From IMGT/mAb-DB to IMGT/3Dtructure-DB: highlighting the antigen and antibody contact amino acids of the target and mAb binding sites

Typhaine Paysan-Lafosse, Souphatta Sasorith, Patrice Duroux, Marie-Paule Lefranc and Sofia Kossida

Université de Montpellier and CNRS, Laboratoire d'ImmunoGénétique Moléculaire (LIGM), Institut de Génétique Humaine (IGH), UPR CNRS 1142, Montpellier (France)

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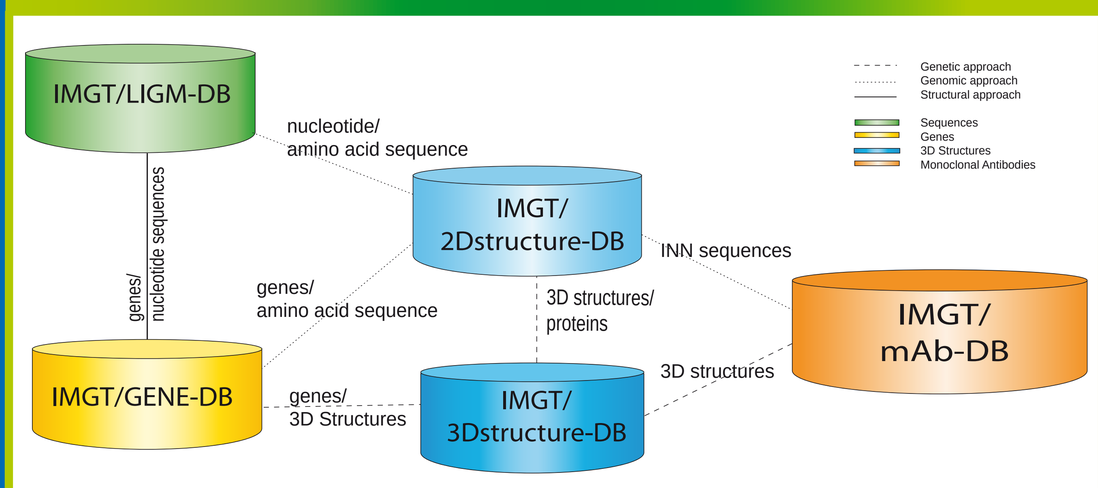
IMGT/mAb-DB is a unique resource of expertized annotations on monoclonal antibodies (mAbs , suffix -mab), fusion proteins for immune applications (FPIA, suffix -cept), composite proteins for clinical applications (CPCA) and relative proteins of the immune system (RPI) with diagnostic or therapeutic indications. The database includes information on antibody identification, format description, specificity, clinical indications, publications, clinical trials and regulations of monoclonal antibodies. IMGT/mAb-DB comprises 413 entries from the World Health Organization (WHO)/International Nonproprietary Name (INN) Programme.

IMGT/2Dstructure-DB and IMGT/3Dstructure-DB contain information about amino acid (AA) sequences, contact analysis, paratope and epitope interactions and IMGT/Colliers de Perles. These annotations are based on the IMGT standards (IMGT gene and allele names, IMGT unique numbering, CDR-IMGT). 286 INN antibodies from IMGT/mAb-DB are provided with their AA sequences and are annotated in IMGT/2Dstructure-DB.

For each antibody, whose experimental 3D structures are available, the corresponding structures are also described and fully annotated in IMGT/3Dstructure-DB using the IMGT standards. In addition, if the antibody has been co-crystallized with an antigen, the user can characterize the complex; for example by identifying the AA involved in the antibody-antigen interaction (using Contact analysis, IMGT/Collier de Perles and the Paratope and epitope description) or by visualizing the complex highlighted by the IMGT labels and standard colors (with the molecular viewer Jmol).

IMGT/mAb-DB and IMGT/3Dstructure-DB: Relations with other IMGT® databases

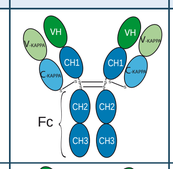
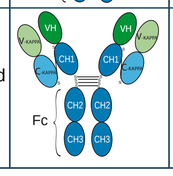


In October 2015, IMGT/mAb-DB contains 552 entries (500 -mab, 21 -cept). 413 have an INN name and, among them, 286 have an amino acid (AA) sequences in IMGT/2Dstructure-DB and 41 have 3D structures in IMGT/3Dstructure-DB.

By providing links to IMGT/2Dstructure-DB and IMGT/3Dstructure-DB for entries available in the databases, IMGT/mAb-DB facilitates comparative studies of antibodies (-mab) and FPIA (-cept), and of their constitutive chains, even if the 3D structures are not yet available.

IMGT/mAb-DB: from specificity target name

Number of results: 2

IMGT/mAb-DB ID	INN (International Nonproprietary Name)	INN Num.	INN Prop. list	INN Rec. list	Common name	Proprietary name	Species	Format	Receptor identification	IMGT/ 2Dstructure-DB	IMGT/ 3Dstructure-DB	Specificity target name [species]	Company	Clinical indication	Development status	Regulatory agency status and year	Clinical trials	Authority decisions
244	canakinumab	8836	97 (2007)	59 (2008)	ACZ885	ILARIS®	*Homo sapiens*		IgG1 - kappa	8836	4g5z 4g6j 5bvj 5bvp	IL1B (interleukin 1 beta, IL-1B, L1F2) [*Homo sapiens*]	Novartis (Basel Switzerland)	Rheumatoid arthritis (RA)				
													Novartis Pharmaceuticals Corp. (East Hanover NJ USA)	Cryopyrin-Associated Periodic Syndromes (CAPS) (including Familial Cold Auto inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 4 and older)	Phase M	FDA approval June 17, 2009	65 studies found, 15 recruiting	EMA: EMEA/H /C/001109 FDA: (BLA) 125319
102	gevokizumab	9310	104 (2010)	66 (2011)	XOMA 052		Humanized		IgG2 - kappa	9310	4g6k 4g6m	IL1B (interleukin 1 beta, IL-1B, L1F2) [*Homo sapiens*]	Xoma (Berkeley CA USA)	Rheumatoid arthritis (RA)	Phase II		24 studies found, 6 recruiting	
														Type 1 diabetes				
														Type 2 diabetes (T2 DM)	Phase II			
														Cardiovascular disease	Phase II			
														Behçet's disease	Phase II			

A query on the specificity target name, based on the HUGO Gene Nomenclature Committee (HGNC) or a synonym allows to retrieve the the corresponding specific mAb, the International Nonproprietary Name (INN) as provided by the WHO/INN Programme, the common name from literature and the proprietary name.

For each entry, IMGT/mAb-DB provides the origin species (human, murine, humanized or chimeric), the isotype, the format, the links to IMGT/2Dstructure-DB (INN amino acid sequences and IMGT Colliers de Perles) and the access to IMGT/3Dstructure-DB (3D structures and structural properties).

IMGT/mAb-DB also provides information on company, clinical indication (more than 200 in the database), development status, organization that approved the drug such as Food and Drugs Administration (FDA) or European Medicines Agency (EMA), application (diagnostic or therapeutic) and clinical domain.

IMGT/3Dstructure-DB: to specificity and binding sites

The antibodies ***canakinumab*** and ***gevokizumab*** are given as examples. The 3D structures are available (4g6j and 4g6m, respectively) in IMGT/3Dstructure-DB. The IMGT Collier de Perles on two layers shows a 2D graphical representation of their VH: conserved amino acids (AA) and hydrogen bonds are shown, and hatched circles correspond to missing positions. The domain alignment shows the VH of ***canakinumab*** and ***gevokizumab*** with the strand delimitations, the framework regions (FR-IMGT), the CDR-IMGT and the dots indicating gaps. The IMGT sequence analysis tools are based on the IMGT unique numbering (Lefranc, M-P. et al., Dev. Comp., 2003). The 2 antibodies have been co-crystallized with the interleukin-1 beta (IL1B), their specific target, so the IMGT paratope and epitope details is provided, as well as the contact analysis table. This table provides pairs of AA (antibody/antigen) involved in the binding site. The specific target sequence is also displayed with its epitope highlighted by the CDR-IMGT standard colors. Using these tools, the user can analyze the complex by identifying the AA involved in the antibody-antigen interaction or by visualizing the complex highlighted by the IMGT standard colors (with the molecular viewer Jmol).

IMGT paratope and epitope details

Ig/Ag interface between canakinumab Fab (FAB-GAMMA-1_KAPPA) *Homo sapiens* (human) [4g6j_H,4g6j_L] and Interleukin-1 Beta (Protein) *Homo sapiens* (human) [4g6j_A]

Paratope in canakinumab Fab (FAB-GAMMA-1_KAPPA) *Homo sapiens* (human) [4g6j_H,4g6j_L]

type	discontinuous
residues	T V Y W Y D N Y L R T S S Y S S S L *IMGT Residue@Position cards*
With positions	T(29_H)+VY(36-37_H)+WYD(57-59_H)+N(64_H)+Y(66_H)+LRT(108-110_H)+S(28_L)+S(38_L)+Y(56_L)+SSSL(107-114_L)

Epitope in Interleukin-1 Beta (Protein) *Homo sapiens* (human) [4g6j_A]

type	discontinuous
residues	V M S G P E K L D E Q Q E K N P K N *IMGT Residue@Position cards*
With positions	VMSGP(16-20_A)+E(22_A)+K(24_A)+L(26_A)+D(32_A)+EQQ(34-36_A)+EKN(61-63_A)+PK(84-85_A)+N(126_A)

IMGT/3Dstructure-DB Domain pair contacts

Contacts of Domain: VH [D1] Chain: 4g6j_H *with* Domain: (Ligand) Chain: 4g6j_A

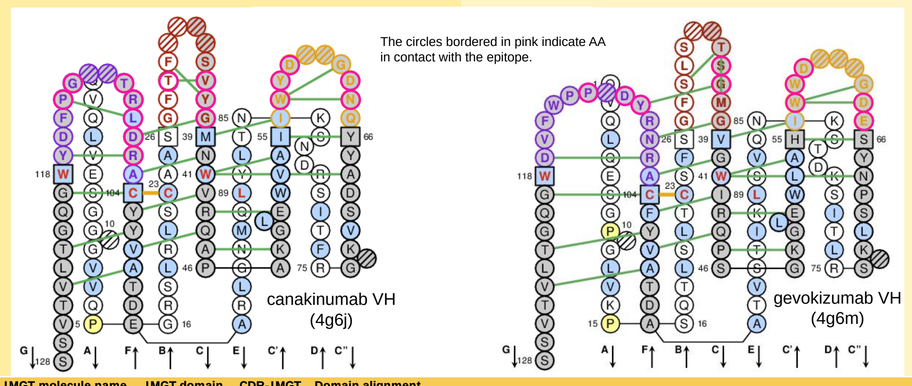
Summary:

Residue pair contacts	Number of residues			Atom pair contact types			
	Total	From 1	From 2	Total	Polar	Hydrogen	Nonpolar
42	34	16	18	395	62	10	333

List of the Residue@Position pair contacts:

Click 'R@P' for IMGT Residue@Position cards

	Order IMGT Num	Residue	Domain	Chain		Order IMGT Num	Residue	Domain	Chain	Atom pair contact types Total	Polar	Hydrogen	Nonpolar
CDR1 R@P	29	THR T	VH [D1]	4g6j_H	R@P	32	ASP D	(Ligand)	4g6j_A	11	3	2	8
R@P	36	VAL V	VH [D1]	4g6j_H	R@P	28	LEU L	(Ligand)	4g6j_A	3	0	0	3
R@P	36	VAL V	VH [D1]	4g6j_H	R@P	32	ASP D	(Ligand)	4g6j_A	6	0	0	6
CDR2 R@P	37	TYR Y	VH [D1]	4g6j_H	R@P	31	GLN Q	(Ligand)	4g6j_A	2	1	0	1
R@P	37	TYR Y	VH [D1]	4g6j_H	R@P	34	GLU E	(Ligand)	4g6j_A	11	2	1	9
R@P	37	TYR Y	VH [D1]	4g6j_H	R@P	35	GLN Q	(Ligand)	4g6j_A	29	2	0	27
R@P	38	GLY G	VH [D1]	4g6j_H	R@P	35	GLN Q	(Ligand)	4g6j_A	1	1	0	0
R@P	57	TRP W	VH [D1]	4g6j_H	R@P	17	MET M	(Ligand)	4g6j_A	14	1	0	13
R@P	57	TRP W	VH [D1]	4g6j_H	R@P	18	SER S	(Ligand)	4g6j_A	22	2	0	20
R@P	57	TRP W	VH [D1]	4g6j_H	R@P	19	GLY G	(Ligand)	4g6j_A	33	2	0	31
R@P	57	TRP W	VH [D1]	4g6j_H	R@P	20	PRO P	(Ligand)	4g6j_A	19	1	0	18
R@P	58	TYR Y	VH [D1]	4g6j_H	R@P	16	VAL V	(Ligand)	4g6j_A	8	0	0	8
R@P	58	TYR Y	VH [D1]	4g6j_H	R@P	18	SER S	(Ligand)	4g6j_A	10	1	0	9
R@P	58	TYR Y	VH [D1]	4g6j_H	R@P	24	LYS K	(Ligand)	4g6j_A	9	1	0	8
R@P	58	TYR Y	VH [D1]	4g6j_H	R@P	26	LEU L	(Ligand)	4g6j_A	9	0	0	9
R@P	58	TYR Y	VH [D1]	4g6j_H	R@P	126	ASN N	(Ligand)	4g6j_A	13	2	1	11
R@P	59	ASP D	VH [D1]	4g6j_H	R@P	18	SER S	(Ligand)	4g6j_A	4	3	0	1
R@P	59	ASP D	VH [D1]	4g6j_H	R@P	24	LYS K	(Ligand)	4g6j_A	9	2	1	7
R@P	59	ASP D	VH [D1]	4g6j_H	R@P	126	ASN N	(Ligand)	4g6j_A	9	3	1	6
R@P	63	ASP D	VH [D1]	4g6j_H	R@P	24	LYS K	(Ligand)	4g6j_A	4	1	0	3
R@P	64	ASN N	VH [D1]	4g6j_H	R@P	18	SER S	(Ligand)	4g6j_A	10	3	1	7
R@P	64	ASN N	VH [D1]	4g6j_H	R@P	19	GLY G	(Ligand)	4g6j_A	6	1	0	5
R@P	64	ASN N	VH [D1]	4g6j_H	R@P	22	GLU E	(Ligand)	4g6j_A	6	3	0	3
R@P	66	TYR Y	VH [D1]	4g6j_H	R@P	20	PRO P	(Ligand)	4g6j_A	5	0	0	5
CDR3 R@P	106	ARG R	VH [D1]	4g6j_H	R@P	34	GLU E	(Ligand)	4g6j_A	4	2	0	2
R@P	107	ASP D	VH [D1]	4g6j_H	R@P	35	GLN Q	(Ligand)	4g6j_A	4	2	0	2
R@P	108	LEU L	VH [D1]	4g6j_H	R@P	34	GLU E	(Ligand)	4g6j_A	12	0	0	12
R@P	108	LEU L	VH [D1]	4g6j_H	R@P	35	GLN Q	(Ligand)	4g6j_A	9	1	0	8
R@P	109	ARG R	VH [D1]	4g6j_H	R@P	34	GLU E	(Ligand)	4g6j_A	14	3	1	11
R@P	109	ARG R	VH [D1]	4g6j_H	R@P	35	GLN Q	(Ligand)	4g6j_A	18	3	0	15
R@P	109	ARG R	VH [D1]	4g6j_H	R@P	36	GLN Q	(Ligand)	4g6j_A	6	1	0	5
R@P	109	ARG R	VH [D1]	4g6j_H	R@P	61	GLU E	(Ligand)	4g6j_A	16	5	0	11
R@P	109	ARG R	VH [D1]	4g6j_H	R@P	62	LYS K	(Ligand)	4g6j_A	2	1	0	1
R@P	110	THR T	VH [D1]	4g6j_H	R@P	17	MET M	(Ligand)	4g6j_A	8	1	0	7
R@P	110	THR T	VH [D1]	4g6j_H	R@P	62	LYS K	(Ligand)	4g6j_A	11	1	1	10
R@P	113	GLY G	VH [D1]	4g6j_H	R@P	62	LYS K	(Ligand)	4g6j_A	1	1	0	0



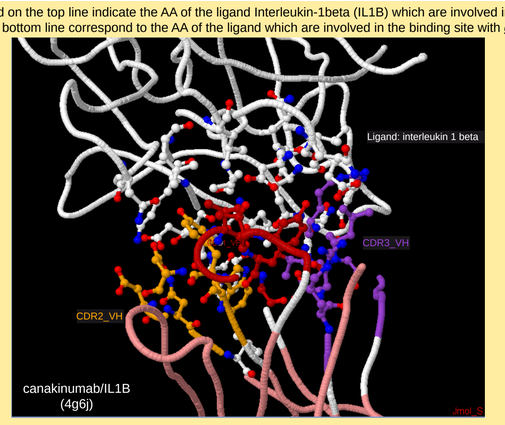
IMGT chain ID	Specie	IMGT molecule name	IMGT domain description	CDR-IMGT length	Domain alignment
8836_H	Homo sapiens	canakinumab; ACZ885	VH	[8.8.11]	QVQLVESGG.GVVQP GRSLRLSCAAS GFTF....SVYG MNWVRQAP GKGLEWVAI IWYD..GDNQ YYADSVK.G RFTISRDNSK NTLYLQMNGLRA EDTAVYYC ARDLRT..GPFDY WGQGTLVTVSS
9310_H	Humanized	gevokizumab; XOMA 052	VH	[10.7.12]	QVQLQESGP.GLVKP SQTLSLTCSFS GFSLS..TSGMG VGWIRQPS GKGLEWLAH IWWD...GDE SYNPSLK.S RLTISKDTSK NQVSLKITSVTA ADTAVYFC ARNRYD.PPWFVD WGQGTLVTVSS

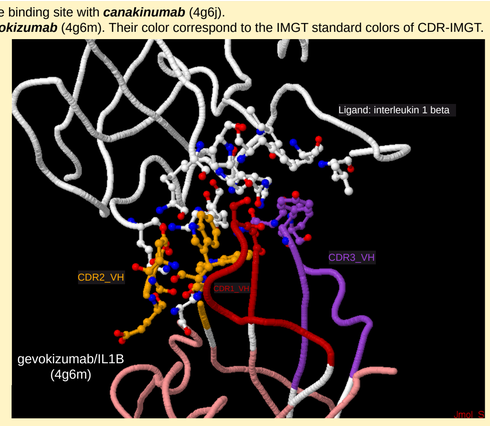
Chain details of **Interleukin-1 Beta**, Protein *Homo sapiens* (human)

Chain length	150
IMGT chain description	Protein
Chain sequence	4g6j_A / 4g6m_A PVRSLNCTLRDSQQKSLVMSGPYELKALHLQGQDMEQQVVFSMSFVQGEESNDKIPVALGLKEKNLYLSCVLKDDKPTLQLESVDPKNYPKKKMEKRFVFNKIEINNKLEFESAQFPNWYISTSQAENMPVFLGGTKGGQDITDFTMQFV

The colored dots located on the top line indicate the AA of the ligand Interleukin-1beta (IL1B) which are involved in the binding site with ***canakinumab*** (4g6j).

The colored dots on the bottom line correspond to the AA of the ligand which are involved in the binding site with ***gevokizumab*** (4g6m). Their color correspond to the IMGT standard colors of CDR-IMGT.





IMGT paratope and epitope details

Ig/Ag interface between gevokizumab Fab (FAB-GAMMA-1_KAPPA) *Chimeric* (chimeric) [4g6m_H,4g6m_L] and Interleukin-1 Beta (Protein) *Homo sapiens* (human) [4g6m_A]

Paratope in gevokizumab Fab (FAB-GAMMA-1_KAPPA) *Chimeric* (chimeric) [4g6m_H,4g6m_L]

type	discontinuous
residues	S G W W D D E S Y D P Q S Y Y K G K M L *IMGT Residue@Position cards*
With positions	SG(35-36_H)+WWD(57-59_H)+DES(64-66_H)+YDP(109-112_H)+Q(27_L)+S(36_L)+Y(38_L)+Y(56_L)+K(66_L)+GKML(107-114_L)

Epitope in Interleukin-1 Beta (Protein) *Homo sapiens* (human) [4g6m_A]

type	discontinuous
residues	V L K D E S D N Y K K E K R A Q F *IMGT Residue@Position cards*
With positions	VLKD(71-74_A)+ES(82-83_A)+D(85_A)+NY(88-89_A)+K(91_A)+K(93_A)+EKR(95-97_A)+AQF(114-116_A)

IMGT/3Dstructure-DB Domain pair contacts

Contacts of Domain: VH [D1] Chain: 4g6m_H *with* Domain: (Ligand) Chain: 4g6m_A

Summary:

Residue pair contacts	Number of residues			Atom pair contact types			
	Total	From 1	From 2	Total	Polar	Hydrogen	Nonpolar
25	23	11	12	269	32	8	237

List of the Residue@Position pair contacts:

Click 'R@P' for IMGT Residue@Position cards

	Order IMGT Num	Residue	Domain	Chain		Order IMGT Num	Residue	Domain	Chain	Atom pair contact types Total	Polar	Hydrogen	Nonpolar
CDR1 R@P	35	SER S	VH [D1]	4g6m_H	R@P	115	GLN Q	(Ligand)	4g6m_A	5	2	0	3
R@P	35	SER S	VH [D1]	4g6m_H	R@P	117	PRO P	(Ligand)	4g6m_A	4	0	0	4
R@P	36	GLY G	VH [D1]	4g6m_H	R@P	115	GLN Q	(Ligand)	4g6m_A	6	1	0	5
CDR2 R@P	57	TRP W	VH [D1]	4g6m_H	R@P	96	LYS K	(Ligand)	4g6m_A	28	0	0	28
R@P	57	TRP W	VH [D1]	4g6m_H	R@P	115	GLN Q	(Ligand)	4g6m_A	2	0	0	2
R@P	58	TRP W	VH [D1]	4g6m_H	R@P	96	LYS K	(Ligand)	4g6m_A	9	0	0	9
R@P	58	TRP W	VH [D1]	4g6m_H	R@P	114	ALA A	(Ligand)	4g6m_A	5	0	0	5
R@P	58	TRP W	VH [D1]	4g6m_H	R@P	115	GLN Q	(Ligand)	4g6m_A	11	0	0	11
R@P	59	ASP D	VH [D1]	4g6m_H	R@P	96	LYS K	(Ligand)	4g6m_A	8	2	1	6
R@P	64	ASP D	VH [D1]	4g6m_H	R@P	93	LYS K	(Ligand)	4g6m_A	8	2	0	6
R@P	64	ASP D	VH [D1]	4g6m_H	R@P	94	MET M	(Ligand)	4g6m_A	1	1	0	0
R@P	64	ASP D	VH [D1]	4g6m_H	R@P	96	LYS K	(Ligand)	4g6m_A	9	2	1	7
R@P	65	GLU E	VH [D1]	4g6m_H	R@P	93	LYS K	(Ligand)	4g6m_A	7	2	1	5
R@P	66	SER S	VH [D1]	4g6m_H	R@P	93	LYS K	(Ligand)	4g6m_A	9	2	1	7
R@P	109	TYR Y	VH [D1]	4g6m_H	R@P	72	LEU L	(Ligand)	4g6m_A	10	0	0	10
CDR3 R@P	109	TYR Y	VH [D1]	4g6m_H	R@P	115	GLN Q	(Ligand)	4g6m_A	33	3	0	30
R@P	109	TYR Y	VH [D1]	4g6m_H	R@P	116	PHE F	(Ligand)	4g6m_A	24	0	0	24
R@P	110	ASP D	VH [D1]	4g6m_H	R@P	70	CYS C	(Ligand)	4g6m_A	1	1	0	0
R@P	110	ASP D	VH [D1]	4g6m_H	R@P	71	VAL V	(Ligand)	4g6m_A	4	0	0	4
R@P	110	ASP D	VH [D1]	4g6m_H	R@P	95	GLU E	(Ligand)	4g6m_A	11	1	0	10
R@P	110	ASP D	VH [D1]	4g6m_H	R@P	96	LYS K	(Ligand)	4g6m_A	15	2	0	13
R@P	110	ASP D	VH [D1]	4g6m_H	R@P	97	ARG R	(Ligand)	4g6m_A	31	6	2	25
R@P	110	ASP D	VH [D1]	4g6m_H	R@P	115	GLN Q	(Ligand)	4g6m_A	15	4	2	11
R@P	112	PRO P	VH [D1]	4g6m_H	R@P	71	VAL V	(Ligand)	4g6m_A	4	0	0	4
R@P	112	PRO P	VH [D1]	4g6m_H	R@P	97	ARG R	(Ligand)	4g6m_A	9	1	0	8

Amino acid color correspondance:

- CDR1-IMGT
- CDR2-IMGT
- CDR3-IMGT

IMGT® director: Sofia Kossida (Sofia.Kossida@igh.cnrs.fr)
IMGT® founder and executive director emeritus: Marie-Paule Lefranc (Marie-Paule.Lefranc@igh.cnrs.fr)
Bioinformatics manager: Véronique Giudicelli (Veronique.Giudicelli@igh.cnrs.fr)
Computer manager: Patrice Duroux (Patrice.Duroux@igh.cnrs.fr)

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