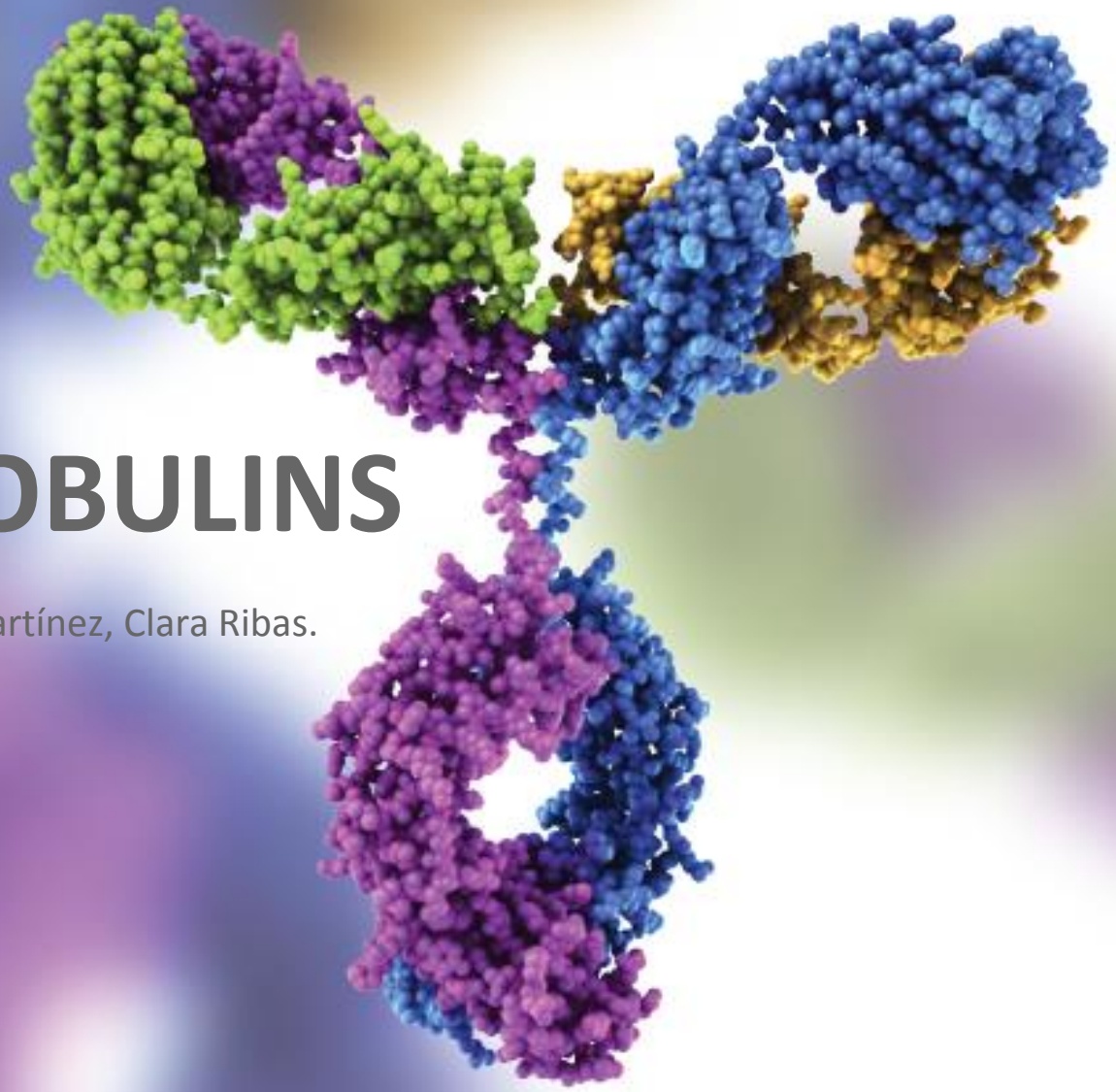
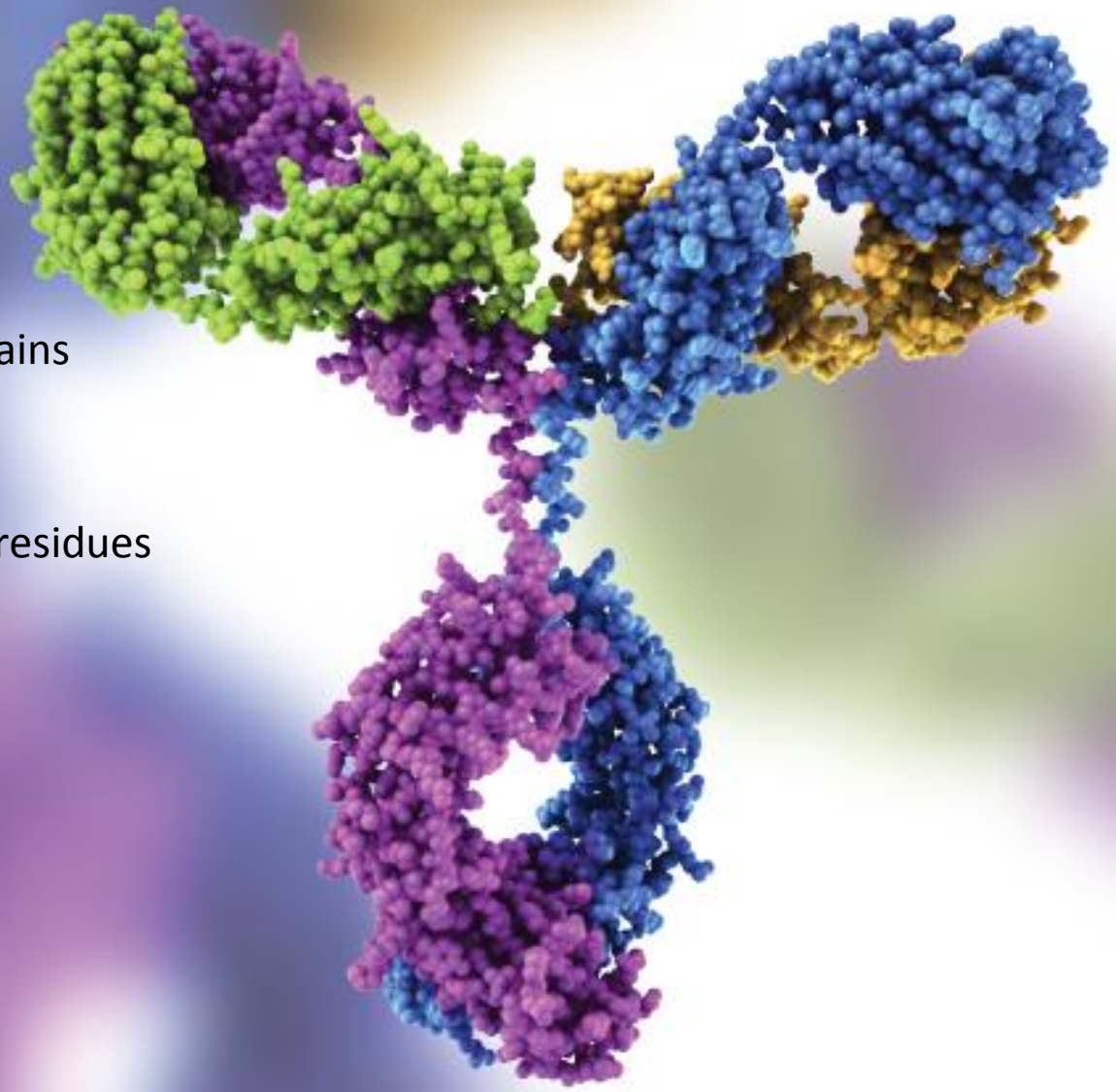


IMMUNOGLOBULINS

Paula Galiana, Núria Isern, Andrea Martínez, Clara Ribas.

1. Introduction
   - immunoglobulin description
   - Ig constant and variable domains
2. Structural alignment
3. Sequence alignment
   - representation of conserved residues
4. Canonical structures
5. Ag-Ab interaction
6. Conclusions
7. References
8. Multiple choice questions



Immunoglobulin description

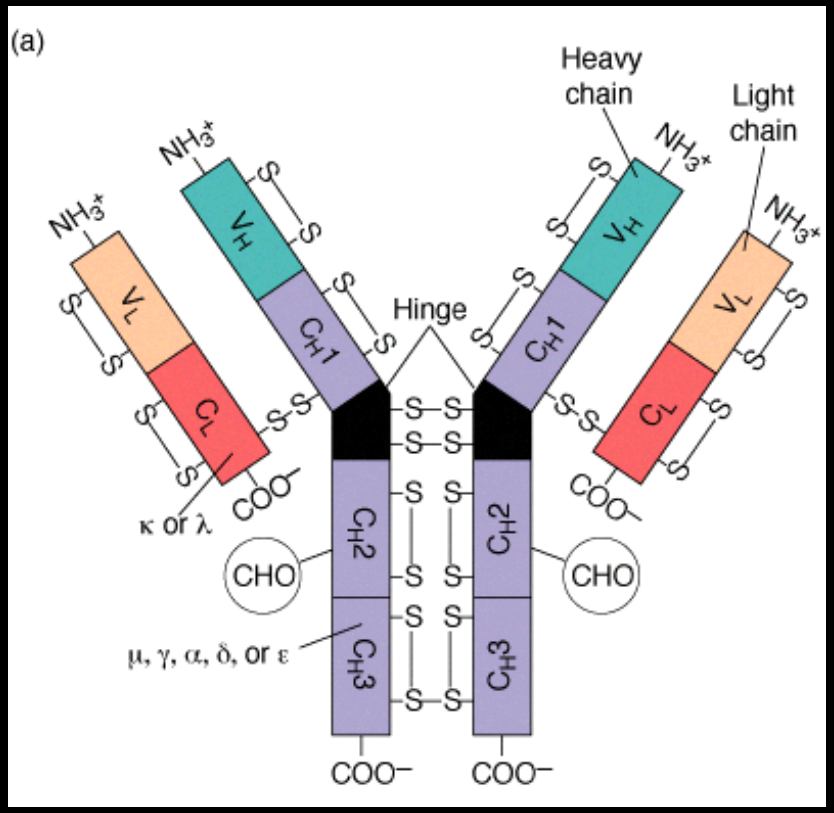
SCOP Classification:

Class: All β protein

Fold: immunoglobulin-like β-sandwich

Superfamily: Immunoglobulin

Family: Vset domains or C1 set domains



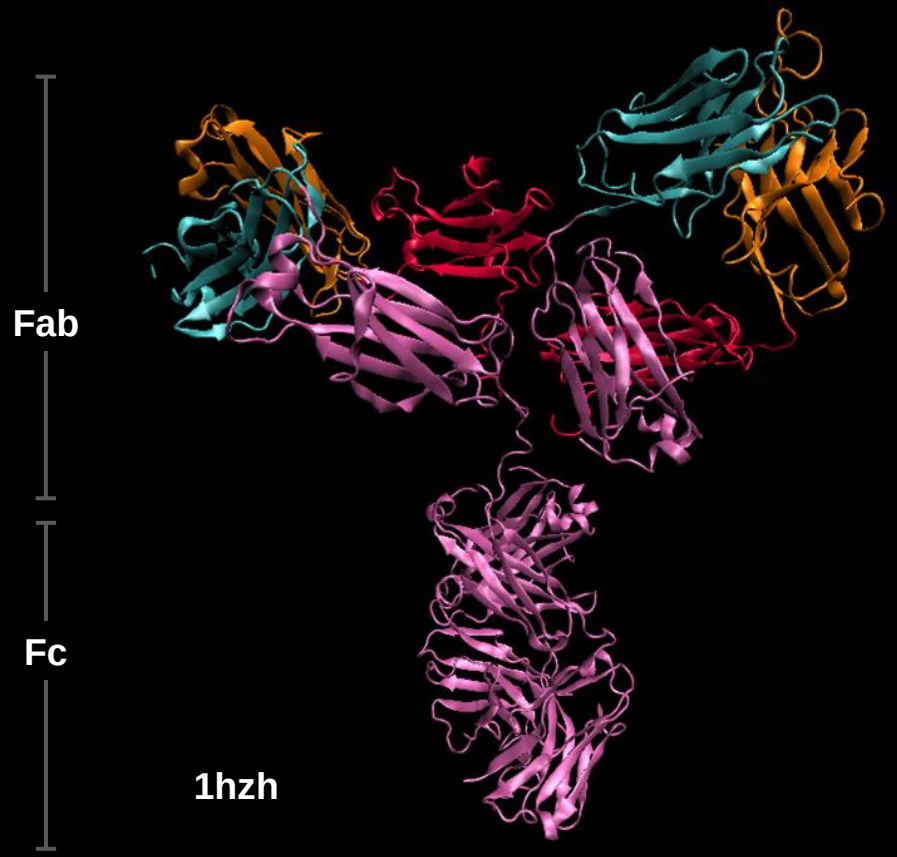
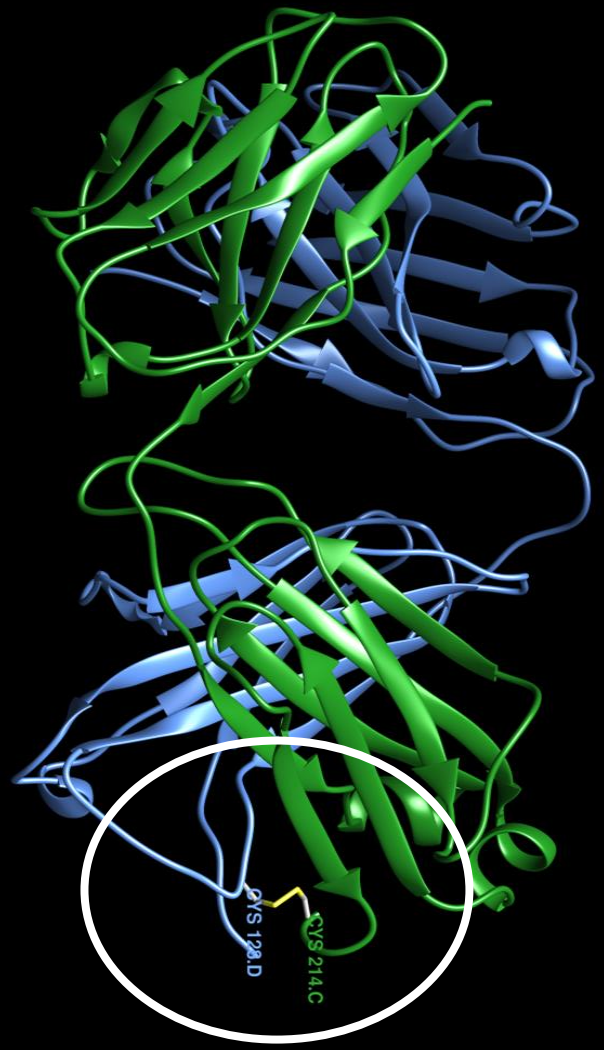
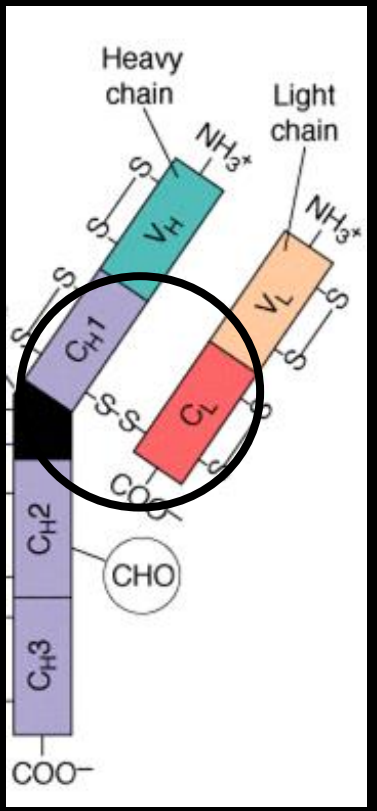


Image from: https://image.slidesharecdn.com/antibodieschpt4-141027033913-conversion-gate01/95/antibodies-chpt-4-2-638.jpg?cb=1414381229

Immunoglobulin description

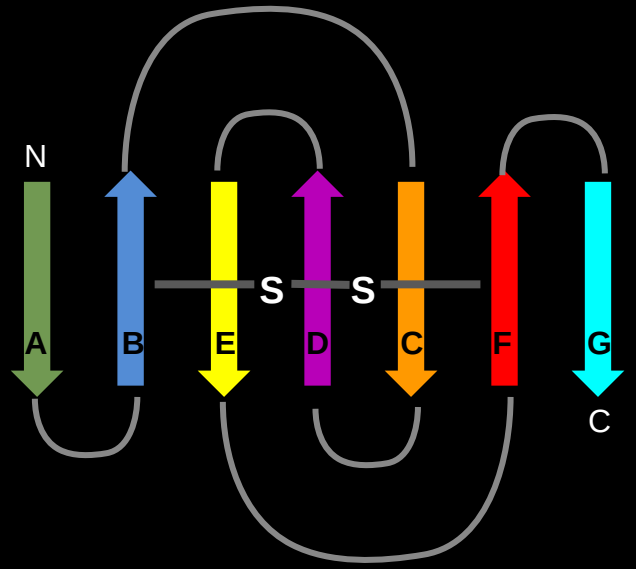


1hzh



Ig constant domain

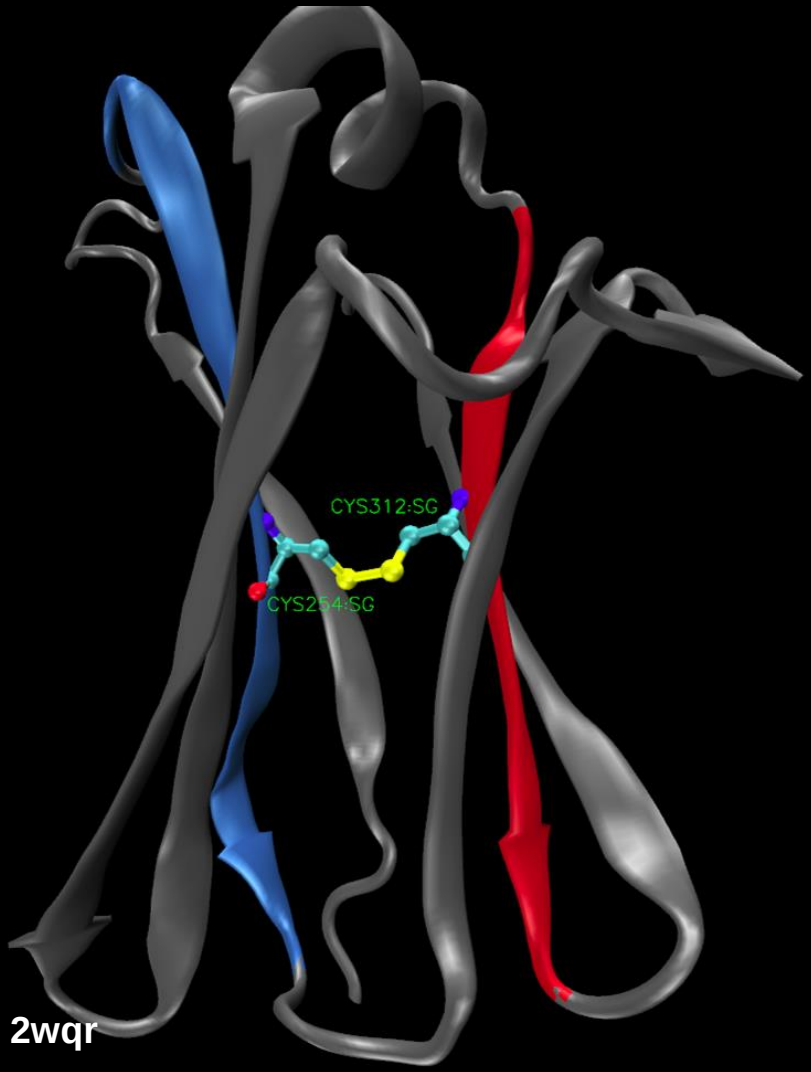
2wqr



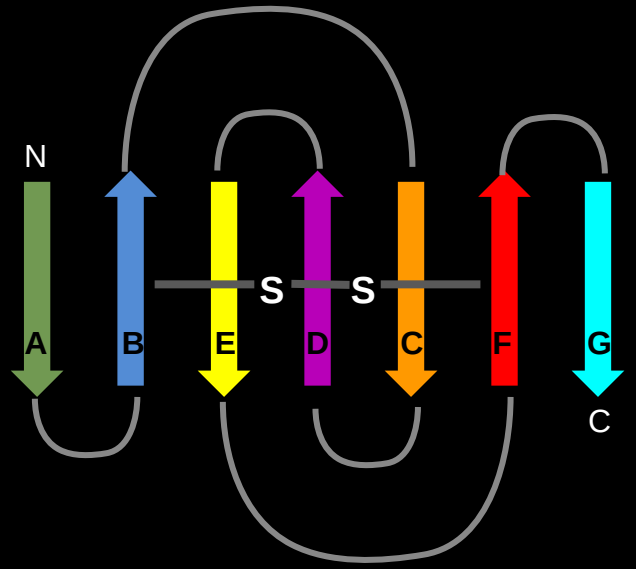
- 7 antiparallel β-strands
- 2 β-sheets:
  - 4-stranded sheet
  - 3-stranded sheet

Immunoglobulin-like β-sandwich

Ig constant domain



2wqr

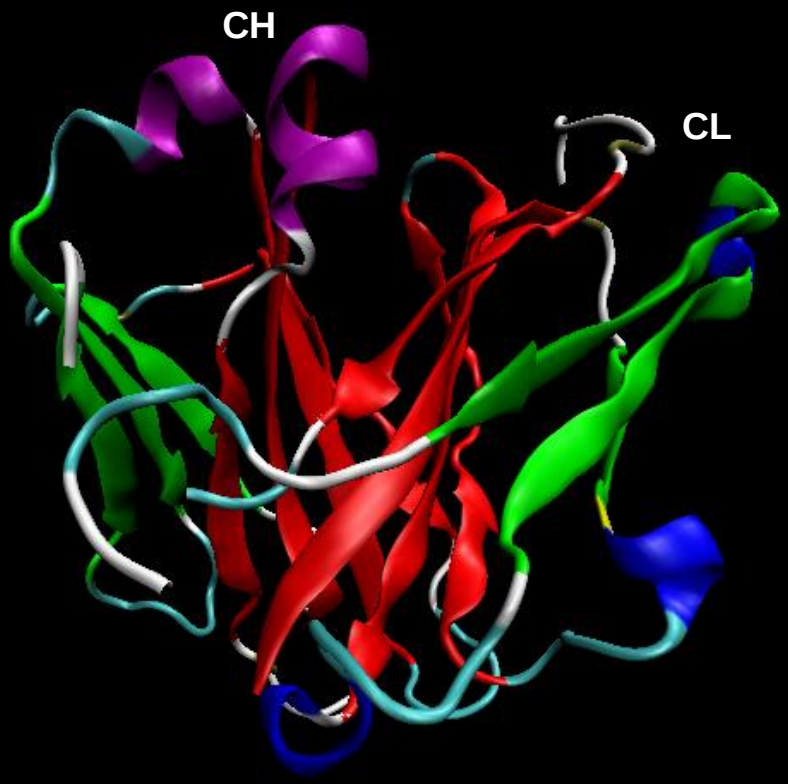


- 7 antiparallel β-strands
- 2 β-sheets:
  - 4-stranded sheet
  - 3-stranded sheet

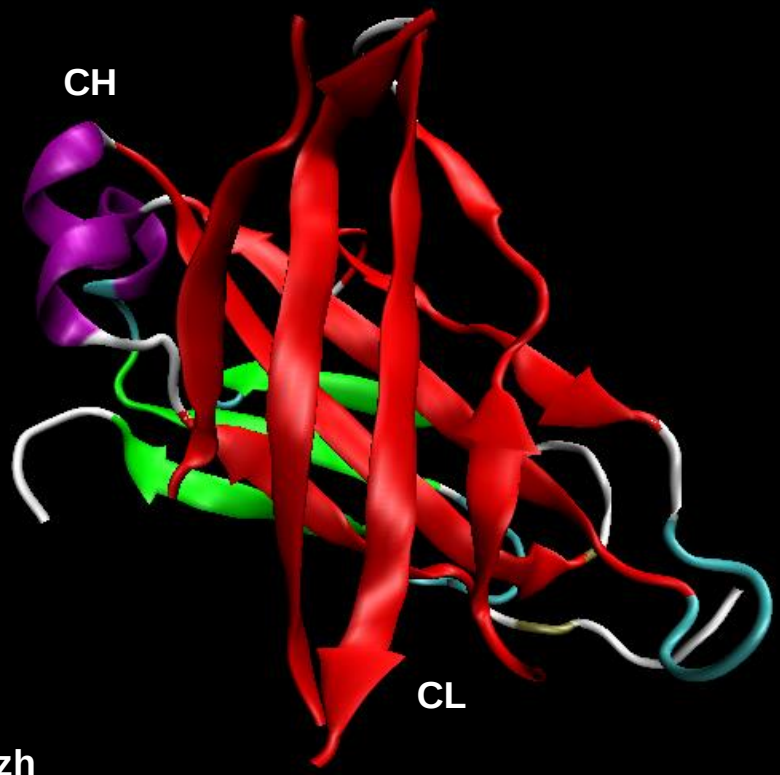
Immunoglobulin-like β-sandwich

Ig constant domain

4-stranded β-sheets interaction

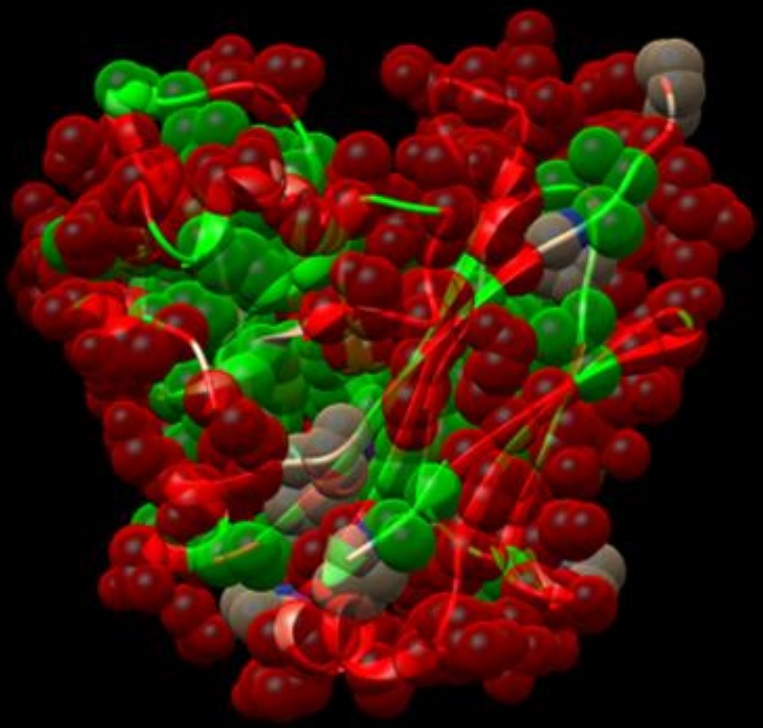


1hzh



1hzh

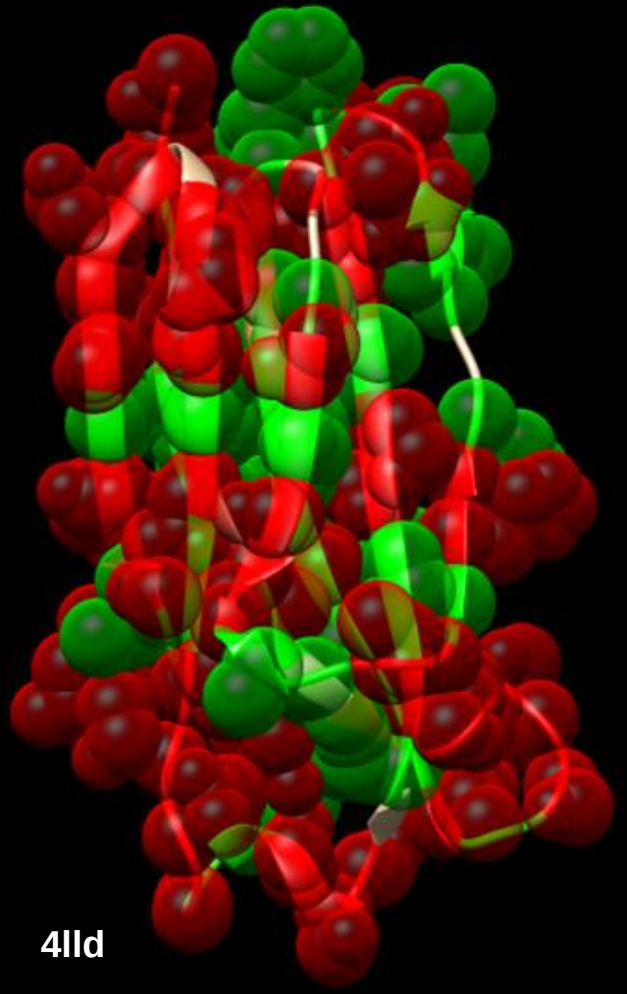
Hydrophobic core



2wqr

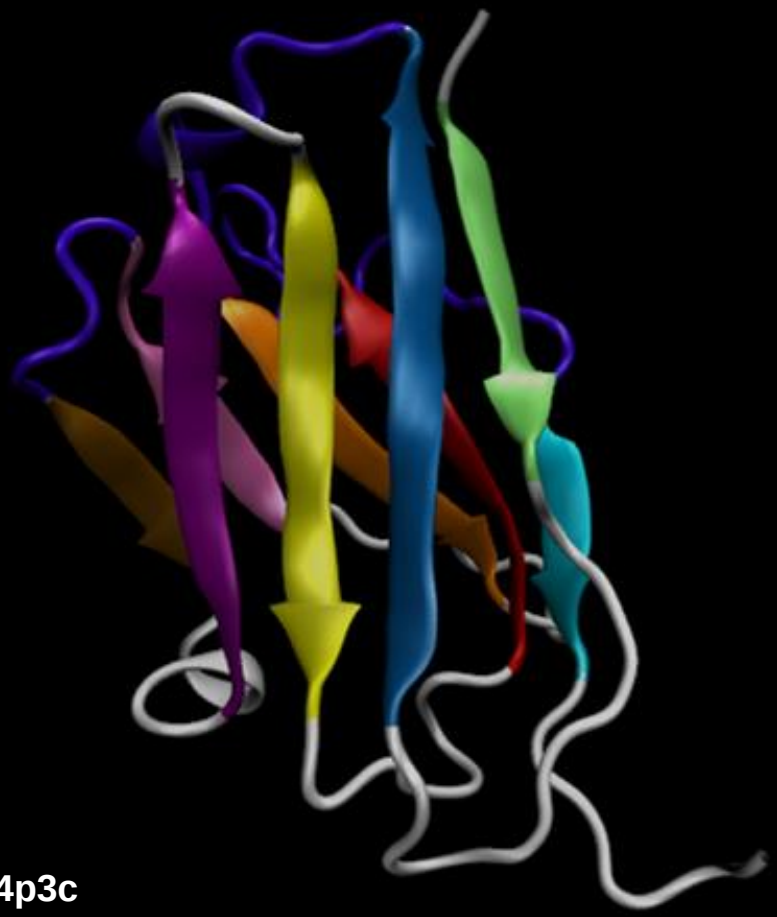
polar

hydrophobic

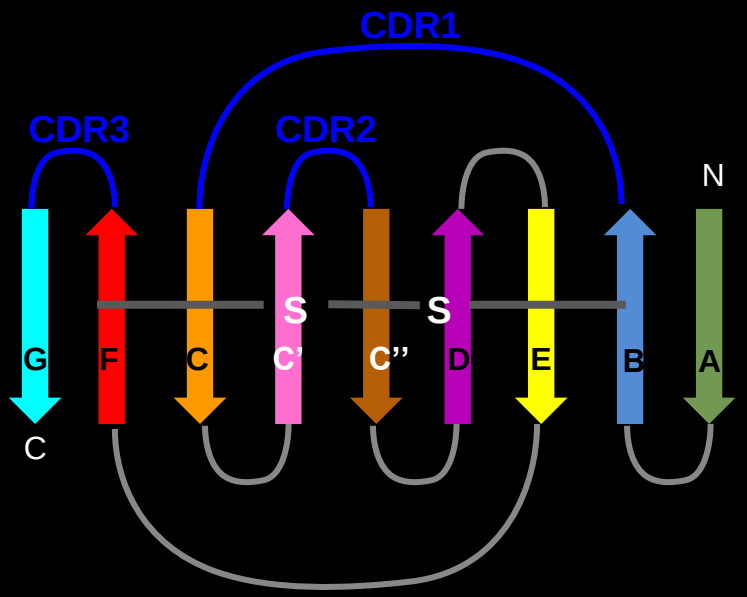


4lld

Ig variable domain



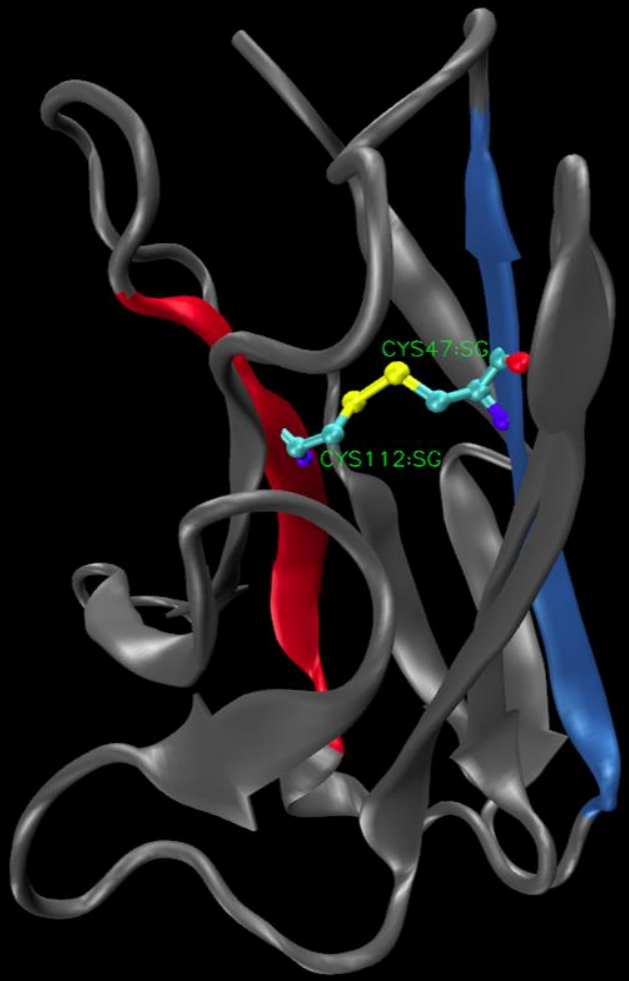
4p3c



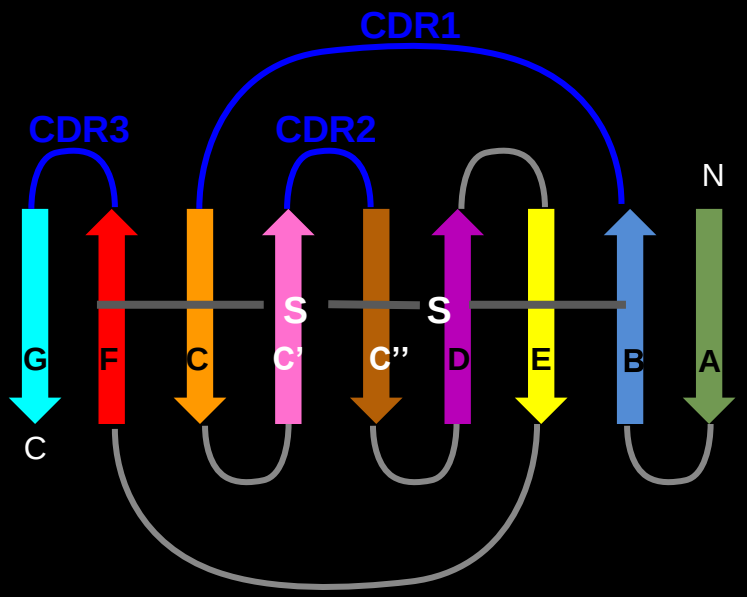
- 7 + 2 antiparallel β-strands: C’ and C’’
- 2 β-sheets:
  - 5-stranded sheet
  - 4-stranded sheet

Immunoglobulin-like β-sandwich

Ig variable domain



5ezj

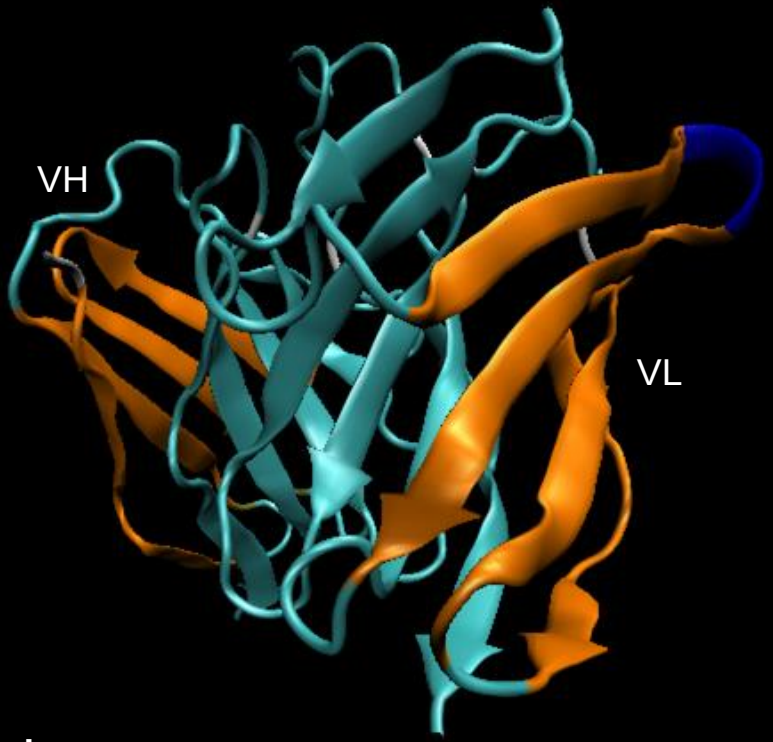


- 7 + 2 antiparallel β-strands: C’ and C’’
- 2 β-sheets:
  - 5-stranded sheet
  - 4-stranded sheet

Immunoglobulin-like β-sandwich

Ig variable domain

5-stranded β-sheets ➡ β-barrel



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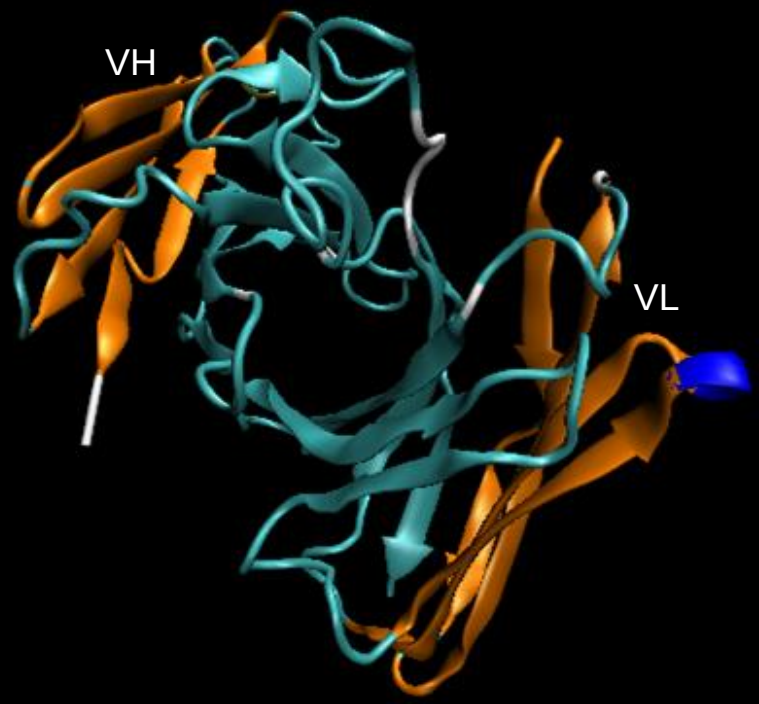
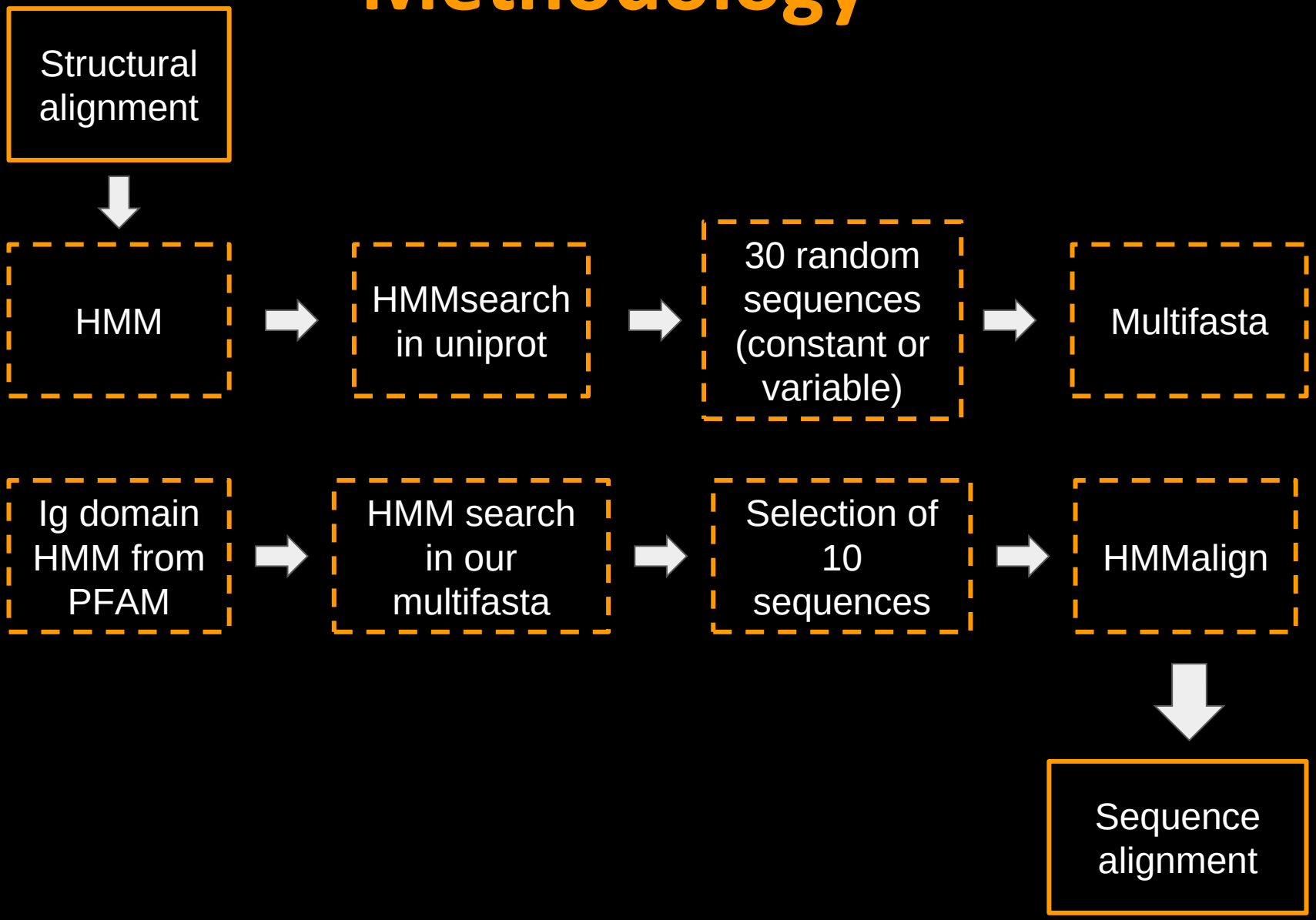
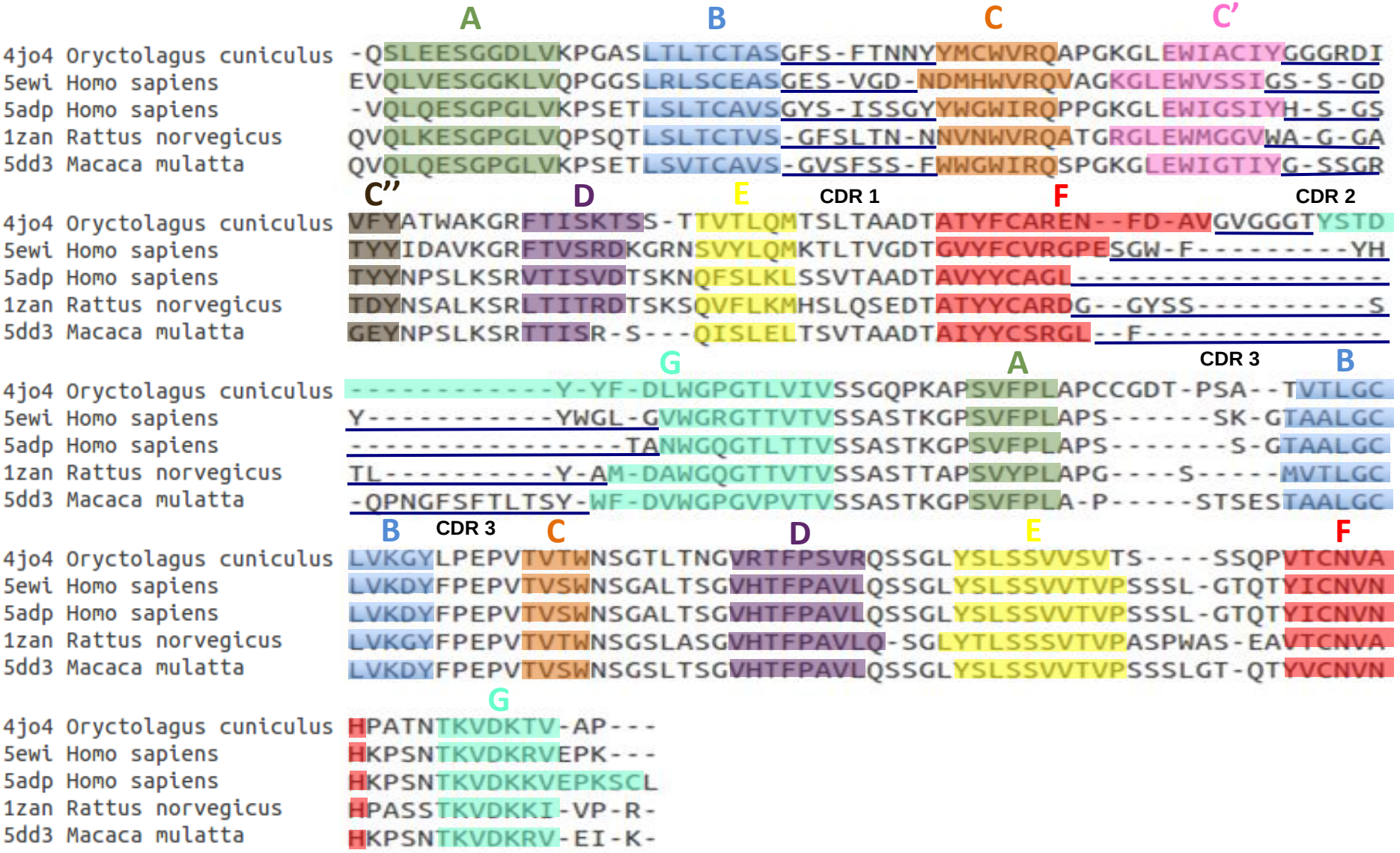


1hzh

Methodology



Structural alignment - heavy chain



Structural alignment - light chain

Sequence alignment - CH1

100% conserved residues

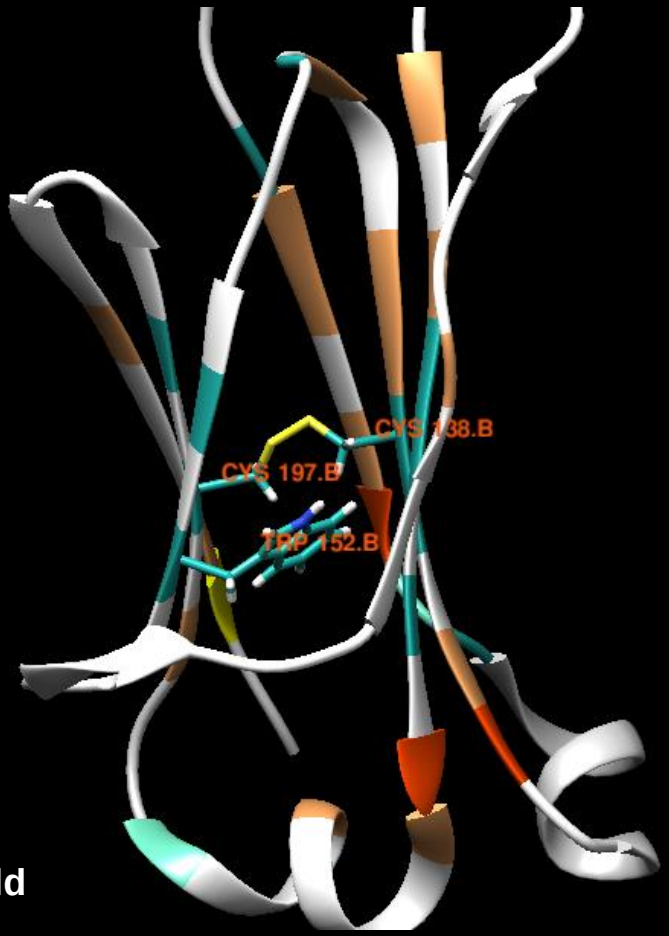
90-80% conserved residues belonging to different groups

90-80% conserved residues belonging to the same group

residues from the same group

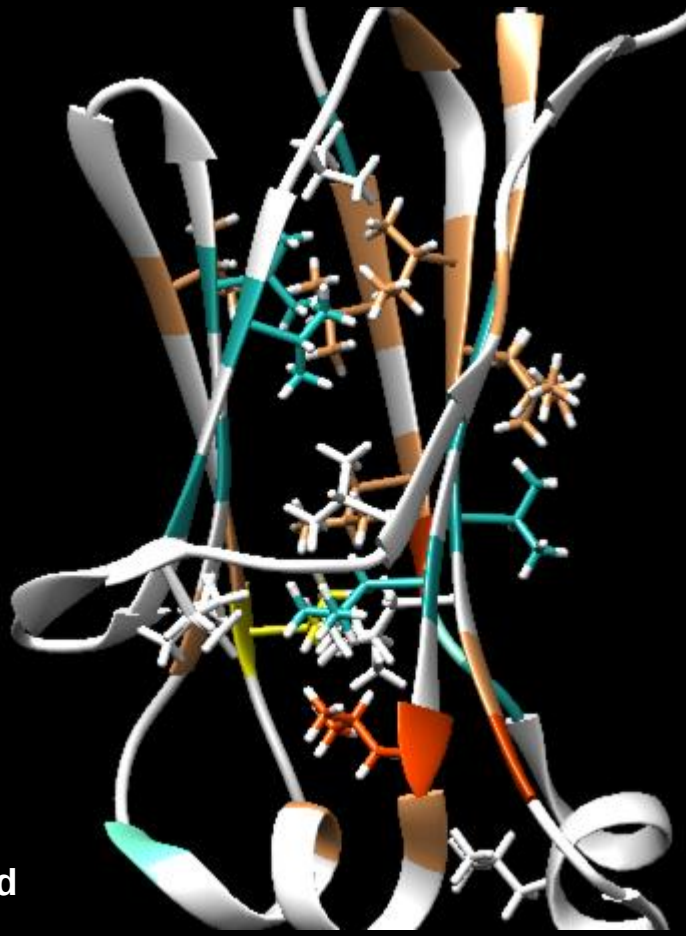
hydrophobic residues (aromatic and none aromatic)

Sequence alignment constant domain



4lld

Cys - Trp - Cys triad

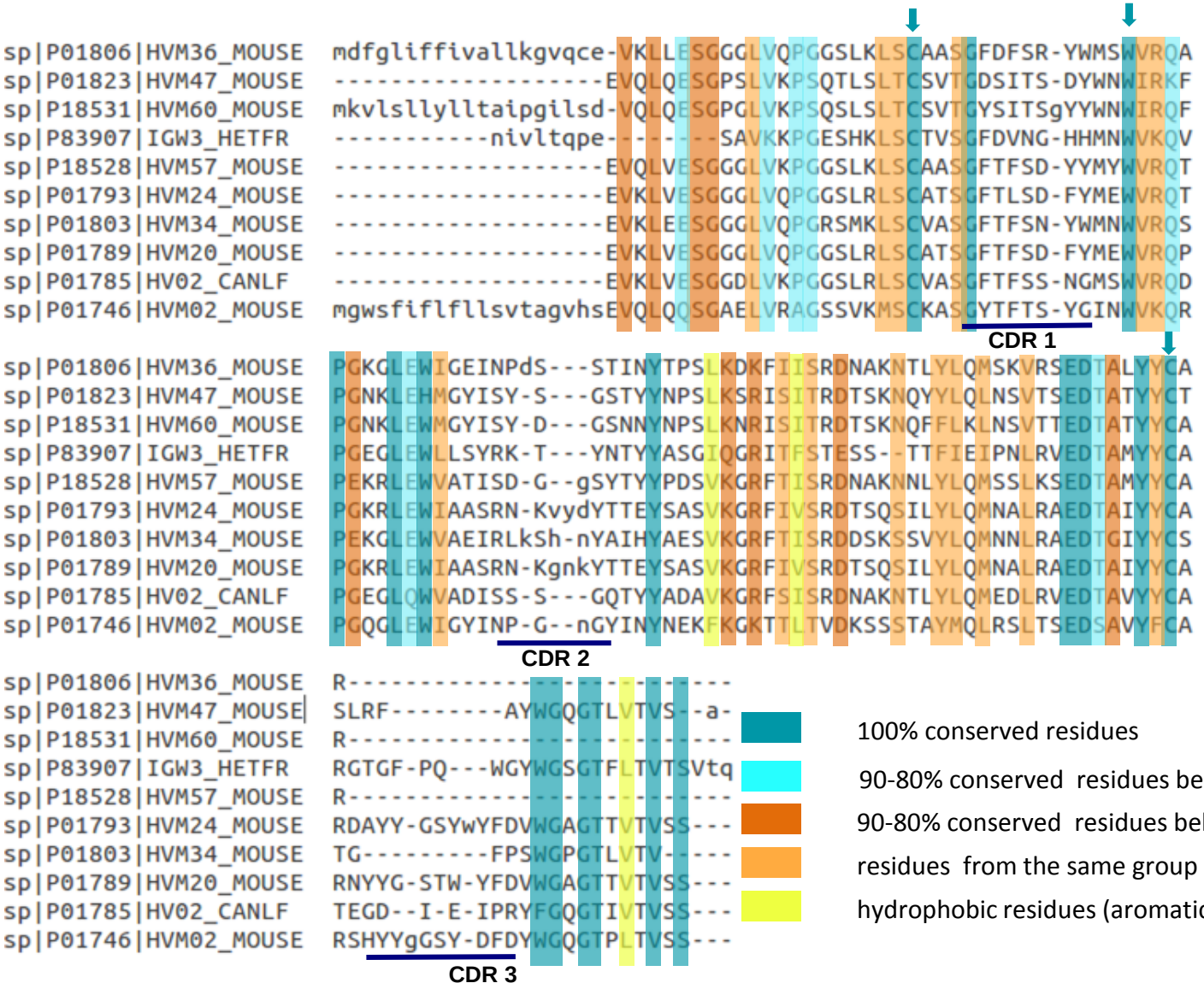


4lld

Conserved Valines, Isoleucines and Leucines

Sequence alignment - CL

Sequence alignment - VH



100% conserved residues

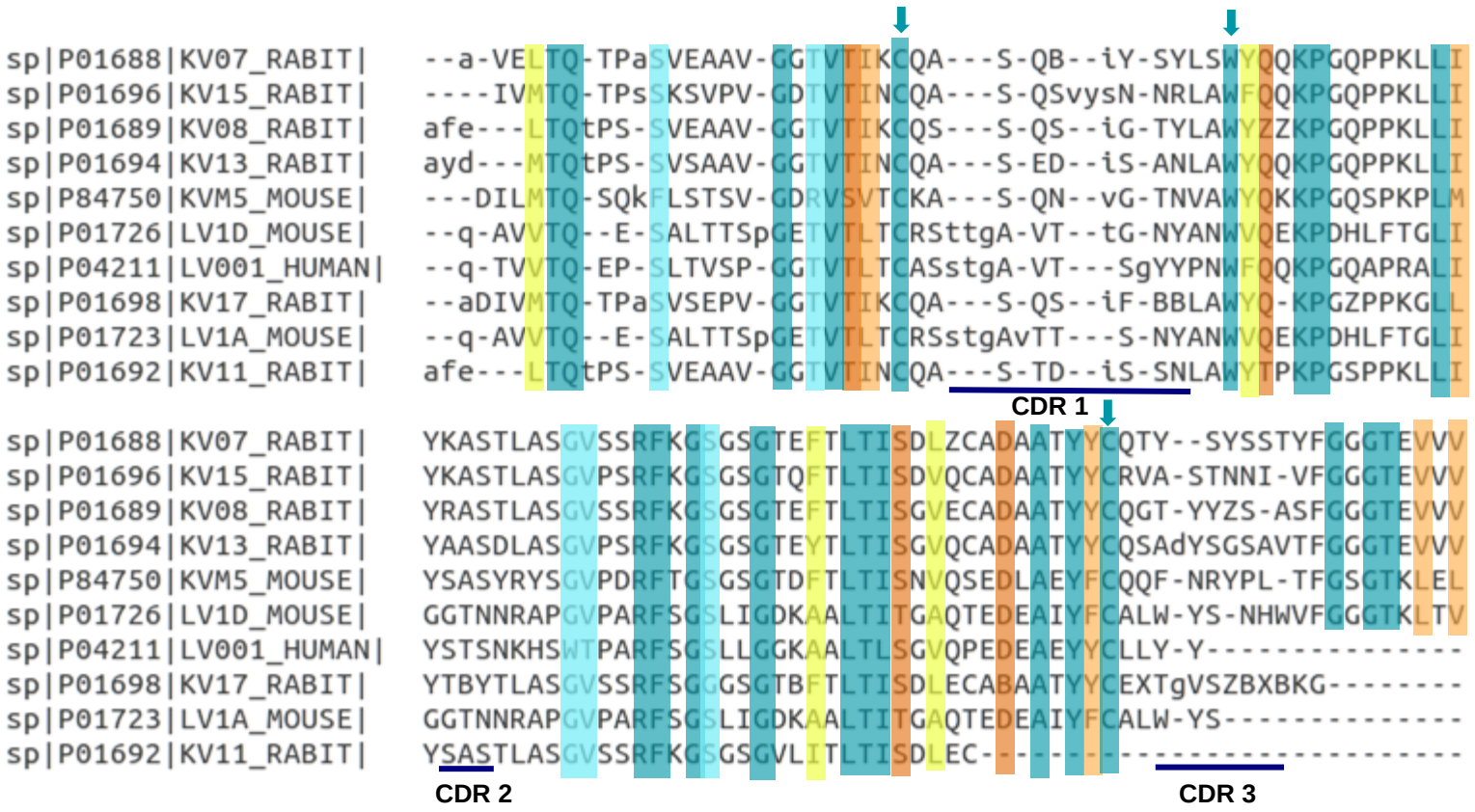
90-80% conserved residues belonging to different groups

90-80% conserved residues belonging to the same group

residues from the same group

hydrophobic residues (aromatic and none aromatic)

Sequence alignment - VL



100% conserved residues

90-80% conserved residues belonging to different groups

90-80% conserved residues belonging to the same group

residues from the same group

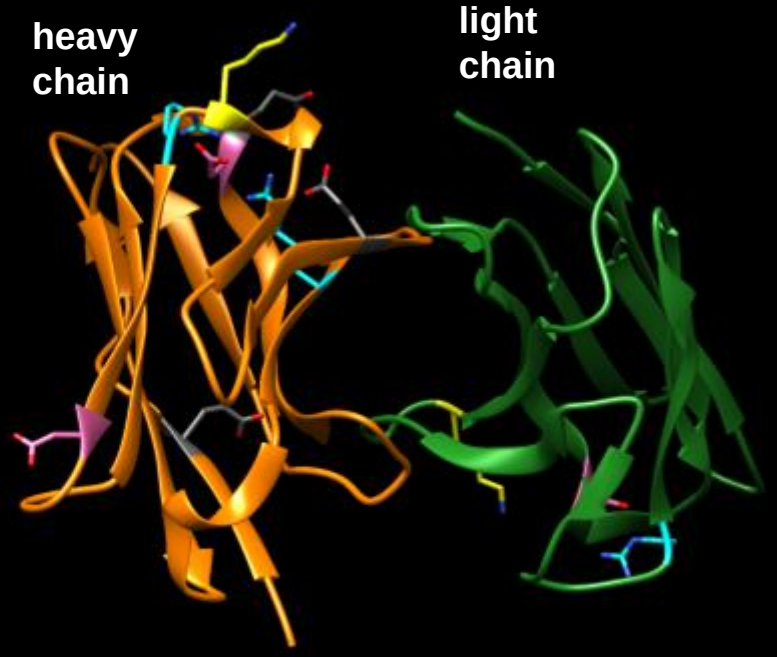
hydrophobic residues (aromatic and none aromatic)

Additional conservations - charged residues

Alignment from the heavy chain:

```
mdfgliffivallkgvqce-VKLLESGGGLVQPGGSLKLSCAASGFDFSR-YWMSWVRQA
------------------EVQLQESGPSLVKPSQTLSLTCSVTGDSITS-DYWNWIRKF
mkvlsllylltaipgilsd-VQLQESGPGLVKPSQSLSLTCSVTGYSITSgYYWNWIRQF
----------nivltqpe-------SAVKKPGESHKLSCTVSGFDVNG-HHMNWVKQV
------------------EVQLVESGGGLVKPGGSLKLSCAASGFTFSD-YYMYWVRQT
------------------EVKLVESGGGLVQPGGSLRLSCATSGFTLSD-FYMEWVRQT
------------------EVKLEESGGGLVQPGRSMKLSCVASGFTFSN-YWMNWVRQS
------------------EVKLVESGGGLVQPGGSLRLSCATSGFTFSD-FYMEWVRQP
------------------EVKLVESGGDLVKPGGSLRLSCVASGFTFSS-NGMSWVRQD
mgwsfiflfllsvtagvhsEVQLQQSGAELVRAGSSVKMSCKASGYTFTS-YGINWVKQR

PGKGLEWIGEINPdS---STINYTPSLKDKFIISRDNAKNTLYLQMSKVRSEDTALYYCA
PGNKLEHMGYISY-S---GSTYYNPSLKSRISITRDTSKNQYYLQLNSVTSEDTATYYCT
PGNKLEWMGYISY-D---GSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCA
PGEGLEWLLSYRK-T---YNTYYASGIQGRITFSTESS--TTFIEIPNLRVEDTAMYYCA
PEKRLEWVATISD-G--gSYTYYPDSVKGRFTISRDNAKNNLYLQMSSLKSEDTAMYYCA
PGKRLEWIAASRN-KvydYTTEYSASVKGRFIVSRDTSQSILYLQMNALRAEDTAIYYCA
PEKGLEWVAEIRLkSh-nYAIHYAESVKGRFTISRDDSKSSVYLQMNNLRAEDTGIYYCS
PGKRLEWIAASRN-KgnkYTTEYSASVKGRFIVSRDTSQSILYLQMNALRAEDTAIYYCA
PGEGLQWVADISS-S---GQTYYADAVKGRFSISRDNAKNTLYLQMEDLRVEDTAVYYCA
PGQGLEWIGYINP-G--nGYINYNEKFKGKTTLTVDKSSSTAYMQLRSLTSEDSAVYFCA
```



1j1o

- Arginine (R)
- Aspartic acid (D)
- Glutamic acid (E)
- Lysine (K)

found in the surface

Additional conservations - charged residues

Salt bridges between charged residues in the heavy chain

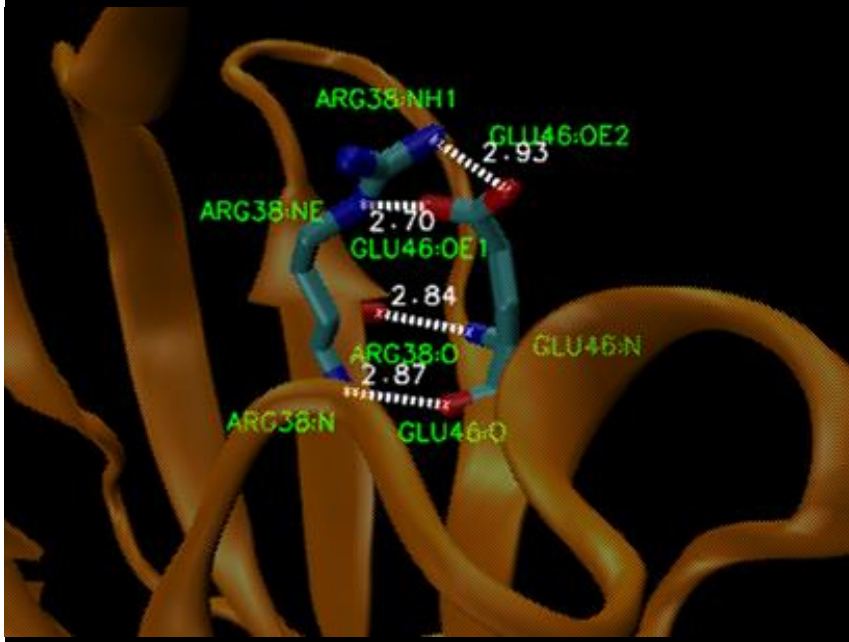
Arg 38

```
mdfgliffivallkgvqce-VKLLESGGGLVQPGGSLKLSCAASGFDFSR-YWMSWVRQA
------------------EVQLQESGPSLVKPSQTLSLTCSVTGDSITS-DYWNWIRKF
mkvlsllylltaipgilsd-VQLQESGPGLVKPSQSLSLTCSVTGYSITSgYYWNWIRQF
-----------nivltqpe--------SAVKKPGESHKLSCTVSGFDVNG-HHMNWVKQV
------------------EVQLVESGGGLVKPGGSLKLSCAASGFTFSD-YYMYWVRQT
------------------EVKLVESGGGLVQPGGSLRLSCATSGFTLSD-FYMEWVRQT
------------------EVKLEESGGGLVQPGRSMKLSCVASGFTFSN-YWMNWVRQS
------------------EVKLVESGGGLVQPGGSLRLSCATSGFTFSD-FYMEWVRQP
------------------EVKLVESGGDLVKPGGSLRLSCVASGFTFSS-NGMSWVRQD
mgwsfiflfllsvtagvhsEVQLQQSGAELVRAGSSVKMSCKASGYTFTS-YGINWVKQR

PGKGLEWIGEINPdS---STINYTPSLKDKFIISRDNAKNTLYLQMSKVRSEDTALYYCA
PGNKLEHMGYISY-S---GSTYYNPSLKSRISITRDTSKNQYYLQLNSVTSEDTATYYCT
PGNKLEWMGYISY-D---GSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCA
PGEGLEWLLSYRK-T---YNTYYASGIQGRITFSTESS--TTFIEIPNLRVEDTAMYYCA
PEKRLEWVATISD-G--gSYTYYPDSVKGRFTISRDNAKNNLYLQMSSLKSEDTAMYYCA
PGKRLEWIAASRN-KvydYTTEYSASVKGRFIVSRDTSQSILYLQMNALRAEDTAIYYCA
PEKGLEWVAEIRLkSh-nYAIHYAESVKGRFTISRDDSKSSVYLQMNNLRAEDTGIYYCS
PGKRLEWIAASRN-KgnkYTTEYSASVKGRFIVSRDTSQSILYLQMNALRAEDTAIYYCA
PGEGLQWVADISS-S---GQTYYADAVKGRFSISRDNAKNTLYLQMEDLRVEDTAVYYCA
PGQGLEWIGYINP-G--nGYINYNEKFKGKTTLTVDKSSSTAYMQLRSLTSEDSAVYFCA
```

Glu 46

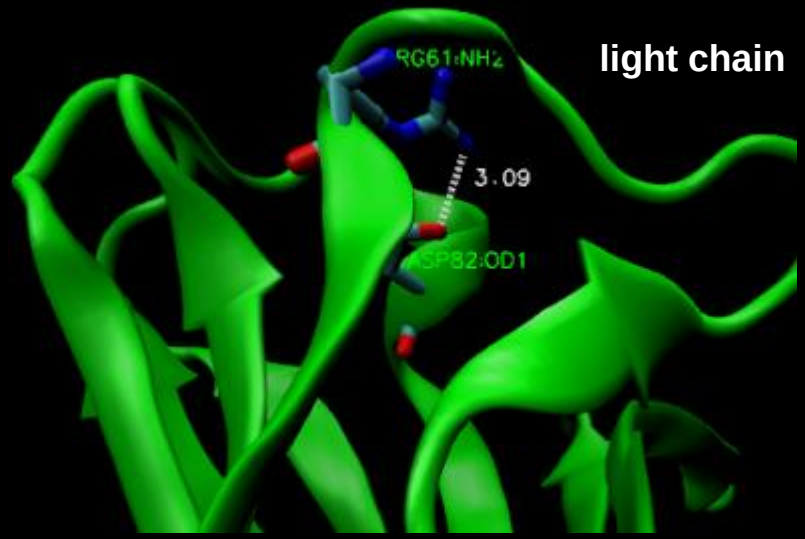
heavy chain



5mvz

Additional conservations - charged residues

Salt bridge between charged residues in the light chain



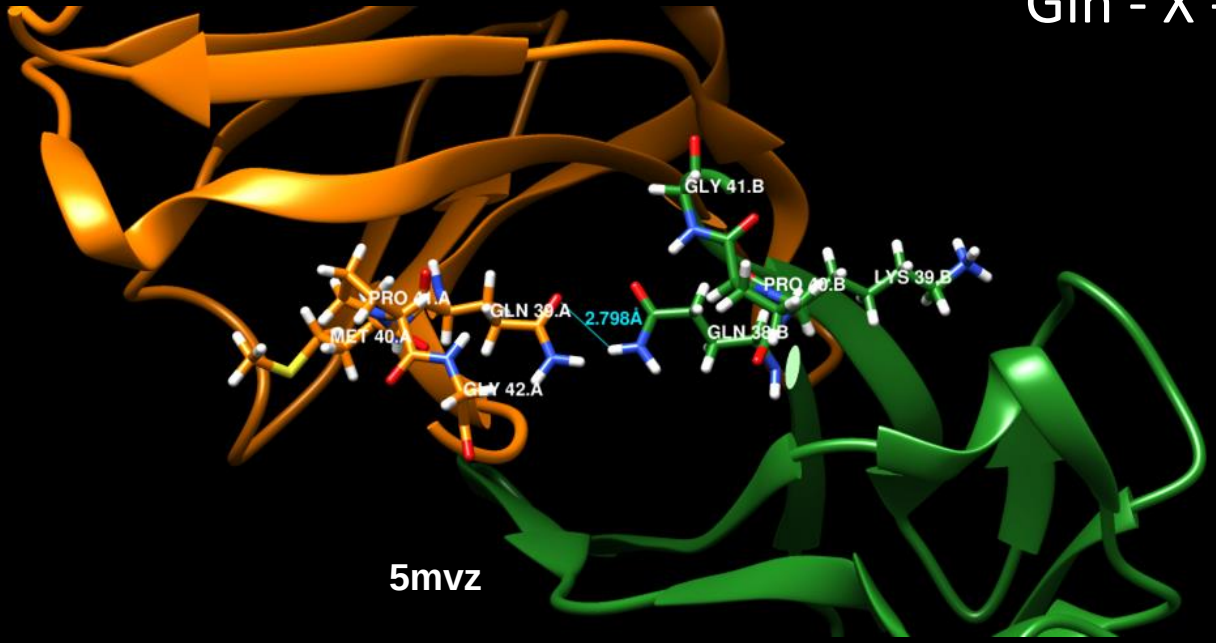
5mvz

Additional conservations - polar residues

```
sp|P01806|HVM36_MOUSE  mdfgliffivallkgvqce-VKLLESGGGLVQPGGSLKLSCAASGFDFSR-YWMSWVRQAPGKGLEWIGEINPdS-
sp|P01823|HVM47_MOUSE  ------------------EVQLQESGPSLVKPSQTLSLTCSVTGDSITS-DYWNWIRKFPGNKLEHMGYISY-S-
sp|P18531|HVM60_MOUSE  mkvlsllylltaipgilsd-VQLQESGPGLVKPSQSLSLTCSVTGYSITSgYYWNWIRQFPGNKLEWMGYISY-D-
sp|P83907|IGW3_HETFR   ----------nivltqpe--------SAVKKPGESHKLSCTVSGFDVNG-HHMNWVKQVPGEGLEWLLSYRK-T-
sp|P18528|HVM57_MOUSE  ------------------EVQLVESGGGLVKPGGSLKLSCAASGFTFSD-YYMYWVRQTPEKRLEWVATISD-G-
sp|P01793|HVM24_MOUSE  ------------------EVKLVESGGGLVQPGGSLRLSCATSGFTLSD-FYMEWVRQTPGKRLEWIAASRN-Kv
sp|P01803|HVM34_MOUSE  ------------------EVKLEESGGGLVQPGRSMKLSCVASGFTFSN-YWMNWVRQSPEKGLEWVAEIRLkSh
sp|P01789|HVM20_MOUSE  ------------------EVKLVESGGGLVQPGGSLRLSCATSGFTFSD-FYMEWVRQPPGKRLEWIAASRN-Kq
sp|P01785|HV02_CANLF   ------------------EVKLVESGGDLVKPGGSLRLSCVASGFTFSS-NGMSWVRQDPGEGLQWVADISS-S-
sp|P01746|HVM02_MOUSE  mgwsfiflfllsvtagvhsEVQLQQSGAELVRAGSSVKMSCKASGYTFTS-YGINWVKQRPGQGLEWIGYINP-G-
```

Gln - X - Pro - Gly

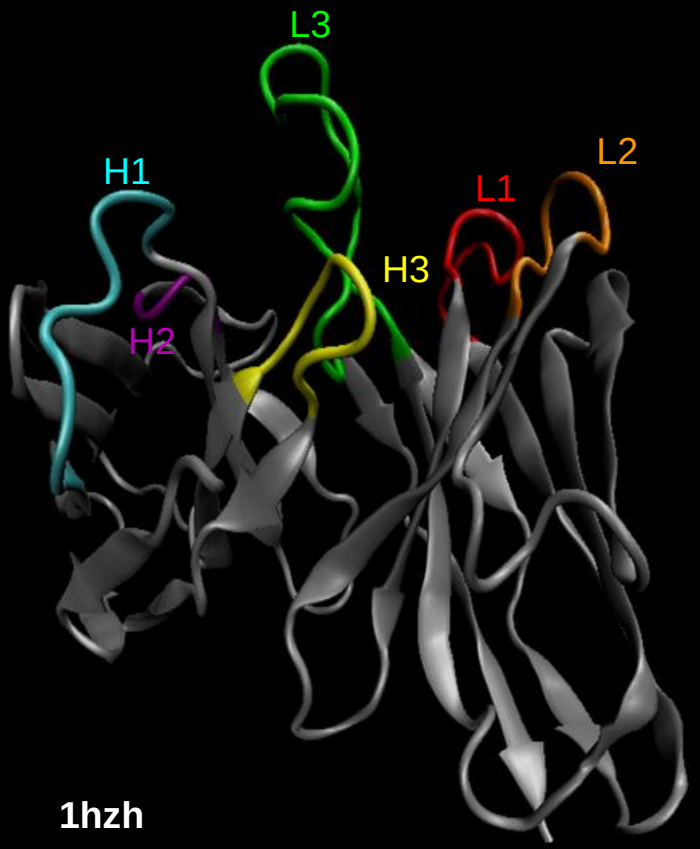
heavy chain



light chain

5mvz

Canonical structures

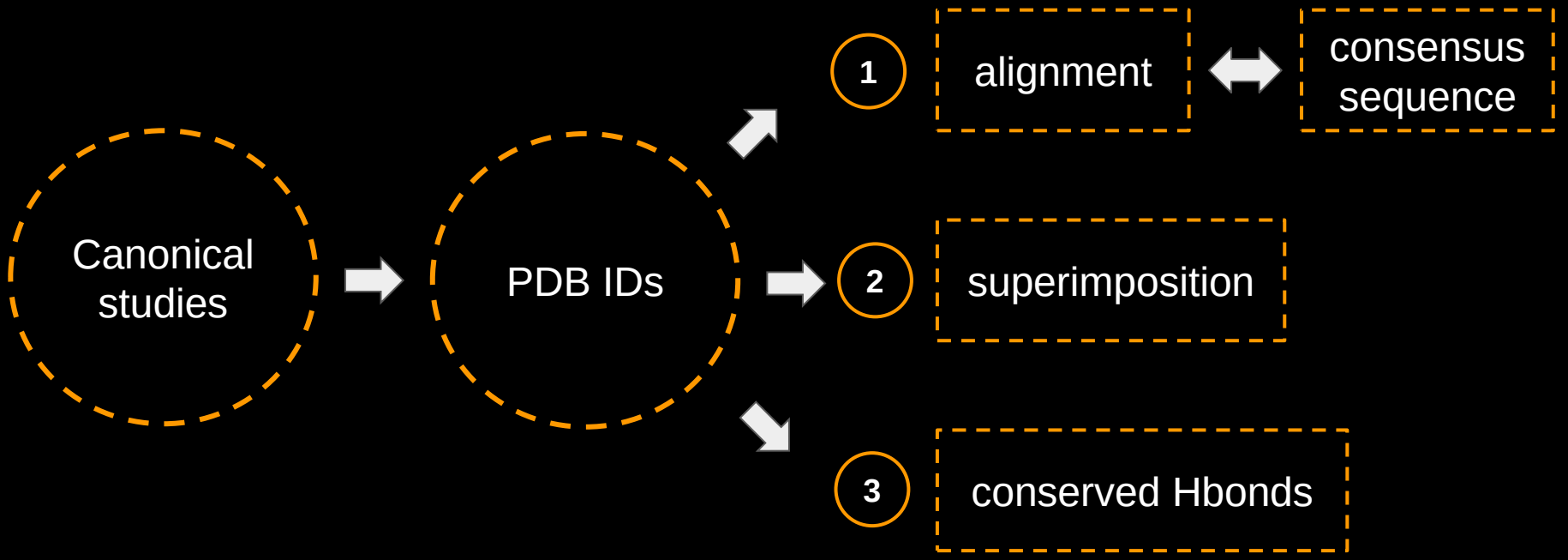


1hzh

Chothia et al classification:

LIGHT	L1	κ 1 **2a** **2b** 3 **4** 5 6 λ 1 2 **3a** **3b** 4
	L2	**1**
	L3	κ **1** 2 3 4 5 λ **1a** **1b** **1c** 2
HEAVY	H1	**1** 2 3
	H2	**1** **2a** 2b 2c 3a 3b **3c** 4

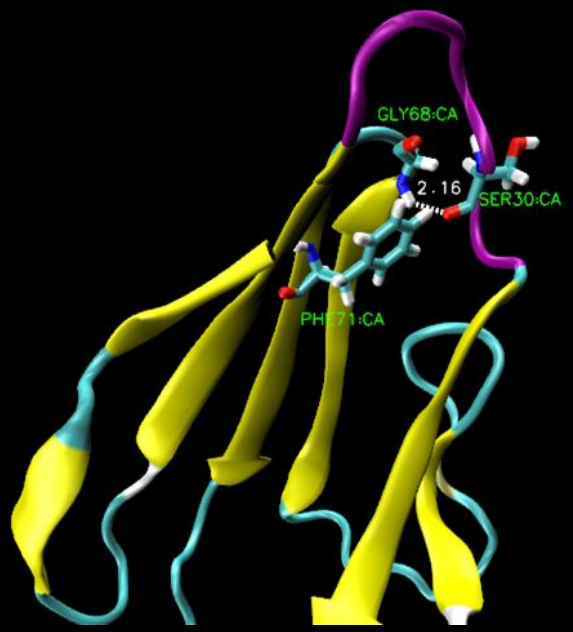
Canonical structures - Methodology



L1 - k2

L1: 24-34

L1-k2a



1dfb

Position 71: Phe, Thr or Gly

Hbond:
Ser 30 (O) --- Gly 68 (N)

L1-k2b

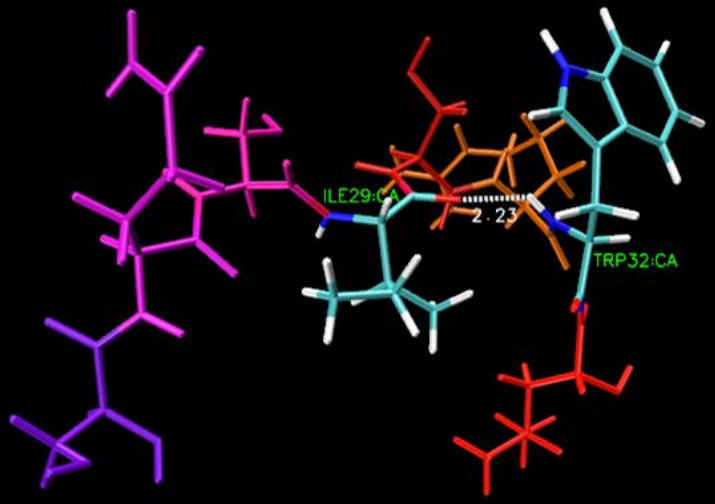
1vfa

Position 71: Tyr

Hbond:
Tyr 71 (O) --- Asn 31 (N)

L1 - k2

L1-k2a



1dfb

Hbond:

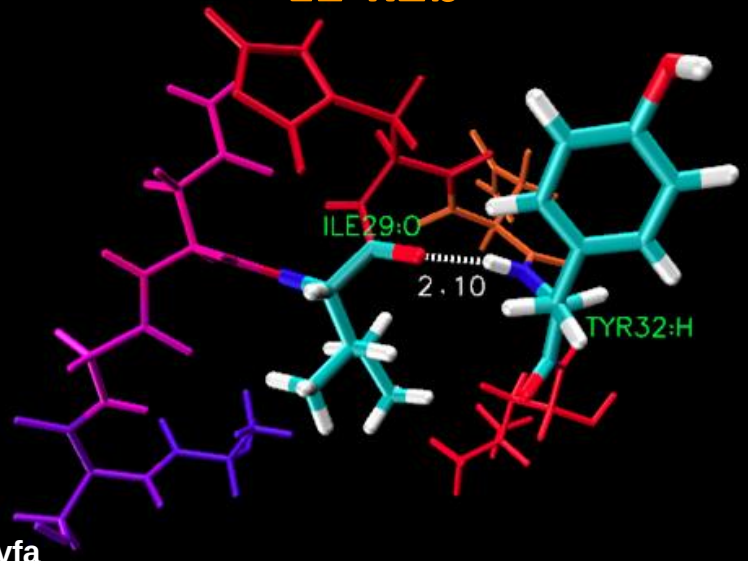
Ile 29 (O) --- Trp 32 (N)

rASQdisnyla

```
idfb RASQSISRWLAWYQQKPG
1igm QASQDISNYLAWYQQKPG
1ivl RASQSIGNRLFWYQQKSH
1fvc RASQDVNTAVAWYQQKPG
```

RMS = 0,62

L1-k2b



1vfa

Hbond:

Ile 29 (O) --- Trp 32 (N)

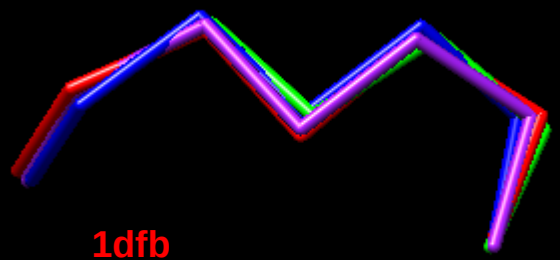
rASqdisnyLa

```
1zan CRASEDIYNALAW
1vfa CRASGNIHNYLAW
1fgv CRASQDINNYLNW
```

RMS = 0,51

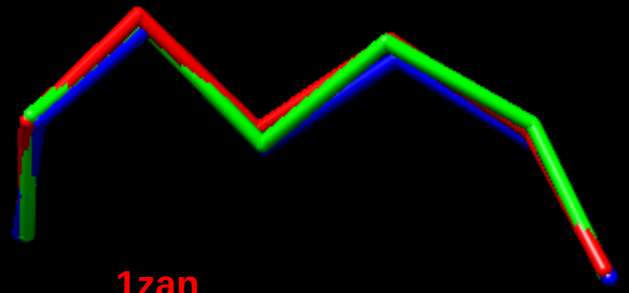
L1 - k2

L1-k2a

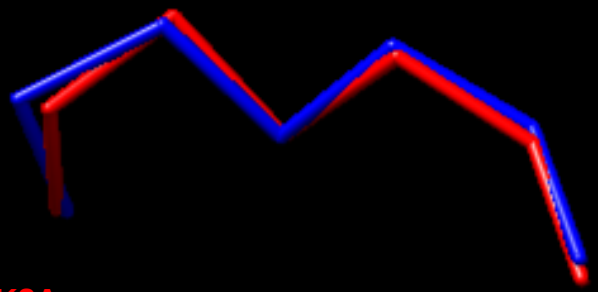


1dfb
1igm
1ivl
7fvc

L1-k2b



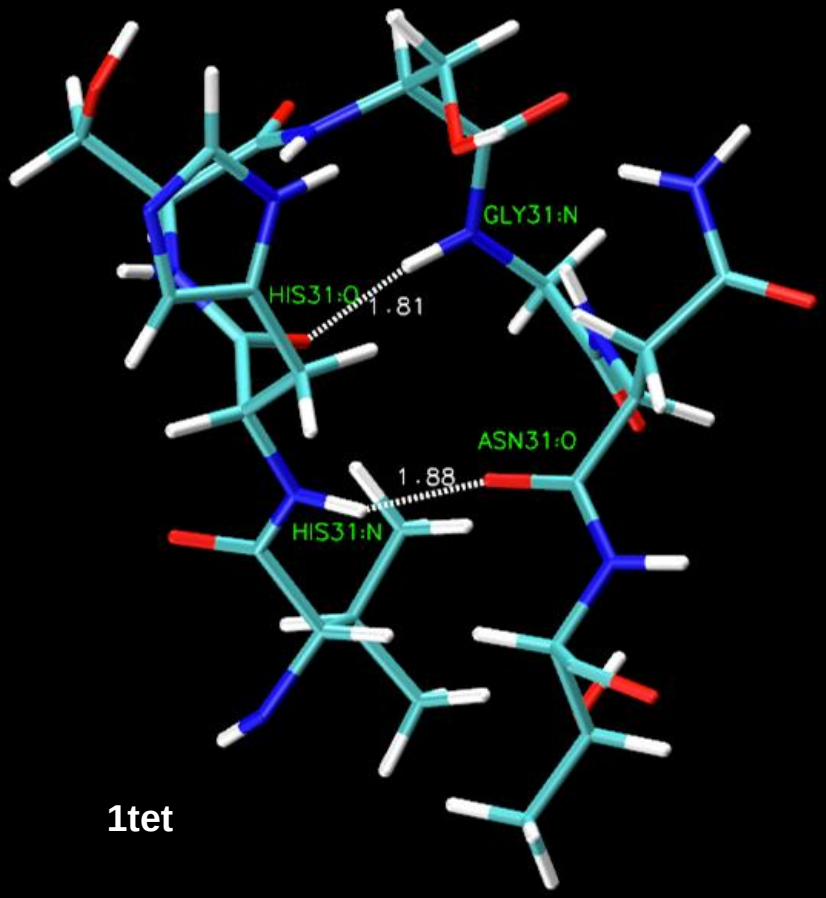
1zan
1vfa
1fgv



L1-K2A
L1-K2B

RMS = 0,70

L1 - k4



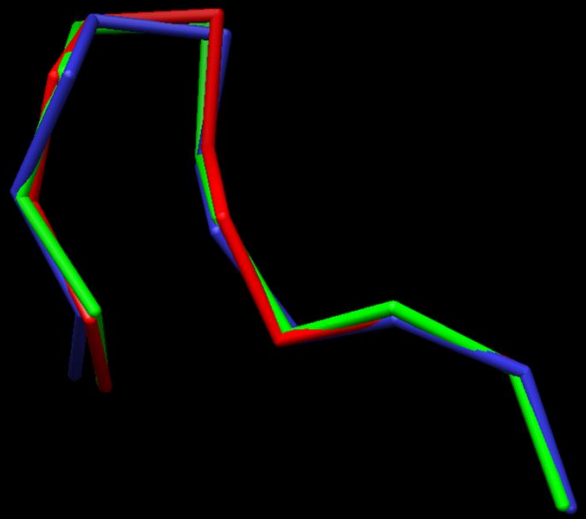
1tet

RSSqslvhsn**G**n**TY**le

```
1flr SISCRSSQSLVHSNGNTYLRW
1tet SISCKSSQSIVHSSGNTYFEW
2cgr SISCRPSQSLVHSNGNTYLHW
```

24

RMS = 0,45



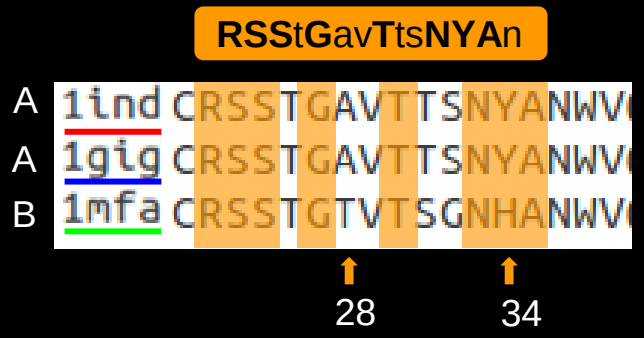
Hydrogen bonds:

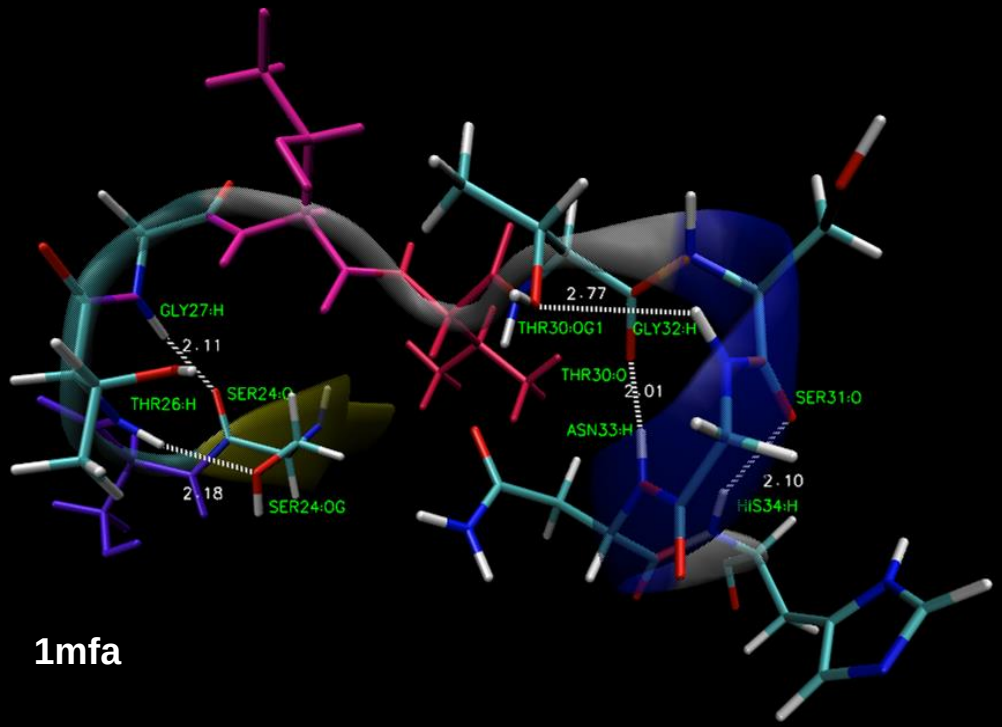
His	31	(O)	---	Gly	31.3	(N)
His	31	(N)	---	Asn	31.4	(O)

L1 - λ3

Hydrogen bonds:

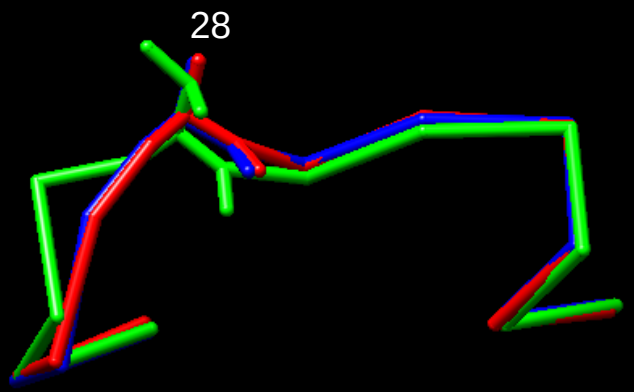
Ser	24	(OG)	---	Thr	26	(N)
Ser	24	(O)	---	Gly	27	(N)
Thr	30	(OG1)	---	Gly	32	(N)
Thr	30	(O)	---	Asn	33	(N)
Ser	31	(O)	---	His	34	(N)





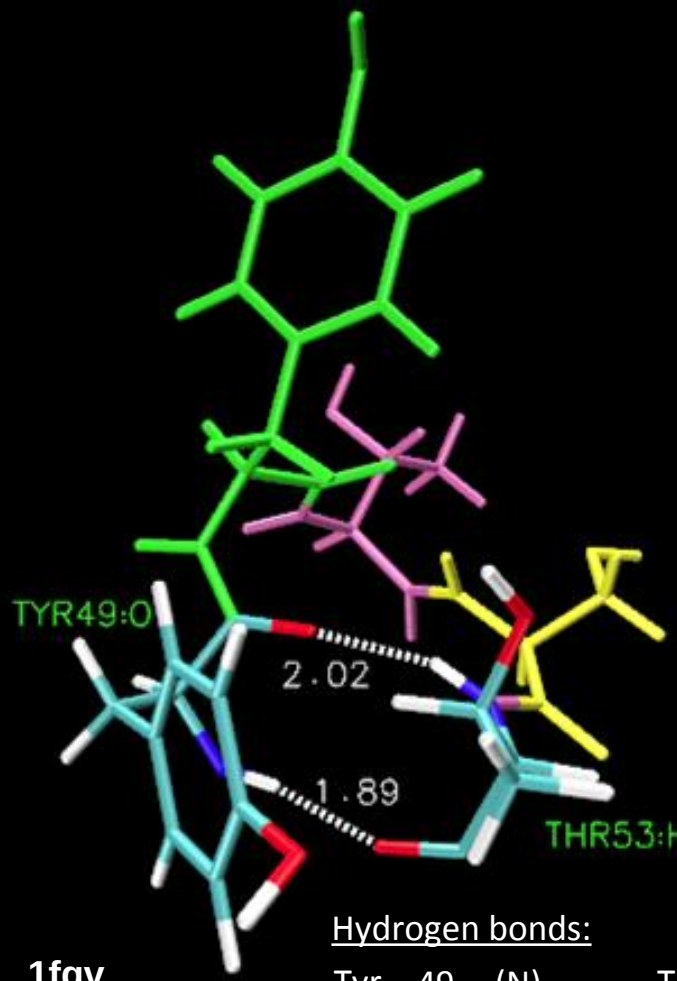
1mfa

RSM = 0,58



L2

positions: 50-52



1fgv

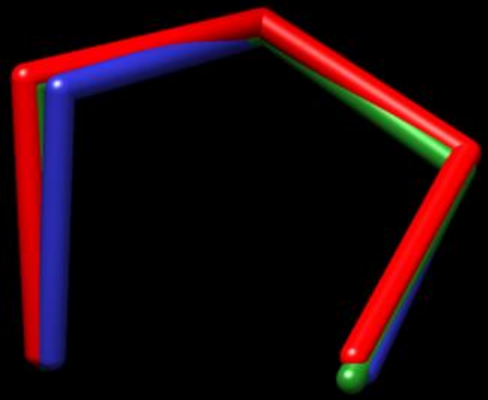
Hydrogen bonds:

Tyr	49	(N)	---	Thr	53	(O)
Tyr	49	(O)	---	Thr	53	(N)

Y-asnlas

```
1flr KVLIYKVSNRF
1fgv KLLIYYTSTLE
1igm ELRIYDASNLE
```

RMS = 0,52

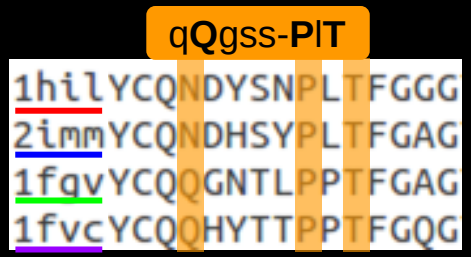


L3 - k1

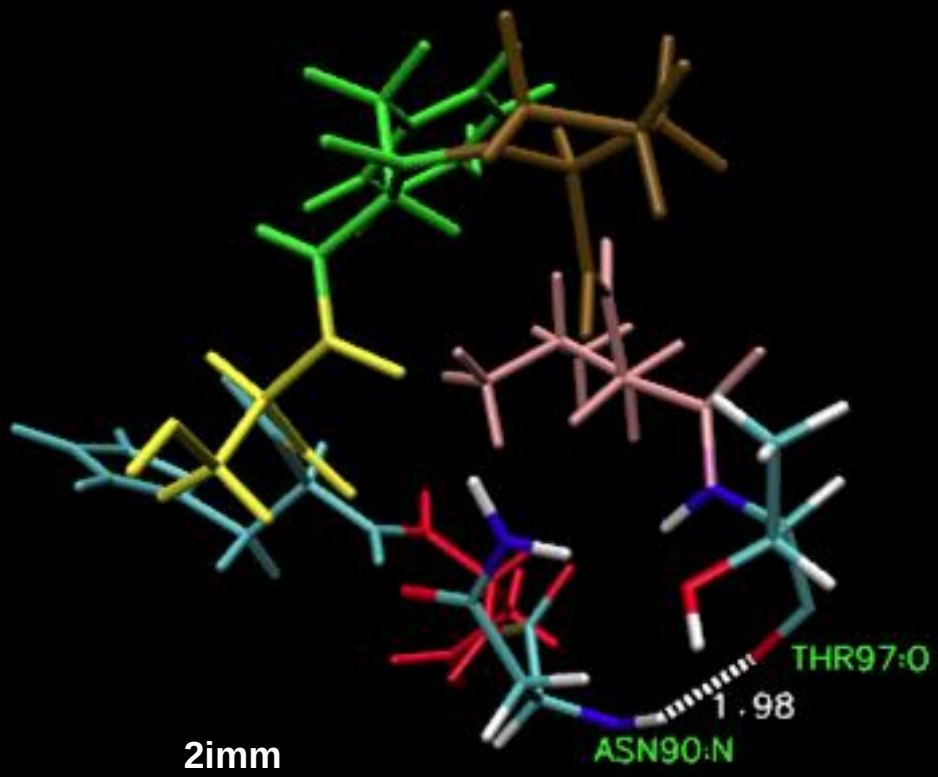
L3: 89-96

Hydrogen bond:

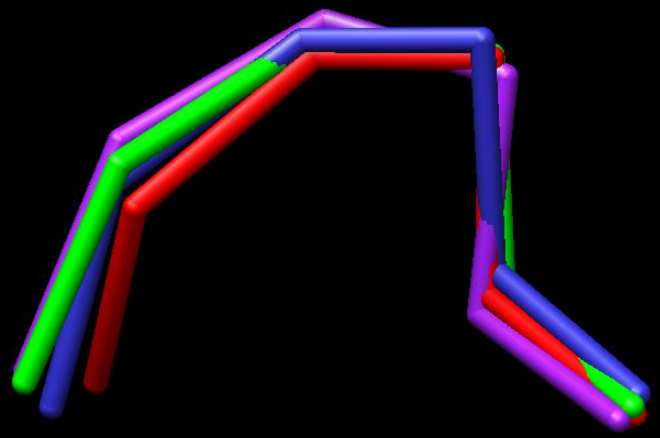
Asn 90 (N) --- Thr 97 (O)



RMS = 0,70



2imm



L3 - λ1

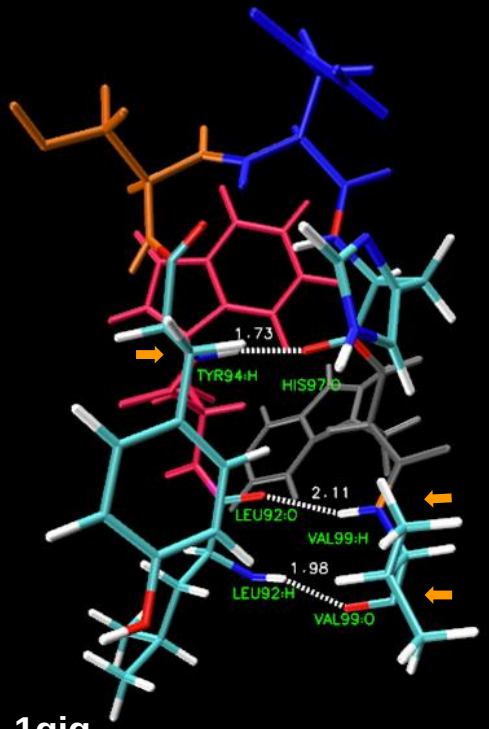
➡ Conserved Hbond between a, b and c
➡ Conserved Hbond between b and c

alw-snhwv

```
A  1ind FCALWYSNLWVFGG
C  1mfa FCALWSNNHWIFGG
A  1gig FCALWYSNHWVFGG
B  7fab YCQSYDRSLRVFGG
```

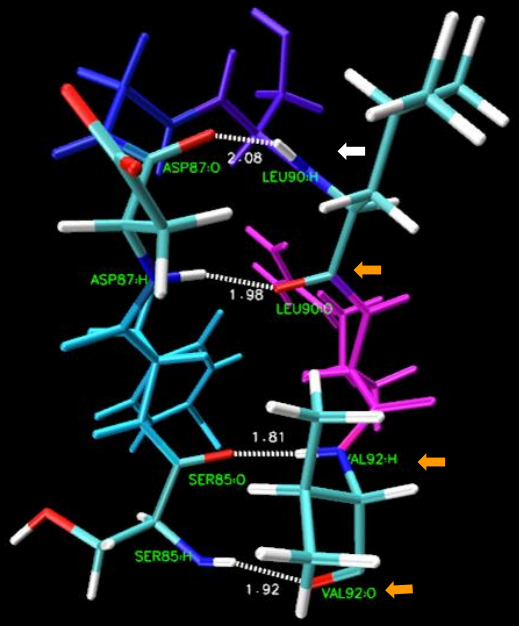
RMS = 0,57

a



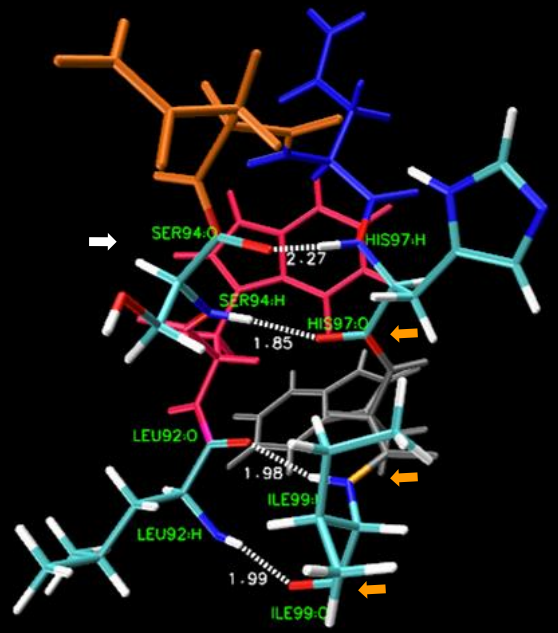
1gig

b



7fab

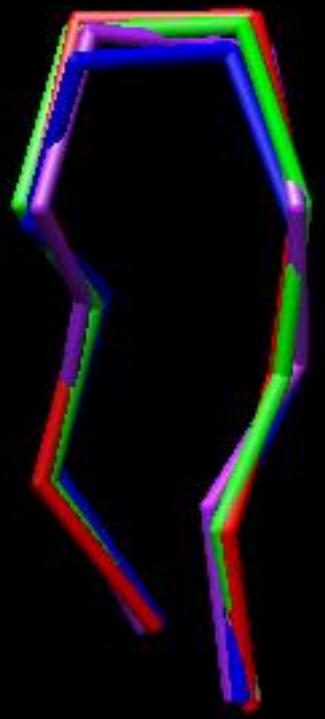
c



1mfa

Different orientation residues 93 and 94

L3 - λ1



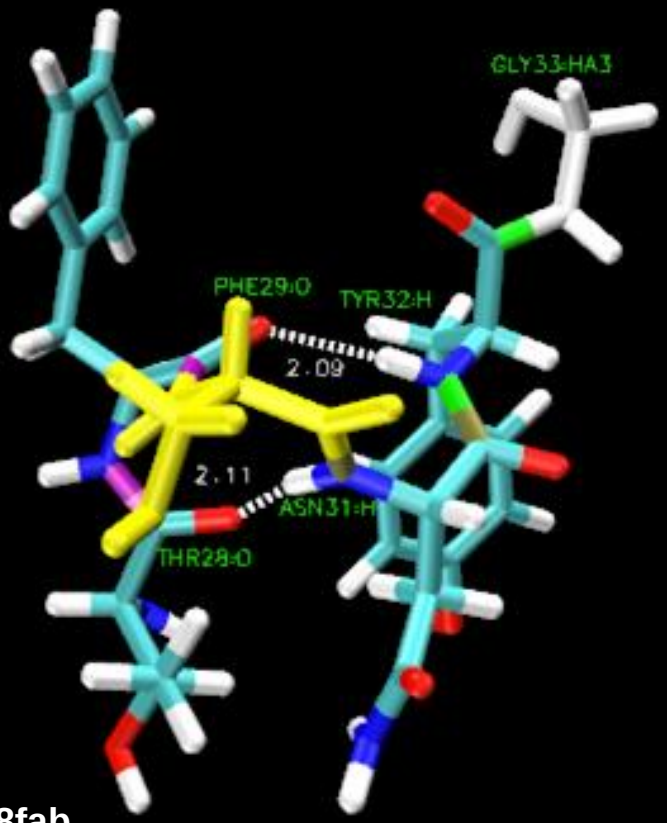
1ind (a)
1mfa (c)
1gig (a)
7fab (b)

H1 - 1

H1: 26-33

Hydrogen bonds:

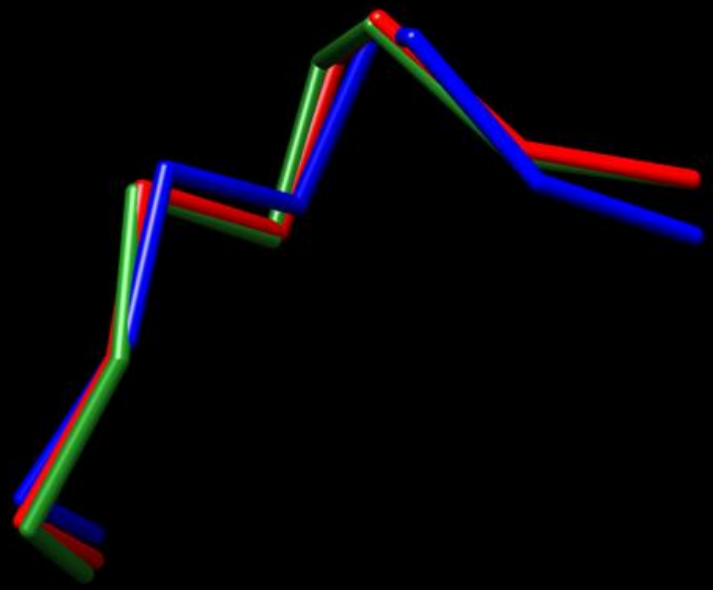
Thr	28	(O)	---	Asn	31	(N)
Phe	29	(O)	---	Tyr	32	(N)



8fab

kaSGftftdyymh

RMS = 0,95

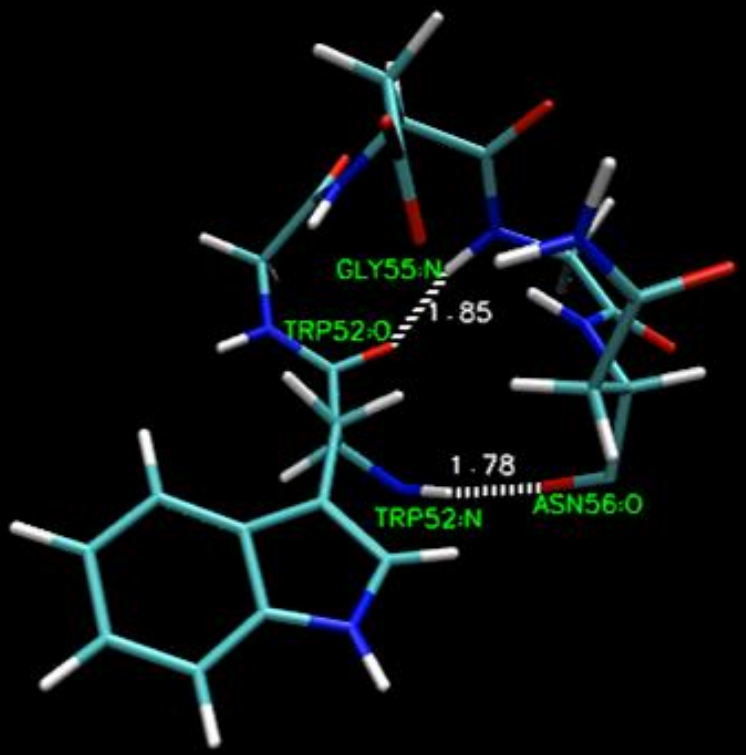


H2 - 1

H2: 52-56

Hydrogen bonds:

Trp	52	(N)	---	Gly	55	(N)
Trp	52	(O)	---	Asn	56	(O)

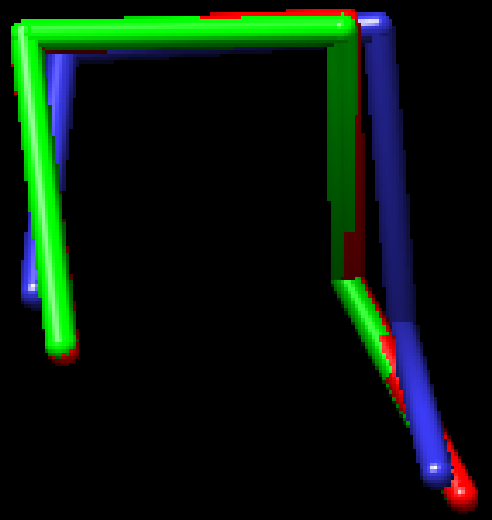


1vfa

yIwysGsty

```
1vfa EWLGMIWGDGNTD
7fab EWIGYVFYTGTTL
1kip EWLGMIWGDGNTD
```

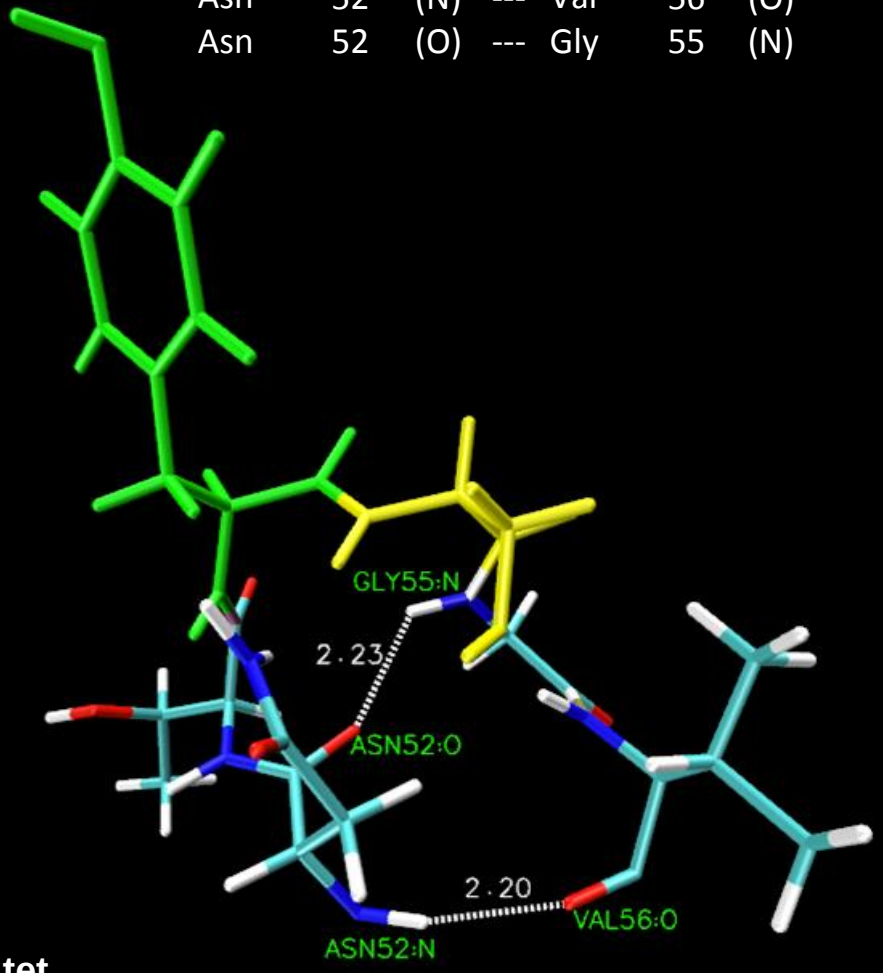
RMS = 0,41



H2 - 2a

Hydrogen bonds:

Asn	52	(N)	---	Val	56	(O)
Asn	52	(O)	---	Gly	55	(N)

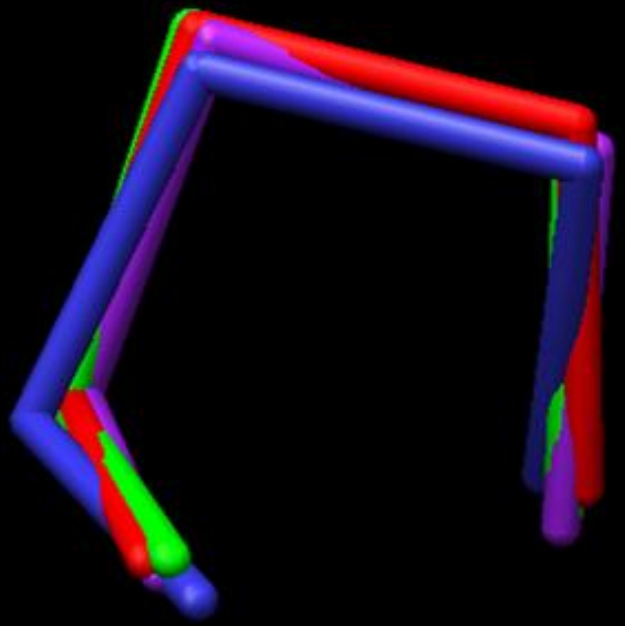


1tet

-I ypgng- t -

```
1tet KWMGWINTYSGVPTY
1mfa EWIGAIYPGNSATFY
1fvc EWVARIYPTNGYTRY
1fgv EWVAGINPKNGGTSY
```

RMS = 0,47



H2 - 3c

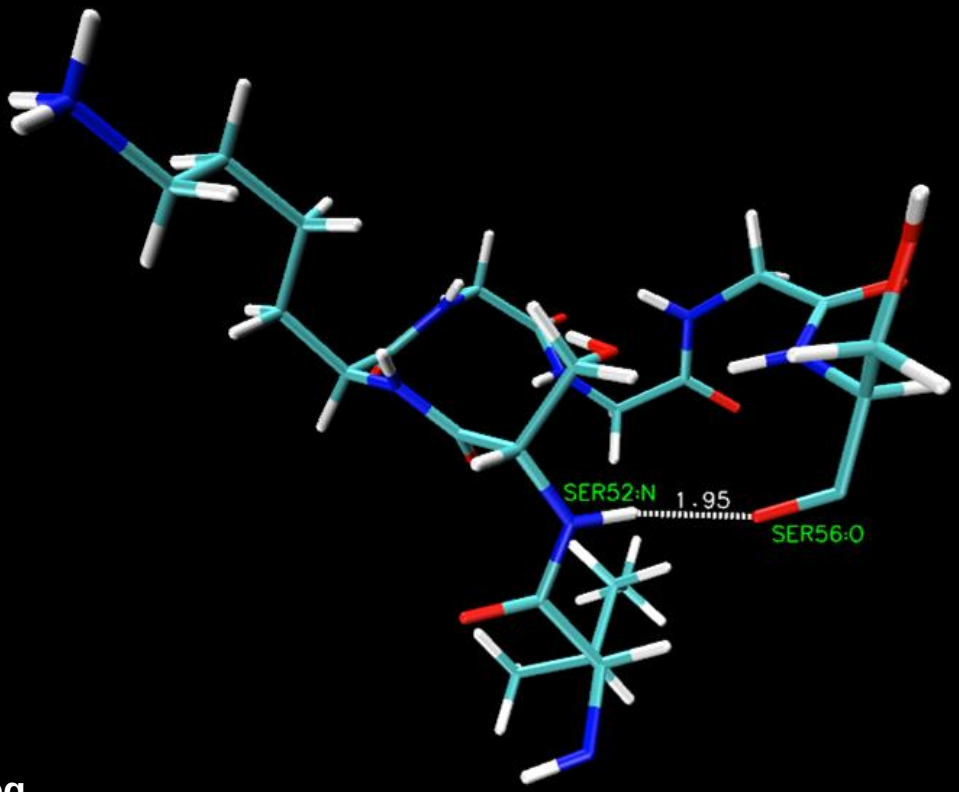
Hydrogen bonds:

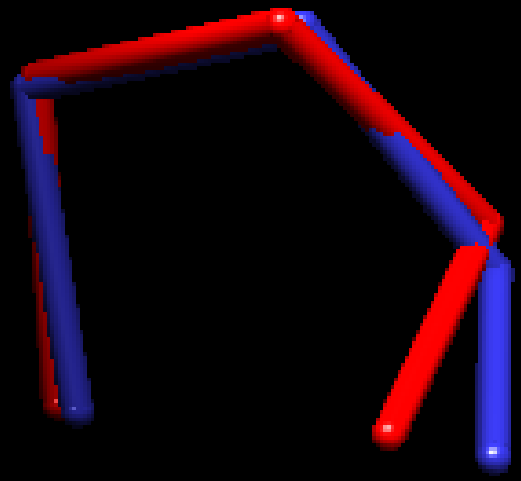
Ser 52 (N) --- Ser 56 (O)

- Issgggnty

```
1igm SGVFGSGGNTDY
1seq AYISKGGGSTYY
```

RMS = 0,51



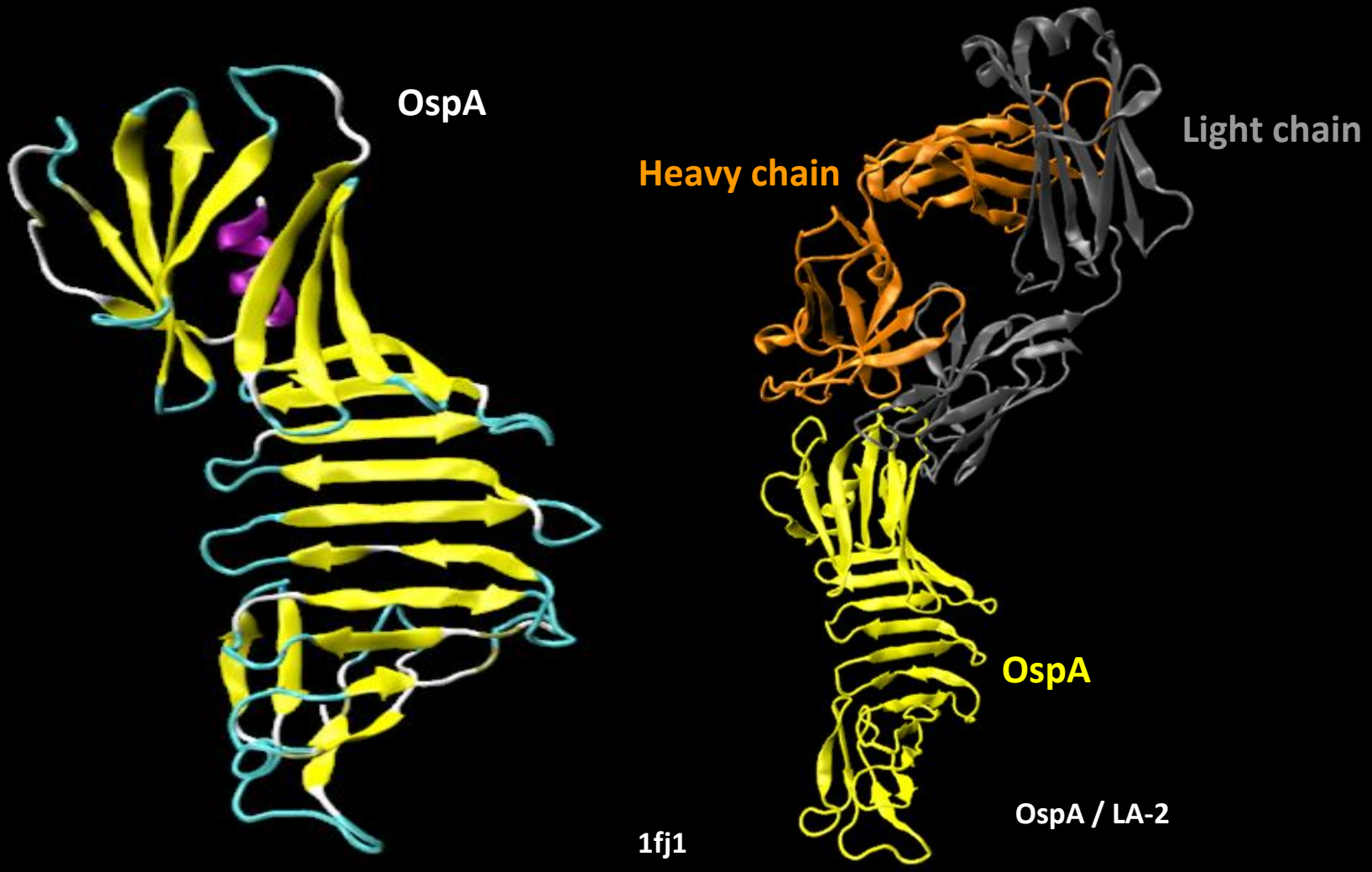


1seq

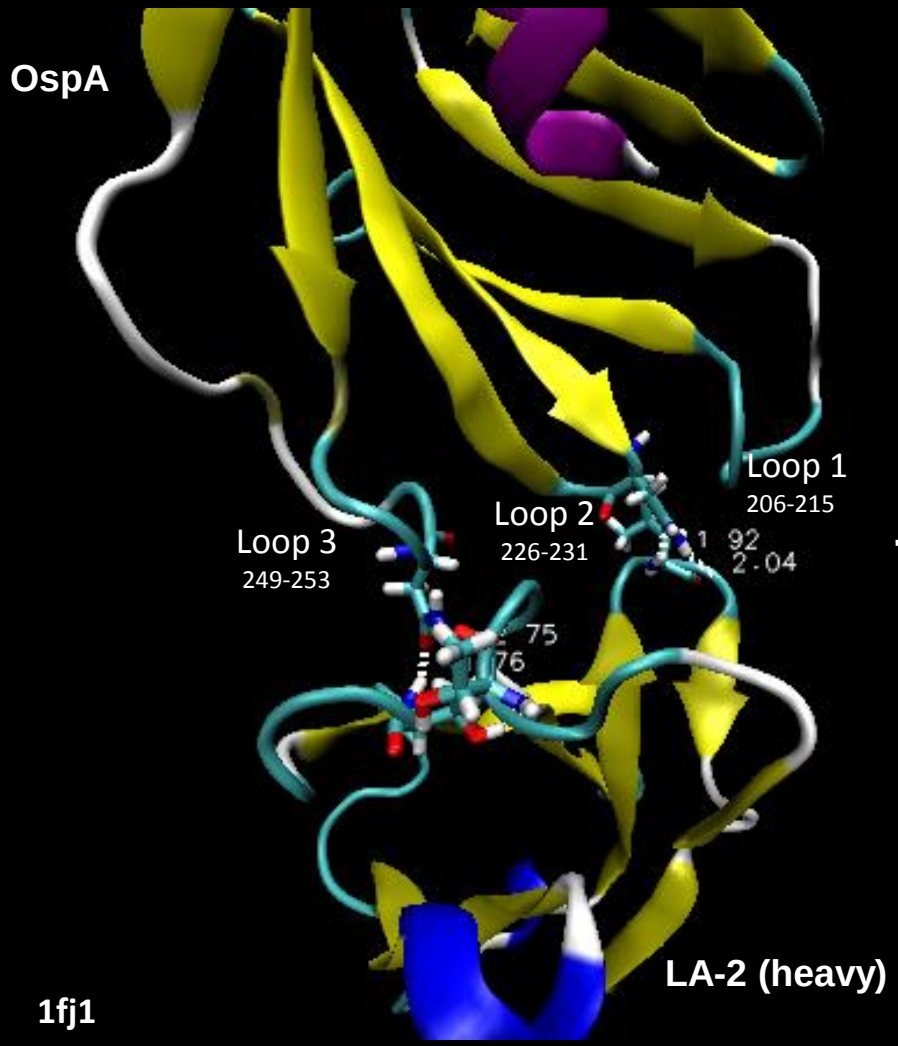
Canonical structures - Conclusions

- Even though the sequence is different, the structure is conserved
- In the spatial conformation of each loop may be also involved residues from the β-strands
- Canonical structures may not be involved in determining specificity but affinity

Ag-Ab interaction: ospA/LA-2



OspA



Borrelia burgdorferi

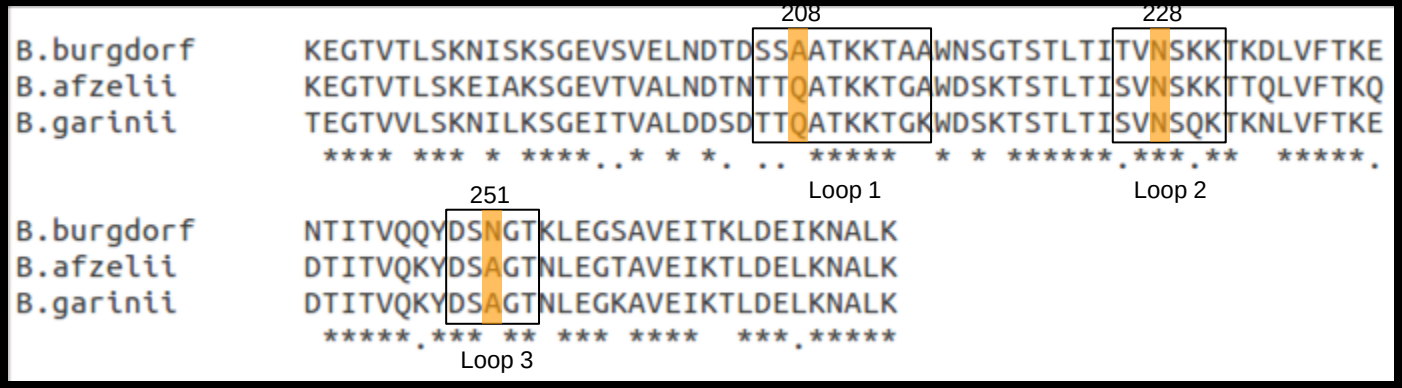
Borrelia afzelii

Borrelia garinii

CONSERVED EPITOPE

Why are the three species **not** recognised by LA-2?

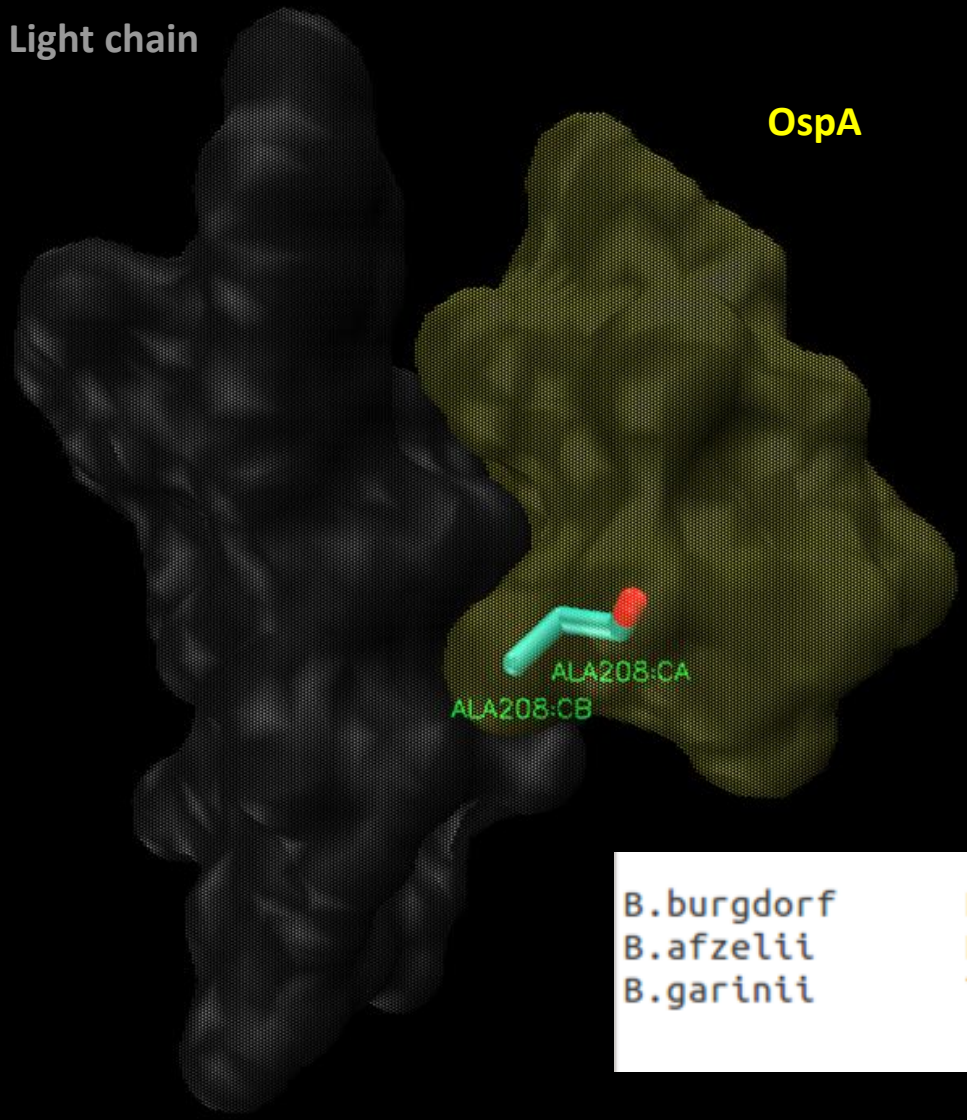
Important residues from OspA



Any mutation in these three residues from OspA abolish binding to LA-2 antibody

WHY?

A208 from OspA (loop 1)

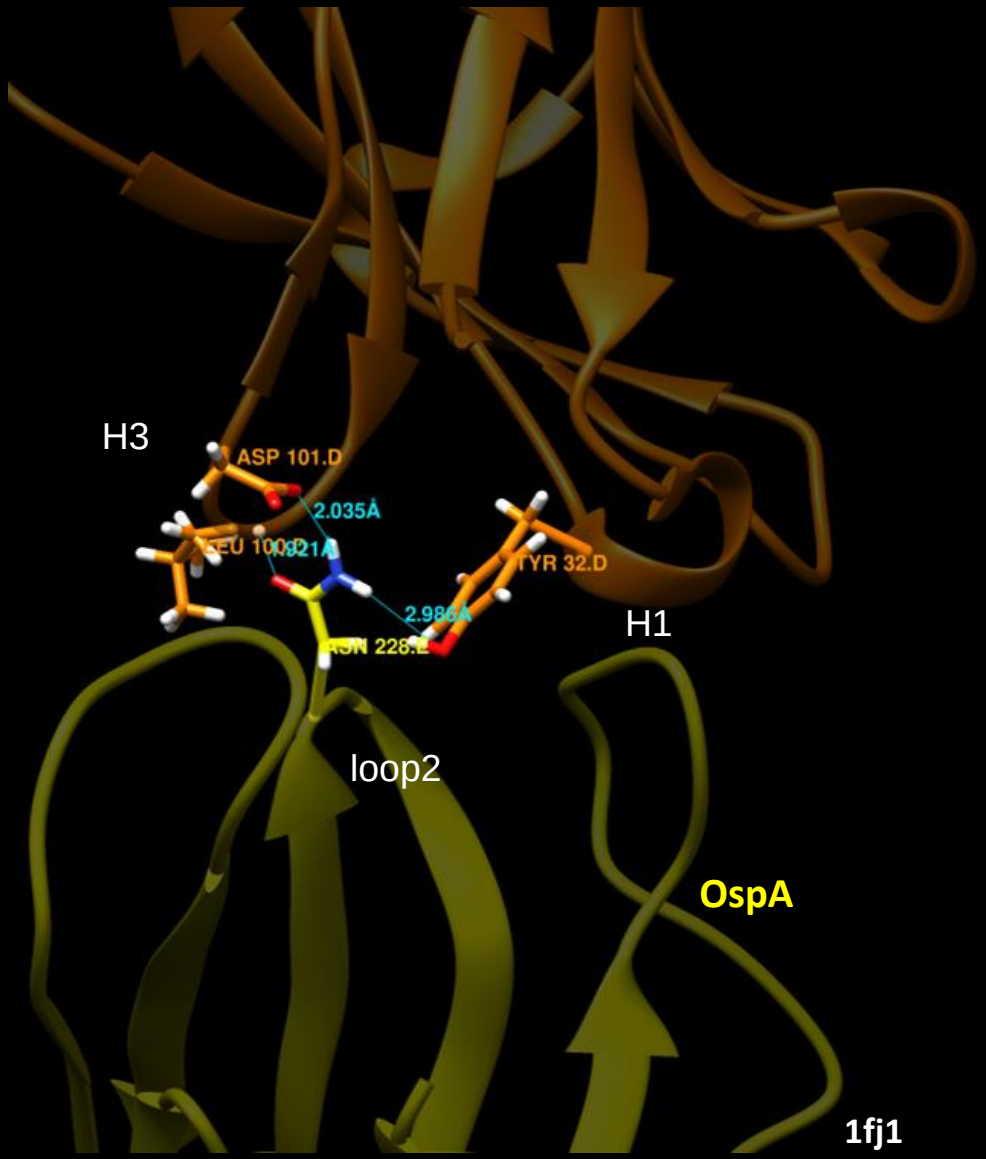


A208 adopts a specific conformation that allows to be bound by LA-2

A208

```
B.burgdorf      KEGTVTLSKNISKSGEVSVELNDTDSSAATKKTAAWNS
B.afzelii       KEGTVTLSKEIAKSGEVTVALNDTNTTQATKKTGAWDS
B.garinii       TEGTVVLSKNILKSGEITVALDDSDTTQATKKTGKWDS
                 **** *** * ****..* * *. .. *****  * *
```

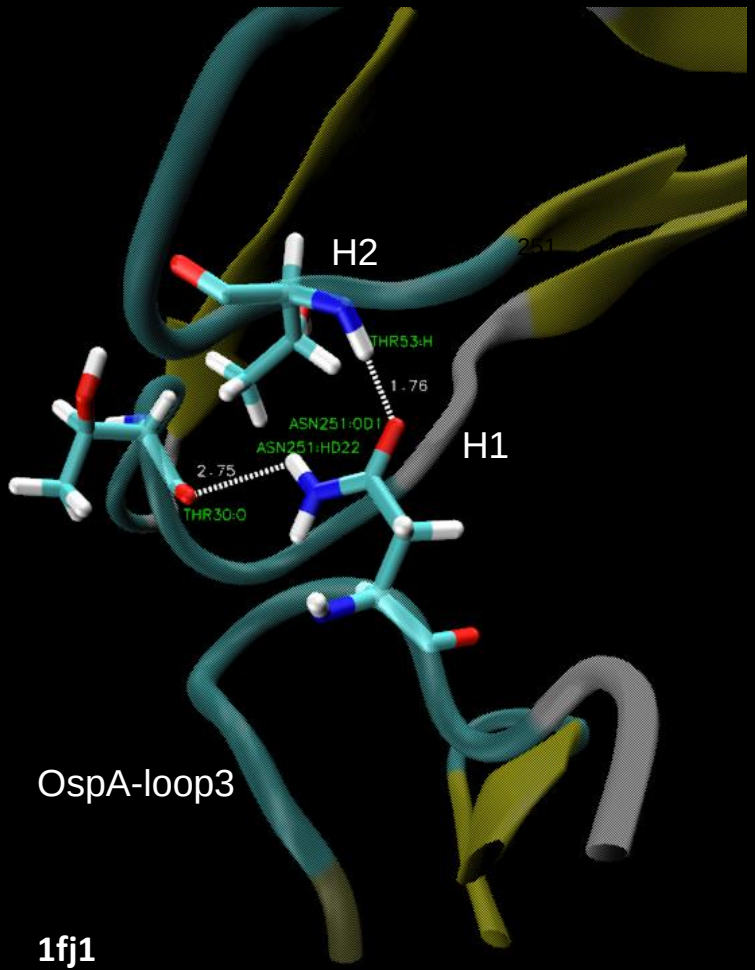
N228 from OspA (loop 2)



Hydrogen bonds:

OspA				LA-2		
Asn	228	(ND2)	---	Asp	101	(OD1)
Asn	228	(OD1)	---	Leu	100	(N)
Asn	228	(ND2)	---	Tyr	32	(OH)

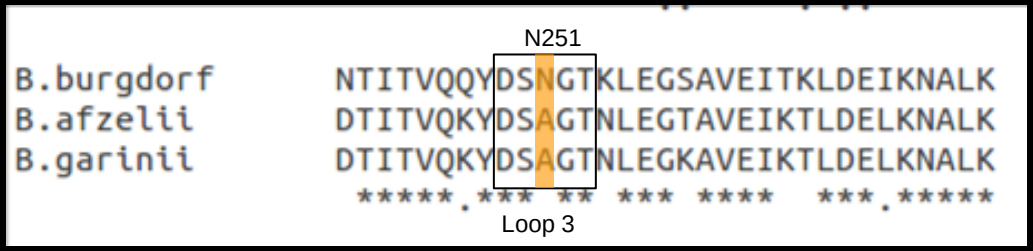
N251 from OspA (loop 3)



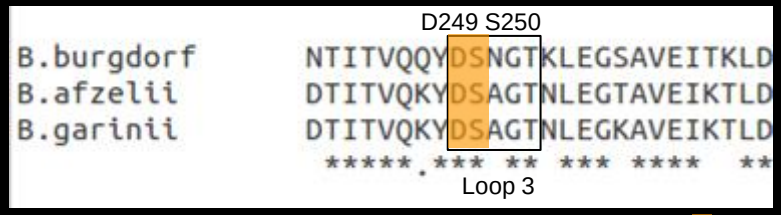
1fj1

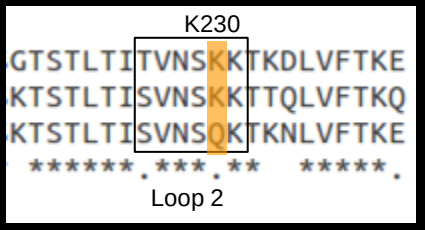
Hydrogen bonds:

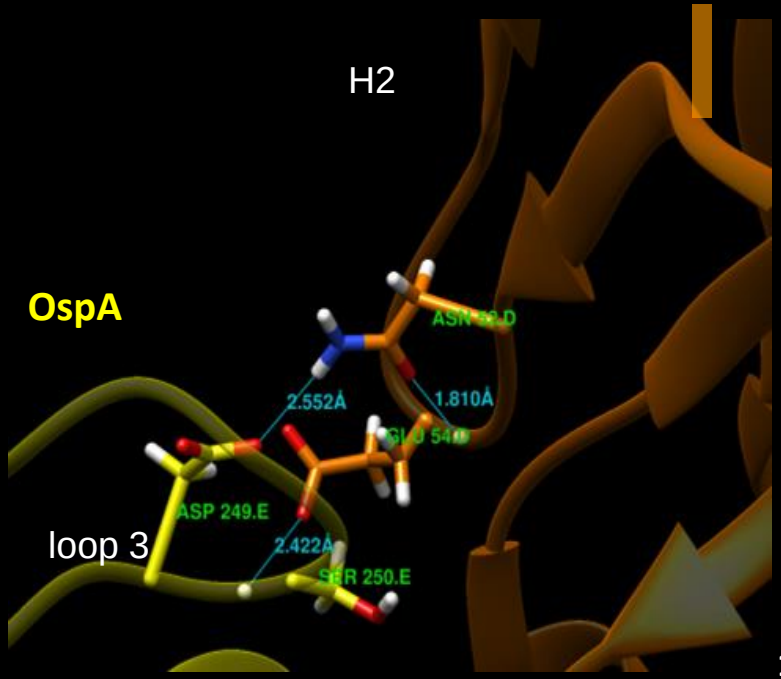
OspA				LA-2		
Asn	251	(ND2)	---	Thr	30	(O)
Asn	251	(OD1)	---	Thr	53	(N)

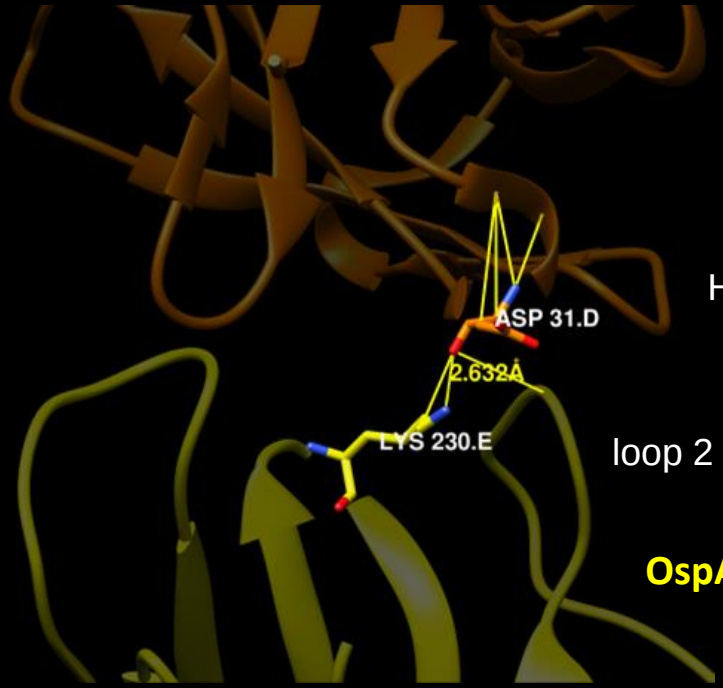


Other interactions between Ag-Ab









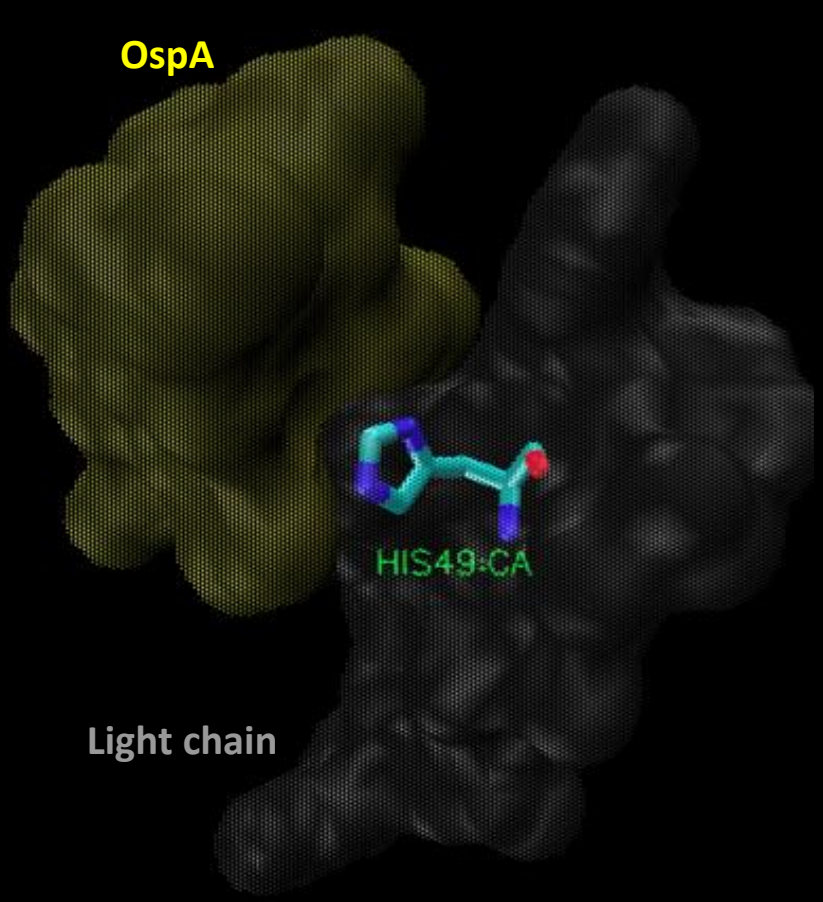
Hydrogen bonds:

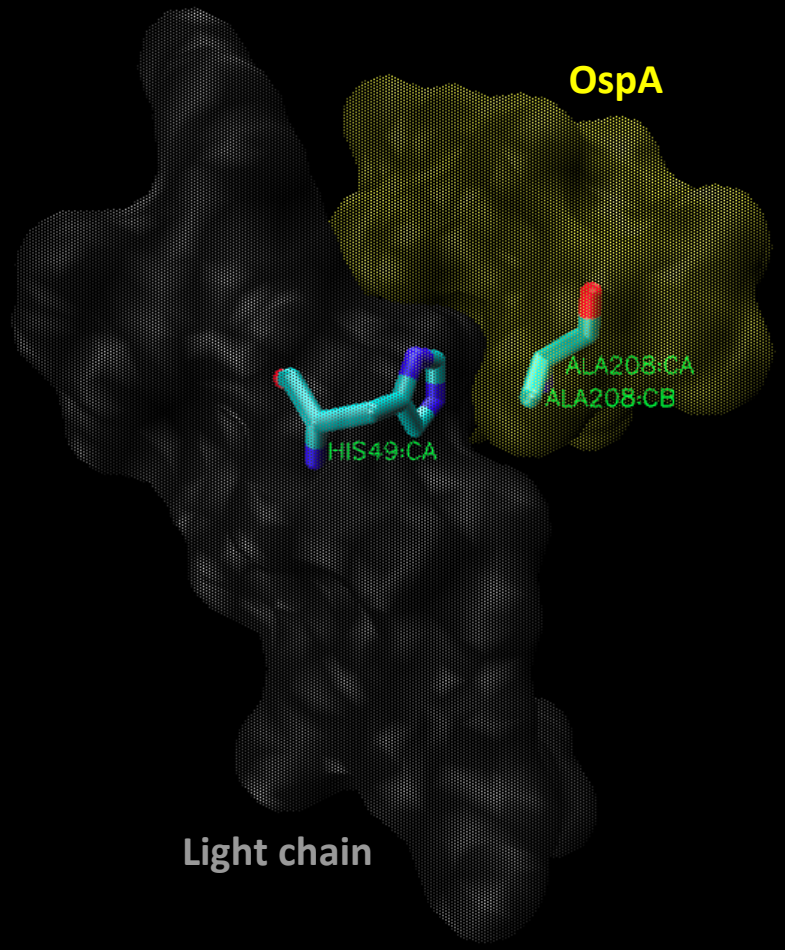
OspA				LA-2		
Asp	249	(OD2)	---	Asn	52	(ND2)
Ser	250	(N)	---	Glu	54	(OE1)

Salt bridge:

OspA				LA-2		
Lys	230	(NZ)	---	Asp	31	(O)

Important residues from LA-2





Ag-Ab: Conclusions

- A208, N228 and N251 from OspA are key for binding to LA-2 being the reason why LA-2 only recognises OspA from *B.burgdorferi*
- H49 from the light chain is essential for the function of the antibody

General conclusions

- The sequence conservation between variable and constant domains is important for the conservation of the structure, but not necessarily for the function
- Even though the CDRs are hypervariable regions there are some structures that are more frequently found than others
- There are key residues for the antigen-antibody interaction but they are different depending on the antigen the antibody has to recognise

References

- Al-Lazikani B, Lesk A, Chothia C. Standard conformations for the canonical structures of immunoglobulins. J Mol Biol. 1997;273(4):927-948.
- Chothia C, Lesk A, Tramontano A, Levitt M, Smith-Gill S, Air G et al. Conformations of immunoglobulin hypervariable regions. Nature. 1989;342(6252):877-883.
- Chothia C, Lesk AM.Canonical structures for the hypervariable regions of immunoglobulins. J Mol Biol. 1987 Aug 20;196(4):901-17.
- Chothia C, Gelfand I, Kister A. Structural determinants in the sequences of the immunoglobulin variable domain. J Mol Biol. 1998;278:475-479.
- Ding W, Huang X, Yang X, Dunn J, Luft B, Koide S et al. Structural identification of a key protective B-cell epitope in lyme disease antigen OspA. J Mol Bio. 2000;302(5):1153-1164.
- Haard H, Kazemier B, Bent A, Oudshoorn P, Boender P, Germen B, et al. Absolute conservation of residue 6 of immunoglobulin heavy chain variable regions of class IIA is required for correct folding. Protein Engineering. 1998;11(12):1267-1276.
- Halaby DM, Pupon A, Mornon JP. The immunoglobulin fold family:sequence analysis and 3D structure comparisons. Protein Eng Des Sel. 1999;12(7):563-571.
- Harris LJ, Larson SB, Hasel KW, Day J, Greenwood A, McPherson A.The three-dimensional structure of an intact monoclonal antibody for canine lymphoma. Nature. 1992 Nov 26;360(6402):369-72.
- Harry W, Schroeder J, Cavacini L. Structure and function of immunoglobulins. J allergy clin immunol. 2010 Feb; 125:41-52.

References

- Joerger TR, Du C, Linthicum DS. Mol immunol. 1999;36(6):373-386.
- Mosca R, Céol A, Aloy P. Interactome3D: adding structural details to protein networks. Nat Methods. 2012;10(1):47-53.
- North B, Lehmann A, Dunbrack R. A New Clustering of Antibody CDR Loop Conformations. J Mol Biol. 2011;406(2):228-256.
- Putnam FW, Takahashi N, Tetaert D, Debuire B, Lien LC. Amino acid sequence of the first constant region domain and the hinge region of the δ heavy chain of the human IgD. Proc Natl Acad. Sci.1981;78(10):6168-6172.
- Shandilya S, Kurt Yilmaz N, Sadowski A, Monir E, Schiller Z, Thomas W et al. Structural and molecular analysis of a protective epitope of Lyme disease antigen OspA and antibody interactions. J Mol Recongit. 2016. Doi: 10.1002/jmr.2595
- Sheriff S, Jeffrey PD, Bajorath J. Comparison of CH1 domains in different classes of murine antibodies. J Mol Biol. 1996;263:385-389.
- Stephen R. Campion. Conserved aromatic residues as determinants in the folding and assembly of immunoglobulin variable domains. Mol Immunol. 2016;70:63-71.
- Vargas-Madrazo E, Lara-Ochoa F, Carlos Almagro J. Canonical Structure Repertoire of the Antigen-binding Site of Immunoglobulins Suggests Strong Geometrical Restrictions Associated to the Mechanism of Immune Recognition. J Mol Biol. 1995;254(3):497-504.

Multiple choice questions

1. Which of the CDR is the most hypervariable and does NOT follow the canonical structures?:

a) L1
b) L3
c) a and b are correct
d) H3
e) a, b and d are correct.

2. What is a CDR ?

a) One of the sheets of a beta barrel in the immunoglobulins
b) all the loops between the beta strands of the immunoglobulin
c) hypervariable region that plays an important role in the antigen recognition
d) A domain of the immunoglobulin
e) a type of immunoglobulin

3. Immunoglobulins in SCOP classification are considered

a) All alpha
b) All beta
c) alpha/beta
d) alpha-beta
e) this group of proteins is not present in the SCOP classification

Multiple choice questions

4. The immunoglobulin structure has:

a) Two variable domains, one from the heavy chain (VH) and another from the light chain (VL)
b) A hinge region that connects CH1 with CH2 and the two heavy chains
c) a and b are correct
d) Only one constant domain in the heavy chain (CH)
e) a, b and d are correct

5. **The intra-domain disulfide bridge:**
a) Is essential for the immunoglobulins folding.
b) Is located between sheet B and F in all domains.
c) a and b are correct.
d) is essential for the functionality of the immunoglobulins.
e) all options are correct.

6. Choose the true sentence about canonical structures:

a) imply a 100% sequence conservation

b) there are only 2 different canonical structures

c) they are different for the heavy and the light chain

d) H3 has canonical structures

e) any of the above is correct

Multiple choice questions

7. The Ig like domain:

a) is only found in proteins of the immune system

b) is found in all proteins in the immunoglobulin superfamily

c) do not require the disulfide bridge

d) has a β - barrel conformation

e) all options are false

8. A canonical structure is:

a) A structure that the b-sheets adopt

b) A structure that all CDR adopt

c) A structure that some CDRs adopt more frequently

d) A and B are true

e) A, B and C are true

9. Choose the correct sentence:

a) LA-2 antibody is able to recognize the OspA antigen only from *Borrelia burgdorferi*

b) Between OspA and the LA-2 antibody there are hydrogen bonds only between the heavy chain and the antigen.

c) There are conserved key residues between all the antigen antibody interactions

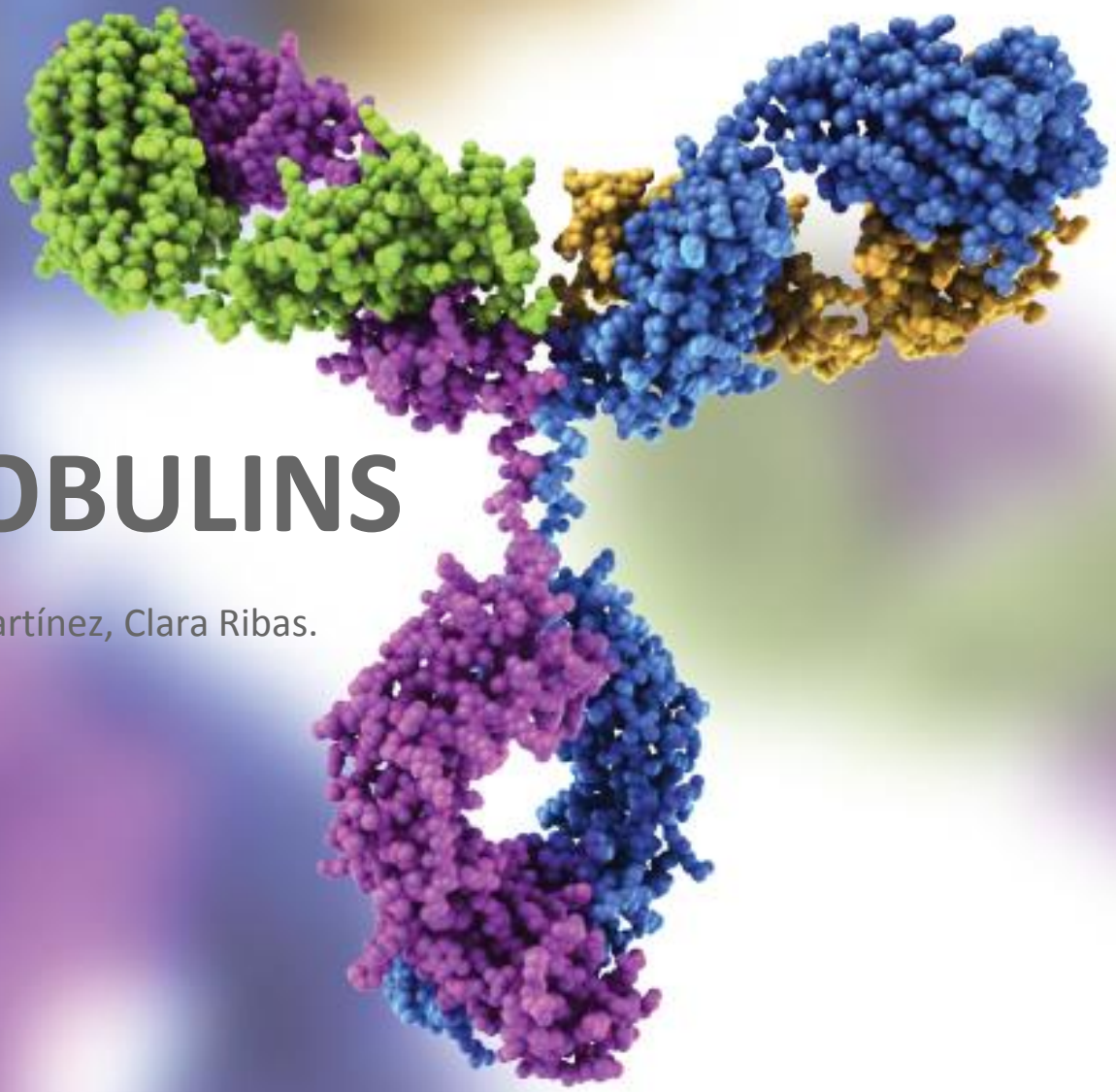
d) A, B and C are true

e) A, B and C are false

Multiple choice questions

10. **In immunoglobulins:**

a) the disulfide bond is made between cysteines that are not conserved.
b) the triad is made between 2 cysteines and one alanine
c) Hydrophobic residues are in the surface
d) Polar residues are located in the surface
e) All of them are false



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