swine, yet is nearly totally unknown. Twenty-two IGL variable (IGLV) genes were identified that belong to seven subgroups. Nine genes appear to be functional. Eight possess stop codons, frameshifts, or both, and one is missing the V-EXON. Two additional genes are missing an essential cysteine residue and are classified as ORF (open reading frame). The IGLV genes are organized in two distinct clusters, a constant (C)-proximal cluster dominated by genes similar to the human IGLV3 subgroup, and a C-distal cluster dominated by genes most similar to the human IGLV8 and IGLV5 subgroups. Phylogenetic analysis reveals that the porcine IGLV8 subgroup genes have recently expanded, suggesting a particularly effective role in immunity to porcine-specific pathogens. Moreover, expression of IGLV genes is nearly exclusively restricted to the IGLV3 and IGLV8 genes. The constant locus comprises three tandem cassettes comprised of a joining (IGLJ) gene and a constant (IGLC) gene, whereas a fourth downstream IGLJ gene has no corresponding associated IGLC gene. Comparison of individual BACs generated from the same individual revealed polymorphisms in IGLC2 and several IGLV genes, indicating that allelic variation in IGLV further expands the porcine antibody light chain repertoire.

Keywords

Sus scrofa; porcine; light chain; lambda; IMGT; gene rearrangement

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Introduction

Adaptive humoral immunity is mediated by a diverse array of genes which recombine during B cell development to generate a vast repertoire of antigen-binding immunoglobulin (IG) proteins. Antigen binding is carried out using the variable domains of both a heavy chain and a light chain. The antibody variable domain is encoded by a variable (V) gene, a diversity (D) gene (heavy chain-only) and a joining (J) gene which rearrange via recognition and cleavage of flanking recombination signal (RS) sequences by the RAG1 and RAG2 complex and subsequent double strand break repair whereby the intervening sequence is excised from the genome (McBlane et al. 1995; Kim and Oettinger 2000). Three complementarity determining regions (CDR) within the variable domain of each heavy and light chain exhibit a large degree of sequence variability. These CDR provide antibodies with an incredibly diverse antigen-binding repertoire (Wu and Kabat 1970; Lefranc and Lefranc 2001).

A large body of knowledge concerning the pig (Sus scrofa domestica) IG heavy (IGH) locus has been accumulated. Its germline organization on chromosome 7q25–q26 (Yerle et al. 1997) of the constant (IGHC) genes and the 15 C-proximal V (IGHV) genes have been mapped, and its expression has been characterized (Eguchi-Ogawa et al. 2010). However, the two light chain loci, kappa (IGK) and lambda (IGL), on chromosomes 3q12-q14 and 14q16–q21, respectively (Yerle et al. 1997), are only partially characterized in the vicinity of their constant genes, and no information is available on the organization of their variable genes (Butler et al. 2006). A search of GenBank and IMGT/LIGM-DB (Giudicelli et al. 2006) reveals the presence of approximately 100 cDNA sequences for the porcine kappa locus and only two partial lambda cDNA sequences, thus highlighting the lack of information on swine light chain loci. Here, we interrogated available porcine genome sequence (Schook et al. 2005; Humphray et al. 2007; Archibald et al. 2010), as well as additional sequence generated by our lab and available in GenBank and IMGT/LIGM-DB to completely characterize the organization, complexity, and expression of the porcine light chain lambda (IGL) locus. Our findings show that the locus organization is typical of mammalian species, but is substantially modified so that expression is dominated by V genes that have undergone a recent expansion.

Materials and methods

Identification and sequencing of bacterial artificial chromosomes

The *Sus scrofa* genome build 9 was queried to identify bacterial artificial chromosomes (BACs) containing IGLV sequences using the Basic Local Alignment Search Tool (BLAST) within the Ensembl database (Altschul et al. 1990; Hubbard et al. 2002). Nucleotide sequences in the region of interest for each BAC were downloaded from GenBank for further analysis. The CHORI (Children's Hospital Oakland Research Institute)-242 BAC library used was derived from a single Duroc sow (http://bacpac.chori.org/porcine242.htm). Four BACs were identified that span the IGL locus (CH242-141B5, CH242-524K4, CH242-158O5, CH242-288F14) and two additional BAC clones (CH242-298L14 and CH242-82N3) were found to overlap and extend upstream of the locus (Fig. 1a). Of these BACs, three represent completely sequenced contigs (CH242-158O5, CH242-298L14, and

CH242-82N3) and the remaining three are only partially sequenced. CH242-288F14 is fragmented into five contigs; however, its content almost completely overlaps CH242-158O5 and CH242-298L14. Additionally, CH242-141B5 is fragmented into seven contigs and CH242-524K4 is fragmented into 19 contigs (not shown). Due to a number of gaps in the overlap between these two BACs, it was uncertain if the entire IGL locus was represented. Thus, the two BAC clones were re-sequenced after overnight growth and BAC DNA purification using the Qiagen Plasmid Midi Prep with Qiagen-tip 500 columns. Purified DNA was submitted to the University of Minnesota Biomedical Genomics Center for library preparation and paired-end sequencing using the Illumina GAIIx platform.

Characterization of the porcine IG lambda locus

Approximately 20 million high-quality reads were sorted by molecular tag to differentiate samples and assembled using a combination of the software programs ABySS and Velvet (Simpson et al. 2009; Zerbino and Birney 2008). Generated contigs were assembled against the existing BAC sequences from GenBank using Sequencher 4.10.1 (Gene Codes Corporation). The insert of CH242-141B5 retained a 651-bp gap in a highly repetitive region of the IGLC locus and CH242-524K4 retained several gaps, primarily in the IGLC locus and further downstream. The entire J-C region was re-sequenced using primer walking, PCR, and chain-termination sequencing to resolve the gaps. It included using primers specific for each IGLJ paired with either a reverse IGLJ-specific primer or with a conserved IGLC primer for PCR amplification and chain-termination sequencing. The resequenced portion encompassed the entire constant region and the first six IGLV genes. All IGLV genes identified by next generation re-sequencing were present on previously shotgun-sequenced contigs. The complete locus was manually annotated and interrogated for immunoglobulin features such as RS (i.e., heptamers and nonamers), promoters (i.e., octamers), and gene structure using the annotation software Artemis (Rutherford et al. 2000).

The sequences of CH242-141B5, CH242-524K4, CH242-158O5, CH242-288F14, CH242-298L14, and CH242-82N3 were acquired from GenBank (accession numbers: CU467669, CU467599, CU468977, CU468665, CT827879, and CU062407, respectively) and assessed for IGLV, IGLJ, and IGLC genes using BLAST. Phylogenetic analyses were performed in CLC Sequence Viewer (CLC Bio) and Dendroscope (Huson et al. 2007) using the Unweighted Pair Group Method with Arithmetic Mean (UPGMA) with 1,000 bootstrap iterations. Genes were annotated according to IMGT®, the international ImMunoGeneTics information system® (Lefranc et al. 2009) (http://www.imgt.org). Translated amino acid sequences of the IGLV genes were compared and CDR and framework (FR) boundaries were annotated according to IMGT unique numbering for V region and V domain (Lefranc et al. 2003). IGLC gene translations were annotated according to IMGT unique numbering for C domain (Lefranc et al. 2005). Expression of germline IGLV genes was deduced using 116 BLAST hits from 398,837 porcine expressed sequence tags (ESTs) obtained from GenBank and deposited at: http://pigest.ku.dk/index.html (Gorodkin et al. 2007) using an *E*-value threshold of 10^{-12} and 98% identity.

Nomenclature

The porcine IGLV genes are named according to IMGT nomenclature (Lefranc and Lefranc 2001; Lefranc 2007, 2008), using human V gene subgroup nomenclature to maintain consistency with porcine heavy chain, light chain, and cattle lambda light chain nomenclature (Eguchi-Ogawa et al. 2010; Butler et al. 2005, 2006; Pasman et al. 2010). The porcine IGLV, IGLJ and IGLC genes were submitted to IMGT/GENE-DB (Giudicelli et al. 2005). BLAST at NCBI was used to organize IGLV genes into subgroups using a 75% identity threshold according to IMGT criteria (Lefranc and Lefranc 2001; Lefranc 2007, 2008). Genes were deemed pseudogenes if they contained a truncation, stop codon, frameshift, or a defective initiation codon. Additionally, genes were described as ORF (open reading frame) if they were missing one (or more) key amino acids (1st-CYS 23, CONSERVED-TRP 41, hydrophobic 89, and 2nd-CYS 104). RS were deemed non-canonical if the heptamer was anything other than "CACAGTG" for V-HEPTAMER (or "CACTGTG" for J-HEPTAMER) or if the nonamer contained at least two nucleotides which were each present in less than 10% of all RS described by Ramsden et al. (1994).

Results

Organization of the porcine immunoglobulin lambda locus

The porcine IGL locus spans approximately 229 kb on chromosome 14 (Fig. 1). The IGLV locus is organized in two distinct clusters containing 22 IGLV genes, fewer as compared to humans and cattle, which have three clusters containing a total of 52 and 25 IGLV genes, respectively (Frippiat et al. 1995; Pasman et al. 2010). The C-proximal cluster contains six IGLV genes, of which one is a pseudogene. The C-distal cluster, approximately 65.1 kb upstream, contains 16 IGLV genes, of which eight are pseudogenes. Two of the pseudogenes possess premature stop codons (IGLV3-1 and IGLV8-21), four have mutated start sites (IGLV(III)-8, IGLV1-15, IGLV1-20, and IGLV5-22), five are frameshifted (IGLV(III)-8, IGLV5-11, IGLV5-17, IGLV1-20, and IGLV5-22), and one (IGLV1-12) is missing the V-EXON (Table 1). In addition, multiple codons are deleted from both IGLV3-1 and IGLV5-11. Two additional genes are classified as ORF (IGLV7-7 and IGLV7-9) since they lack the highly conserved cysteine residue at IMGT position 104 (2nd-CYS), which is critical for intrachain disulfide bond formation with the cysteine at position 23 (1st-CYS) and are therefore unlikely to be functional (Tables 1 and 2) (Lefranc et al. 2003; Bergman and Kuehl 1979). IGLV8-16 contains an insertion within CDR3, creating a premature stop codon at the 3' end of the gene. However, due to exonuclease and terminal deoxynucleotidyl transferase (TdT) activity in the V–J junction during recombination, it is plausible for this stop codon to be altered and generate a functional V region. The intervening region between the IGLV clusters contains the genes PRAME and ZNF280B, syntenic with cattle (Pasman et al. 2010).

The presence of additional IGLV clusters farther upstream was ruled out by analyzing contiguous, overlapping sequence represented by the fully sequenced BACs CH242-298L14 and CH242-82N3 (Fig. 1a). These BACs extend approximately 445 kb upstream from the most upstream IGLV gene, IGLV5-22. Flanking the IGL locus upstream from IGLV5-22 on these BACs are the genes *SLC5A4*, *SLC5A1*, *YWHAH*, and *DEPCD5* (ordered from IGL-

proximal to distal), syntenic with the cattle upstream flanking genes (UCSC Genome Browser, assembly: bos_taurus_UMD_3.1/bosTau6). This effectively rules out the possibility of additional upstream IGLV clusters and makes the germline porcine IGL locus more compact than that of cattle.

In contrast to the mouse IGL locus which is organized in tandem V–J–C cassettes (Sanchez et al. 1991), the organization of the porcine IGL locus is similar to most other mammals having tandem J–C cassettes downstream of the IGLV genes (Fig. 1d). Approximately 91 kb of sequence on CH242-524K4 lies downstream of IGLJ4, the most 3' IGLJ gene. However, no corresponding IGLC gene was identified, based on both chain-termination and next generation sequencing. Likewise, PCR failed to amplify a product when using an IGLJ4-specific forward primer when paired with either of two conserved constant region reverse primers, despite positive results with the other IGLJ-specific primers (data not shown). The canonical amino acid motif W/F-G-X-G was present in the IGLJ genes save IGLJ1, which also has a non-canonical RS, indicating that swine only possess two functional J–C cassettes: IGLJ2–IGLC2 and IGLJ3–IGLC3 (Table 3).

Phylogenetic analysis of IGLV genes

The C-proximal IGLV cluster contains five genes (four functional and one pseudogene) all belonging to either the IGLV3 or IGLV2 subgroups. The second cluster is comprised of 16 genes, six of which belong to the IGLV8 subgroup, four belong to IGLV5, three belong to IGLV1, two belong to IGLV7, and one, which most closely resembles members of IGLV clan III yet is distinct from any defined subgroup. This organization differs from cattle, which possess four IGLV2 subgroup genes and four IGLV3 subgroup genes in the most C-proximal IGLV cluster and exclusively contain IGLV1 genes in their second and third IGLV clusters (Pasman et al. 2010). Interestingly, IGLV8 subgroup genes are at least 92.4% identical to each other compared to IGLV1, IGLV3, and IGLV5 genes which are only 84.5%, 74.2%, and 79.5% identical, respectively. This suggests that porcine IGLV8 genes result from a recent expansion by gene duplication (Fig. 2).

Allelic variation

BACs at the 5' and 3' ends of the IGLV locus overlap with approximately 99% identity. All eight IGLV genes in these overlaps differ by at least a single nucleotide (Table 1). IGLV3-3, IGLV3-4, IGLV8-19, and IGLV8-21 differ by two, four, six, and eight amino acids between alleles, respectively (Table 2). A gene order polymorphism was found in the second IGLV cluster at the 5' end of the locus, where the last four IGLV genes have a different order (Fig. 1b and c). However, it is not certain if it is real or is an artifact due to whole genome shotgun sequencing and assembly error.

The CH242-141B5 insert terminates downstream of IGLJ3 and is therefore missing IGLC3 and IGLJ4. There are no nucleotide substitutions in any of the first three IGLJ genes or their respective RS between BACs. Sequence analysis revealed, however, that IGLC2 on CH242-524K4 contains a non-synonymous SNP resulting in an A1>T (using IMGT numbering) amino acid substitution. Other than this polymorphism, all of the constant region exons are identical (Table 4).

Expression of IGLV genes

Only IGLV3 and IGLV8 subgroup genes are predicted to be expressed based on functionality and RS (Table 5), in agreement with a previous report (Butler et al. 2006). BLAST analysis of a porcine EST database revealed that all functional IGLV8 subgroup genes are expressed, with IGLV8-13 and IGLV8-18 expressed most abundantly, but only two IGLV3 subgroup genes were expressed (Fig. 3). In contrast, IGLV3 family members were reported to dominate the expressed pre-immune lambda repertoire in neonatal pigs (Butler et al. 2006). Additionally, low level expression of IGLV5-14 was observed despite the presence of non-canonical heptamer and nonamer sequences (Table 5).

A canonical octamer (ATTTGCAT) necessary for transcription was present upstream of all IGLV genes except for six (IGLV2-6, IGLV-7, IGLV5-11, IGLV5-14, IGLV1-15, and IGLV5-17). The octamer was located 106 bp upstream of the seven most highly expressed IGLV genes (six IGLV8 subgroup genes and IGLV3-3). The mean distance among all IGLV genes was 94 bp and ranged from 82 to 108 bp (Table 5), which is typical of mammals (Parslow et al. 1984).

Discussion

The porcine IGL locus organization is typical among mammalian species, containing multiple V genes followed by tandem J–C cassettes. Among described species, it is most similar in organization to, but is more compact than cattle, another member of the order Cetartiodactyla. The capacity for recombinatorial diversity is significantly limited since more than half of the V genes are pseudogenes or ORFs and one of four J genes lacks a paired C gene. The lack of IGLC4 downstream of IGLJ4 and a non-canonical heptamer and mutated W/F-G-X-G motif associated with IGLJ1 suggest that swine use only two J–C cassettes (IGLJ2–IGLC2 and IGLJ3–IGLC3). The only porcine lambda cDNA previously described is identical to IGLJ3 (Lammers et al. 1991).

Screening of EST databases indicates that the vast majority of expressed IGLV genes belong to the IGLV8 subgroup, followed by IGLV3 and IGLV5. The IGLV8 subgroup is the result of a recent expansion, presumably by gene duplication, suggesting that its products have provided a strong selective advantage. Our EST analysis differs from an earlier report which showed that the C-proximal IGLV3 is the most highly expressed IGLV subgroup in the porcine pre-immune repertoire (Butler et al. 2006). The preferential use of C-proximal IGLV2 and IGLV3 subgroup genes has been reported in humans (Frippiat et al. 1995). Similarly, C-proximal IGHV gene preference has been reported in mice (Yancopolous et al. 1984; Malynn et al. 1990), rabbits (Knight and Becker 1990), and humans (Berman et al. 1991). However, in mice, IGHV gene usage shifts upstream with animal age, possibly due to an increased presence of peripheral B cells bearing more distal genes as a result of environmental stimulation, since the number of pre-B cells possessing C-proximal rearrangements remains unchanged in the bone marrow of adult mice (Malynn et al. 1990; Jung et al. 2006). It is plausible that swine may similarly shift IGLV usage upstream with age and peripheral antigenic stimulation. In addition, several IGLV3 genes containing canonical RS were not detected in the EST database, due possibly to poor reactivity to

exogenous antigen so that the B cells expressing these genes are rare, or the B cells may have been deleted due to reactivity to self-antigens.

The size of the expressed repertoire may be increased by allelic variation. Polymorphisms, comprising from two to eight amino acid differences, were identified in four of the eight IGLV genes that were present in overlapping BACs from the single animal used to construct the BAC library. Thus, allelic variation in swine V regions may significantly increase the complexity of the lambda repertoire.

The two most C-proximal human IGLV clusters are dominated by 34 IGLV genes largely belonging to IGLV2 and IGLV3. The reduced complexity of C-proximal IGLV in pigs compared to cattle suggests that this cluster has undergone contraction and expansion during the divergent evolution of these two species. The third human IGLV cluster is dominated by IGLV1, IGLV5, and IGLV7 which correspond to the swine IGLV genes of the distal cluster. IGLV8, however, only occurs as a single gene in the most distal region of the third human IGLV cluster, suggesting that significant gene order reshuffling as well as expansion and/or contraction has occurred specifically during suid evolution. Thus, the immunogenetic loci may represent ideal regions for identifying intra-species gene order and gene content polymorphisms.

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Fig. 1.

Organization of the porcine (*Sus scrofa domestica*) immunoglobulin lambda (*IGL*) locus. **a** BACs used to determine locus organization. *Grey and black bars* represent allelic variation. **b** IGL locus gene organization. Genes are displayed along a scaffold line as *vertical bars* representing functional genes (*long bars*), pseudogenes (*short bars*), or ORF (*intermediate bars*). **c** Rearranged gene order in IGLV1-19 to IGVL1-22 in BAC CH242-288F14. **d** Organization of the IGL J–C locus. The non-Ig genes *ZNF280B*, *PRAME*, and *SLC5A4* are shown for genomic context



Fig. 2.

Phylogenetic analysis of porcine (*Sus scrofa domestica*) IGLV nucleotide sequences using UPGMA with 1,000 bootstrap iterations. Genes comprising the most highly expressed subgroup, IGLV8, are very tightly clustered, suggestive of a relatively recent expansion. Nodes are labeled with bootstrap values



Fig. 3.

Expression of porcine (*Sus scrofa domestica*) IGLV genes. BLAST analysis revealed 116 hits to germline IGLV sequences from 398,837 expressed sequence tags in GenBank and deposited at http://pigest.ku.dk/index.html (Gorodkin et al. 2007). The *x*-axis is organized by gene order in the locus with the most 5' (most C-distal) IGLV genes on the left. Genes belonging to the IGLV8 subgroup dominate the expression profile

Table 1

Porcine (Sus scrofa domestica) IGLV subgroups, gene and allele names (allele functionality, clone names and accession numbers are provided)

IMGT subgroup	IMGT gene name	IMGT allele name	Fct	Clone names	Clone accession numbers
IGLV1	IGLV1-12	IGLV1-12*01	ьa	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2
	IGLV1-15	IGLV1-15*01	$q\mathrm{d}$	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2
	IGLV1-20	IGLV1-20*01	\mathbf{P}^{c}	CH242-15805	CU468977.2
		IGLV1-20*02	\mathbf{b}^{c}	CH242-141B5	CU467669.2
IGL V2	IGLV2-6	IGLV2-6*01	ц	CH242-141B5	CU467669.2
IGL V3	IGLV3-1	IGLV3-1*01	pd	CH242-141B5	CU467669.2
		IGLV3-1*02	pd	CH242-524K4	CU467599.3
	IGLV3-2	IGLV3-2*01	ц	CH242-141B5	CU467669.2
		IGLV3-2*02	Ц	CH242-524K4	CU467599.3
	IGLV3-3	IGLV3-3*01	ц	CH242-141B5	CU467669.2
		IGLV3-3*02	ц	CH242-524K4	CU467599.3
	IGLV3-4	IGLV3-4*01	Ц	CH242-141B5	CU467669.2
		IGLV3-4*02	ц	CH242-524K4	CU467599.3
	IGLV3-5	IGLV3-5*01	ц	CH242-141B5	CU467669.2
IGL V5	IGLV5-11	IGLV5-11*01	\mathbf{P}^{e}	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2
	IGLV5-14	IGLV5-14*01	Ц	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2
	IGLV5-17	IGLV5-17*01	\mathbf{P}^{f}	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2
	IGLV5-22	IGLV5-22*01	P^{g}	CH242-15805	CU468977.2
		IGLV5-22*02	P^{g}	CH242-288F14	CU468665.2
IGL V7	IGLV7-7	IGLV7-7*01	ORF ^h	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2

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IMGT subgroup	IMGT gene name	IMGT allele name	Fct	Clone names	Clone accession numbers
	6-LV7-91	IGLV7-9*01	ORF ⁱ	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2
IGL V8	IGLV8-10	IGLV8-10*01	ц	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2
	IGLV8-13	IGLV8-13*01	ц	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2
	IGLV8-16	IGLV8-16*01	ц	CH242-15805	CU468977.2
				CH242-141B5	CU467669.2
	IGLV8-18	IGLV8-18*01	ц	CH242-15805	CU468977.2
	IGLV8-19	IGLV8-19*01	ц	CH242-15805	CU468977.2
		IGLV8-19*02	ц	CH242-288F14	CU468665.2
	IGLV8-21	IGLV8-21*01	Ρį	CH242-15805	CU468977.2
		IGLV8-21*02	Pj.	CH242-288F14	CU468665.2

Fct functionality, F functional, P pseudogene, ORF open reading frame

CU468977.2

CH242-15805

Ρķ

IGLV(III)-8*01

IGLV(III)-8

IGLV(III)

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^aV-EXON is missing

^bINIT-CODON replaced by Val (ATG>GTG)

^cINIT-CODON replaced by Arg (ATG>CGG); frameshift at position 98; 2nd-CYS replaced by Val; STOP-CODON at pos. 105

 d STOP-CODON in L-PART1, codons 80–87 are deleted

 e 14 nt deletion and frameshift from codons 2–6, frameshift at position 45

 $f_{\rm Frameshift}$ at position 57

 g L-PART1 and V-EXON are fused, INIT-CODON is replaced by Leu (ATG>CTG), frameshift in FR3-IMGT

 $h_{2nd-CYS}$ replaced by Tyr

i 2nd-CYS replaced by Ser

^jSTOP-CODON in L-PART1

 $k_{\rm INIT}\text{-}{\rm CODON}$ replaced by Lys (ATG>AAG); frameshift in FR1-IMGT

Table 2

IMGT protein display of in-frame porcine (Sus scrofa domestica) IGLV genes

	FR1-	IMGT	CDR1-IMGT	FR2 - 1	IMGT	CDR2-IMGT		FR3	-IMGT		CDR3-IMGT
	(1-	26)	(27-38)	(39	-55)	(56-65)		(66	-104)		(105-117)
	A	в	BC	C	C'	C'C"	C"	D	E	F	FG
	(1-15)	(16-26)	(27-38)	(39-46)	(47-55)	(56-65)	(66-74)	(75-84)	(85-96)	(97-104)	
	>	>		>	>		>	>	>	>	
	1 15	16 26	27 38	39 46	47 55	56 65	66 74	75 84	85 96	97 104	105 11
			[[]	[]			
IGLV1-15*01	QAVLTQPPS.ESGSL	GQRVTLSCTGS	SSNIGGGNS	VNWSQPLP	GKVPRSVFT	YAN	LMAIAAP.D	QFSGFKSG	SSGTLTITGLQA	EDDAEYYC	TAGGDSLDG
IGLV1-20*01	QAVLTQLLS.TSGSL	GQRVTLSCTGS	SSNIGSGNT	VNWSQQLP	GKAPRTIID	$\texttt{GN}\ldots \texttt{S}$	NRPSGVP.D	QFSGSKSG	SSGTLTITGLQA	ELRLSITV	* PGRTASMV
IGLV2-6*01	QSALTQPPS.VSRNL	KEMETISCAGT	SSDIGGY	VSWYQQHP	GLAPKFLIY	$\texttt{YV} \dots \dots \texttt{N}$	TRASGIP.D	GFCGSKSG	NTASLTISGLQA	EDEADYYC	SSPRSGGTL
IGLV3-1*01	SCELTQPPS.LSVSL	GQMARITCGGN	NIGYKH	TFWYQQKV	GQAPVLVMY	SDS	HQLSGIP.E	LFSGS	TLTISRARA	EDEEDYYC	AVADGKGSS
IGLV3-2*01	SYEVTQPPS.VSVNP	GQRASITCEGN	NIGRKD	IQWYQQKP	GQAPVLFIY	EDT	NRPSGIP.E	RFSASKSG	NTATLTISGAQA	EDEADYYC	QSYDDSYTP
IGLV3-3*01	SYELTQPSS.ESVAL	GNTAKITCSGD	LLDEKY	TQWYQQKP	GQAPLLLIY	KDS	ERPSGIP.E	RFSGSSSG	KTATLTITGAQA	EDEADYYC	QSADSIDNA
IGLV3-3*02	SYELTQPSS.ESVAL	GNTAKITCSGD	LLDEKY	TRWYQQKP	GQAPLLLIY	KDS	ERPSGIP.E	RFSGSSSG	KTATLTITGAQA	EDEADYYC	QSADSSDNA
IGLV3-4*01	SSKLTQPPG.VSVSL	GGTASIACQGD	NFGSYY	AHWYQQKP	GQSPMLVIY	EYN	KRASGIP.D	RFSGSKSG	NTATLTISGAQA	EDEADYYC	QSSDDSYTP
IGLV3-4*02	SSQLTQPPG.VSVSL	GGTASITCQGG	NFGSYY	AHWYKQKP	GQSPMLVIY	EYN	KRASGIP.D	RFSGSKSG	NTATLTISGAQA	EDEADYYC	QSSDDSYTP
IGLV3-5*01	SSKLTQPPG.VSVSL	GGTASITCQGA	NFGSYY	AHWYQQKP	GQSPELVIY	EYP	EIFLGFL.E	RFSVSRTG	DTATLTISGAQA	EDEADYYC	QVYDGGYHV
IGLV5-14*01	QAVLTQPPS.LSASP	GPSARLPCTLS	SGSSVGSYH	ISWYQRKP	GRPPWYLLR	FHFAS.SKDQ	GSGVPSC.F	SGDKDASA	HAGLLLISGLQP	EDKADCDC	LNWQSSAS
IGLV7-7*01	SQMVTQEIS.LSTTS	GETVTLTCGSS	AGAVTTSNY	ASWVQQKP	YEVLWGLIG	$GT\ldots S$	TQIPGVP.A	RFSGSLLG	DKAALTRSGAQS	KDEADYYY	VLWFSNV
IGLV7-9*01	PSCVTQEPS.KTVSP	GVTVTFTCGSS	MGVVTIGHY	PCWFQQKP	GQAPRTLIY	$DT \dots N$	SKLSWTP.A	WFSGSFLG	DKAALILSRAQP	QDQVEYYS	GAQ
IGLV8-10*01	SQTVIQEPA.MSVSP	GGTVTLTCAFS	SGSVTTSNY	PSWFQQTP	GQPPRLLIY	RTN	NRPTGVP.S	RFSGAISG	NKAALTITGAQA	NDEADYFC	TLYKSSAN
IGLV8-13*01	SQTVIQEPA.MSVSP	GGTVTLTCAFS	SGSVTTSNY	PSWFQQTP	GQPPRQLIY	STN	NRPTGVP.S	RFSGAISG	NKAALTITGAQA	EDEADYFC	ALYKSSAN
IGLV8-16*01	SQTVIQEPA.MSVSL	GGTVTLTCAFS	SGSVTSSNY	PSWYQQTP	GQPPRQLIY	STN	SRPTGVP.S	RFSGAISG	NKATLTITGAQA	EDEADYFC	ALYKGSGTYT
IGLV8-18*01	SQTVIQEPA.MSVSL	GGTVTLTCAFS	SGSVTSSNY	PGWFQQTP	GQPPRTVIY	STN	SRPTGVP.S	RFSGAISG	NKATLTITGAQA	EDEADYFC	ALYKSCTN
IGLV8-19*01	SQTVIQEPA.MSVSL	GGTVTLTCAFS	SGSVTSSNN	PGWFQQTP	GQPPRTVIY	QTN	NRPTGVP.S	RFSGAISG	NKATLTITGAQA	EDEADYFC	ALGKSCTN
IGLV8-19*02	SQTVIQEPA.MSVSL	GGTVTLTCAFS	SGSVTSSNY	PGWYQQTP	GQPPRQLIY	STN	SRPTGVP.S	RFSGAISG	NKATLTITGAQA	EDEADYFC	ALYKSCTN
IGLV8-21*01	SQTVIQEPA.MSVSP	GGTVTLTCAFS	SGSVTTSNY	PGWYQQTP	GQPPRQLIY	QTN	SRPTGVP.S	RFSGAISG	NKATLTITGAQA	EDEADYFC	ALEKSSAN
IGLV8-21*02	SQTVIQEPA.MSVSP	GGTVTLTCAFS	SGSVTTSNY	PSWFQQTP	GQPPRQLIY	QTN	SRPTGVP.S	RFSGAISG	NKATLTITGAQA	EDEADYFC	ALEKSSAN

The protein display is shown using IMGT header (IMGT Repertoire, http://www.imgt.org) and IMGT unique numbering for V region and V domain (Lefranc et al. 2003)

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IGLV gene	Fct	J-NONAMER	J-SPACER	J-HEPTAMER	J-REGION nt and AA sequences
IGLJI	4	GGGTTITGT	TCGAGCCTCAGT	CAGCGTG	GTATTTTTCCGGCAGCGAGGAGTCTAGCGCCTTAG Y F S G S E T Q F T A L
IGLJ2	щ	GGTTTATGT	TTGAGGCTGTAT	CACTGTG	TAATATTTTCGGCGCGGGGGGGCCCATCTGACCGTCCTCG N I F G G G T H L T V L
IGLJ3	ц	GGTTTATGT	TTGAGGCTGTAT	CACTGTG	TGTTCCCTTCGGCGCTGGGACCCATCTGACCGTCCTCG V P F G G G T H L T V L
IGLJ4	щ	GGTTTATGT	TTGAGGCTGTAT	CACTGTG	CGATAGGTTCGGCCGAGGGACCCGTCTCC D R F G R G T R L S V L

 ${\it Fct}$ functionality, ${\it F}$ functional, ${\it P}$ pseudogene

Table 4

MGT protein display of porcine (Sus scrofa domestica) IGLC genes

	A	AB	В	BC	С	CD	D	DE	E	EF	F	FG	G
	(1-1	5)	(16-26)	(27-38)	(39-45)		(77-84)		(85-96)		(97-104)	(105-117)	(118-128)
		>	>		>		>		·	->	>		
	1	15	16 26	27 38	39 45		77 84		85 9	96	97 104	105 117	118
	87654321	123	8	·····	1	234567	7 12345	5677654323	ι]	12	[]]
GLC1*01	QPKAAPTVNLFP:	PSSEELG	TNKATLVCLIS	DFYPGAVT	VTWKAGGI	TVTQ.	GVETTKPSKQSN	NKY2	AASSYLALSASI	DW	KSSSGFTC	QVTHEGTIV	EKTVTPSEC
GLC2*01	QPKAAPTVNLFP:	PSSEELG	TNKATLVCLIS	DFYPGAVT	VTWKAGGI	TVTQ.	GVETTKPSKQSN	NKY/	ASSYLALSASI	DW	KSSSGFTC	QVTHEGT IV	EKTVTPSEC
GLC2*02	QPKATPTVNLFP:	PSSEELG	TNKATLVCLIS	DFYPGAVT	VTWKAGGI	TVTQ.	GVETTKPSKQSN	NKY/	ASSYLALSASI	DW	KSSSGFTC	QVTHEGTIV	EKTVTPS EC
GLC3*01	QPKAAPTVNLFP:	PSSEELG	TNKATLVCLIS	DFYPGAVT	VTWKAGGI	TVTQ.	GVETTKPSKQSN	NKY/	AAS SYLALSASI	DW	KSSSGFTC	QVTHEGTIV	EKTVTPSE

The protein display is shown using IMGT header (IMGT Repertoire, http://www.imgt.org) and IMGT unique numbering for C domain (Lefranc et al. 2005)

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IGLV gene	Fct	Octamer (promoter)	Ħ	Ini.	L-PART1 (nt)	5' Splice site	Intron (nt)	3' Splice site	V-EXON (nt)	V-HEPTAMER	V-SPACER (nt)	V-NONAMER
IGLV3-1*01	Ч	ATTTGCAT	96	ATG	46	GT	358	AG	282	CCCAGTG	37	ACACAAACT
IGLV3-2*01	ц	ATTTGCAT	96	ATG	46	GT	370	AG	299	CACAGTG	23	ACACAAACT
IGLV3-2*02	Ц	ATTTGCAT	96	ATG	46	GT	363	AG	299	CACAGTG	17	ACACAAACT
IGLV3-3*01	ц	ATTTGCAT	106	ATG	46	GT	143	AG	299	CACAGTG	23	ACACAAACC
IGLV3-4*01	Ц	ATTTGCAT	82	ATG	46	GT	151	AG	299	CACAGTG	23	ACACAAACC
IGLV3-5*01	Ц	ATTTGCAT	82	ATG	46	GT	151	AG	299	CACAGTG	23	ACACAAACT
IGLV3-5*02	ц	ATTTGCAT	82	ATG	46	GT	151	AG	299	CACAGTG	23	ACACAAACC
IGLV2-6*01	ц	ATTTGTAT	101	ATG	46	GT	116	AG	302	TACAGTG	23	ACACAAACC
IGLV7-7*01	ORF	ATCTGCAT	101	ATG	46	GT	97	AG	301	CACCGTG	23	ACATGAGCC
IGLV(III)-8	Ь	ATTTGCAT	93	AAG	47	GT	111	AG	267	CACAGTG	21	ACTCAAACC
IGLV7-9*01	ORF	ATTTGCAT	108	ATG	43	GT	85	AG	288	CACAGTG	23	GACACAAAG
IGLV8-10*01	ц	ATTTGCAT	106	ATG	46	GT	97	AG	304	CACAGTG	23	ACCCAAACC
IGLV5-11*01	Ч	ACTGGCAT	87	ATG	46	GT	109	TG	303	CACAATG	23	AAAAACAT
IGLV1-12*01	Ь	ATTTGCAT	108	ATG	46	GA	I	Ι	I	1	I	1
IGLV8-13*01	Ц	ATTTGCAT	106	ATG	46	GT	97	AG	304	CACAGTG	23	ACCCAAACC
IGLV5-14*01	ц	ACTGGCAT	88	ATG	46	GT	121	AG	323	CACTGTG	23	AGAAGAATC
IGLV1-15*01	Ч	ATTGGCAT	107	GTG	46	GT	106	AG	310	CACAGTG	23	ACCAAAACC
IGLV8-16*01	Ц	ATTTGCAT	106	ATG	46	GT	97	AG	312	CACAGTG	23	ACCCAAACC
IGLV5-17*01	Ч	ACTGGCAT	87	ATG	46	GT	121	AG	302	CACTGTA	23	TGGGAACGG
IGLV8-18*01	ц	ATTTGCAT	106	ATG	46	GT	97	AG	304	CACAGTG	23	ACTCAAACC
IGLV8-19*01	ц	ATTTGCAT	106	ATG	46	GT	97	AG	304	CACAGTG	23	ACCCAAACC
IGLV8-19*02	ц	ATTTGCAT	105	ATG	46	GT	98	AG	304	CACAGTG	23	ACCCAAACC
IGLV1-20*01	Ч	ATTTGCAT	88	CGG	46	GT	108	AG	309	CACAGTG	23	ACCAAAACC
IGLV1-20*02	Ч	ATTTGCAT	91	CGG	46	GT	108	AG	309	CACAGTG	23	ACCAAAACC
IGLV8-21*01	Ч	ATTTGCAT	106	ATG	46	CC	96	AG	304	CACAGTG	23	ACCCAAACC
IGLV5-22*01	Р	ATTTGCAT	103	CTG		ı			354	CACAGTG	23	AGAAGAATC
IMGT standardiz	zed labels	s are written in <i>capital let</i> .	ters									

Immunogenetics. Author manuscript; available in PMC 2015 April 02.

 Fct functionality, F functional, P pseudogene, ORF open reading frame