FIGURES LEGENDS

Supplemental Figure 1: MS/MS fragmentation of the peptides allowing assignment of two distinct IGHG3 AA alleles for the same NP49 sample

Left panel: MS/MS fragmentation of the tryptic peptide R.WQEGNVFSCSVMHEALHNR.F from the NP49 purified IgG sample and assignable to IGHG3*03, as listed in the Table 2; Right panel: MS/MS fragmentation of the tryptic peptide R.WQQGNIFSCSVMHEALHNHYTQK.S from the NP49 purified IgG sample and assignable to IGHG3*17*18*19, as listed in the Table 2.

Supplemental Figure 2: MS/MS fragmentation of a putatively new IGHG4 peptide identified in two distinct samples of purified IgG

Left panel: MS/MS fragmentation of the tryptic peptide R.VVSVLTILHQDWLNGK.E included in the amino acid sequence FMN|AS50|G4|V308I|N325H|Q355R|T394|L410 from the AS50 purified IgG sample, as listed in the Supplemental Table S1; Right panel: MS/MS fragmentation of the tryptic peptide R.VVSVLTILHQDWLNGK.E included in the amino acid sequence FMN|PA16|G4|V308I|N325H|Q355R|T394|L410 from the PA16 purified IgG sample, as listed in the Supplemental Table S1.

Supplemental Table S1: Database of IGHG CH2 and CH3-CHS amino acid sequences from the 10 patients included in the study (60 sequences; 13,004 amino acids)

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>FMN|PA45|G1|02

APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>FMN|PA45|G2|01030405|V308|T394

APPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>FMN|PA45|G2|01030405|V308|T394|T437

APPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>FMN|PA45|G3|01040510

APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYVDGVEVHNAKTKPREEQYNSTFRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKTKGQPREPQVYTLPPSREEM
TKNQVSLTCLVKGFYPSDIAVEWESSGQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRWQQGNIFSCSVMHEALHNRFTQKSLSLSPGK
>FMN|PA45|G4|01
APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
>FMN|PA48|G1|02
APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELT
KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
>FMN|PA48|G2|01030405|V308
APPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEM
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
>FMN|PA48|G3|03
APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYVDGVEVHNAKTKPREEQYNSTFRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKTKGQPREPQVYTLPPSREEM
TKNQVSLTCLVKGFYPSDIAVEWESSGQPENNYNTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNRFTQKSLSLSPGK
>FMN|PA48|G4|0104|E233
APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

[a]: ">": FASTA format; "FMN": origin; "|AS50|": sample ID; "|G1|": IG heavy chain type 1; "|02": IG heavy chain type-related AA allele already referenced in IMGT®. For each sample and each IG heavy chain, one to two AA alleles are mentioned according to the homozygous or heterozygous allele carriage, respectively.

[b]: For an AA sequence which is not yet referenced in IMGT®, each SAAV (with or without substitution) is mentioned between vertical bars, according to IMGT® (http://www.imgt.org) amino acid EU numbering (23).

[c]: Novel IGHG2 and IGHG4 IMGT AA alleles identified in this study and approved by the IMGT Nomenclature committee (IMGT-NC).

[d]: Combination of IGHG3*01, IGHG3*04, IGHG3*05 and IGHG3*10 alleles sharing the same AA sequence.

[e]: AA sequence already referenced in IMGT® under IGHG4*01 or IGHG4*04 allele but whose nucleotide sequence carries synonymous variations at the codon corresponding to amino acid E233.

Supplemental Table S2: Nucleotide positions of the IGHG gene components from the hinge exon (and for IGHG3 from the most 3' hinge exon) to the CH3-CHS exons

Nt numbering	Hinge exon	Intron	CH2 exon	Intron	CH3-CHS exon
IMGT/LIGM-DB numbering [a]:					
IGHG1*01 (J00228)	892-936	937-1054	1055-1384	1385-1480	1481-1800
IGHG2*01 (J00230)	902-937	938-1055	1056-1382	1383-1479	1480-1799
IGHG3*01 (X03604)	1471-1515	1516-1633	1634-1963	1964-2060	2061-2380
IGHG4*01 (K01316)	900-935	936-1053	1054-1383	1384-1480	1481-1800
IMGT unique numbering for C-DOMAIN [b]:					
all IGHG	1-45 or 1-36 [c]		1.6-375		1.4-375 (1-6) [d]

The five IGHG gene components are represented in the 5'➔3' direction, starting with the hinge exon (most 3' hinge exon (H4) for IGHG3*01) and ending with the CH3-CHS exon. Allele*01 of each IGHG is given with its accession number in IMGT/LIGM-DB reference sequence (24).

[a]: The numbering position is according to IMGT/LIGM-DB (http://www.imgt.org) accession number.

[b]: The numbering position is according to IMGT Scientific chart (2, 25).

[c]: 1-45 for IGHG1*01 and for IGHG3*01 H4 hinge exon; 1-36 for IGHG2*01 and IGHG4*01.

[d]: The numbering in brackets corresponds to CHS.

Supplemental Table S3: Validation of IGHG1, IGHG2, IGHG3 and IGHG4 gene amplification according to IGHG gene specific codons

IMGT Nt numbering [c]	**AA numbering**		**Contigs** [a]					**Samples** [b]				
	IMGT [c]	**EU** [d]	**IGHG1**	**IGHG2**	**IGHG3**	**IGHG4**	**IGHGP**	**IGHG1**	**IGHG2**	**IGHG3**	**IGHG4**	**IGHGP** [e]
CH2 exon			5 (5)	6 (8)	19 (57)	4 (4)						
1.6-3.6	1.6	231	gca	gca	gca	gca	**aca**					**no aca**
1.5-3.5	1.5	232	cct	**cca**	cct	cct	**act**		**cca**			**no act**
1.4-3.4	1.4	233	gaa	**---**	gaa	**gag**	gaa		**---**		**gag** [f]	
1.3-3.3	1.3	234	ctc	**cct**	ctc	**ttc**	**ccc**		**cct**		**ttc**	**no ccc**
1.2-3.2	1.2	235	ctg	**gtg**	ctg	ctg	ctg		**gtg**			
1.1-3.1	1.1	236	ggg	**gca**	**gga**	ggg	ggg		**gca**	**gga**		
4-6	2	238	ccg	ccg	ccg	**cca**	ccg				**cca**	
16-18	6	242	ctc	ctc	ctc	**ctg**	ctc				**ctg**	
40-42	14	250	acc	acc	acc	**act**	acc				**act** [f]	
43-45	15	251	ctc	ctc	**ctt**	ctc	ctc			**ctt**		
43.2-45.2	15.2	253	atc	atc	**att**	atc	atc			**att**		
64-66	22	260	**aca**	acg	acg	acg	acg	**aca**				
88-90	30	268	cac	cac	cac	**cag**	cac				**cag**	
118-120	40	276	aac	aac	**aag**	aac	aac			**aag**		
130-132	44	280	gac	gac	gac	**gat**	gac				**gat**	
244-246	82	291	ccg	**cca**	ccg	ccg	ccg		**cca**			
253.1-255.1	85.1	301	cgt/cgg [g]	cgt	cgt	cgt	**cat**					**no cat**
283-285	95	312	gac	gac	gac	gac	**aac**					**no aac**
292-294	98	315	**aat**	aac	aac	aac	aac	**aat**				
340-342	114	329	cca	cca	cca	**ccg**	cca				**ccg**	
343-345	115	330	gcc	gcc	gcc	**tcc**	gcc				**tcc**	
346-348	116	331	ccc	ccc	ccc	**tcc**	ccc				**tcc**	
CH3-CHS exons												
1-3	1	345	gaa	gaa	gaa	**gag**	gaa				**gag**	
34-36	12	356	gat/gag [h]	gag	gag	gag	**aag**					**no aag**
37-39	13	357	gag	gag	gag	gag	**---**					**no deletion**
58-60	20	364	agc	agc	agc	agc	**acc**					**no acc**
85-87	29	373	**tat**	tac	tac	tac	tac	**tat**				
112-114	38	378	gcc	gcc/tcc [i]	gcc	gcc	**acc**					**no acc**

250.4-252.4	84.4	401	gac	gac	gac	gac	**aac**					**no aac**
328-330	110	431	gct	gct	gct	gct	**ggt**					**no ggt**
373-375	125	445	ccg	ccg	ccg	**ctg**	ccg				**ctg**	

Number of alleles for each IGHG gene (and between parentheses number of sequences) is shown below the four IGHG functional genes (IMGT Alignments of alleles, IMGT Repertoire, http://www.imgt.org) (3); specific codons in bold.

[a] : sequence compilations of 5 IGHG1, 6 IGHG2, 19 IGHG3, 4 IGHG4 and 2 IGHGP alleles according to IMGT® http://www.imgt.org.

[b] : contigs results for the 10 samples under study (AS50, NP49, PA01, PA07, PA09, PA16, PA31, PA42, PA45 and PA48).

[c] : Nucleotide (Nt) and amino acid (AA) numbering according to IMGT® http://www.imgt.org, IMGT unique numbering for C-DOMAIN (2, 25).

[d] : amino acid EU numbering according to IMGT® http://www.imgt.org (23).

[e] : verification of the absence of IGHGP amplification

[f] : this specific codon was not validated in several cases (CH2 g3.4>a and CH2 t42>c), see Table 5 for more precisions.

[g] : cgt for all IGHG1 except for IGHG1*01 (cgg).

[h] : gat for all IGHG1 except for IGHG1*03 (gag).

[i] : gcc for all IGHG2 except for IGHG2*06 (tcc).

Supplemental Table S4: Decision tree reading for IGHG nucleotide sequences with the representation of the CH2 and CH3-CHS polymorphisms

	CH2 domain												CH3 domain																				
IMGT	1.5	1.4	1.1	9	45.1	82	83	84.3	85.1	91	92	124	1.4	12	14	38	39	44	79	81	84	86	88	89	90	98	100	101	115	116	117	124	IGHG alleles
EU index	232	233	236	245	282	291	292	296	301	308	309	339	341	356	358	378	379	384	392	394	397	407	409	410	411	419	421	422	435	436	437	444	
	P	-	A	P	M	P	R	F	R	V	V	T	G	E	M	A	V	N	K	T	M	Y	K	L	T	Q	N	V	H	Y	T	S	IGHG2*02
	cca	---	gca	cca	atg	cca	cgg	ttc	cgt	gtc	gtg	acc	ggg	gag	atg	gcc	gtg	aat	aag	aca	atg	tac	aag	ctc	acc	cag	aac	gtc	cac	tac	aca	tct	
					V	P	R	F	R	V	V	T	G	E	M	S	V	N	K	T	M	Y	K	L	T	Q	N	V	H	Y	T	S	IGHG2*06
					gtg	cca	cgg	ttc	cgt	gtc	gtg	acc	ggg	gag	atg	tcc	gtg	aat	aag	aca	atg	tac	aag	ctc	acc	cag	aac	gtc	cac	tac	aca	tct	
										V	V	T	G	E	M	A	V	N	K	T	M	Y	K	L	T	Q	N	V	H	Y	T	S	IGHG2*01*03*04
										gtt	gtg	acc	ggg	gag	atg	gcc	gtg	aat	aag	aca	atg	tac	aag	ctc	acc	cag	aac	gtc	cac	tac	acg	tct	
																				T	M	Y	K	L	T	Q	N	V	H	Y	T	S	IGHG2*05
																				acg	atg	tac	aag	ctc	acc	cag	aac	gtc	cac	tac	acg	tct	
	P	E	G	P	V	P	R	Y	R	V	L	A	G	D	L	A	V	N	K	T	V	Y	K	L	T	Q	N	V	H	Y	T	S	IGHG1*01
	cct	gaa	ggg	cca	gtg	ccg	cgg	tac	cgg	gtc	ctg	gcc	ggg	gat	ctg	gcc	gtg	aat	aag	acg	gtg	tac	aag	ctc	acc	cag	aac	gtc	cac	tac	acg	tct	
									R	V	L	A	G	E	M	A	V	N	K	T	V	Y	K	L	T	Q	N	V	H	Y	T	S	IGHG1*03
									cgt	gtc	ctg	gcc	ggg	gag	atg	gcc	gtg	aat	aag	acg	gtg	tat	aag	ctc	acc	cag	aac	gtc	cac	tac	acg	tcc	
														D	L	A	V	N	K	T	V	Y	K	L	T	Q	N	I	H	Y	T	S	IGHG1*04
														gat	ctg	gcc	gtg	aat	aag	acg	gtg	tac	aag	ctc	acc	cag	aac	atc	cac	tac	acg	tct	
																												V	H	Y	T	S	IGHG1*02
																												gtc	cac	tac	acg	tct	
																															T	S	IGHG1*05
																															aca	tct	
			G	P															N	T	M												IGHG3*02
			gga	cct															aac	acg	atg												
				P	V	L	R	Y	R	V	L	A	G	E	M	A	V	N	N	T	M	Y	K	L	T	Q	N	I	R	Y	T	S	IGHG3*16
				cca	gtg	ctg	cgg	tac	cgt	gtc	ctg	gcc	gga	gag	atg	gcc	gtg	aat	aac	acg	atg	tac	aag	ctc	acc	cag	aac	atc	cgc	tac	acg	tct	
												T	G	E	M	A	V	N	K	T	M	Y	K	L	T	Q	N	I	R	Y	T	S	IGHG3*15
												acc	gga	gag	atg	gcc	gtg	aat	aag	acg	atg	tac	aag	ctc	acc	cag	aac	atc	cgc	tac	acg	tct	
																			N	T	M	Y	K	L	T	Q	N	I	R	Y	T	S	IGHG3*14
																			aac	acg	atg	tac	aag	ctc	acc	cag	aac	atc	cgc	tac	acg	tct	
						P	W	Y	R	V	L	T	G	E	M	A	M	S	K	T	V	Y	K	L	T	Q	N	I	H	Y	T	S	IGHG3*18*19
						ccg	tgg	tac	cgt	gtc	ctg	acc	gga	gag	atg	gcc	atg	agc	aag	acg	gtg	tac	aag	ctc	acc	cag	aac	atc	cac	tac	acg	tct	
							R	F	R	V	L	T	G	E	M	A	V	S	N	T	M	Y	K	L	T	Q	N	I	R	F	T	S	IGHG3*11*12
							cgg	ttc	cgt	gtc	ctg	acc	gga	gag	atg	gcc	gtg	agc	aac	acg	atg	tac	aag	ctc	acc	cag	aac	atc	cgc	ttc	acg	tct	
								Y	R	V	V	T	G	E	M	A	V	S	N	T	M	Y	K	L	T	Q	N	I	R	F	T	S	IGHG3*09
								tac	cgt	gtc	gtg	acc	gga	gag	atg	gcc	gtg	agc	aac	acg	atg	tac	aag	ctc	act	cag	aac	atc	cgc	ttc	acg	tct	
											L	T	G	E	M	A	V	S	K	T	M	Y	K	L	T	Q	N	I	R	F	T	S	IGHG3*06*07
											ctg	acc	ggg	gag	atg	gcc	gtg	agc	aag	acg	atg	tac	aag	ctc	acc	cag	aac	atc	cgc	ttc	acg	tct	
													G	E	M	A	M	S	K	T	V	Y	K	L	T	Q	N	I	H	Y	T	S	IGHG3*17
													gga	gag	atg	gcc	atg	agc	aag	acg	gtg	tac	aag	ctc	acc	cag	aac	atc	cac	tac	acg	tct	
																	V	N	N	T	M	Y	K	L	T	Q	N	I	R	F	T	S	IGHG3*08
																	gtg	aat	aac	acg	atg	tac	aag	ctc	acc	cag	aac	atc	cgc	ttc	acg	tct	
																		S	K	T	M	Y	K	L	T	E	N	I	R	F	T	S	IGHG3*13
																		agc	aag	aca	atg	tac	aag	ctc	acc	gag	aac	atc	cgc	ttc	acg	tct	
																			N	T	V	Y	R	L	T	E	N	V	R	F	T	S	IGHG3*03
																			aac	acg	gtg	tac	agg	cta	acc	gag	aat	gtc	cgc	ttc	acg	tct	
																					M	Y	K	L	T	Q	N	I	R	F	T	S	IGHG3*01*04*05*10
																					atg	tac	aag	ctc	acc	cag	aac	atc	cgc	ttc	acg	tct	
		E	G	P	V	P	R	F	R	V	V	A	G	E	M	A	V	N	K	T	V	Y	R	L	T	E	N	V	H	Y	T	S	IGHG4*02
		gag	ggg	cca	gtg	ccg	cgg	ttc	cgt	gtc	gtg	gcc	ggg	gag	atg	gcc	gtg	aat	aag	acg	gtg	tac	agg	cta	acc	gag	aat	gtc	cac	tac	acg	tct	
											L	A	G	E	M	A	V	N	K	T	V	Y	K	L	T	E	N	V	H	Y	T	S	IGHG4*03
											ctg	gcc	ggg	gag	atg	gcc	gtg	aat	aag	acg	gtg	tac	aag	ctc	acc	gag	aac	gtc	cac	tac	acg	tct	
																							R	L	T	E	N	V	H	Y	T	S	IGHG4*01
																							agg	cta	acc	gag	aat	gtc	cac	tac	aca	tct	
																								L	T	E	N	V	H	Y	T	S	IGHG4*04
																								ctc	acc	gag	aat	gtc	cac	tac	aca	tct	

Supplemental Table S5: Discriminatory nucleotide and/or AA positions along the alignment of *Homo sapiens* IGHG2 alleles, including the 5 (exon) IGHG2 novel alleles

GenBank Accession N°	IMGT allele name			CH1 exon					CH2 exon				CH3-CHS exon		
			IMGT UN[a]	19	82	92	95	96	35	45.1	91	92	38	81	117
J00230	IGHG2*01	F	AA	A	P	P	N	F	P	V	V	V	A	T	T
			gDNA	gcc	cca	ccc	aac	ttc	ccc	gtg	gtt	gtg	gcc	aca	acg
Z49802	IGHG2*01	F	AA			No data									
			gDNA						---	---	---	---	---	---	---
AJ250170	IGHG2*02	F	AA			**T**				**M**					
			gDNA	**--g**	**--g**	**a--**	---	---	---	**a--**	**--c**	---	---	---	**--a**
Z49801	IGHG2*02	F	AA			No data				**M**					
			gDNA						---	**a--**	**--c**	---	---	---	**--a**
AF449616	IGHG2*03	F	AA												
			gDNA	**--g**	---	---	---	---	---	---	---	---	---	---	---
AF449617	IGHG2*04	F	AA												
			gDNA	**--g**	---	---	**--g**	**--g**	---	---	---	---	---	---	---
AF449618	IGHG2*05	F	AA												
			gDNA	**--g**	---	---	---	---	---	---	---	---	---	**--g**	---
AL928742	IGHG2*06	F	AA										**S**		
			gDNA	**--g**	**--g**	---	---	---	---	---	**--c**	---	**t--**	---	**--a**
KX670549	IGHG2*07i[b]		AA			No data						**L**			
			gDNA						---	---	**--c**	**c--**	---	**--g**	---
KX670550[c]	IGHG2*08i[b]		AA			No data									
			gDNA						---	---	**--c**	---	---	---	---
KX670551[c]	IGHG2*08i[b]		AA			No data									
			gDNA						---	---	**--c**	---	---	---	---
KX670552	IGHG2*09i[b]		AA			No data									
			gDNA						---	---	**--c**	---	---	**--g**	---
KX670553	IGHG2*10i[b]		AA			No data									
			gDNA						**--t**	---	**--c**	---	---	**--g**	**--a**
KX670554	IGHG2*11i[b]		AA			No data									
			gDNA						---	---	**--c**	---	---	**--g**	**--a**

[a]: IMGT Unique Numbering, according to IMGT® scientific chart (http://www.imgt.org).

[b]: the denomination of IGHG2*07*08*09*10*11 alleles is followed by "i" to signify that this denomination is in process and not yet formalized in IMGT® repertoire.

[c]: KX670550 and KX670551 sequences are different in the intron between the CH2 and CH3-CHS exons.

F: functional. AA: amino acid. gDNA: genomic DNA.

No letter at AA position indicates identical amino acid in comparison with IGHG2*01. Dashes at gDNA position indicate identical nucleotides in comparison with allele IGHG2*01. Nucleotide and amino acid changes (for a given codon) are indicated in bold letter.

Supplemental Table S6: Discriminatory nucleotide and/or AA positions along the alignment of *Homo sapiens* IGHG4 alleles, including the 4 IGHG4 alleles newly identified

GenBank Accession N°	IMGT allele name		IMGT UN[a]	CH1 exon	CH2 exon					CH3-CHS exon					
				3	1.4	14	91	92	108	11	81	88	89	100	117
K01316	IGHG4*01	F	AA	S	E	T	V	L	N	Q	T	R	L	N	T
			gDNA	tcc	gag	act	gtc	ctg	aac	cag	acg	agg	cta	aat	aca
AJ001563	IGHG4*02	F	AA	No data				**V**							
			gDNA		---	---	---	**g**--	---	---	---	---	---	---	--**g**
AJ001564	IGHG4*03	F	AA	No data								K			
			gDNA		---	---	---	---	---	---	---	-**a**-	--**c**	--**c**	--**g**
AL928742	IGHG4*04	F	AA												
			gDNA	--**g**	---	---	---	---	---	---	---	---	--**c**	---	---
KX670555	IGHG4*05i[b]		AA	No data			**I**		**H**	**R**					
			gDNA		---	---	**a**--	---	**c**--	-**g**-	--**a**	---	--**c**	---	---
KX670556	IGHG4*06i[b]		AA	No data			**I**		**H**						
			gDNA		---	---	**a**--	---	**c**--	---	---	---	--**c**	---	---
KX670557	IGHG4*07i[b]		AA	No data											
			gDNA		--**a**	---	---	---	---	---	---	---	---	---	---
KX670558	IGHG4*08i[b]		AA	No data											
			gDNA		--**a**	--**c**	---	---	---	---	---	---	---	---	---

[a]: IMGT Unique Numbering, according to IMGT® scientific chart (http://www.imgt.org).

[b]: the denomination of IGHG4*05*06*07*08 alleles is followed by "i" to signify that this denomination is in process and not yet formalized in IMGT® repertoire.

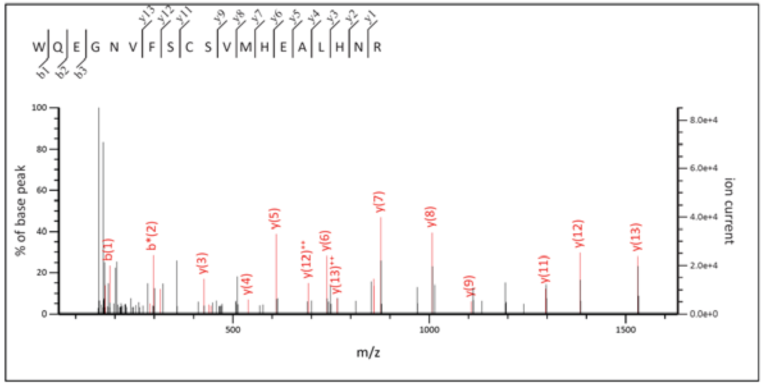
F: functional. AA: amino acid. gDNA: genomic DNA.

No letter at AA position indicates identical amino acid in comparison with IGHG4*01. Dashes at gDNA position indicate identical nucleotides in comparison with allele IGHG4*01. Nucleotide and amino acid changes (for a given codon) are indicated in bold letter.

Supplemental Figure 1: MS/MS fragmentation of the peptides allowing assignment of two distinct IGHG3 AA alleles for the same NP49 sample

MS/MS Fragmentation of **WQEGNVFSCSVMHEALHNR**
Found in **X16110** in **IGHGhaplotypes**, IGHG3*03|Homo

Match to Query 12882: 2242.997472 from(748.673100,3+) intensity(357626.9688) rtinseconds(1700) scans(12318) index(9712)
Title: File14018 Spectrum9797 scans: 12318
Data file \\10.114.108.227\qexdata\Data\2014\Pharma\FlMI140719_Q695aQ704\FlMI140719_NP49_Q704.mgf

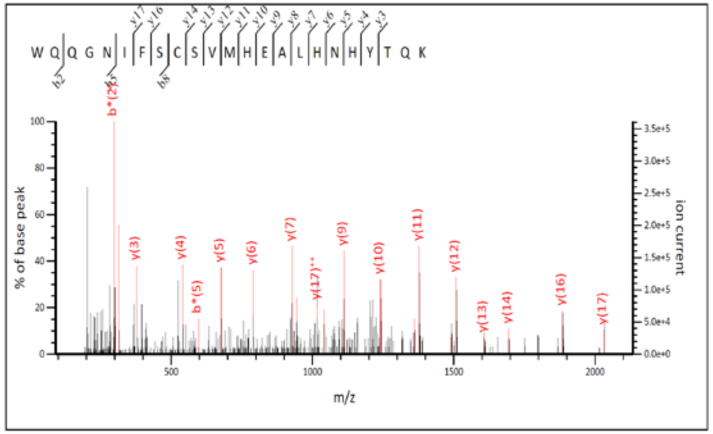


```
Monoisotopic mass of neutral peptide Mr(calc): 2243.0000
Ions Score: 37  Expect: 0.00021
Matches : 21/200 fragment ions using 76 most intense peaks   (help)
```

#	b	b^{++}	b^{*}	b^{*++}	b^{0}	b^{0++}	Seq.	y	y^{++}	y^{*}	y^{*++}	y^{0}	y^{0++}	#
1	187.0866	94.0469					W							19
2	315.1452	158.0762	298.1186	149.5629			Q	2057.9280	1029.4676	2040.9015	1020.9544	2039.9174	1020.4624	18
3	444.1878	222.5975	427.1612	214.0842	426.1772	213.5922	E	1929.8694	965.4384	1912.8429	956.9251	1911.8589	956.4331	17
4	501.2092	251.1082	484.1827	242.5950	483.1987	242.1030	G	1800.8268	900.9171	1783.8003	892.4038	1782.8163	891.9118	16
5	615.2522	308.1297	598.2256	299.6164	597.2416	299.1244	N	1743.8054	872.4063	1726.7788	863.8930	1725.7948	863.4010	15
6	714.3206	357.6639	697.2940	349.1506	696.3100	348.6586	V	1629.7624	815.3849	1612.7359	806.8716	1611.7519	806.3796	14
7	861.3890	431.1981	844.3624	422.6849	843.3784	422.1928	F	1530.6940	765.8507	1513.6675	757.3374	1512.6835	756.8454	13
8	948.4210	474.7141	931.3945	466.2009	930.4104	465.7089	S	1383.6256	692.3164	1366.5991	683.8032	1365.6150	683.3112	12
9	1051.4302	526.2187	1034.4036	517.7055	1033.4196	517.2135	C	1296.5936	648.8004	1279.5670	640.2872	1278.5830	639.7951	11
10	1138.4622	569.7347	1121.4357	561.2215	1120.4517	560.7295	S	1193.5844	597.2958	1176.5579	588.7826	1175.5738	588.2906	10
11	1237.5306	619.2690	1220.5041	610.7557	1219.5201	610.2637	V	1106.5524	553.7798	1089.5258	545.2665	1088.5418	544.7745	9
12	1368.5711	684.7892	1351.5446	676.2759	1350.5606	675.7839	M	1007.4840	504.2456	990.4574	495.7323	989.4734	495.2403	8
13	1505.6300	753.3187	1488.6035	744.8054	1487.6195	744.3134	H	876.4435	438.7254	859.4169	430.2121	858.4329	429.7201	7
14	1634.6726	817.8400	1617.6461	809.3267	1616.6621	808.8347	E	739.3846	370.1959	722.3580	361.6826	721.3740	361.1906	6
15	1705.7097	853.3585	1688.6832	844.8452	1687.6992	844.3532	A	610.3420	305.6746	593.3154	297.1613			5
16	1818.7938	909.9005	1801.7673	901.3873	1800.7832	900.8953	L	539.3049	270.1561	522.2783	261.6428			4
17	1955.8527	978.4300	1938.8262	969.9167	1937.8421	969.4247	H	426.2208	213.6140	409.1942	205.1008			3
18	2069.8956	1035.4515	2052.8691	1026.9382	2051.8851	1026.4462	N	289.1619	145.0846	272.1353	136.5713			2
19							R	175.1190	88.0631	158.0924	79.5498			1

MS/MS Fragmentation of **WQQGNIFSCSVMHEALHNHYTQK**
Found in **AJ390272** in **IGHGhaplotypes**, IGHG3*17|Homo

Match to Query 15326: 2757.252822 from(920.091550,3+) intensity(6484194.0000) rtinseconds(1684) scans(12154) index(9558)
Title: File14018 Spectrum9643 scans: 12154
Data file \\10.114.108.227\qexdata\Data\2014\Pharma\FlMI140719_Q695aQ704\FlMI140719_NP49_Q704.mgf



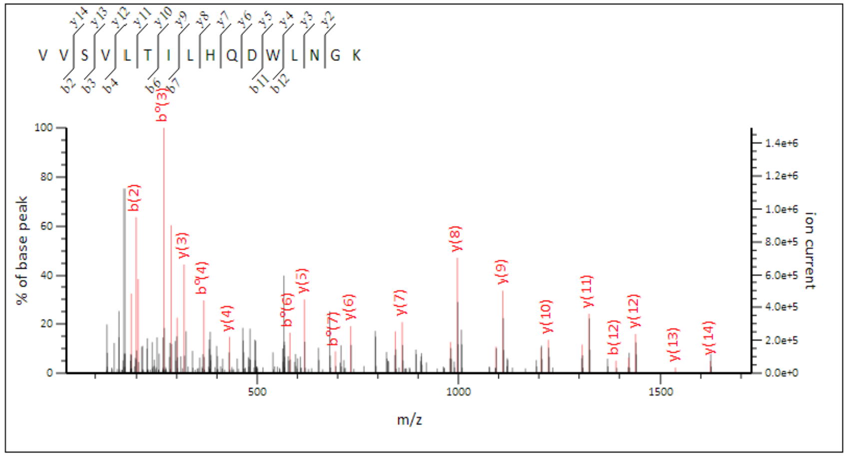
```
Monoisotopic mass of neutral peptide Mr(calc): 2757.2540
Ions Score: 66  Expect: 2.3e-07
Matches : 21/244 fragment ions using 52 most intense peaks   (help)
```

#	b	b^{++}	b^{*}	b^{*++}	b^{0}	b^{0++}	Seq.	y	y^{++}	y^{*}	y^{*++}	y^{0}	y^{0++}	#
1	187.0866	94.0469					W							23
2	315.1452	158.0762	298.1186	149.5629			Q	2572.1820	1286.5946	2555.1554	1278.0814	2554.1714	1277.5893	22
3	443.2037	222.1055	426.1772	213.5922			Q	2444.1234	1222.5653	2427.0969	1214.0521	2426.1128	1213.5601	21
4	500.2252	250.6162	483.1987	242.1030			G	2316.0648	1158.5361	2299.0383	1150.0228	2298.0543	1149.5308	20
5	614.2681	307.6377	597.2416	299.1244			N	2259.0434	1130.0253	2242.0168	1121.5120	2241.0328	1121.0200	19
6	727.3522	364.1797	710.3257	355.6665			I	2145.0004	1073.0039	2127.9739	1064.4906	2126.9899	1063.9986	18
7	874.4206	437.7139	857.3941	429.2007			F	2031.9164	1016.4618	2014.8898	1007.9486	2013.9058	1007.4565	17
8	961.4526	481.2300	944.4261	472.7167	943.4421	472.2247	S	1884.8480	942.9276	1867.8214	934.4143	1866.8374	933.9223	16
9	1064.4618	532.7346	1047.4353	524.2213	1046.4513	523.7293	C	1797.8159	899.4116	1780.7894	890.8983	1779.8054	890.4063	15
10	1151.4939	576.2506	1134.4673	567.7373	1133.4833	567.2453	S	1694.8068	847.9070	1677.7802	839.3937	1676.7962	838.9017	14
11	1250.5623	625.7848	1233.5357	617.2715	1232.5517	616.7795	V	1607.7747	804.3910	1590.7482	795.8777	1589.7642	795.3857	13
12	1381.6028	691.3050	1364.5762	682.7917	1363.5922	682.2997	M	1508.7063	754.8568	1491.6798	746.3435	1490.6957	745.8515	12
13	1518.6617	759.8345	1501.6351	751.3212	1500.6511	750.8292	H	1377.6658	689.3365	1360.6393	680.8233	1359.6553	680.3313	11
14	1647.7043	824.3558	1630.6777	815.8425	1629.6937	815.3505	E	1240.6069	620.8071	1223.5804	612.2938	1222.5963	611.8018	10
15	1718.7414	859.8743	1701.7148	851.3610	1700.7308	850.8690	A	1111.5643	556.2858	1094.5378	547.7725	1093.5538	547.2805	9
16	1831.8254	916.4164	1814.7989	907.9031	1813.8149	907.4111	L	1040.5272	520.7672	1023.5007	512.2540	1022.5166	511.7620	8
17	1968.8843	984.9458	1951.8578	976.4325	1950.8738	975.9405	H	927.4431	464.2252	910.4166	455.7119	909.4326	455.2199	7
18	2082.9273	1041.9673	2065.9007	1033.4540	2064.9167	1032.9620	N	790.3842	395.6958	773.3577	387.1825	772.3737	386.6905	6
19	2219.9862	1110.4967	2202.9596	1101.9835	2201.9756	1101.4914	H	676.3413	338.6743	659.3148	330.1610	658.3307	329.6690	5
20	2383.0495	1192.0284	2366.0230	1183.5151	2365.0390	1183.0231	Y	539.2824	270.1448	522.2558	261.6316	521.2718	261.1396	4
21	2484.0972	1242.5522	2467.0706	1234.0390	2466.0866	1233.5470	T	376.2191	188.6132	359.1925	180.0999	358.2085	179.6079	3
22	2612.1558	1306.5815	2595.1292	1298.0683	2594.1452	1297.5762	Q	275.1714	138.0893	258.1448	129.5761			2
23							K	147.1128	74.0600	130.0863	65.5468			1

Supplemental Figure 2: MS/MS fragmentation of a putatively new IGHG4 peptide identified in two distinct samples of purified IgG

MS/MS Fragmentation of **VVSVLTILHQDWLNGK**
Found in **FMN|AS50|G4|V308I|N325H|Q355R|T394|L410** in **FIMIAS50**, FMN|AS50|G4|V308I|N325H|Q355R|T394|L410

Match to Query 9406: 1821.011208 from(911.512880,2+) intensity(18404198.0000) rtinseconds(2090) scans(16738) index(13848)
Title: File14016 Spectrum14014 scans: 16738
Data file \\10.114.108.227\qexdata\Data\2014\Pharma\FIMI140719_Q695aQ704\FIMI140719_AS50_Q695.mgf

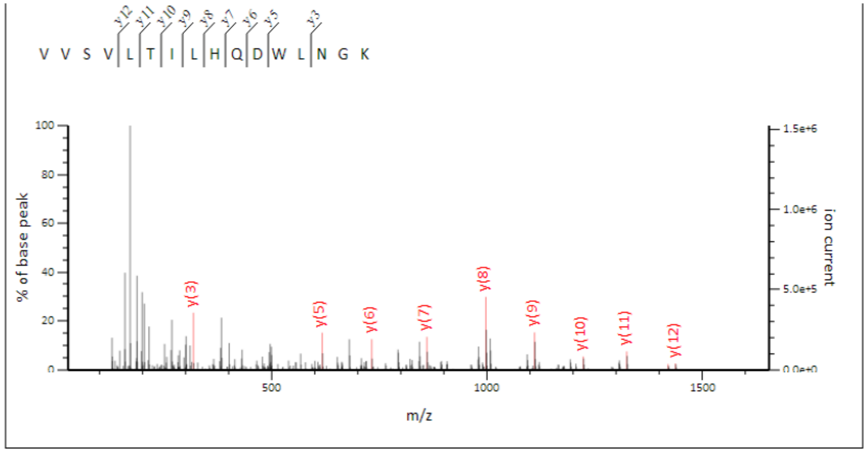


```
Monoisotopic mass of neutral peptide Mr(calc): 1821.0149
Ions Score: 78  Expect: 1.6e-08
Matches : 28/148 fragment ions using 59 most intense peaks   (help)
```

#	b	b^{++}	b^{*}	b^{*++}	b^{0}	b^{0++}	Seq.	y	y^{++}	y^{*}	y^{*++}	y^{0}	y^{0++}	#
1	100.0757	50.5415					V							16
2	**199.1441**	100.0757					V	1722.9537	861.9805	1705.9272	853.4672	1704.9432	852.9752	15
3	**286.1761**	143.5917			268.1656	134.5864	S	***1623.8853***	812.4463	1606.8588	803.9330	1605.8748	803.4410	14
4	385.2445	193.1259			367.2340	184.1206	V	***1536.8533***	768.9303	1519.8267	760.4170	1518.8427	759.9250	13
5	498.3286	249.6679			480.3180	240.6627	L	***1437.7849***	719.3961	1420.7583	710.8828	1419.7743	710.3908	12
6	599.3763	300.1918			581.3657	291.1865	T	***1324.7008***	662.8540	1307.6743	654.3408	1306.6902	653.8488	11
7	712.4604	356.7338			694.4498	347.7285	I	***1223.6531***	612.3302	1206.6266	603.8169	1205.6426	603.3249	10
8	825.5444	413.2758			807.5339	404.2706	L	***1110.5691***	555.7882	1093.5425	547.2749	1092.5585	546.7829	9
9	962.6033	481.8053			944.5928	472.8000	H	***997.4850***	499.2461	980.4585	490.7329	979.4744	490.2409	8
10	1090.6619	545.8346	1073.6354	537.3213	1072.6513	536.8293	Q	***860.4261***	430.7167	843.3995	422.2034	842.4155	421.7114	7
11	**1205.6889**	603.3481	1188.6623	594.8348	1187.6783	594.3428	D	***732.3675***	366.6874	715.3410	358.1741	714.3569	357.6821	6
12	**1391.7682**	696.3877	1374.7416	687.8744	1373.7576	687.3824	W	***617.3406***	309.1739	600.3140	300.6606			5
13	1504.8522	752.9298	1487.8257	744.4165	1486.8417	743.9245	L	***431.2613***	216.1343	414.2347	207.6210			4
14	1618.8952	809.9512	1601.8686	801.4379	1600.8846	800.9459	N	***318.1772***	159.5922	301.1506	151.0790			3
15	1675.9166	838.4619	1658.8901	829.9487	1657.9061	829.4567	G	***204.1343***	102.5708	187.1077	94.0575			2
16							K	147.1128	74.0600	130.0863	65.5468			1

MS/MS Fragmentation of **VVSVLTILHQDWLNGK**
Found in **FMN|PA16|G4|V308I|N325H|Q355R|T394|L410** in **FIMIPA16**, FMN|PA16|G4|V308I|N325H|Q355R|T394|L410

Match to Query 9760: 1821.011142 from(608.010990,3+) intensity(2270489.5000) rtinseconds(2091) scans(16469) index(13608)
Title: File14026 Spectrum13745 scans: 16469
Data file \\10.114.108.227\qexdata\Data\2014\Pharma\FIMI140719_Q695aQ704\FIMI140719_PA16_Q699.mgf



```
Monoisotopic mass of neutral peptide Mr(calc): 1821.0149
Ions Score: 64  Expect: 4.2e-07
Matches : 10/148 fragment ions using 15 most intense peaks   (help)
```

#	b	b^{++}	b^{*}	b^{*++}	b^{0}	b^{0++}	Seq.	y	y^{++}	y^{*}	y^{*++}	y^{0}	y^{0++}	#
1	100.0757	50.5415					V							16
2	199.1441	100.0757					V	1722.9537	861.9805	1705.9272	853.4672	1704.9432	852.9752	15
3	286.1761	143.5917			268.1656	134.5864	S	1623.8853	812.4463	1606.8588	803.9330	1605.8748	803.4410	14
4	385.2445	193.1259			367.2340	184.1206	V	1536.8533	768.9303	1519.8267	760.4170	1518.8427	759.9250	13
5	498.3286	249.6679			480.3180	240.6627	L	***1437.7849***	719.3961	1420.7583	710.8828	1419.7743	710.3908	12
6	599.3763	300.1918			581.3657	291.1865	T	***1324.7008***	662.8540	1307.6743	654.3408	1306.6902	653.8488	11
7	712.4604	356.7338			694.4498	347.7285	I	***1223.6531***	612.3302	1206.6266	603.8169	1205.6426	603.3249	10
8	825.5444	413.2758			807.5339	404.2706	L	***1110.5691***	555.7882	1093.5425	547.2749	1092.5585	546.7829	9
9	962.6033	481.8053			944.5928	472.8000	H	***997.4850***	499.2461	980.4585	490.7329	979.4744	490.2409	8
10	1090.6619	545.8346	1073.6354	537.3213	1072.6513	536.8293	Q	***860.4261***	430.7167	843.3995	422.2034	842.4155	421.7114	7
11	1205.6889	603.3481	1188.6623	594.8348	1187.6783	594.3428	D	***732.3675***	366.6874	715.3410	358.1741	714.3569	357.6821	6
12	1391.7682	696.3877	1374.7416	687.8744	1373.7576	687.3824	W	***617.3406***	309.1739	600.3140	300.6606			5
13	1504.8522	752.9298	1487.8257	744.4165	1486.8417	743.9245	L	431.2613	216.1343	414.2347	207.6210			4
14	1618.8952	809.9512	1601.8686	801.4379	1600.8846	800.9459	N	***318.1772***	159.5922	301.1506	151.0790			3
15	1675.9166	838.4619	1658.8901	829.9487	1657.9061	829.4567	G	204.1343	102.5708	187.1077	94.0575			2
16							K	147.1128	74.0600	130.0863	65.5468			1