

The Human Immunoglobulin Heavy Diversity (IGHD) and Joining (IGHJ) Segments

Manuel Ruiz Nathalie Pallarès Valérie Contet Valérie Barbié
Marie-Paule Lefranc

Laboratoire d'ImmunoGénétique Moléculaire CNRS, Université Montpellier II,
Montpellier, France

Key Words

Human · IMGT · Immunoglobulin · Heavy

Abstract

The 'Human Immunoglobulin Heavy Diversity (IGHD) and Joining (IGHJ) segments', fifth report of the 'IMGT Locus on Focus' section, comprises six tables entitled: (1) 'Human germline IGHD segments at 14q32.33'; (2) 'Human IGHD alleles'; (3) 'Human germline IGHJ segments at 14q32.33'; (4) 'Human IGHJ alleles'; (5) 'Human germline IGHD orphans on chromosome 15 (15q11.2)'; (6) 'Correspondence between the different human IGHD nomenclatures', and two figures: (1) 'Protein display of human IGH D-REGIONS'; (2) 'Protein display of human IGH J-REGIONS'. These tables and figures are available at the IMGT Marie-Paule page from **IMGT**, the international ImMunoGeneTics database (<http://imgt.cnusc.fr:8104>) created by Marie-Paule Lefranc, Université Montpellier II, CNRS, France.

Introduction

'Human Immunoglobulin Heavy Diversity (IGHD) and Joining (IGHJ) segments' is the fifth report of the 'IMGT Locus on Focus' section launched in the April 1998 issue of *Experimental and Clinical Immunogenetics* [1], with the first report on the human IGLV genes and IGLJ segments [2], the second report on human IGKV genes and IGKJ segments [3], the third report on mouse (*Mus musculus*) IGKV genes and IGKJ segments [4] and the fourth report on humanIGHV genes [5].

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Prof. Marie-Paule Lefranc, Université Montpellier II
Lab. d'ImmunoGénétique Moléculaire, LIGM, UPR CNRS 1142, IGH
141 rue de la Cardonille, F-34396 Montpellier Cedex 5 (France)
Tel. +33 (0)4 99 61 99 65, Fax +33 (0)4 99 61 99 01
E-Mail lefranc@ligm.igh.cnrs.fr, IMGT: <http://imgt.cnusc.fr:8104>

Table 1

Human germline IgHD segments at 14q32.33

Fct: FUNCTIONALITY

F : Functional

ORF : Open Reading Frame

IgHD subgroup	IgHD name	Fct	Reference sequences	Accession numbers	Position in X97051 (a)	Position in X97051 (b)	Sequences from the literature
1	1-1	F	D1-1	X97051 [8]	23599-35048	33686-33758	M4 [9]
	1-7	F	DM1	X13972 [5]	43057-44649	43272-43344	M37277 [5], D1-7 [X97051][8]
	1-14	ORF	DM2	X13972 [5]	52325-53909	52540-52612	M37277 [5], D1-14 [X97051][8]
	1-20	F	D1-20	X97051 [8]	61770-63337	61987-62059	M3 [9]
	1-26	F	D1-26	X97051 [8]	71927-79765	72141-72216	M'3 [9]
	2	F	D4	J00232 [1]		LR4 [9]	
		F	D2-2	X97051 [8]	35049-37615	36339-36425	
		F	D4	M35648 [3]		M35649 [3]	
	2-8	F	DLR1	X13972 [5]	44650-47262	45954-46040	M37277 [5], D2-8 [X97051][8], M35650 [3]
	2-15	F	D2	J00234 [1]	53910-56408	55207-55293	D2-15 [X97051][8], LR2 [9]
2	2-21	F	D3	J00235 [1]		LR3 [9]	
		F	D2-21	X97051 [8]	63338-65916	64616-64699	
	3	F	DXP4	X13972 [5]	37616-39425	38806-38892	M37277 [5], D3-3 [X97051][8]
		F	D23/7	X93618 [4]			
	3-9	F	DXP1	X13972 [5]	47263-48619	48484-48570	M37277 [5], M37485 [7], D21/0,5 [X93613][4], D3-9 [X97051][8]
	3-10	F	DXP ⁺ 1	X13972 [5]	48620-49158	48668-48754	M37277 [5], M37485 [7], D3-10 [X97051][8]
		F	D21/7	X93615 [4]			
	3-16	F	D21/10	X93614 [4]	56409-58143	57524-57616	D3-16 [X97051][8], XP2 [9]
	3-22	F	D21/9	X93616 [4]	65917-67762	67133-67219	D3-22 [X97051][8], XP3 [9]
	4	F	DA4	X13972 [5]	39426-40474	39958-40029	M37277 [5], D4-4 [X97051][8]
4	4-11	ORF	DA1	X13972 [5]	49159-50078	49563-49634	M37277 [5], (2), D4-11 [X97051][8]
	4-17	F	D4-17	X97051 [8]	58144-59187	58671-58742	A2 [9]
	4-23	ORF	D4-23	X97051 [8]	67763-68226	68306-68380	A3 [9]
	5	F	DK4	X13972 [5]	40475-41880	40919-40994	M37277 [5], D5-5 [X97051][8]
	5-12	F	DK1	X13972 [5]	50079-51316	50523-50601	M37277 [5], D5-12 [X97051][8]
	5-18	F	D5-18	X97051 [8]	59188-60591	59633-59708	K2 [9]
	5-24	ORF	D5-24	X97051 [8]	68827-70492	69272-69347	K3 [9]

6	6-6	F	DN4	X13972 [5]	41881-43056	42767-42840	M37277 [5], D6-6 [X97051][8]
	6-13	F	DN1	X13972 [5]	51317-52324	52032-52108	M37277 [5], D6-13 [X97051][8]
	6-19	F	D6-19	X97051 [8]	60592-61769	61475-61551	N2 [9]
	6-25	F	D6-25	X97051 [8]	70493-71926	71638-71711	N3 [9]
7	7-27	F	DHQ52	J00256 [2]	87428-87515	87431-87497	D7-27 [X97051][8], X86355 [6], X86356 [6], X86357 [6], X86358 [6], X86359 [6]

(a) Arbitrary limits of the DNA sequence assigned to the different D-SEGMENTS

(b) Limits from the 5D-NONAMER to the 3D-NONAMER

Notes

- (1) The g29>c and c30>g substitutions in X97051 EMBL flat file are probably typing errors.
- (2) The deletion of one nucleotide (t) in M37277 EMBL flat file is probably a typing error. This deletion does not exist in the paper.

References

- [1] Siebenlist, U. et al., *Nature*, 294: 631-635 (1981)
- [2] Ravetch, J.V. et al., *Cell*, 27: 583-591 (1981)
- [3] Zong, S.Q. et al., *Immunol.Lett.*, 17: 329-334 (1988)
- [4] Buluwela, L. et al., *EMBO J.*, 7: 2003-2010 (1988)
- [5] Ichihara, Y. et al., *EMBO J.*, 7: 4141-4150 (1988)
- [6] Mattila, P.S. et al., *Eur.J.Immunol.*, 25: 2578-2582 (1995)
- [7] Huang, C. et al., Unpublished
- [8] Corbett, S. Unpublished
- [9] Matsuda, F. et al., *J.Exp.Med.*, 188: 2152-2162 (1998). Accession number AB019441 is not yet available (March 99).

Analyst/Contact : Manuel Ruiz (manu@ligm.igh.cnrs.fr)

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Table 2**Human IGHD alleles**

Fct : FUNCTIONALITY

F : Functional

ORF : Open Reading Frame

D-REGION alleles are only described at the nucleotide level since D-REGION can be used in the three reading frames. The numbering starts with the first nucleotide following the heptamer.

The accession number of a reference sequence is given for each allele.

IGHD subgroup	IGHD name	Fct	IGHD allele name	Accession number	confirmed by genetics and/or data	Description of mutations
1	1-1	F	D1-1*01	X97051		
	1-7	F	D1-7*01	X13972	+	
	1-14	ORF	D1-14*01	X13972	+	
	1-20	F	D1-20*01	X97051		
	1-26	F	D1-26*01	X97051		
2	2-2	F	D2-2*01	J00232		a1 g29
		F	D2-2*02	X97051		g29>a
		F	D2-2*03	M35648	+	a1>t
	2-8	F	D2-8*01	X13972	+	a14 a15
		F	D2-8*02	J00233		a14>g a15>g
	2-15	F	D2-15*01	J00234	+	
	2-21	F	D2-21*01	J00235	+	t19
		F	D2-21*02	X97051		t19>c
3	3-3	F	D3-3*01	X13972	+	c7 g8
		F	D3-3*02	X93618		c7>g g8>c
	3-9	F	D3-9*01	X13972	+	
	3-10	F	D3-10*01	X13972	+	g12
		F	D3-10*02	X93615		g12>del
	3-16	F	D3-16*01	X93614	+	
	3-22	F	D3-22*01	X93616	+	
4	4-4	F	D4-4*01	X13972	+	
	4-11	ORF	D4-11*01	X13972	+	
	4-17	F	D4-17*01	X97051		
	4-23	ORF	D4-23*01	X97051		
5	5-5	F	D5-5*01	X13972	+	
	5-12	F	D5-12*01	X13972	+	
	5-18	F	D5-18*01	X97051		
	5-24	ORF	D5-24*01	X97051		
6	6-6	F	D6-6*01	X13972	+	
	6-13	F	D6-13*01	X13972	+	
	6-19	F	D6-19*01	X97051		
	6-25	F	D6-25*01	X97051		
7	7-27	F	D7-27*01	J00256	+	

Analyst/Contact : Nathalie Pallarès (ligm@ligm.igh.cnrs.fr)

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Table 3**Human germline IGHJ segments at 14q32.33**

Fct : FUNCTIONALITY
 F : Functional
 P : Pseudogene

IGHJ name	Fct sequences	Accession numbers	Sequences from the literature
IGHJ1P	P J1P	J00256 1	X86355/X86356/X86357/X86358/X86359 [3](2), X97051 [4]
IGHJ1	F J1	J00256 1	X86355/X86356/X86357/X86358/X86359 [3](2), X97051 [4]
IGHJ2	F J2	J00256 1	X86355/X86356/X86357/X86358/X86359 [3](2), X97051 [4]
IGHJ2P	P J2P	J00256 1	X86355/X86356/X86357/X86358/X86359 [3](2), X97051 [4]
IGHJ3	F J3	J00256 1	M25625 [2]
	F	X86355/X86356/X86357/X86358/X86359 [3](2)	X97051 [4]
IGHJ4	F J4	J00256 1	X86355/X86356/X86357/X86358/X86359 [3](2)
	F	X86355/X86356/X86357/X86358/X86359 [3](2)	X97051 [4]
	F	M25625 [2](5)	
IGHJ5	F J5	J00256 1	M25625 [2]
	F	X86355/X86356/X86357/X86358/X86359 [3](2)	X97051 [4]
IGHJ3P	P J3P	J00256 1	M25625 [2]
	P	X86355/X86356/X86357/X86358/X86359 [3](2)	X97051 [4]
IGHJ6	F J6	J00256 1	
	F	X86355/X86357/X86358/X86359 3	X97051 [4], M63031 [5], M25625 [2](5)
	F	X86356/X86359 [3](4)	M63030 [5]

Notes

- Haplotypes have been described in Mattila et al., Eur. J. Immunol., 25, 2578-2582 (1995) [1] Ravelich et al., Cell, 27, 583-591 (1981)
 (1) sequenced in haplotype a.
 (2) sequenced in haplotypes b1, b1c, b2, b3 and c, respectively.
 (3) sequenced in haplotypes b1, b2 and b3, respectively.
 (4) sequenced in haplotypes b1c and c, respectively.
 (5) sequenced in haplotype d.

Analyst/Contact : Nathalie Pallarès (nigm.igh.cns.fr)
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References

- [2] Rabbits, Biochem. Soc. Trans., 11, 119-126 (1983)
 [3] Mattila et al., Eur. J. Immunol., 25, 2578-2582 (1995)
 [4] Corbett. Unpublished.
 [5] Nottembourg and Hasenstab. Unpublished.

Table 4**Human IGHJ alleles**

Fct : FUNCTIONALITY

F : Functional

The accession number of a reference sequence is given for each allele.

IMGT numbering and description of alleles for germline J-REGIONS start with the first nucleotide of the first codon.

IGHJ name	Fct	IGHJ Allele name	Accession number	confirmed by genetics and/or data	Description of mutations	
IGHJ1	F	J1*01	J00256	+		
IGHJ2	F	J2*01	J00256	+		
IGHJ3	F	J3*01	J00256	+	g10 , V4	
	F	J3*02	X86355	+	g10>a, V4>I	
IGHJ4	F	J4*01	J00256		a21 a24	
	F	J4*02	X86355	+	a21>g	
	F	J4*03	M25625		a24>g	
IGHJ5	F	J5*01	J00256	+	t13 , S5 a24	
	F	J5*02	X86355	+	t13>c, S5>p a24>g	
IGHJ6	F	J6*01	J00256		g16 , g17 , t18 , G6 g33 c34 , Q12	
	F	J6*02	X86355	+		g33>c
	F	J6*03	X86356	+	g16>t, g17>a, t18>c, G6>Y g33>c c34>a, Q12>k	

Analyst/Contact : Nathalie Pallarès (ligm@ligm.igh.cnrs.fr)

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This report completes the tables of the immunoglobulin germline genes in humans and comprises six tables entitled:

- (1) 'Human germline IGHD segments at 14q32.33';
- (2) 'Human IGHD alleles';
- (3) 'Human germline IGHJ segments at 14q32.33';
- (4) 'Human IGHJ alleles';
- (5) 'Human germline IGHD orphans on chromosome 15 (15q11.2)';
- (6) 'Correspondence between the different human IGHD nomenclatures',

and two figures:

- (1) 'Protein display of human IGH D-REGIONS';
- (2) 'Protein display of human IGH J-REGIONS'.

Table 5**Human germline IGHD orphans on chromosome 15 (15q11.2)**

Fct : FUNCTIONALITY

ORF : Open Reading Frame

IGHD subgroup	IGHD name	Fct	Reference sequences	Accession numbers	Sequences from the literature
1	1/OR15-1a	ORF	DM5-a	X55575 [3]	
	1/OR15-1b	ORF	DM5-b	X55576 [3]	
2	2/OR15-2a	ORF	D5-a	X55577 [3]	M35647 [1]
	2/OR15-2b	ORF	D5-b	X55578 [3]	M35647 [1]
3	3/OR15-3a	ORF	DXP5-a	X55579 [3]	D22/12 [X93617][2]
	3/OR15-3b	ORF	DXP5-b	X55580 [3]	D22/12 [X93617][2]
4	4/OR15-4a	ORF	DA5-a	X55581 [3]	
	4/OR15-4b	ORF	DA5-b	X55582 [3]	
5	5/OR15-5a	ORF	DK5-a	X55583 [3]	
	5/OR15-5b	ORF	DK5-b	X55584 [3]	

References

- [1] Zong, S.Q. et al., Immunol. Lett., 17: 329-334 (1988)
- [2] Buluwela, L. et al., EMBO J., 7: 2003-2010 (1988)
- [3] Matsuda, F. et al., EMBO J., 9: 2501-2506 (1990)

Analyst/Contact : Manuel Ruiz (manu@ligm.igh.cnrs.fr)

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These tables and figures are available at the IMGT Marie-Paule page from **IMGT**, the international ImMunoGeneTics database (<http://imgt.cnusc.fr:8104>) created by Marie-Paule Lefranc, Université Montpellier II, CNRS, France [6-8].

Description of functionality (FUNCTIONAL, ORF, PSEUDOGENE) and description of mutations [1] are according to the IMGT scientific chart available at the IMGT Marie-Paule page [8].

Table 6**Correspondence between the different human IGHD nomenclatures**

IGHD segments are listed from 5' (top of the table) to 3' (bottom of the table).

IMGT IGHD name	Other designations from the literature	
1-1		M4 [5]
2-2	D4 [1]	LR4 [5]
3-3	23/7 [3]	XP4 [4]
4-4		A4 [4]
5-5		K4 [4]
6-6		N4 [4]
1-7		M1 [4]
2-8	D1 [1]	LR1 [4]
3-9	21/0,5 [3]	XP1 [4]
3-10	21/7 [3]	XP'1 [4]
4-11		A1 [4]
5-12		K1 [4]
6-13		N1 [4]
1-14		M2 [4]
2-15	D2 [1]	LR2 [5]
3-16	21/10 [3]	XP2 [5]
4-17		A2 [5]
5-18		K2 [5]
6-19		N2 [5]
1-20		M3 [5]
2-21	D3 [1]	LR3 [5]
3-22	21/9 [3]	XP3 [5]
4-23		A3 [5]
5-24		K3 [5]
6-25		N3 [5]
1-26		M'3 [5]
7-27	DHQ52 [2]	

Note

IGHD segments are designated by a number for the subgroup followed by a dash and a number for the localisation from 5' to 3' in the locus [6].

References:

- [1] Siebenlist, U. et al., *Nature*, 294, 631-635 (1981).
- [2] Ravetch, J.V. et al., *Cell*, 27, 583-591 (1981).
- [3] Buluwela, L. et al., *EMBO J.*, 7, 2003-2010 (1988).
- [4] Ichihara, Y. et al., *EMBO J.*, 7, 4141-4150 (1988).
- [5] Matsuda F. et al., *J.Exp.Med.*, 188, 2151-2162 (1998).
- [6] Corbett, S. Unpublished X97051

Author: Manuel Ruiz manu@lgm.igh.cnrs.fr

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		Direct 5' - 3' orientation	Inverted orientation
IGHD1-1	X97051, IGHD1-1*01	G T T G T V Q L E R Y N W N D ggtacaactggaaacgac	V V P V V S F Q L Y R S S C T gtcgttccagttgtacc
IGHD1-7	X13972, IGHD1-7*01	G I T G T V * L E L Y N W N Y ggtataactggaaactac	V V P V I * F Q L Y S S S Y T gtagttccaggtaacc
IGHD1-14	X13972, IGHD1-14*01	G I T G T V * P E P Y N R N H ggtataaccggaaaccac	V V P V I W F R L Y G S G Y T gtggttccggtaacc
IGHD1-20	X97051, IGHD1-20*01	G I T G T V * L E R Y N W N D ggtataactggaaacgac	V V P V I S F Q L Y R S S Y T gtcgttccagttacc
IGHD1-26	X97051, IGHD1-26*01	G I V G A T V * W E L L Y S G S Y Y ggtataatgtggagactactac	V V A P T I * * L P L Y S S S H Y T gttagtagctcccactataacc
IGHD2-2	J00232, IGHD2-2*01	R I L * * Y Q L L C G Y C S S T S C Y A D I V V V P A A M aggatattgttagtagtaccagctgttatgcc	G I A A G T T T I S A * Q L V L L Q Y P H S S W Y Y Y N I ggcatagcagctggtaactacaatatccct
	X97051, IGHD2-2*02	R I L * * Y Q L L C G Y C S S T S C Y T D I V V V P A A I aggatattgttagtagtaccagctgttatacc	G I A A G T T T I S A * Q L V L L Q Y P H S S W Y Y Y N I ggtagatagcagctggtaactacaatatccct
	M35648, IGHD2-2*03	W I L * * Y Q L L C G Y C S S T S C Y A D I V V V P A A M tggatattgttagtagtaccagctgttatgcc	G I A A G T T T I S A * Q L V L L Q Y P H S S W Y Y Y N I ggcatagcagctggtaactacaatatccct
IGHD2-8	X13972, IGHD2-8*01	R I L Y * W C M L Y G Y C T N G V C Y T D I V L V Y A I aggatattgtactatgggtatgttatacc	G I A Y T I S T I S V * H T P L V Q Y P Y S I H H * Y N I ggtagatagcatacaccattagtacaatatccct
	J00233, IGHD2-8*02	R I L Y W W C M L Y G Y C T G G V C Y T D I V L V Y A I aggatattgtactatgggtatgttatacc	G I A Y T T S T I S V * H T P B V Q Y P Y S I H H Q Y N I ggtagatagcatacaccatccactacaatatccct
IGHD2-15	J00234, IGHD2-15*01	R I L * W W * L L L G Y C S G G S C Y S D I V V V V A A T aggatattgttagtggtggtagctactcc	G V A A T T T T I S E * Q L P P L Q Y P S S S Y H H Y N I ggagtagcagctaccaccactacaatatccct
IGHD2-21	J00235, IGHD2-21*01	S I L W W * L L F A Y C G G D C Y S H I V V V I A I agcatattgtgggtggtagctattcc	G I A I T T T I C E * Q S P P Q Y A N S N H H H N M ggaatagaatcaccaccacaatatgct
	X97051, IGHD2-21*02	S I L W W * L L F A Y C G G D C Y S H I V V V T A I agcatattgtgggtggtagctattcc	G I A V T T T I C E * Q S P P Q Y A N S S H H H N M ggaatagaatcaccaccacaatatgct
IGHD3-3	X13972, IGHD3-3*01	V L R F L E W L L Y Y Y D F W S G Y Y T I T I F G V V I I gtattacgattttggagtgggttattataacc	G I I T T P K I V I V * * P L Q K S * Y Y N N H S K N R N ggtataataaccactccaaaaatcgtaataac

1a

(For legend 1 see p. 184.)

		Direct 5' - 3' orientation	Inverted orientation
X93618, IGHD3-3*02	IGHD3-9 X13972, IGHD3-9*01	<pre> V L A F L E W L L Y Y * H F W S G Y Y T I S I F G V V I I gtattagcattttggagtggttataacc </pre>	<pre> G I I T T P K M L I V * * P L Q K C * Y Y N N H S K N A N ggtataataaccactccaaaatgctaatac </pre>
IGHD3-10 X13972, IGHD3-10*01	IGHD3-16 X93614, IGHD3-16*01	<pre> V L L W F G E L L * Y Y Y G S G S Y Y N I T M V R G V I I gtattactatggtcggggagttataac </pre>	<pre> V I I T S Q N I V I L * * P V K I S * Y Y N N Q S K Y R N gttataataaccagtcaaaatatcgtaatac </pre>
IGHD3-16 X93614, IGHD3-16*01	IGHD3-22 X93616, IGHD3-22*01	<pre> V L * L R L G E L C L Y Y Y D Y V W G S Y A Y T I M I T F G V M L I gtattatgattacgtttggggagttatgtttatacc </pre>	<pre> V I I T P R T * * Y L * * L P E H S N Y N N S P N I V I gttataataactccccgaac.atagaatac </pre>
IGHD4-4 X13972, IGHD4-4*01	IGHD4-11 X13972, IGHD4-11*01	<pre> * L Q * L D Y S N Y T T V T tgactacagtaactac </pre>	<pre> V V I T T I I V I * * * P L L S * * Y S N N H Y Y H S N gttagtaataaccactatcatagtaatac </pre>
IGHD4-17 X97051, IGHD4-17*01	IGHD4-23 X97051, IGHD4-23*01	<pre> * L R * L D Y G D Y T T V T tgactacggtgactac </pre>	<pre> V V T V V * L L * S S Y C S gtagttactgttagtca </pre>
IGHD5-5 X13972, IGHD5-5*01	IGHD5-12 X13972, IGHD5-12*01	<pre> * L R W * L D Y G G N S T T V V T tgactacggtgactcc </pre>	<pre> V T I A V S * P * L Y P N H S C I H gtaaccatactgttatccac </pre>
IGHD5-12 X13972, IGHD5-12*01	IGHD5-18 X97051, IGHD5-18*01	<pre> V D I V A T I W I * W L R L G Y S G Y D Y gtggatatagtggctacgattac </pre>	<pre> V I V A T I S * S * P L Y P N R S H Y I H gtaatcgtagccactatccac </pre>
IGHD5-18 X97051, IGHD5-18*01	IGHD5-24 X97051, IGHD5-24*01	<pre> V D T A M V W I Q L W L G Y S Y G Y gtggatatacgatgtggttac </pre>	<pre> V T I A V S * P * L Y P N H S C I H gtaaccatactgttatccac </pre>
IGHD5-24 X97051, IGHD5-24*01		<pre> V E M A T I * R W L Q L R D G Y N Y gtagagatggctacaattac </pre>	<pre> V I V A I S * L * P S L N C S H L Y gtaattgttagccatctctac </pre>

1b

(For legends 1 and 2 see p. 184.)

		Direct 5' - 3' orientation	Inverted orientation
IGHD6-6	X13972, IGHD6-6*01	E Y S S S S S I A A R V * Q L V gagtatagcagctcgatcc	G R A A I L D E L L Y T S C Y T ggacgagctgtataactc
IGHD6-13	X13972, IGHD6-13*01	G Y S S S W Y G I A A A G V * Q Q L V gggtatagcagcagctggta	V P A A A I P Y Q L L L Y T S C C Y T gtaccagctgtatacc
IGHD6-19	X97051, IGHD6-19*01	G Y S S G W Y G I A V A G V * Q W L V gggtatagcagtgctggta	V P A T A I P Y Q P L L Y T S H C Y T gtaccaggcaactgtatacc
IGHD6-25	X97051, IGHD6-25*01	G Y S S G Y G I A A A V * Q R L gggtatagcagcgctac	V A A A I P * P L L Y S R C Y T gtagccgcgtgtatacc
IGHD7-27	J00256, IGHD7-27*01	L T G * L G N W G ctaactggga	S P V P Q L P S * tccccagttag

Author: Manuel Ruiz (manu@igm.igh.cnrs.fr)

1c

Analyst/Contact: Valérie Barbié (valerie@ligm.igh.cnrs.fr)

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Fig. 1. Protein display of human IGH D-REGIONS. Amino acids are shown with one-letter abbreviations. D-REGIONS are shown in the three reading frames. Some of the D-REGIONS having been found in inverted orientations [9, 10], the IGH D-REGIONS are shown in both direct 5'-3' and inverted orientations.

Fig. 2. Protein display of human IGH J-REGIONS. Amino acids are shown with one-letter abbreviations. The conserved W-G-X-G (Trp-Gly-X-Gly) motif is underlined. Note that the JUNCTIONs of rearranged IGHV-D-J-GENEs extend from 2nd-CYS (cystein 104 of the V-REGION) to J-TRP (conserved Trp of the J-REGION), whereas the CDR3-IMGT extend from amino acid 105 of the V-REGION to J-TRP not included.