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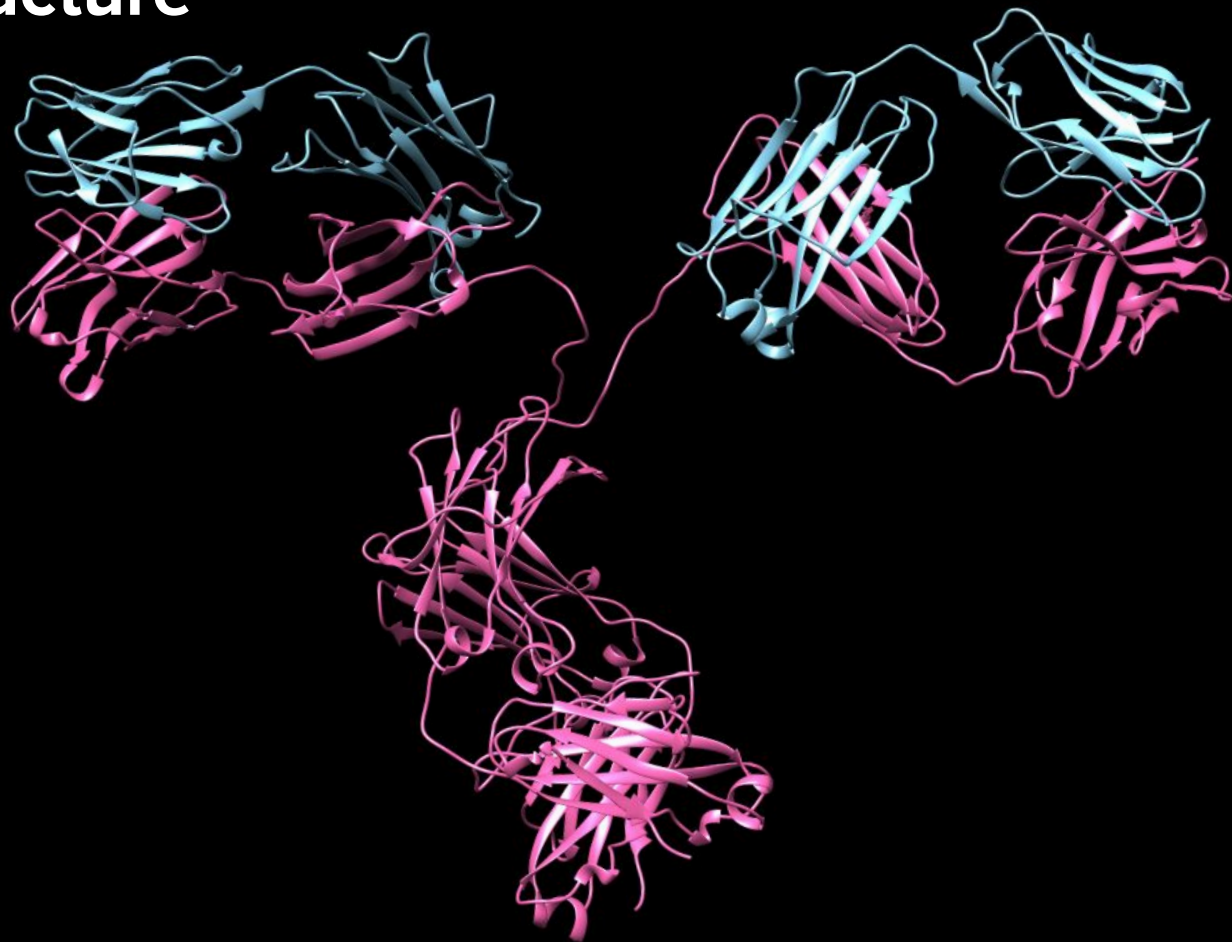
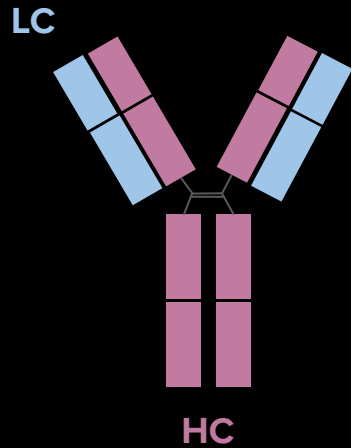
6. IgG - antigen interaction

- g. IgG - Hyalorunidase

7. IgG - FcγR interaction

BASIC CONCEPTS

Introduction: Structure



Introduction: Structure

Variable
domain

VL

CL

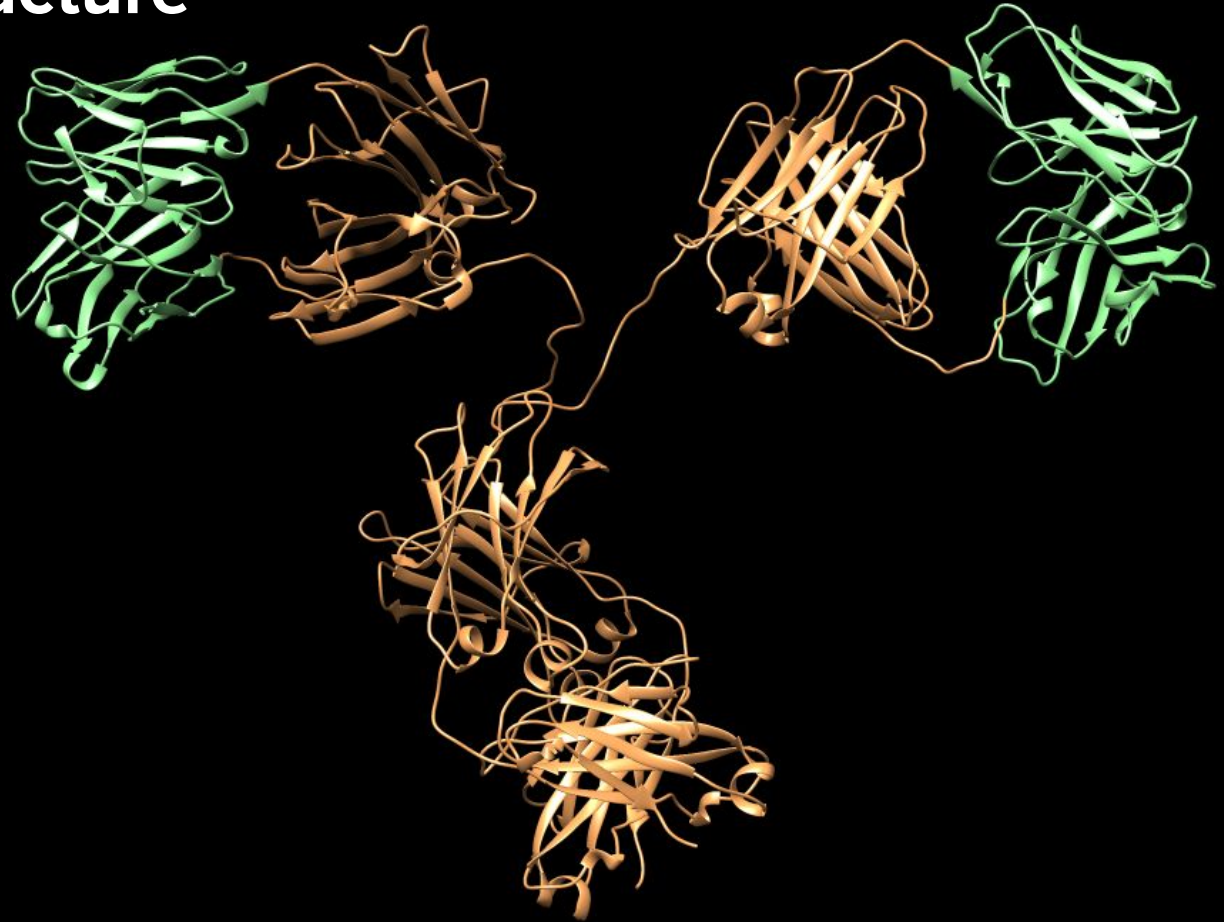
VH

CH1

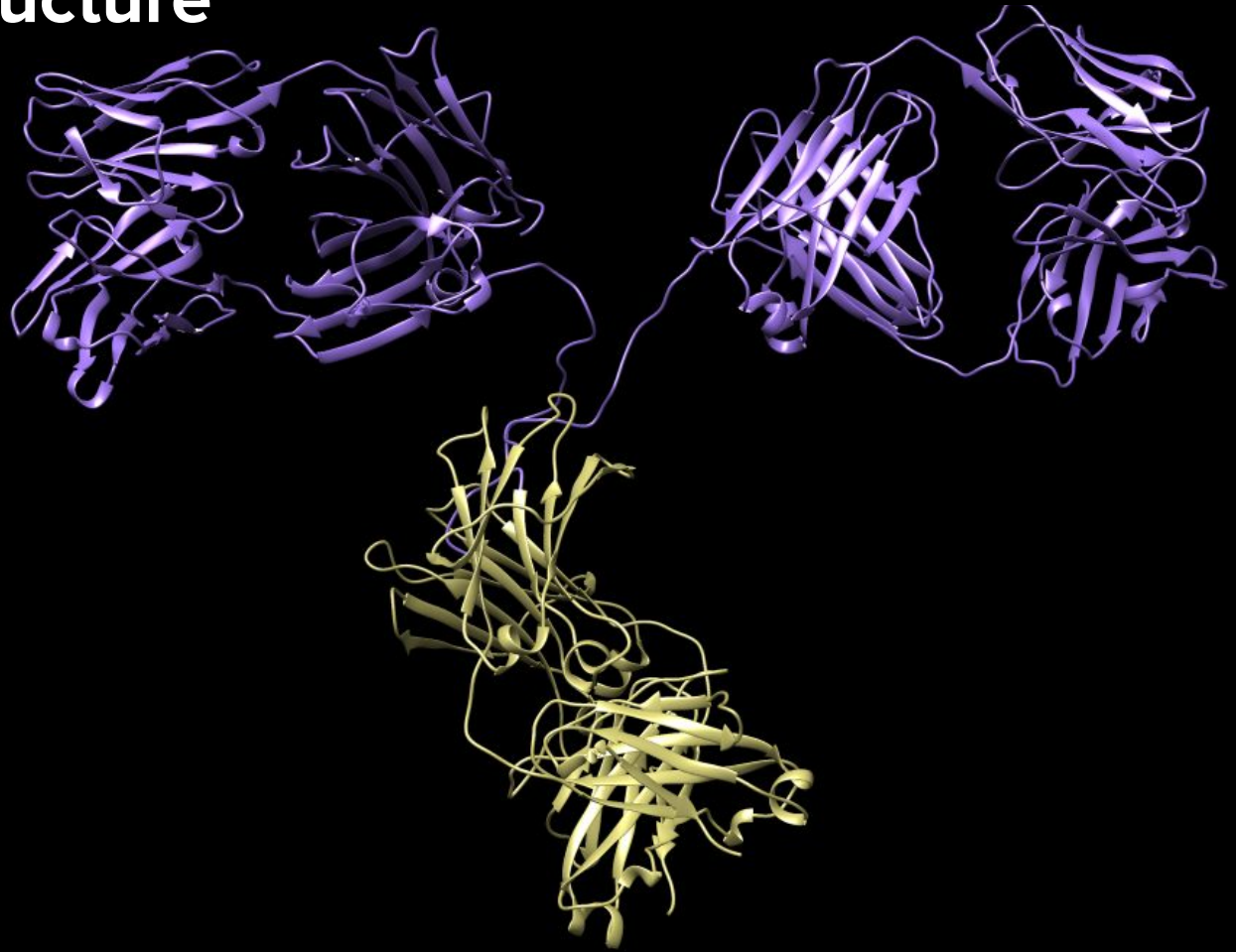
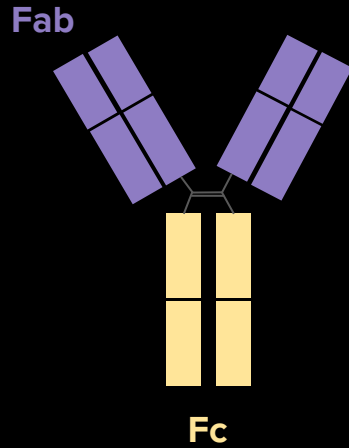
CH2

CH3

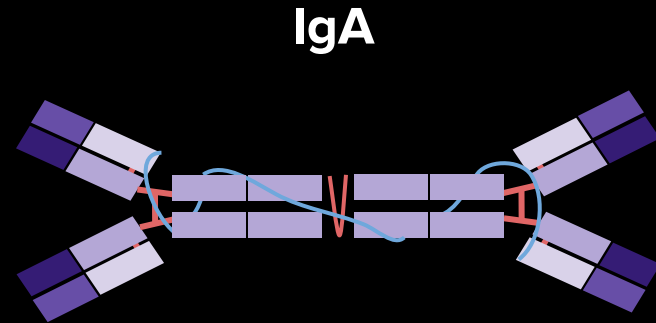
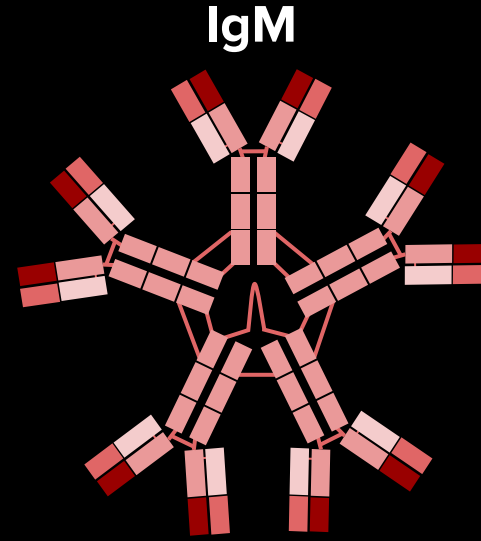
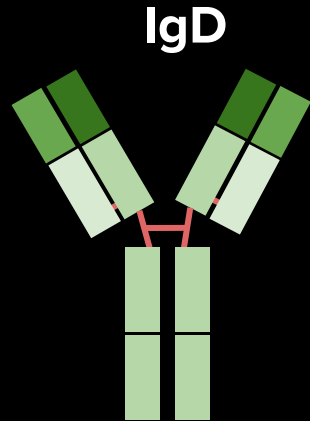
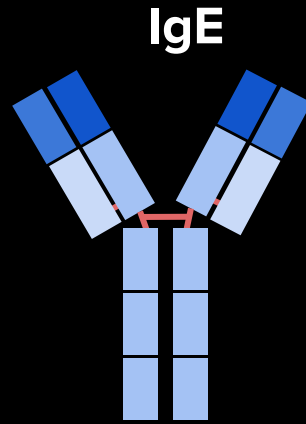
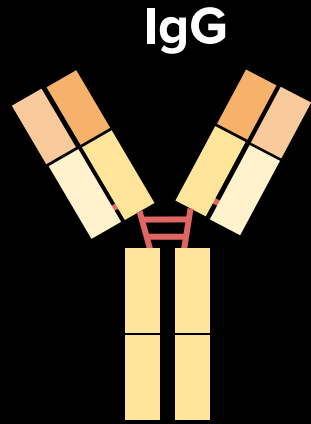
Constant
domain

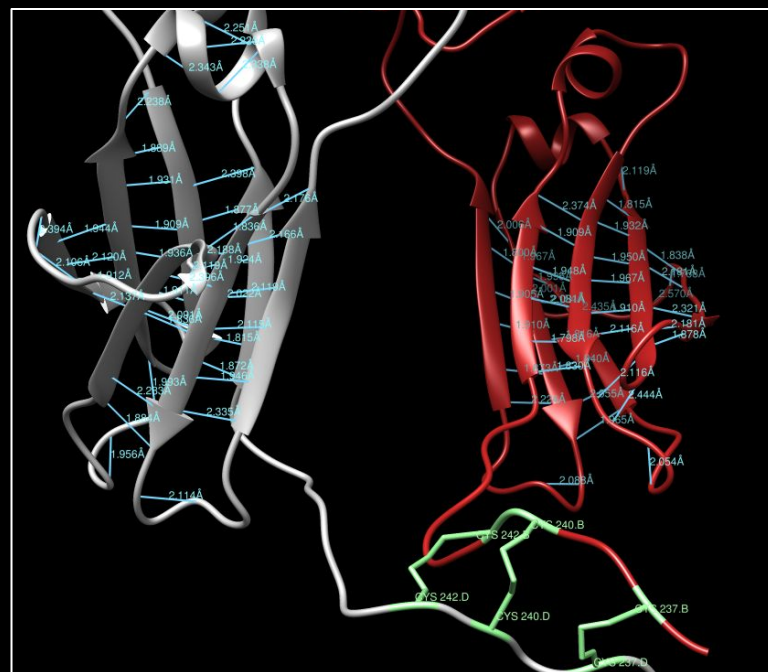


Introduction: Structure



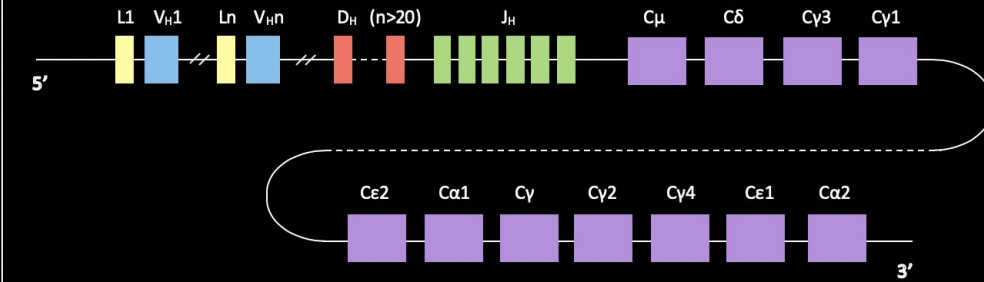
Introduction: Isotypes





Introduction: Immunoglobulin rearrangement

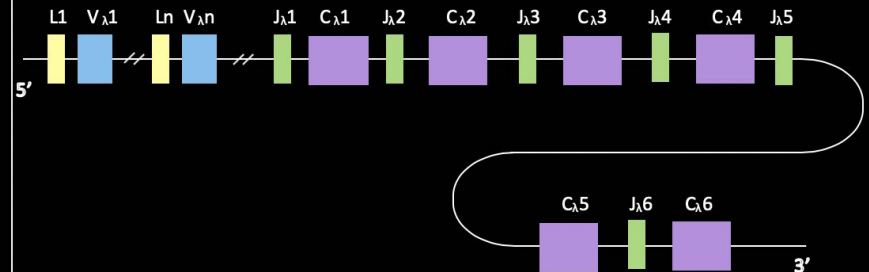
H chain locus (chromosome 14)



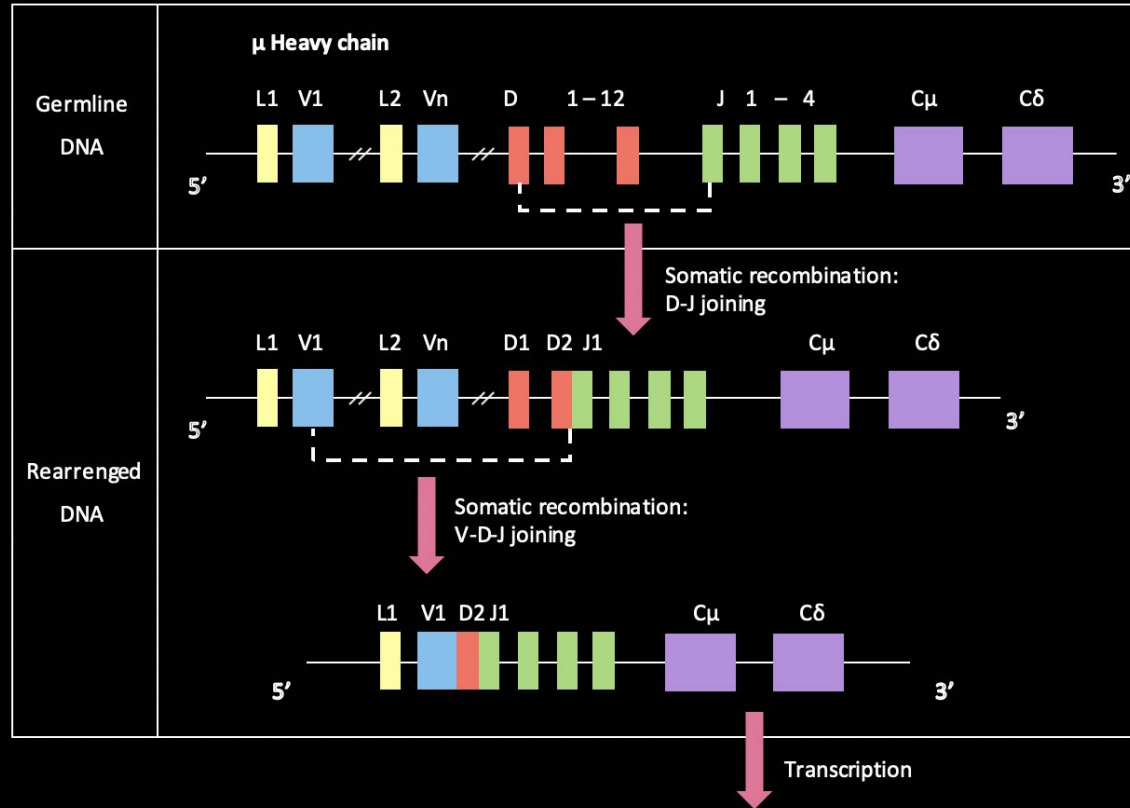
K chain locus (chromosome 2)



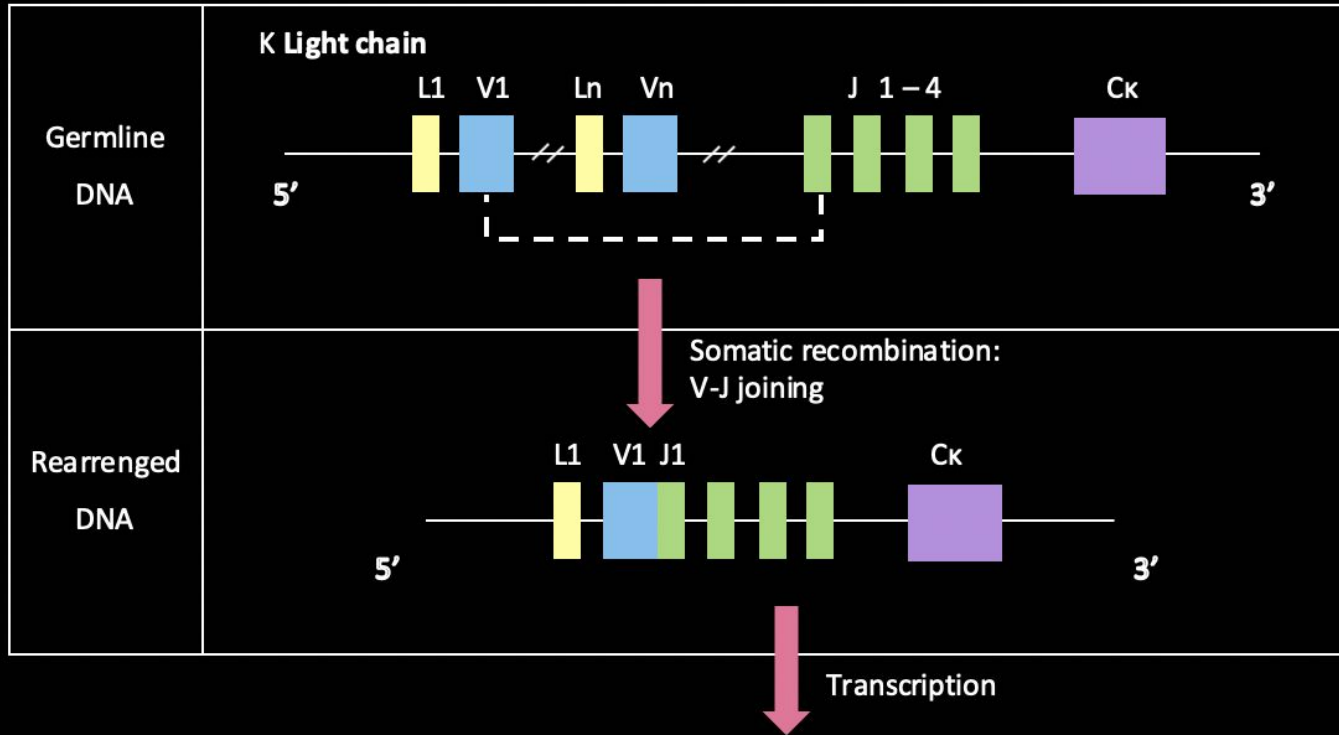
λ chain locus (chromosome 22)



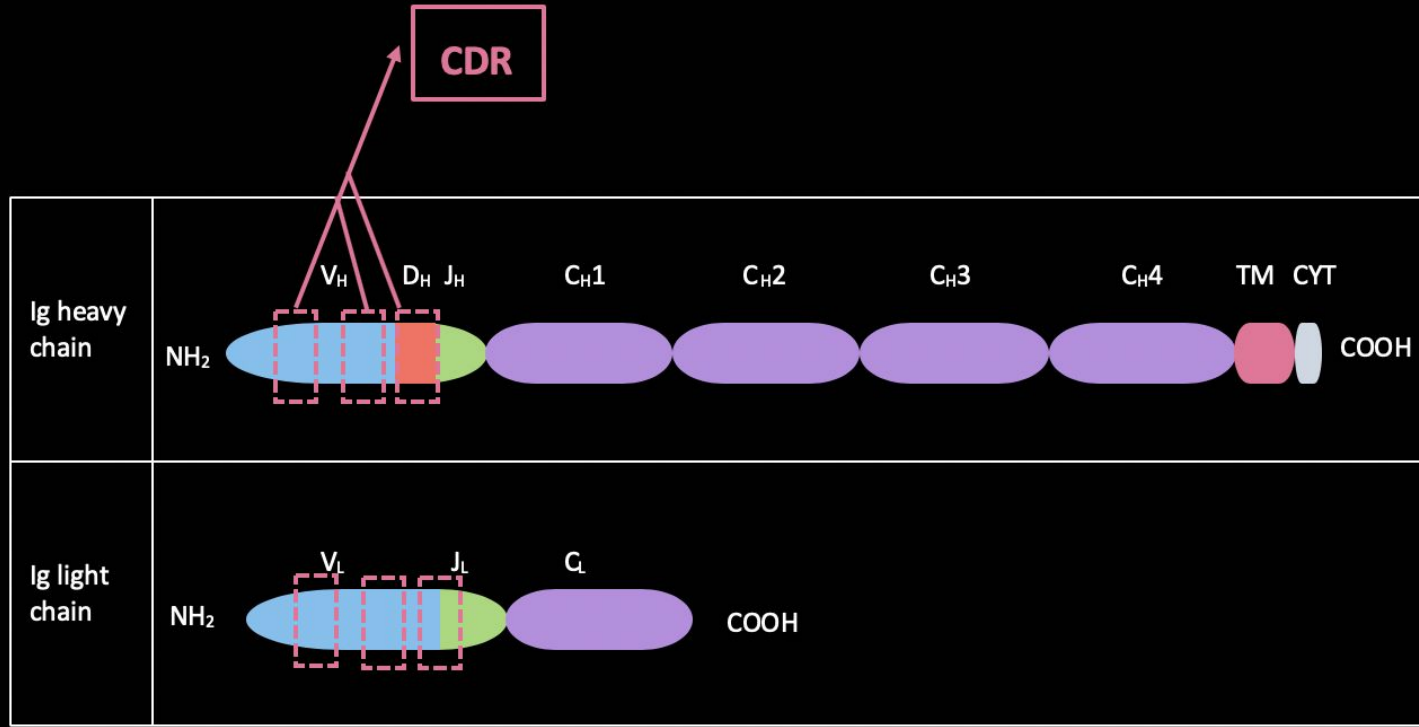
Introduction: Immunoglobulin rearrangement



Introduction: Immunoglobulin rearrangement



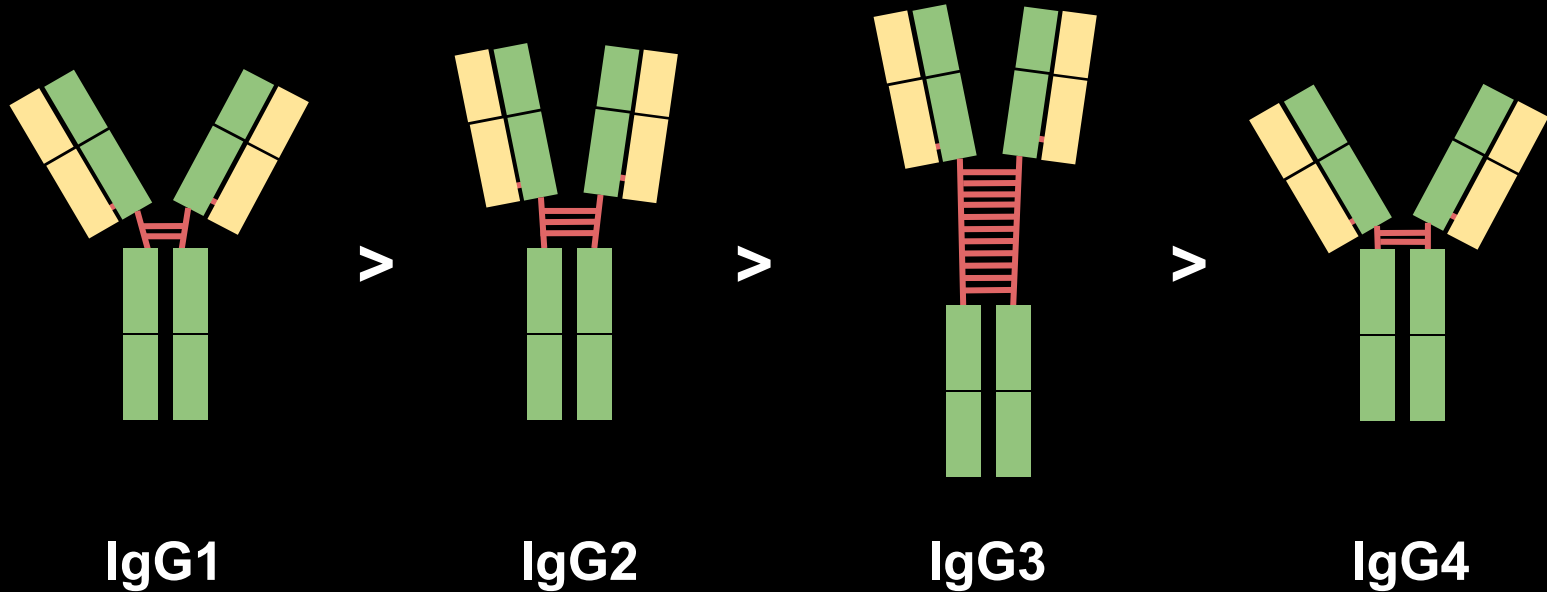
Introduction: Immunoglobulin rearrangement



IMMUNOGLOBULIN G

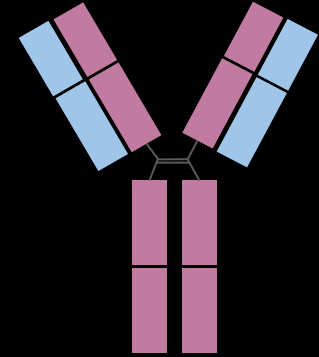
Immunoglobulin G: subclasses

The four subclasses of IgG differ in the structure of the hinge

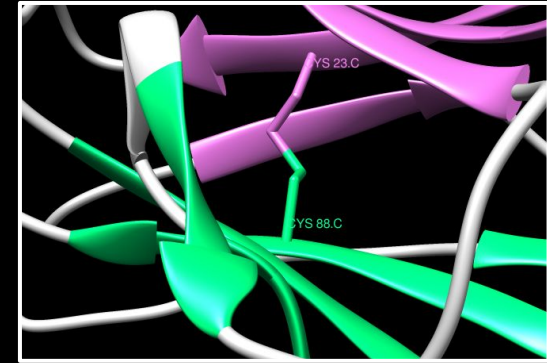
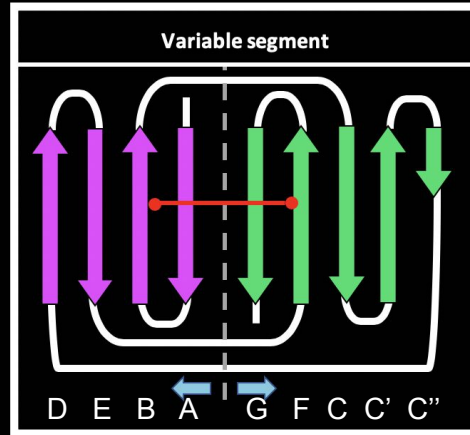
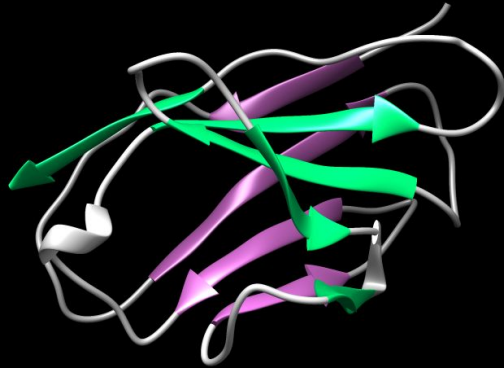
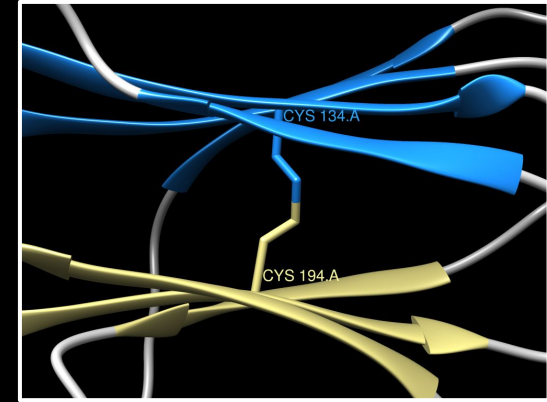
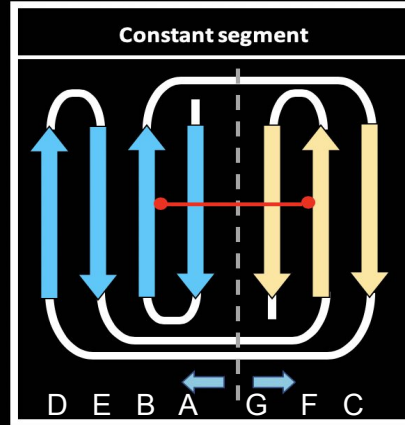
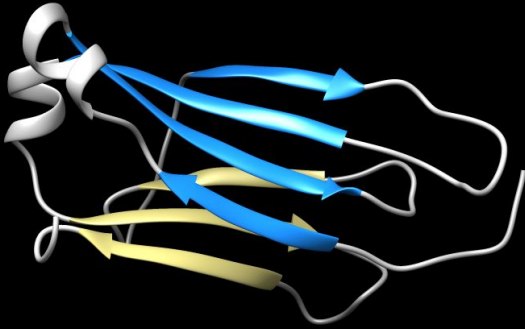
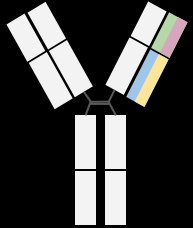


Immunoglobulin G: SCOP classification

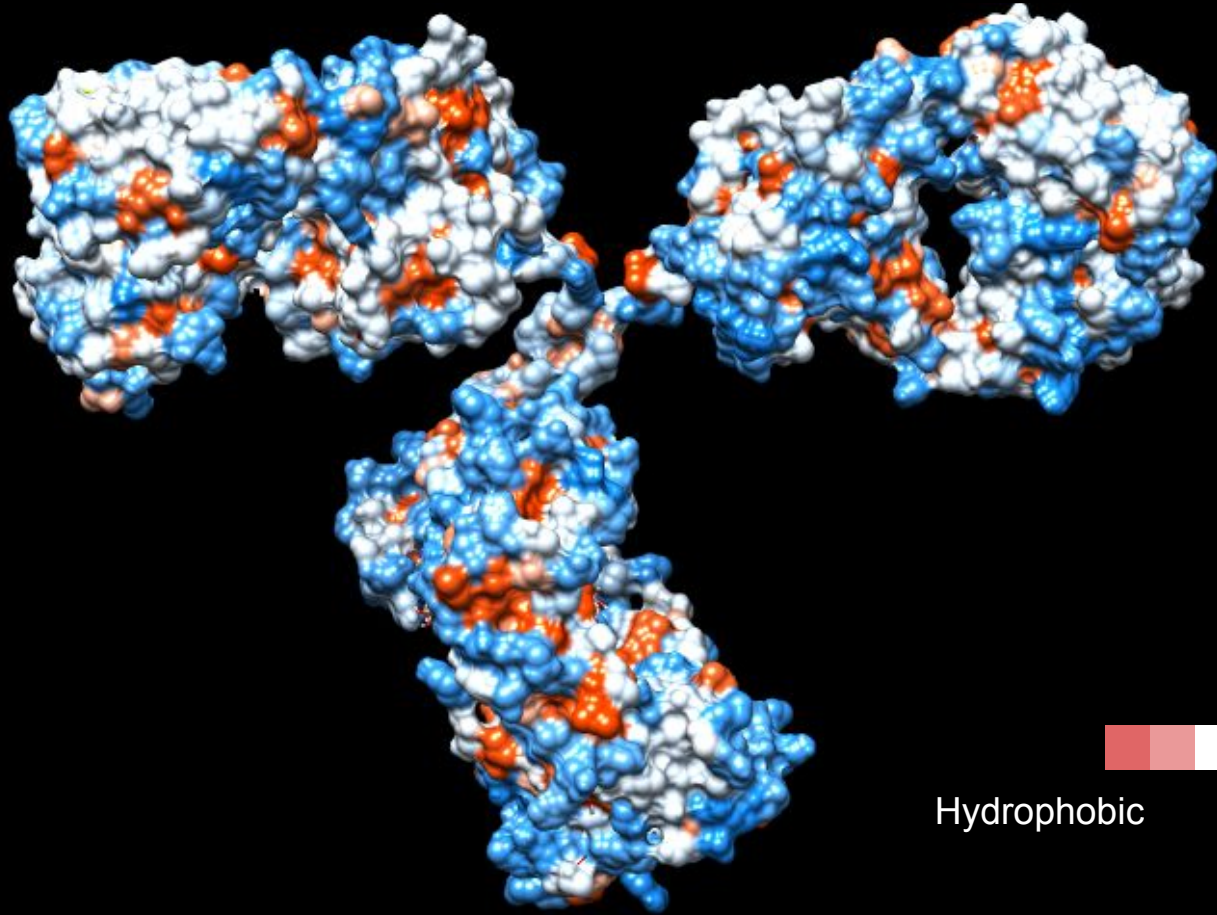
- Class → All- β proteins
- Fold → Immunoglobulin like
- Superfamily → Immunoglobulin
- Family:
 - **V set domains: antibody variable domain-like**
 - I set domains: are found in several cell adhesion molecules.
 - **C1 set domains: antibody constant domain-like**
 - C2 set domains: Ig-like domains resembling the antibody constant domain



Immunoglobulin G: Fold



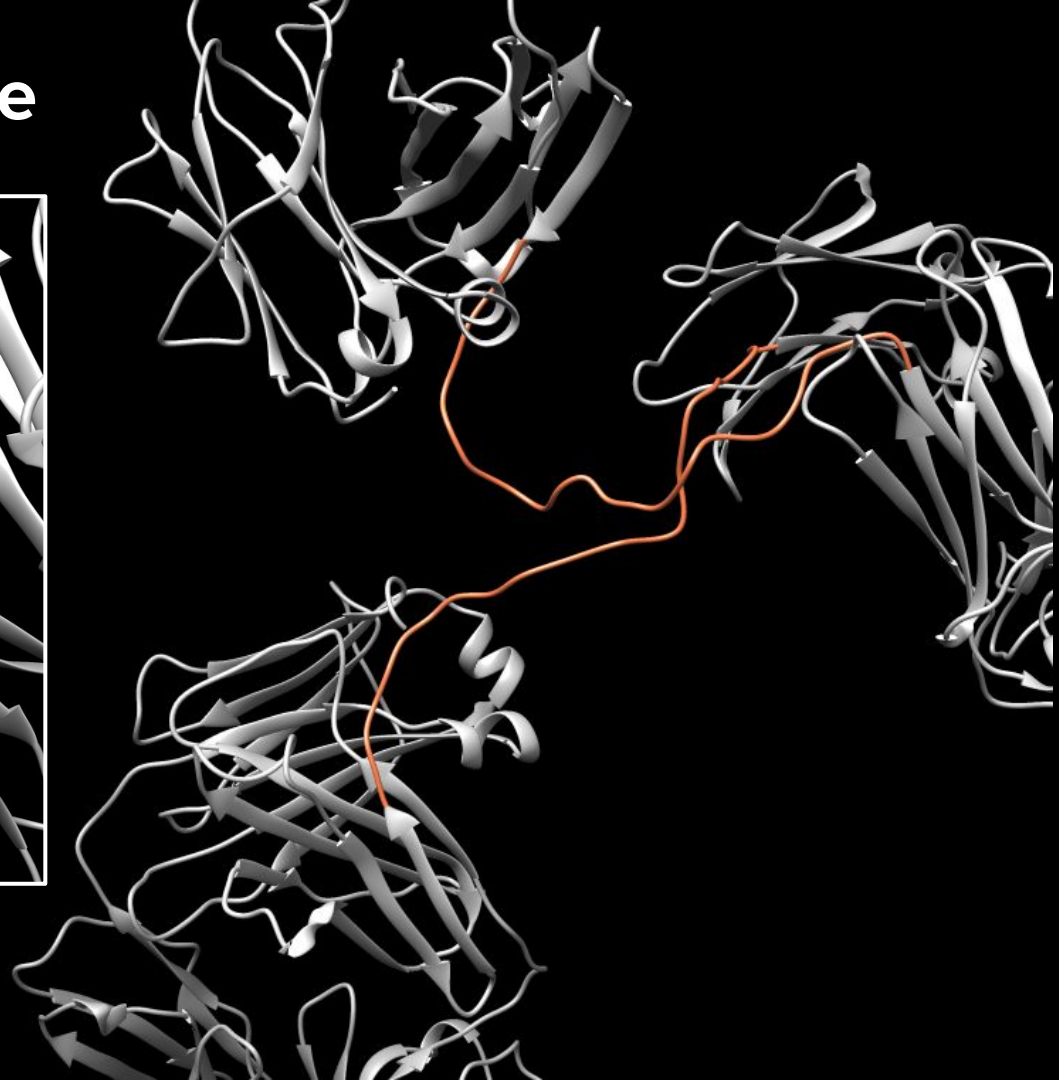
Immunoglobulin G: Architecture



Hydrophobic

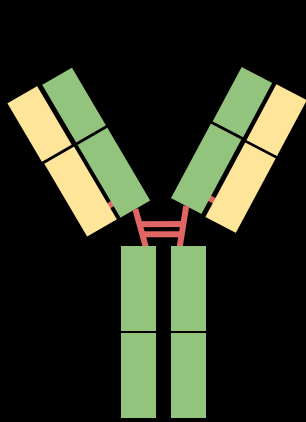
Hydrophilic

Immunoglobulin G: Hinge

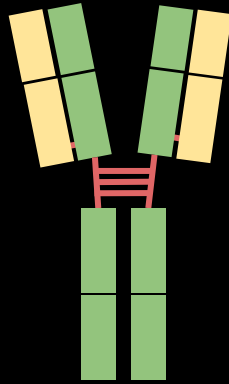


Immunoglobulin G: hinge

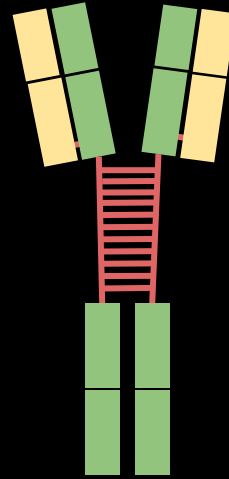
The four subclasses of IgG differ in the structure of the hinge



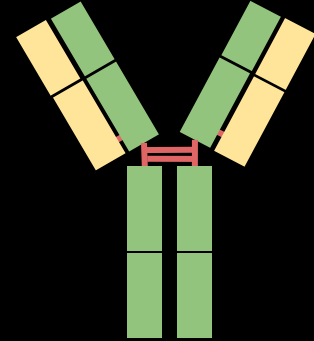
IgG1



IgG2



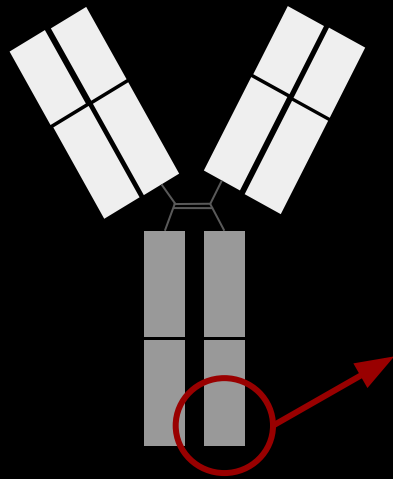
IgG3



IgG4

**IgG FRAGMENT
CRYSTALLIZABLE
REGION (Fc)**

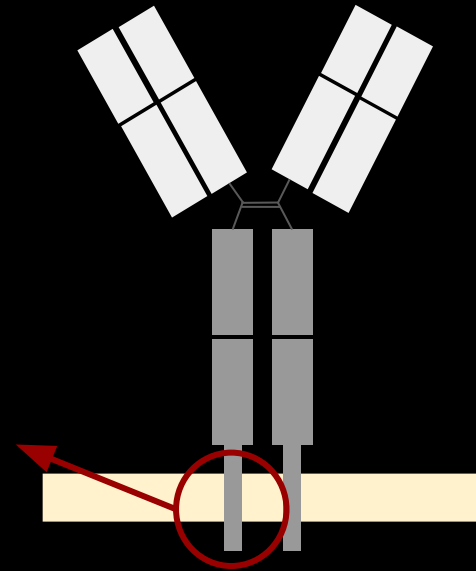
Fc: Soluble vs Surface



Soluble antibody



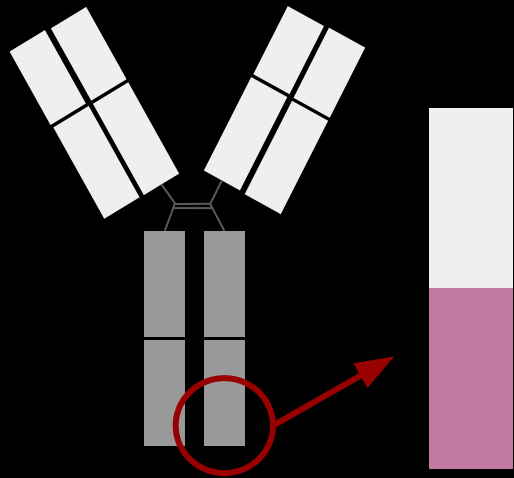
Hydrophilic
Hydrophobic



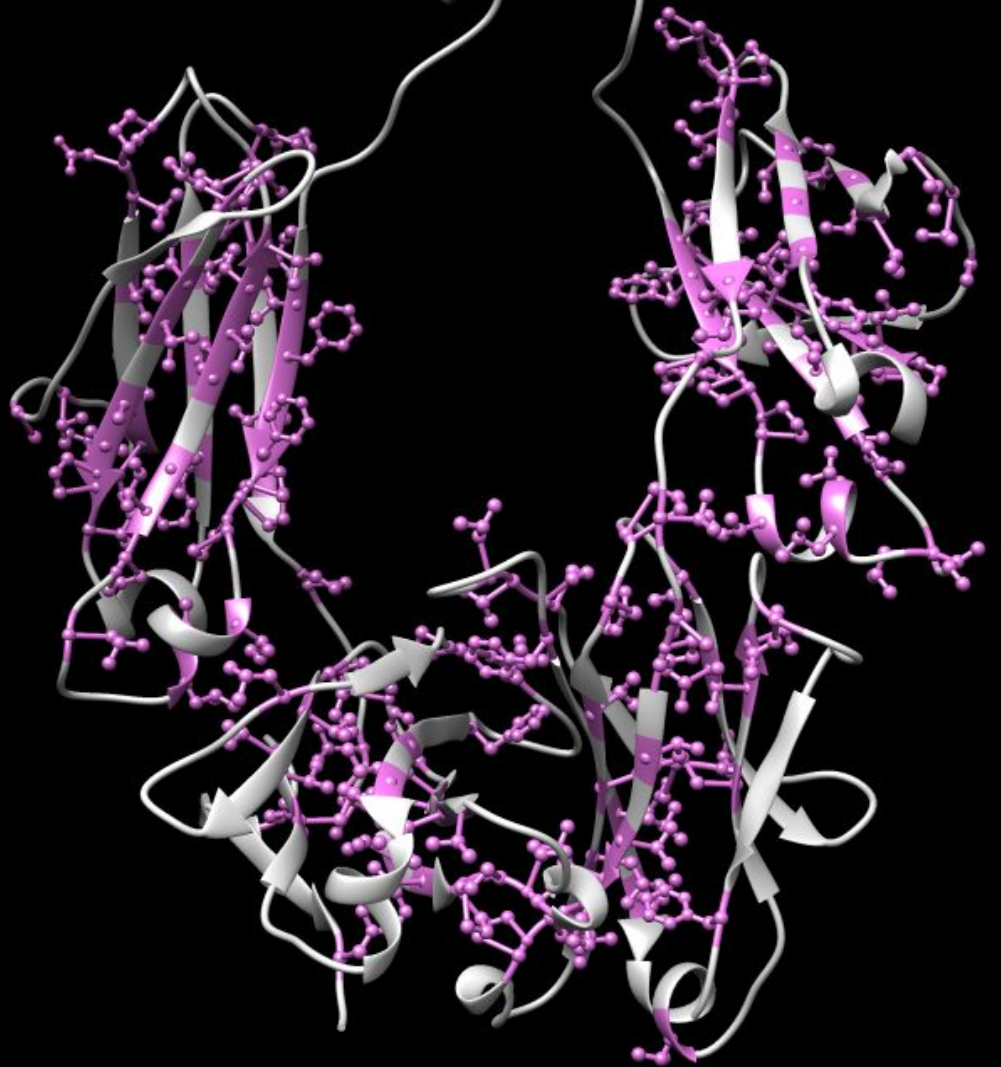
Plasma
membrane

Surface antibody

Fc: Soluble IgG



Soluble antibody



Fc: Subtypes comparison

```

4HAG_A      --VECPCPAP-PVAGPSVFLFPPKPKDTLMISRTP EVT CVVDV SHEDP
4BYH_A      GTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTP EVT CVVDV SHEDP
4C55_A      -----PAPEFLGGPSVFLFPPKPKDTLMISRTP EVT CVVDV SQEDP
6D58_A      -----LLGGPSVFLFPPKPKDTLMISRTP EVT CVVDV SHEDP
              :.*****:

4HAG_A      EVQFNWYVDGVEVHNAKTKPREEQFNSTFRVSVLTVVHQDWLNGKEYKC
4BYH_A      EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKC
4C55_A      EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVSVLTVLHQDWLNGKEYKC
6D58_A      EVQFKWYVDGVEVHNAKTKPREEQYNSTFRVSVLTVLHQDWLNGKEYKC
              **:.*:*****:***:*****:*****:

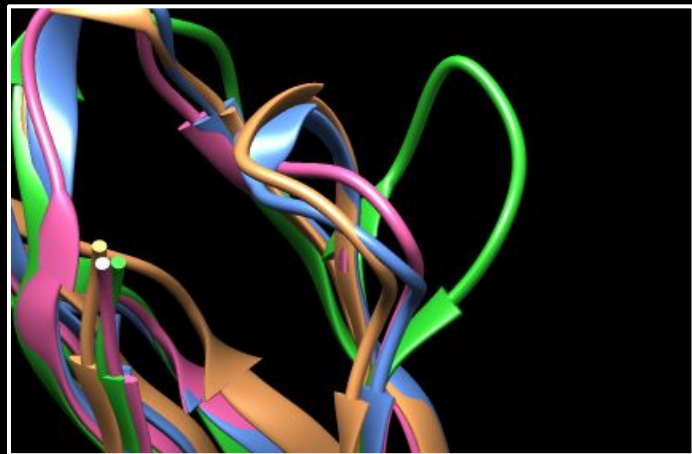
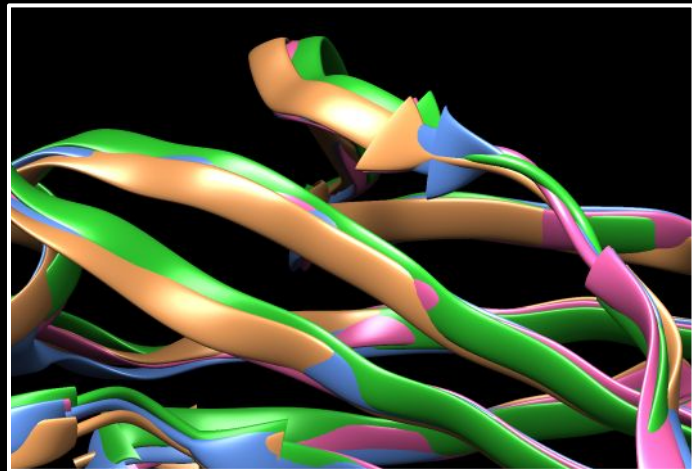
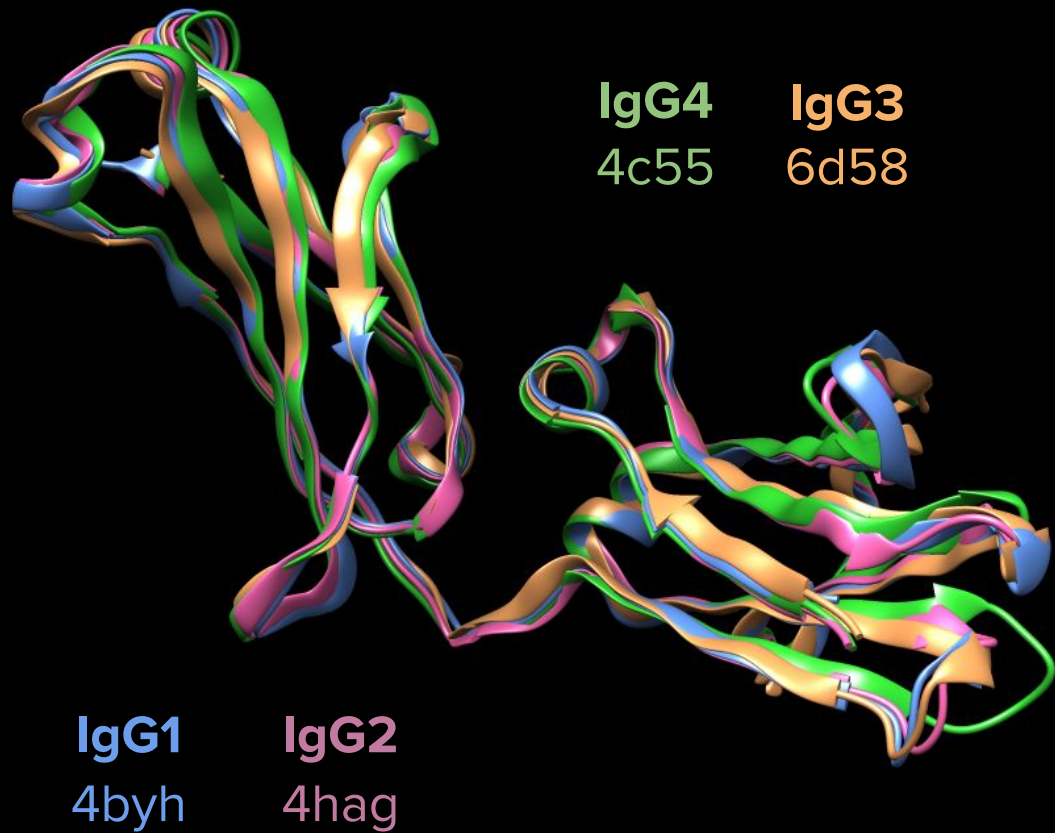
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4BYH_A      KVSNGKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG
4C55_A      KVSNGKLPSSEIETISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKG
6D58_A      KVSNGKALPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG
              *****:.*:*****:*****:*****:*****:

4HAG_A      FYPSDI AVEWESNGQPENNYKTPPM L DSDGSFFLYSKLTVDKSRWQQGN
4BYH_A      FYPSDI AVEWESNGQPENNYKTPPM L DSDGSFFLYSKLTVDKSRWQQGN
4C55_A      FYPSDI AVEWESNGQPENNYKTPPM VL DSDGSFFLYSRLTVDKSRWQEGN
6D58_A      FYPSDI AVEWESSGQPENNYNTTPM L DSDGSFFLYSKLTVDKSRWQQGN
              *****:*****:****:*****:*****:*****:

4HAG_A      VFSCSVMHEALHNHYTQKSLSLSPGK-----
4BYH_A      VFSCSVMHEALHNHYTQKSLSLSPGKHHHHHH
4C55_A      VFSCSVMHEALHNHYTQKSLSLSPGK-----
6D58_A      IFSCSVMHEALHNHFTQKSLSLSPGK-----
              :*****:*****:

```

Fc: Subtypes comparison



Fc: IgG2 among species

4HAF VECPPCPAP -PVAGP SVFLF PPKPKDTLMIS RTP EVT C V V D V S HEDPEV
6BHQ KECPPCAAPDLLGGP SVFI F PPKIKDVL MISLSP MVT C V V D V S EDDPDV
6D4I STCPPCPAE -LLGGP SVFLF PPKPKDTLMIS RTP EVT C V V D V S QEEP DV

4HAF QFNWYV DGV E V H N A K T K P R E E Q F N S T F R V V S V L T V V H Q D W L N G K E Y K C K V
6BHQ Q I S W F V N N V E V H T A Q T Q T H R E D Y N S T L R V V S A L P I Q H Q D W M S G K E F K C K V
6D4I K F N W Y V D G V E V H N A O T K P R E E Q F N S T Y R V V S V L T V T H O D W L N G K E Y T C K V

* * *

4HAF SNKGLPAP IEKTI SKTKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFY
6BHQ NNRALPSP IEKTI SKPRGPVRAPQVYVL PPPAEEMTKKEFSLTCMITGFL
6D4I SNKALPAP ROKTVS KTKGQPREPOVYTL PPPREELTKNOVSLTCLVKGFY

[illegible]

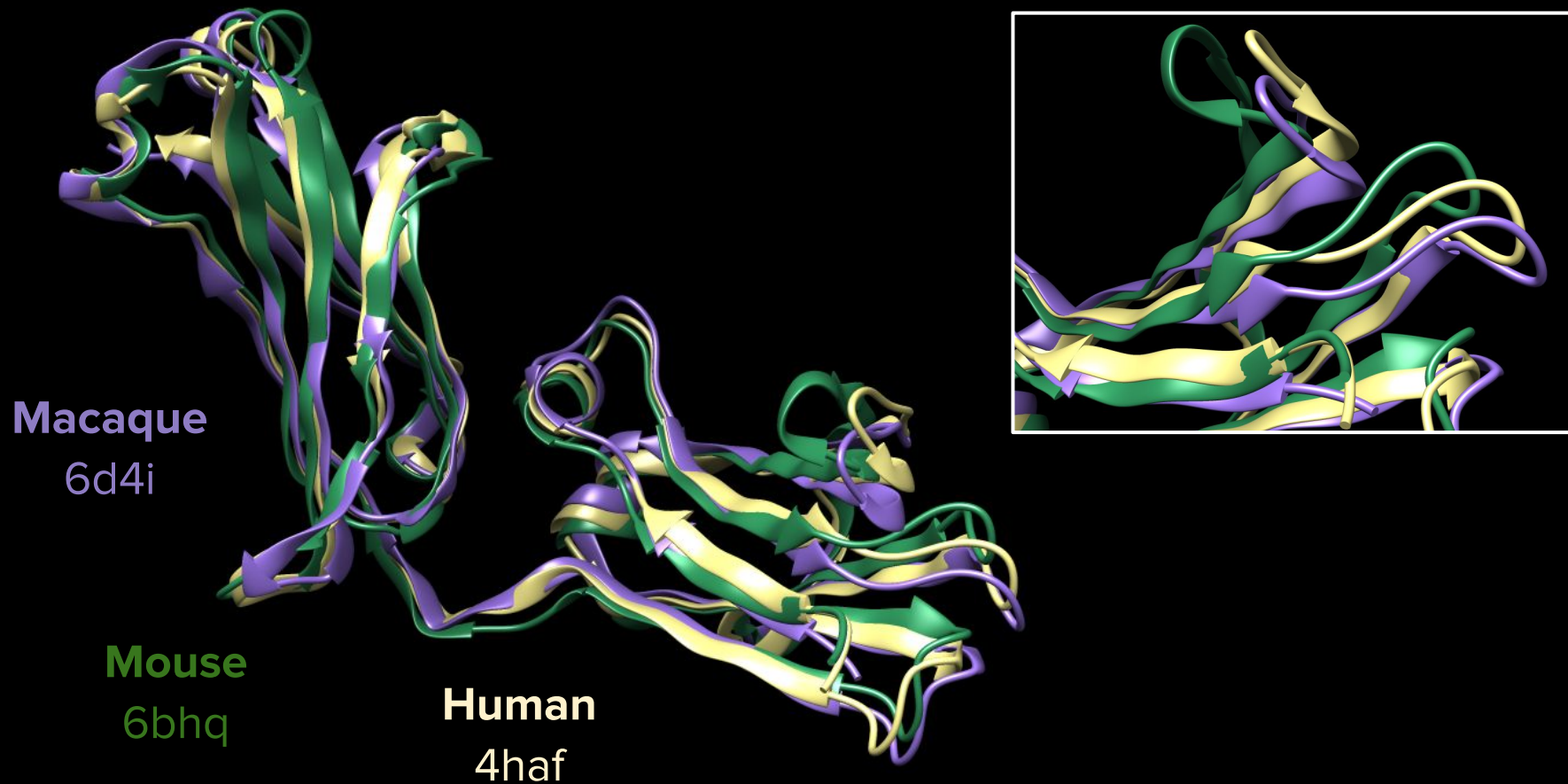
4HAF PSDI AVEWESNGQPENNYKTPPMLDSDGSFFLYSKLTVDKSRWQQGNVF
6BHQ PAEI AVDWTSNGRTEQNYKNATVLDSDGSYFMYSKLRVQKSTWERGSLF
6D4I PSDI VVEWASNGOPENTYKTPPVLDSDGSYFLYSKLTVDKSRWQOOGNTF

* * * * *

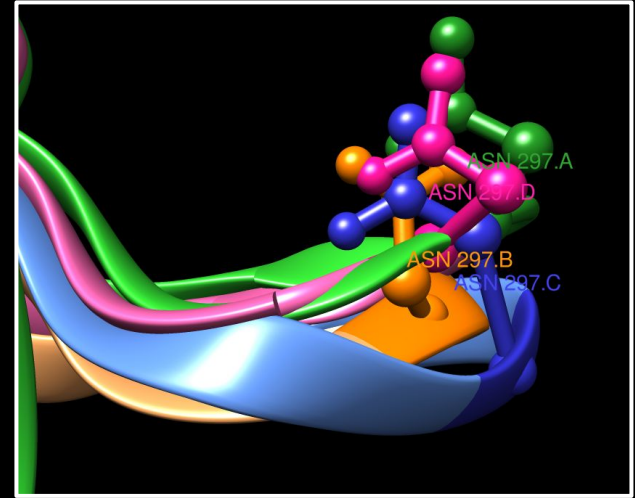
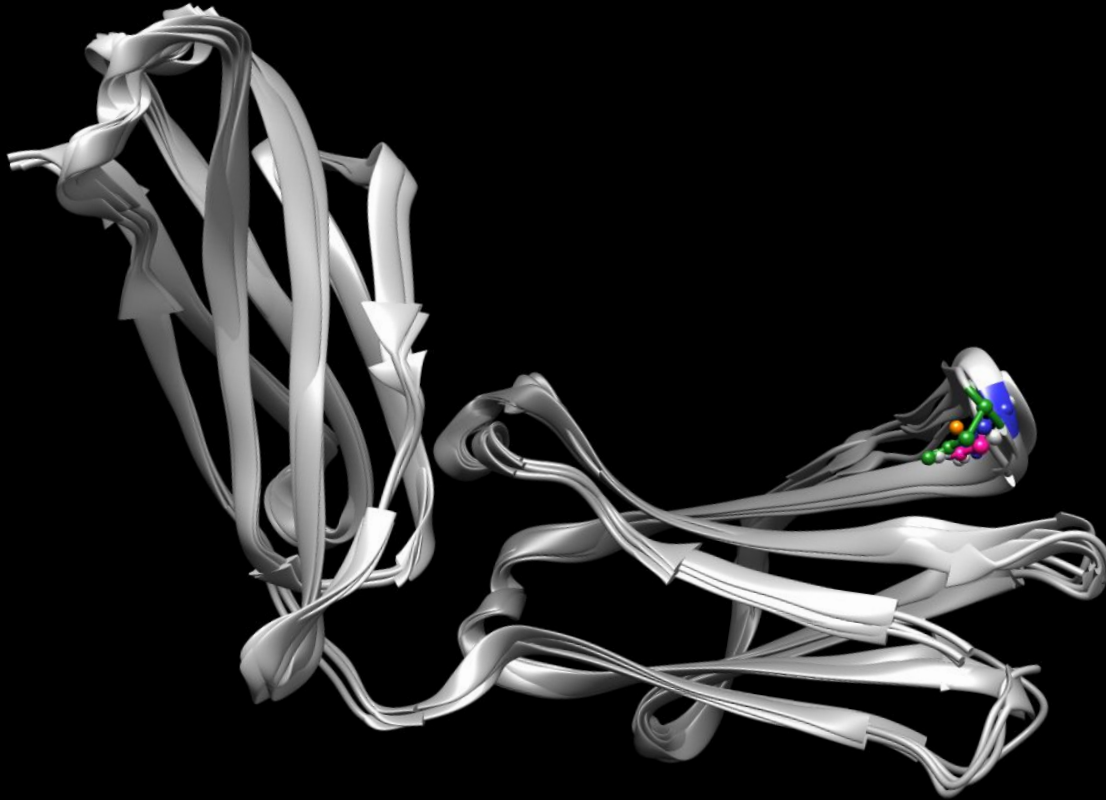
4HAF SCSVMHEALHNHYTQKSLSPGK
6BHQ ACSVMHEGLHNHLTTKTISRSLGK
6D4I SCSVMHEALHNHYTQKSLSPGK

* * *

Fc: IgG2 superimposition

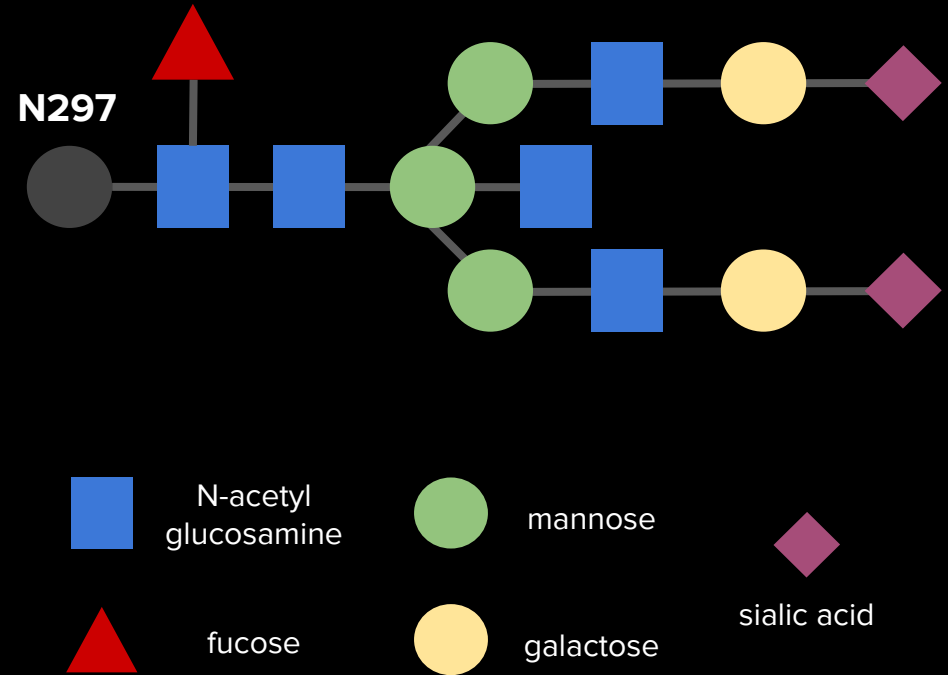
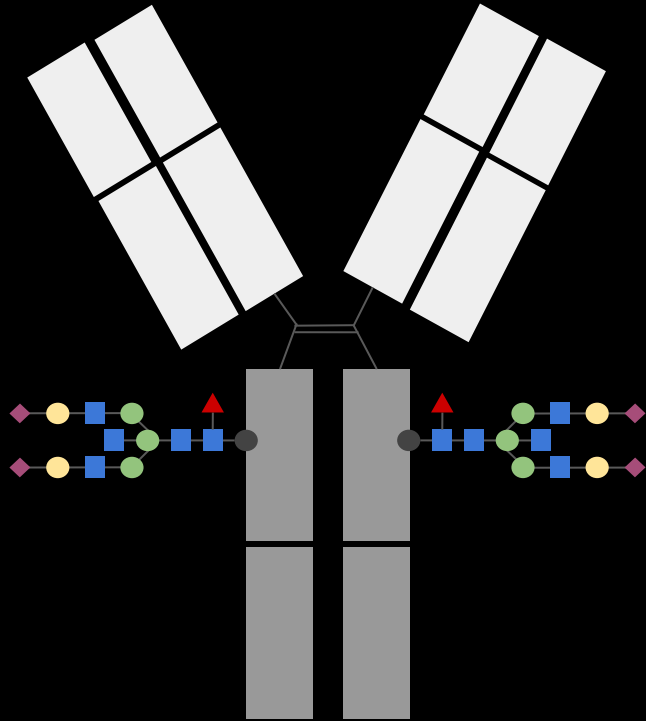


Fc: N-glycosilation



Asn 297

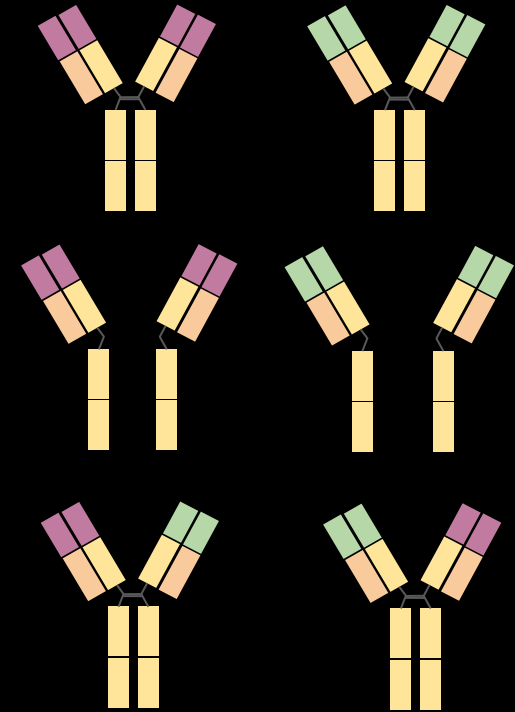
Fc: N-Glycosylation



IgG4 Fab-ARM EXCHANGE (FAE)

FAE

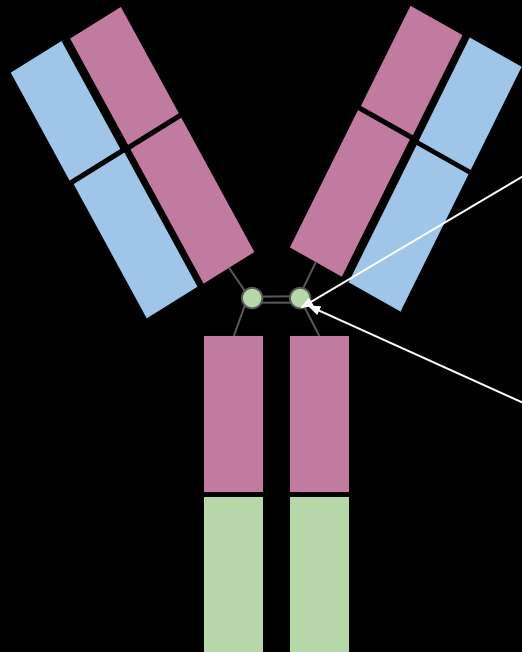
- Separation of the 2 IgG4 heavy chains to form 'half-molecules' comprising just 1 heavy and light chain. They recombine to create bispecific antibodies.
- Two determinants enable IgG4 to undergo FAE, namely the core hinge and the Cy3–Cy3 domain interface
- Imply both covalent and non-covalent interactions



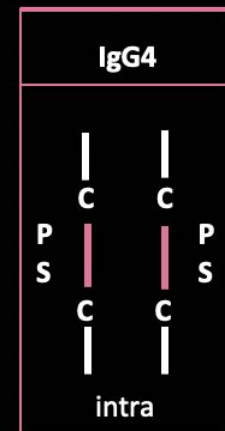
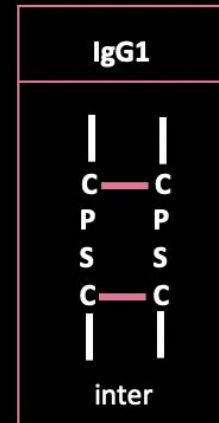
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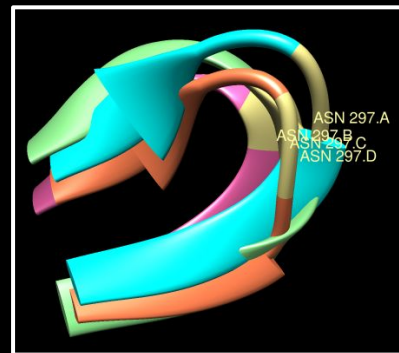
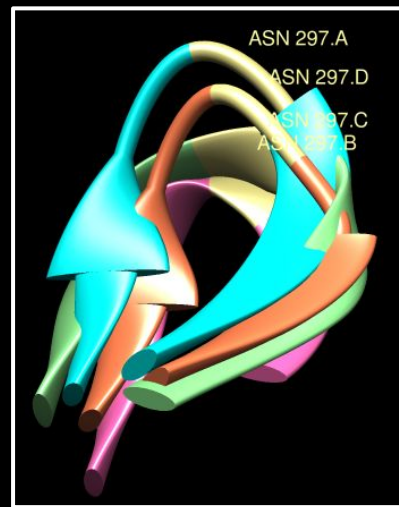
IgG1	EPKSCDKTHTCPPCPAPELLGGP
IgG4	ESKYGPPCPSCPAPELLGGP

FAE



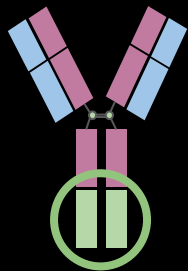
IgG1	IgG4
E	
P	
K	
S	E
C	S
D	K
K	Y
T	G
H	P
T	P
C	C
P	P
P	S (228)
C	C
P	P
A	A





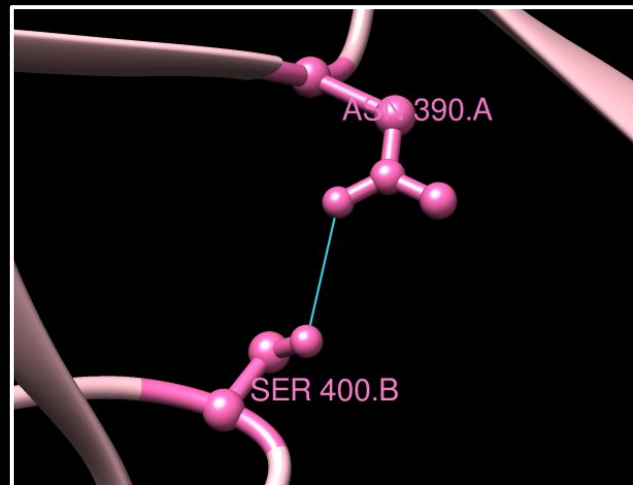
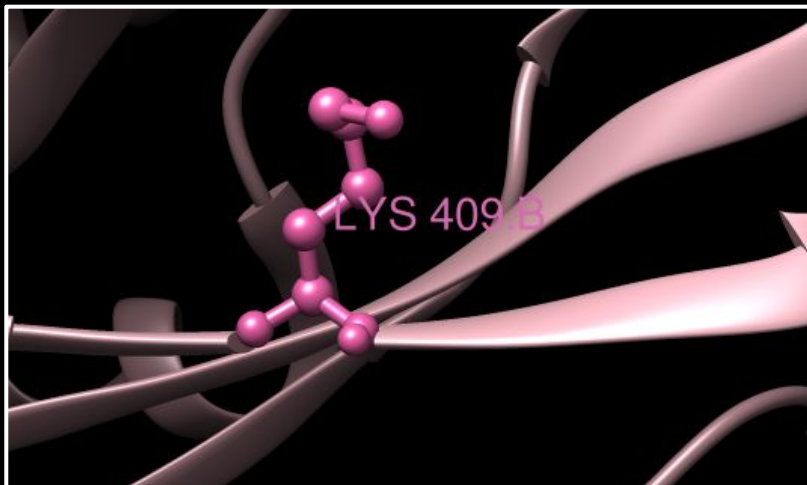
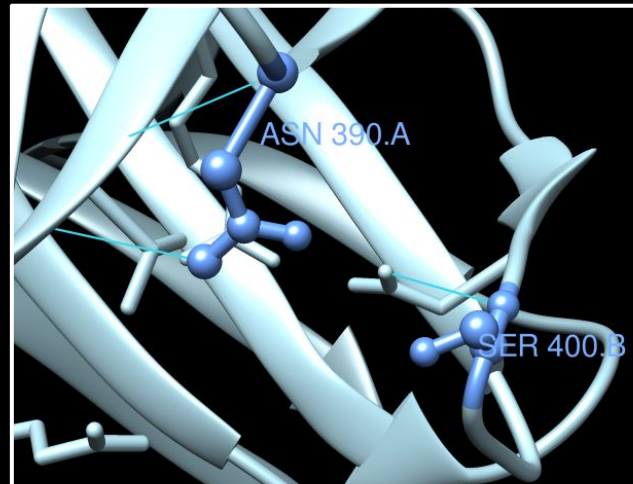
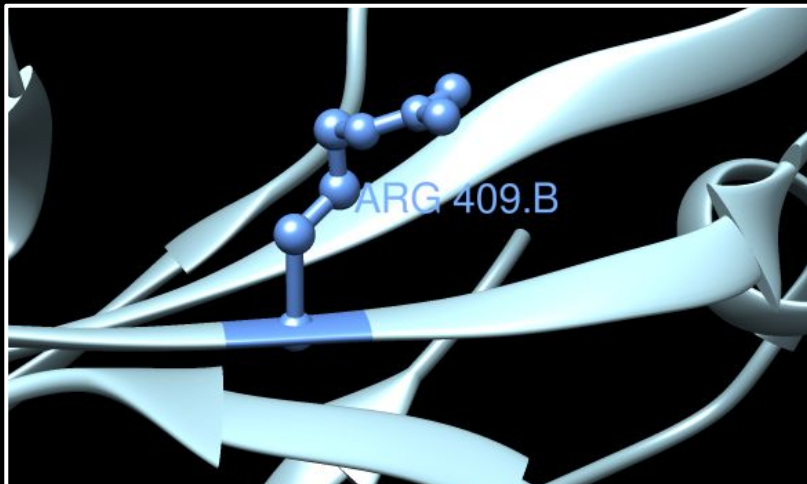
IgG4

4b53

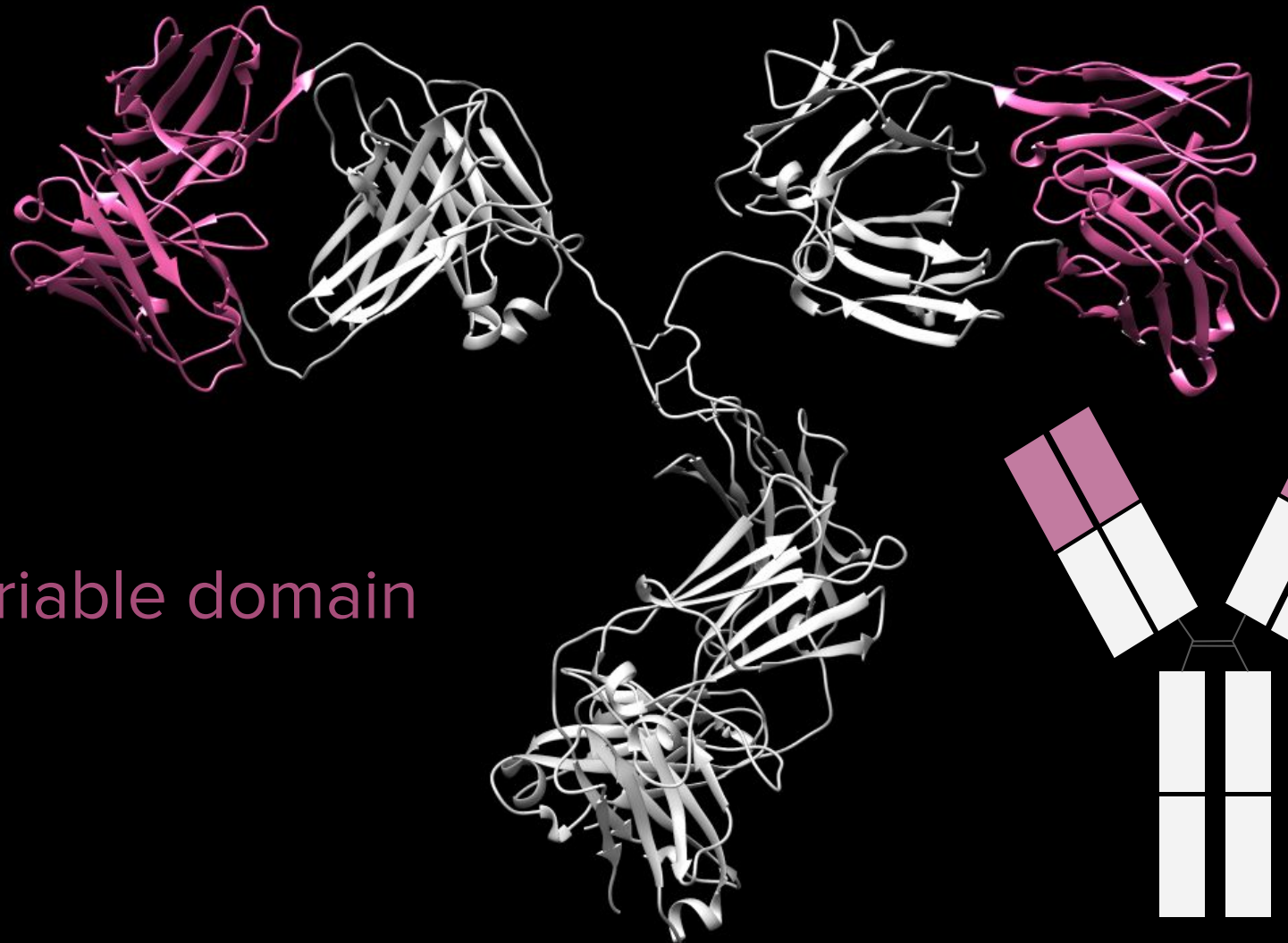


IgG1

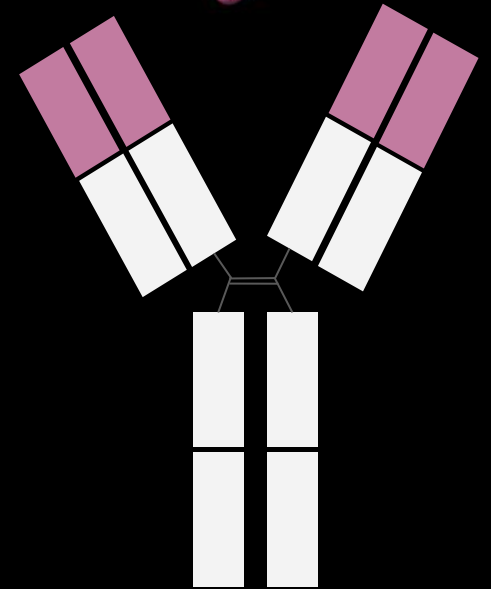
3ave



IgG VARIABLE DOMAIN

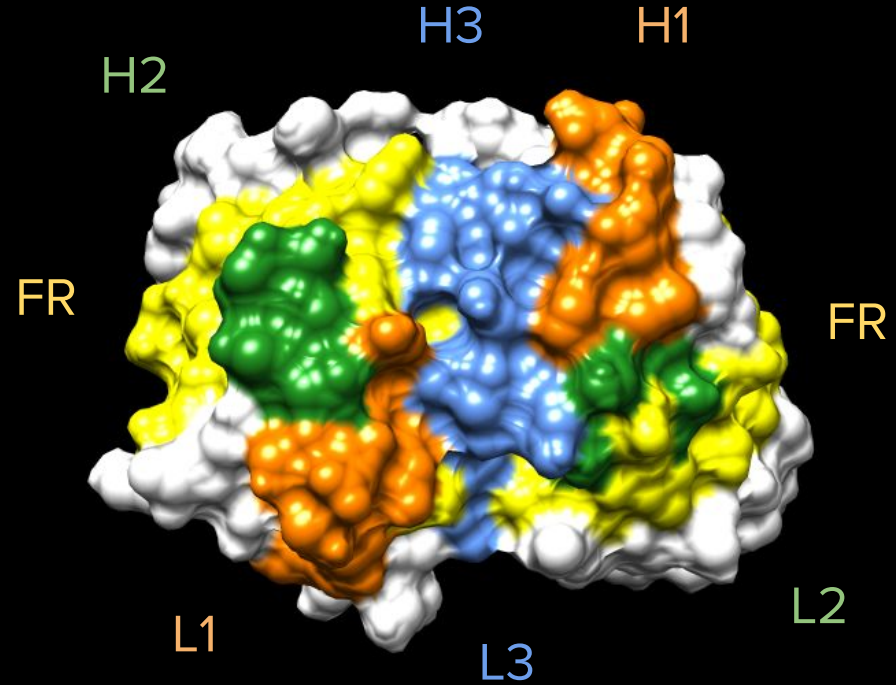
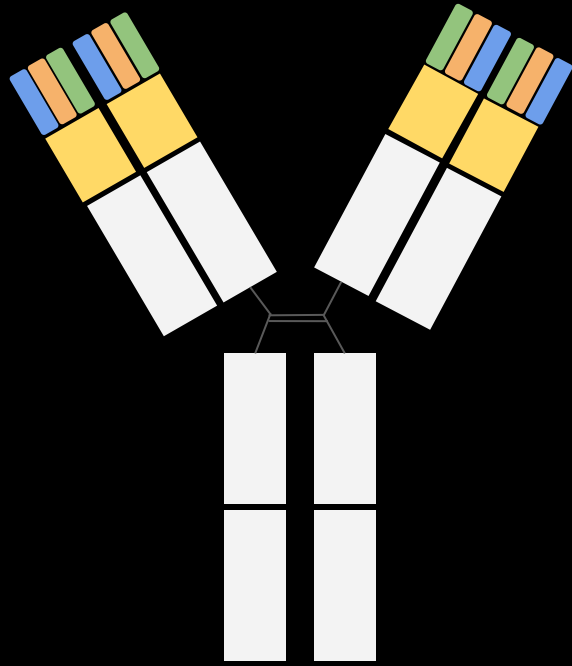


Variable domain



HYPERVARIABILITY

Complementarity-determining regions (CDRs)



HYPERVARIABILITY

Light chains
(lambda type)

Framework

L1

L2

L3

1gigl
1mfal
1indl
2fb4l
2rhea
8faba

1gigl
1mfal
1indl
2fb4l
2rhea
8faba

```
QAVVTQESALTTSPGETVTLTCSRSTGAVTTSNYANWVQEKPDHLFTGLI GGTNNRAPGV
QIVVTQESALTTSPGETVTLTCSRSTGTVTSGNHANWVQEKPDHLFTGLI GDTNNRAPGV
-AVVTQESALTTSPGETVTLTCSRSTGAVTTSNYANWVQEKPDHLFTGLI GGTNNRAPGV
QSVLTQPPSASGTPGQRTISCSGTSSNIGS-STVNWYQQLPGMAPKLLI YRDAMRPSGV
ESVLTQPPSASGTPGQRTISCTGSATDIGS-NSVIWYQQVPGKAPKLLI YYNDLLPSGV
--ELTQPPSVSVSPGQTARITCS--ANALPN-QYAYWYQQKPGRAPVMVI YKDTQRPSGI
: ** . : : : ** : . : ** : : : . . . * * : * . : * . . . *
```

```
PARFSGSLIGDKAALTITGAQTEDEAIYFCA LWYSNHW--VFGGGTKLTVLGQPKSSPSV
PARFSGSLIGDKAALTITGAQPEDEAIYFCA LWSNNHW--IFGGGTKLTVLGQG-----
PARFSGSLIGDKAALTITGAQTEDEARYFCA LWYSNLW--VFGGGTKLTVLGQPKSSPSV
PDRFSGSKSGASASLAIGGLQSEDETDYYCA AWDVSLNAYVFGTGKTVTLGQPKANPTV
SDRFSASKSGTSASLAISGLESEDEADYYCA AWNDLDEPGFGGGTKLTVLGQPK-----
PQRFSSSTSGTTVTLTISGVQAEDEADYYCA AWDNSAS--IFGGGTKLTVLGQPKAAPSV
. *** . * . . : ** : * : . *** : * : * . * . ** *** : *****
```

HYPERVARIABILITY

Light chains
(kappa type)

1fgvl
1fvca
1igml
1vfaa
1flrl
2cgrl
1tetl
2fbjl
1hila
2imma

```
DIQMTQSPSSLSASVGDRVTITCRASQDINN-----YLNWYQKPGKAPKLLIYYTSTL
DIQMTQSPSSLSASVGDRVTITCRASQDVNT-----AVAWYQKPGKAPKLLIYSASFLL
DIQMTQSPSSLSASVGDRVTITCQASQDISN-----YLAWYQKPGKAPELRIYDASNLL
DIVLTQSPASLSASVGETVTITCRASGNIHN-----YLAWYQKQKQKSPQLLVYYTTTLL
DVVMTQTPLSLPVSLGDQASISCRSSQSLVHS-NGNTYLRWYLQKPGQSPKVLIIYKVSNNR
ELVMTQSPLSLPVSLGDQASISCRPSQSLVHS-NGNTYLHWYLQKPGQSPKLLIYRVSNRR
DVLMTQTPLSLPVSLGDQASISCKSSQSIVHS-SGNTYFEWYLQKPGQSPKLLIYKVSNNR
EIVLTQSPAITAASLGQKVITITCSASSSVSS-----LHWYQKSGTSPKPWIYEISKLL
DIVMTQSPSSLTVTAGEKVTMSCTSSQSLFNSGKQKNYLTWYQKPGQPPKVLIIYWASTRR
DIVMTQSPSSLSVSAGERVTMSCKSSQSLLNQKQKNFLAWYQKPGQPPKLLIYGASTRR
:: :***:  .:. *: .:*** .* .:  . ** ** * .*: :* :
```

Framework

L1

L2

L3

1fgvl
1fvca
1igml
1vfaa
1flrl
2cgrl
1tetl
2fbjl
1hila
2imma

```
ESGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCQGNTLPPTFGAGTKVEIK-----
YSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQHYTTPTFGQGTKVEIKRT-----
ETGVPSRFSGSGSGTDFFTTISSLQPEDIAATYYCQYQNLPLTFGPGTKVDIKRTVAAPS
ADGVPSRFSGSGSGTQYSLKINSLQPEDFGSYCCQFWSTPRTFGGGTKLEIKR-----
FSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPWTFGGGKLEIKRADAAPT
FSGVPDRFSGSGSGTAFTLKISRVEAEDLGVYFCSQGTHVPYTFGGGKLEIKRADAAPT
FSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYCFQGSHIPFTFGSGTKLEIKRADAAPT
ASGVPARFSGSGSGTSYSLTINTMEAEDAAIYYCQWPTYPLITFGAGTKLEIKRADAAPT
ESGVPPDRFTGSGSGTDFTLTISSVQAEDLAVYYCQNDYSNPLTFGGGKLEIKRADAAPT
ESGVPPDRFTGSGSGTDFTLTISSVQAEDLAVYYCQNDHSYPLTFGAGTKLEIKR-----
*** **:* *** :...: .:..* . ** : *** ***:***
```

HYPERVARIABILITY

Heavy chains

1mfah
2cgrh
1teth
1hilb
1indh
1flrh
1gigh
1vfab
1fgvh
1fvcb
1igmh
2fbjh
2fb4h
8fabb

```
EVQVQQSGTVVARPGASVKMSCKASGYTFTNYWMHWIKQRPGQGLEWIGAIYPG---NSAT
RVQLLESGAELMKPGASVQISCKATGYTFSEYWI EWVKERPGHGLEWIGEILPG---SGRT
QIQLVQSGPELKTTPGETVRISCKASGYTFTTYGMSVVKQTPGKGFKWMGWINTY---SGVP
EVQLVESGGDLVKPGGSLKLSCAA SGFSFSSYGM SVWRQTPDKRLEWVATISNG---GGYT
EVTLVESGGDSVKPGGSLKLSCAA SGFTLSGETMSVWRQTPDKRLEWVATLSG---GGFT
EVKLDDETGGLVQPGRPMLKSCVASGFTFSDYWMNVWRQSPEKGLEWVAQIRNKPYN YET
QVQLKESGPGLVAPSQSL SITCTVSGFLLISNGVHWVRQPPGKGLEWLGVIWAG---GNT
QVQLQESGPGLVAPSQSL SITCTVSGFSLTGYGVNVWRQPPGKGLEWLGMIWGD---GNT
EVQLVESGGGLVQPGGSLRLSCATSGYTTFEYTMHWMRQAPGKGLEWVAGINPK---NGGT
EVQLVESGGGLVQPGGSLRLSCAA SGFNIKDTYIHWVRQAPGKGLEWVARIYPT---NGYT
EVHLLSEGGNLVQPGGSLRLSCAA SGFTFNIFVMSVWRQAPGKGLEWVSGVFGS---GGNT
EVKLLSEGGGLVQPGGSLKLSCAA SGDFDSKYWMSVWRQAPGKGLEWIGEIHDPD---SGTI
EVQLVQSGGGVVQPGRSRLRLSCSSSGFIFSSYAMYVWRQAPGKGLEWVAIIWDD---GSDQ
AVKLVQAGGGVVQPGRSRLRLSCIASGFTFSNYGMHWVRQAPGKGLEWVAI WYN---GSRT
: : :*: * . . :*: *: : : :*: * : :*:.
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Framework

H1

H2

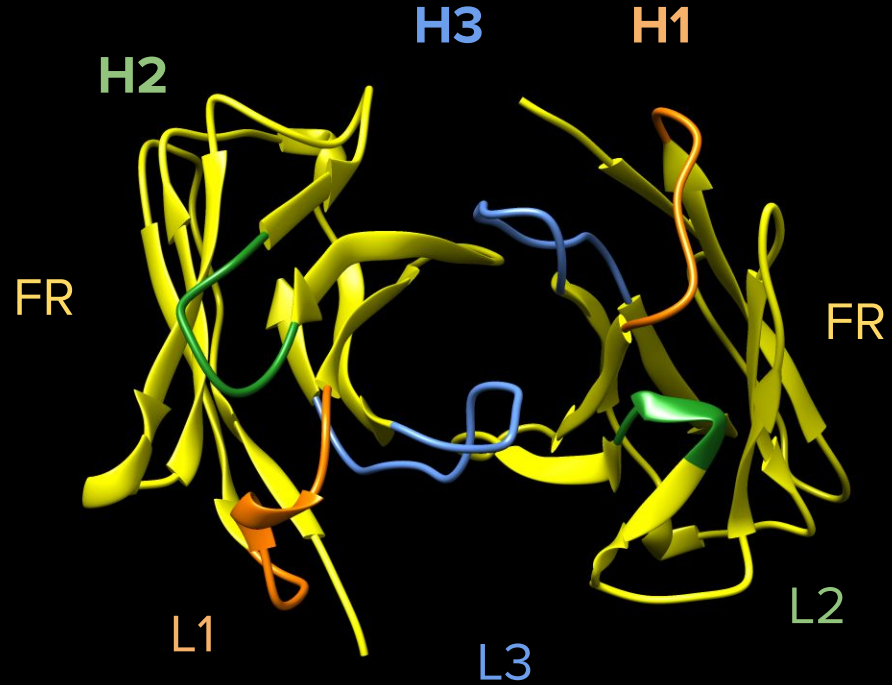
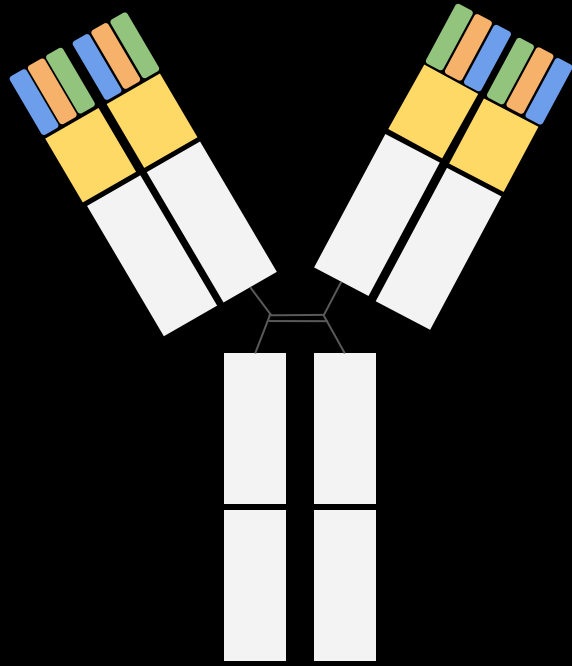
H3

1mfah
2cgrh
1teth
1hilb
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1flrh
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2fbjh
2fb4h
8fabb

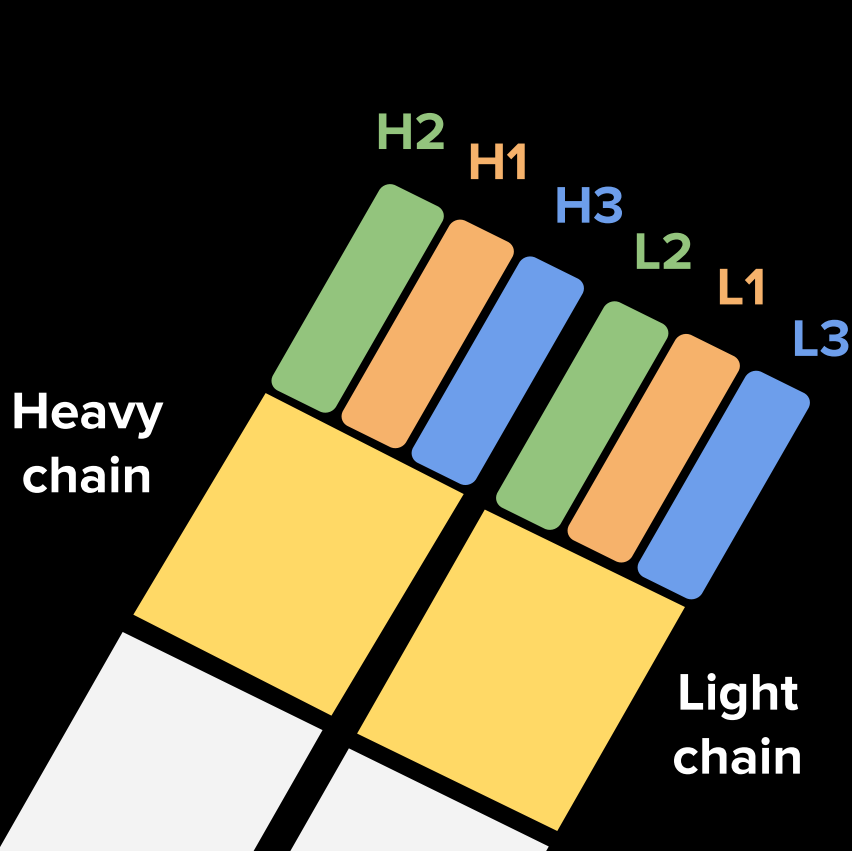
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TYADDFKGRFAFSLETSASTAYLQINN LKNE DTATYFCARR-----SWYFDVWGT
YYPDSVKGRFTISRDN AKNTLYLQMSSLKSEDSAMYYCARRERYD-----ENGFAYWGQ
FYSASVKGRFTISRDN AQNNLYLQLNSLRSEDTALYFCASHR-----FVHWGH
YYSDSVKGRFTISRDDSS---VYLQMNNLRVEDMGIYYCTGSYYG-----MDYWGQ
NYNSALMSRVSISKDNSKSQVFLKMKSLQTDDTAMYYCARDFYDYD---VFYYAMDYWGQ
DYN SALKSRLSISKDNSKSQVFLKMNSLHTDDTARYYCARERD-----YRLDYWGQ
SYADSVKGRFTISVDKSKNTLYLQMNSLRAEDTAVYYCARWRG-----LDVRYFDVWGQ
RYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGG-----DGFYAMDYWGQ
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YYGDSVKGRFTISRDN SKRTLYMQMNSLRTE DTAVYYCARDP-----DILTAFSFDYWGQ
* . : : : : :*: * . :*: **
```

HYPERVARIABILITY

Complementarity-determining regions (CDRs)



CANONICAL STRUCTURES



H1

1	2	3
---	---	---

H2

1	2
3	4

H3

No canonical structure

L1

Kappa			
1	2a	2b	3
4	5	6	
Lambda			
1	2	3	4

L3

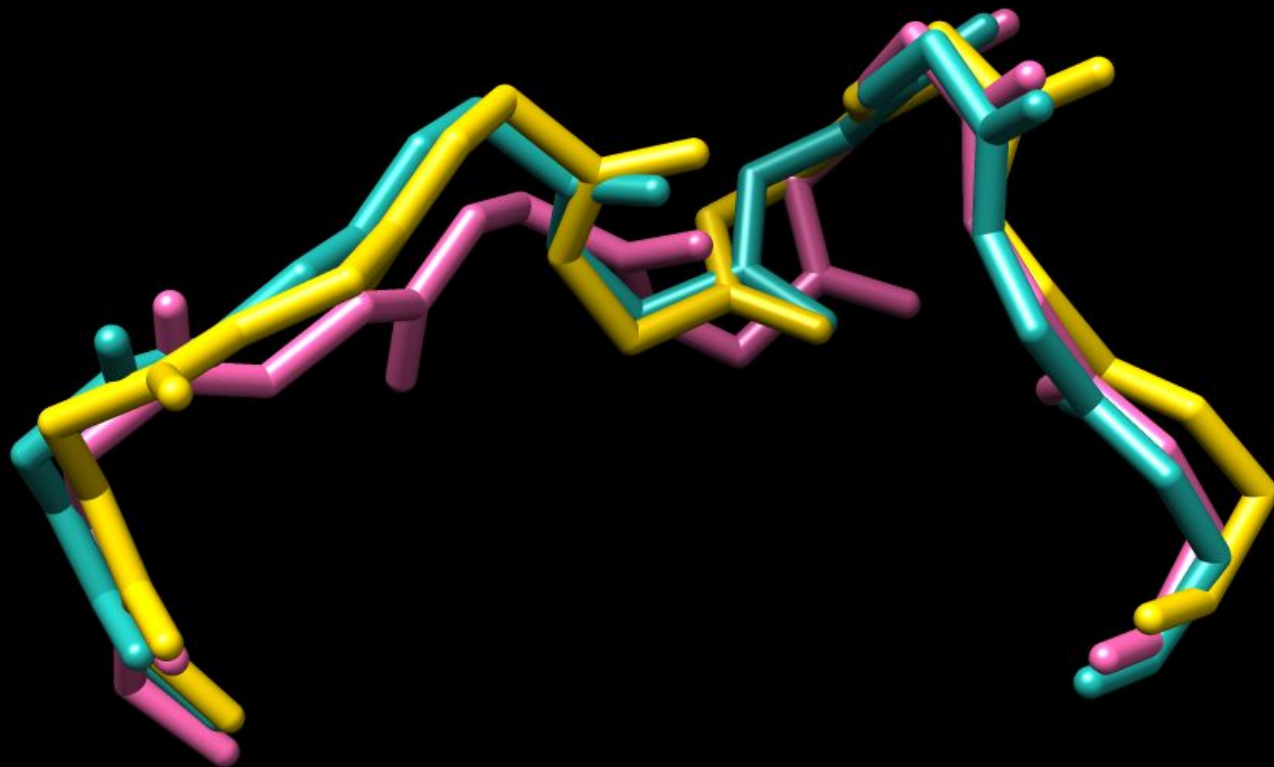
Kappa					
1	2	3	4	5	6
Lambda					
1	2				

L2

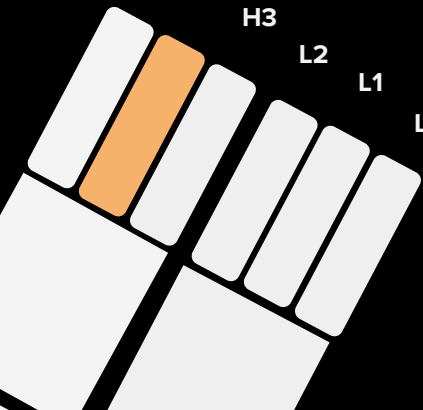
Only 1

CANONICAL STRUCTURES

H1



H2
H1
H3
L2
L1
L3



CANONICAL STRUCTURES

H1



H2

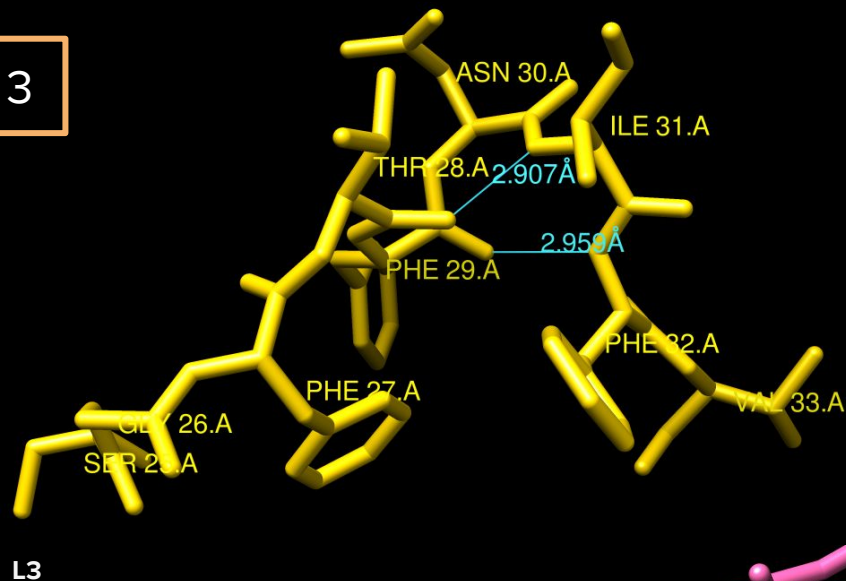
H1

H3

L2

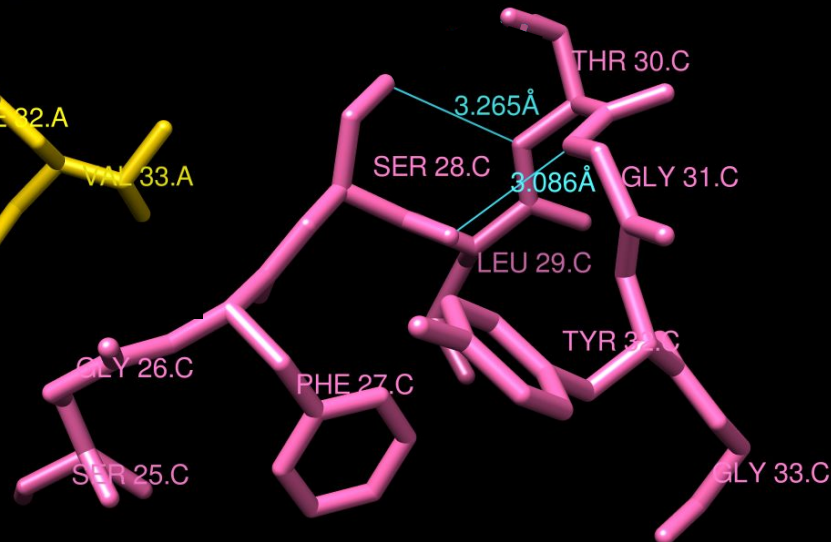
L1

L3



1igm

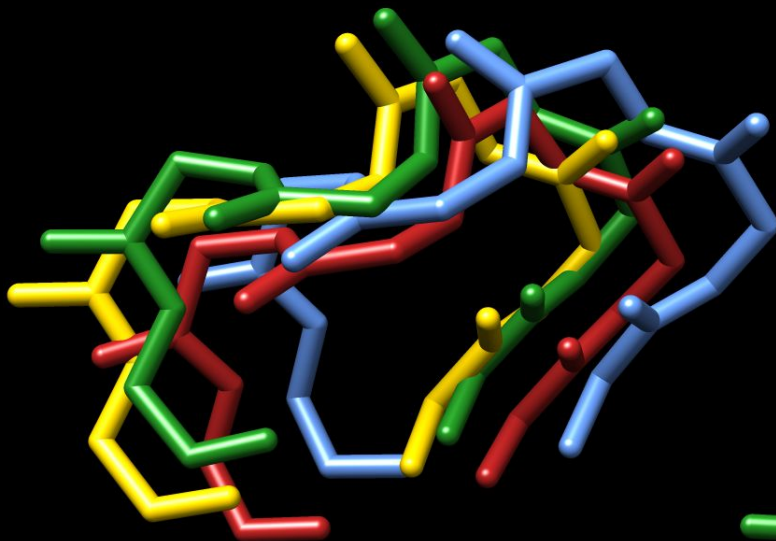
1vfa



CANONICAL STRUCTURES

H2

1	2
3	4



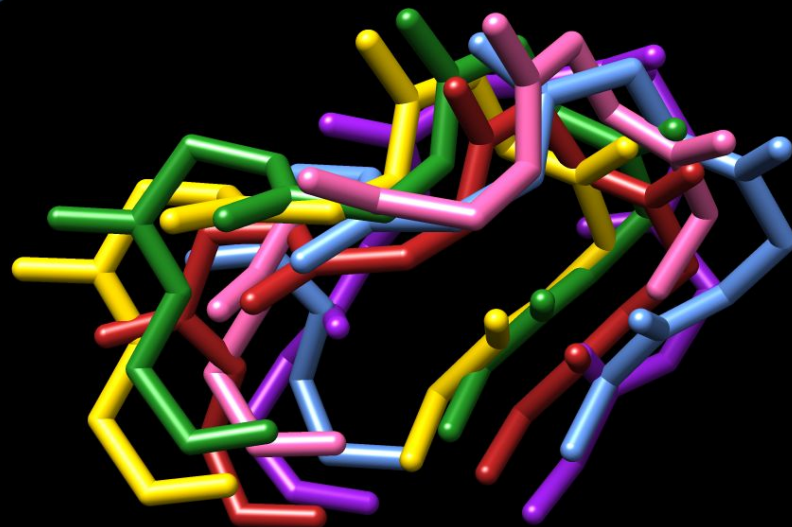
2fb4

1hil

2fbj

8fab

A



H2

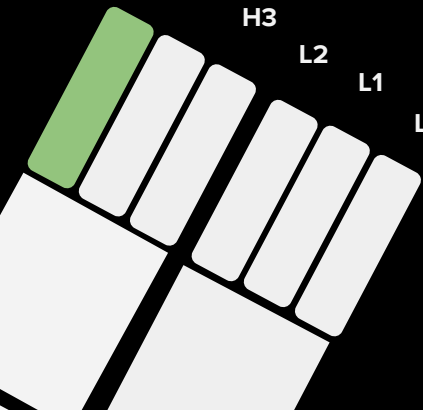
H1

H3

L2

L1

L3



1ind

B

1igm

C

CANONICAL STRUCTURES

H2

1	2
3	4

H2

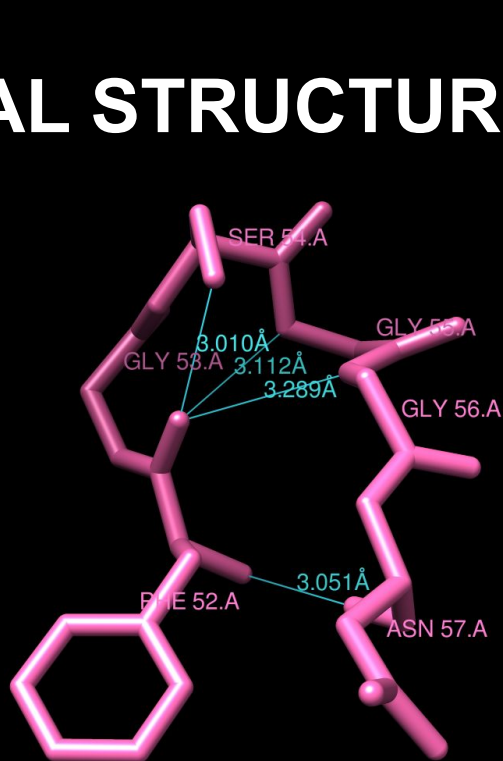
H1

H3

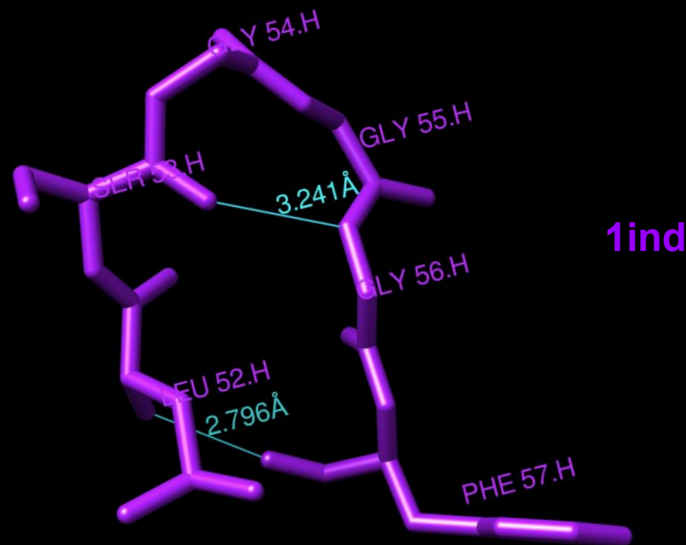
L2

L1

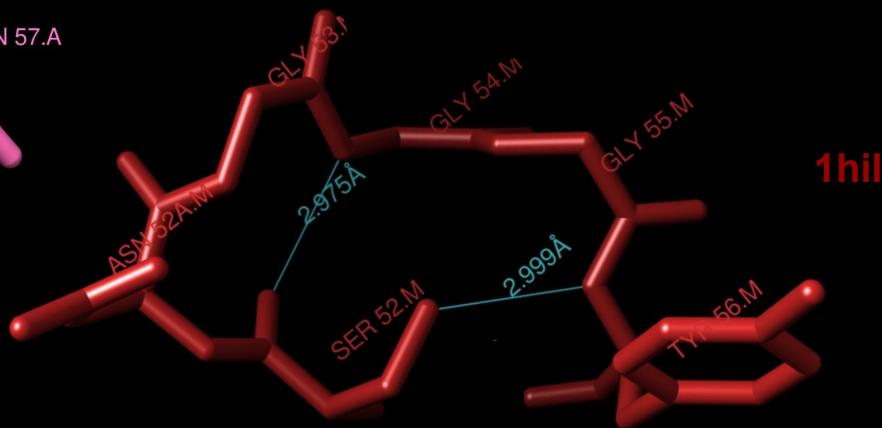
L3



1igm



1ind

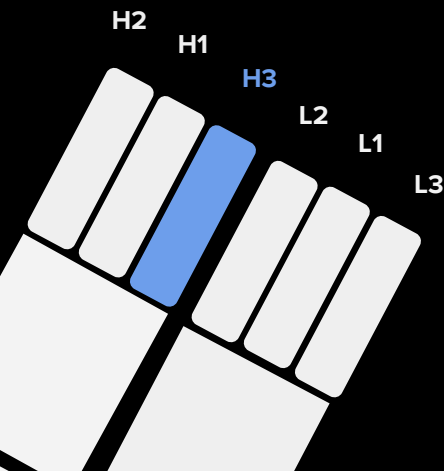


1hil

CANONICAL STRUCTURES

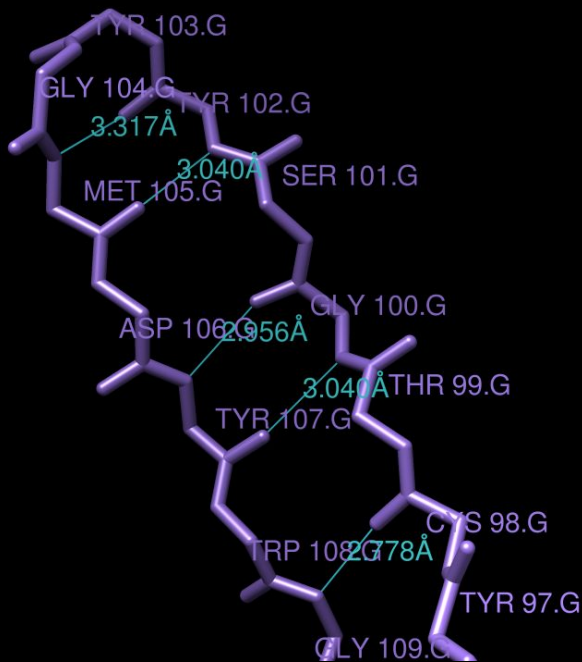
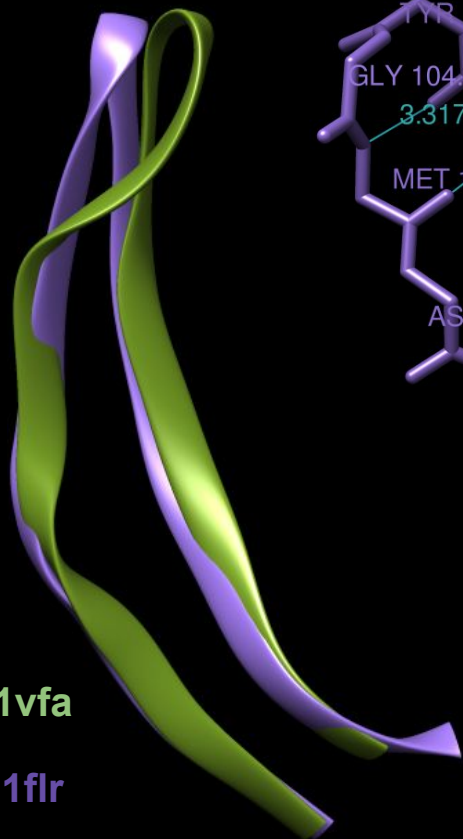
H3

No
canonical
structure

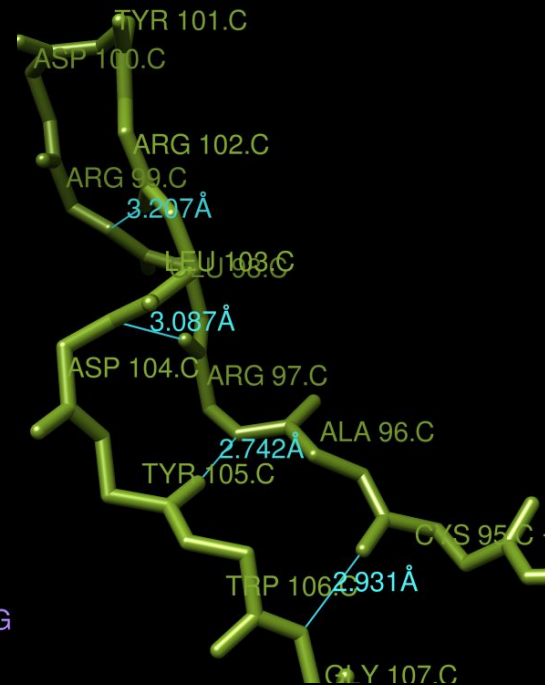


1vfa

1flr



Non-bulged
Extended

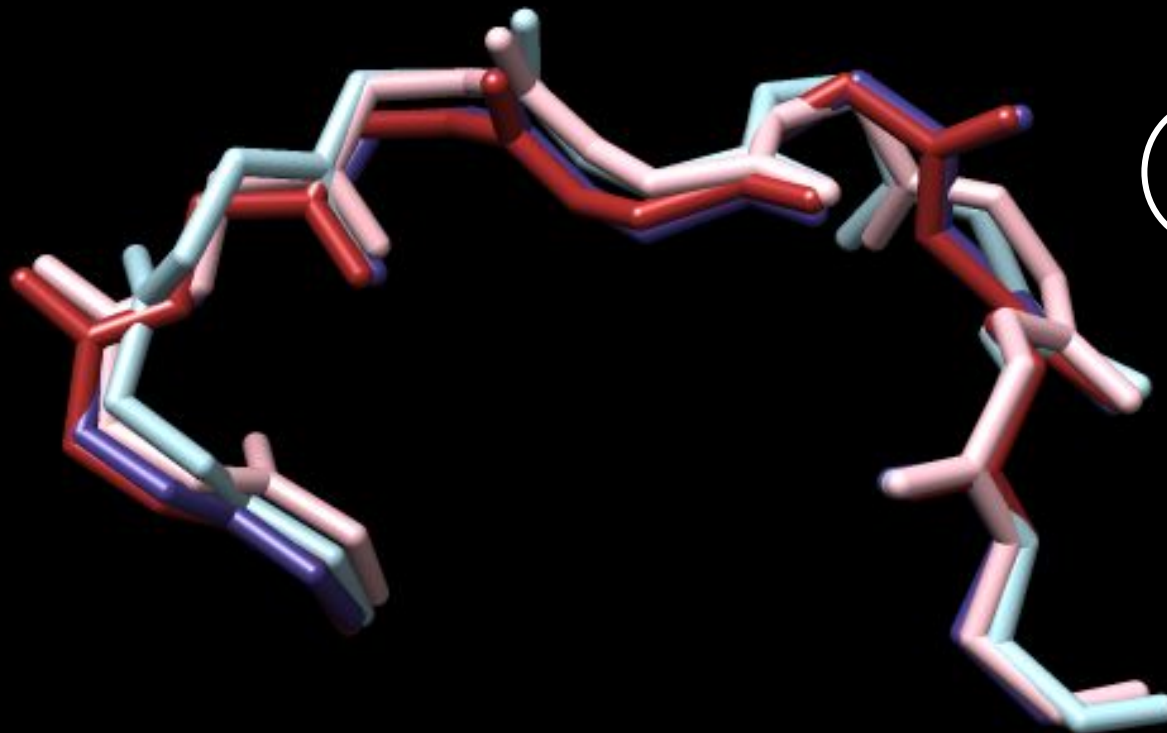
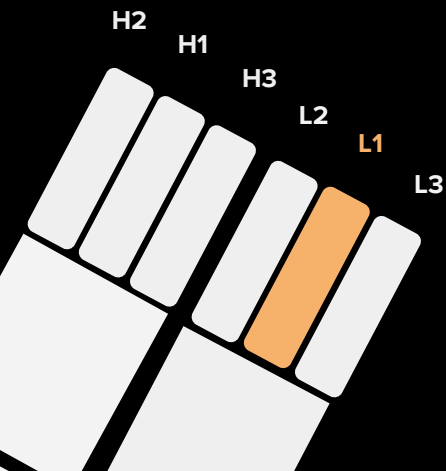


Bulged
Kinked

CANONICAL STRUCTURES

L1

Kappa			
1	2	3	
4	5	6	
Lambda			
1	2	3	4



1igm
1fvc

A

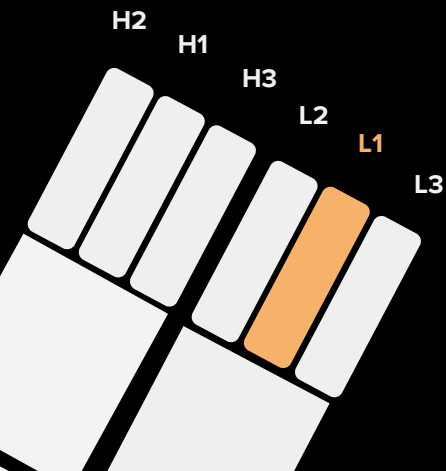
1fgv
1vfa

B

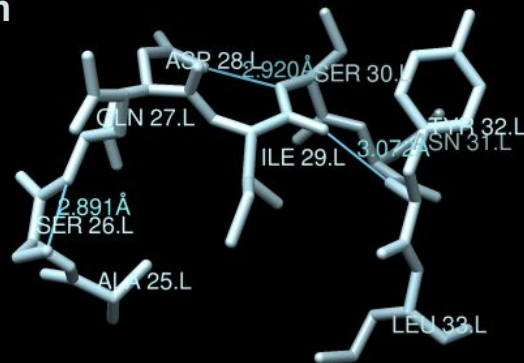
CANONICAL STRUCTURES

L1

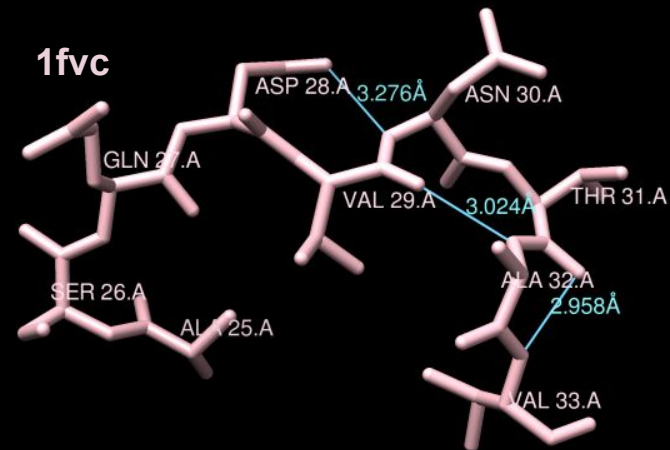
Kappa			
1	2	3	
4	5	6	
Lambda			
1	2	3	4



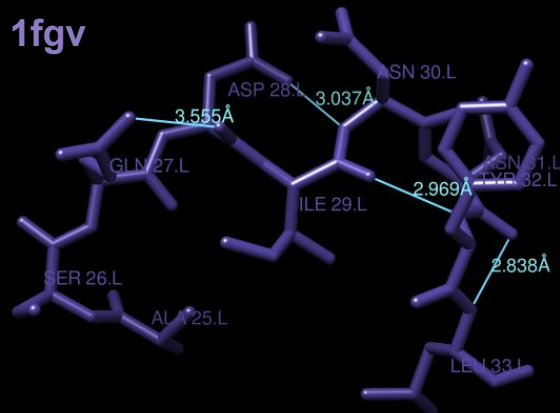
1igm



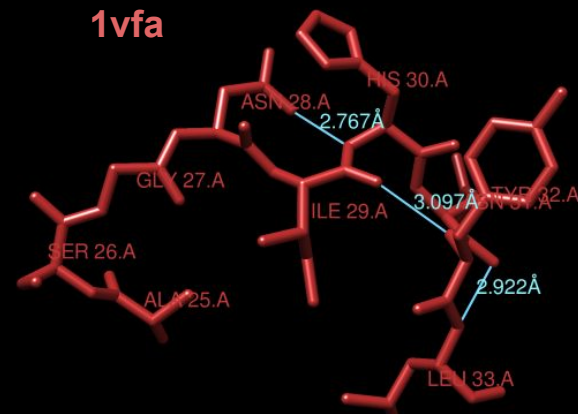
1fvc



1fgv



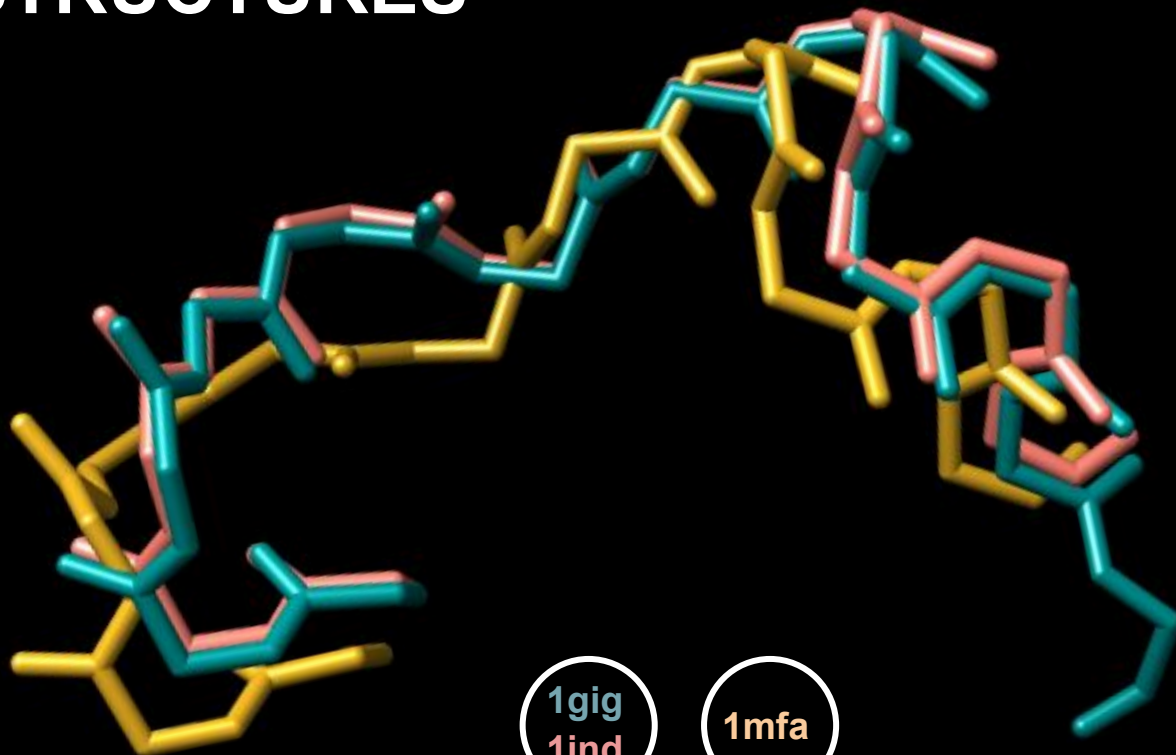
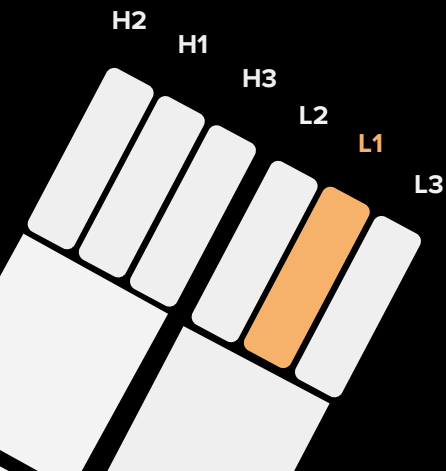
1vfa



CANONICAL STRUCTURES

L1

Kappa		
1	2	3
4	5	6
Lambda		
1	2	3
4	5	6



1gig
1ind

A

1mfa

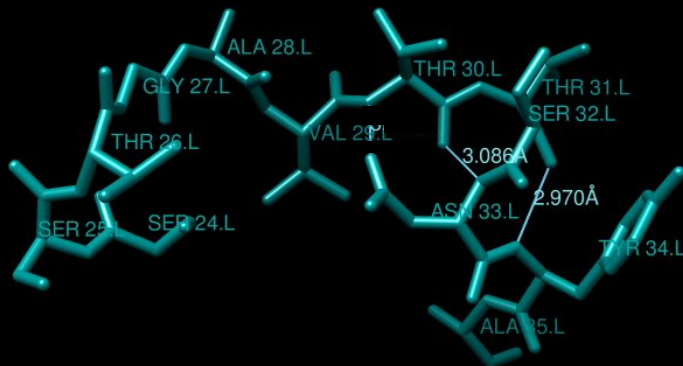
B

CANONICAL STRUCTURES

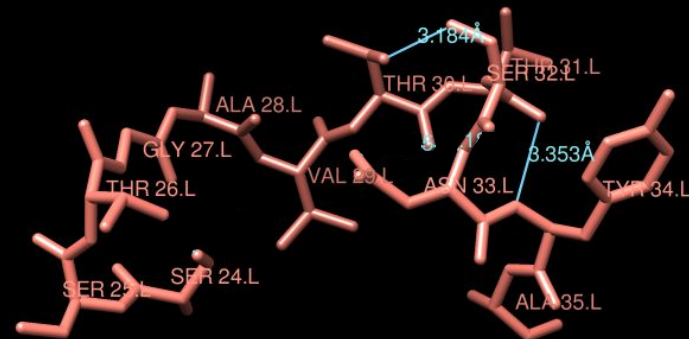
L1

Kappa		
1	2	3
4	5	6
Lambda		
1	2	3
		4

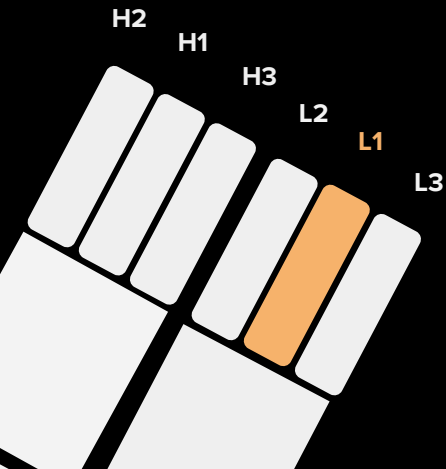
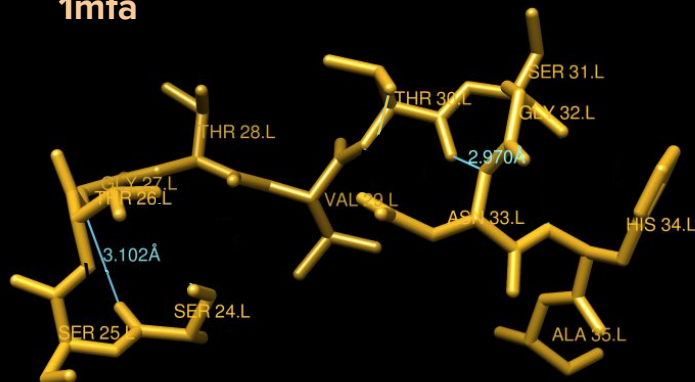
1gig



1ind



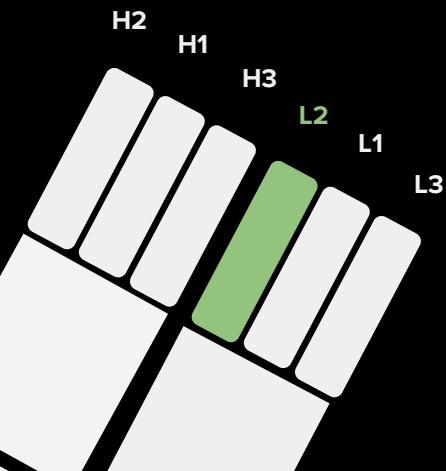
1mfa



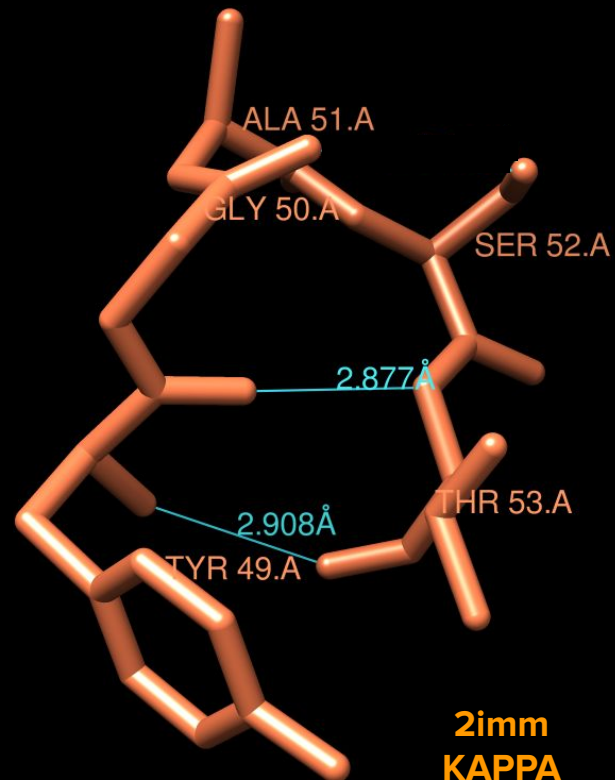
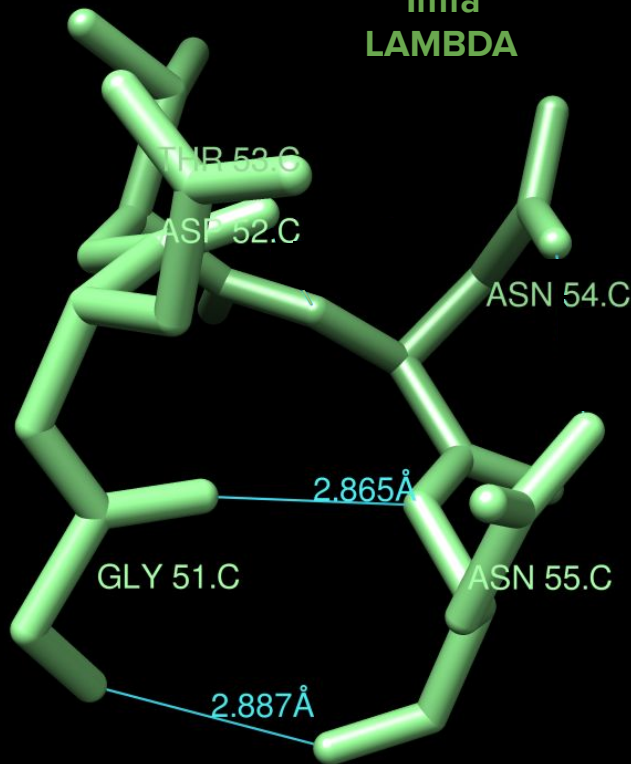
CANONICAL STRUCTURES

L2

Only 1



1mfa
LAMBDA

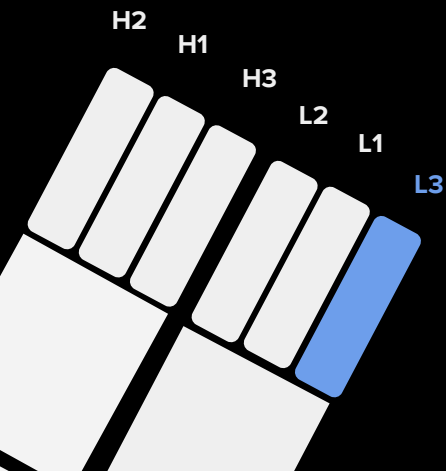


2imm
KAPPA

CANONICAL STRUCTURES

L3

Kappa					
1	2	3	4	5	6
Lambda					
		1	2		



2imm

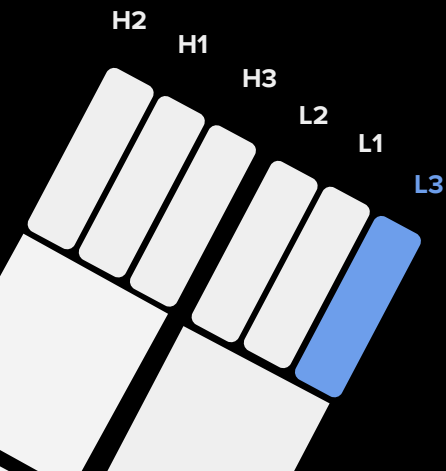
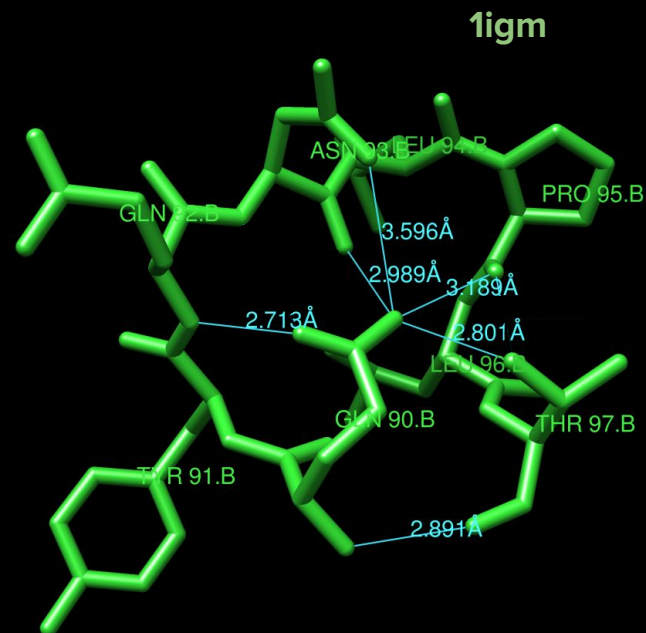
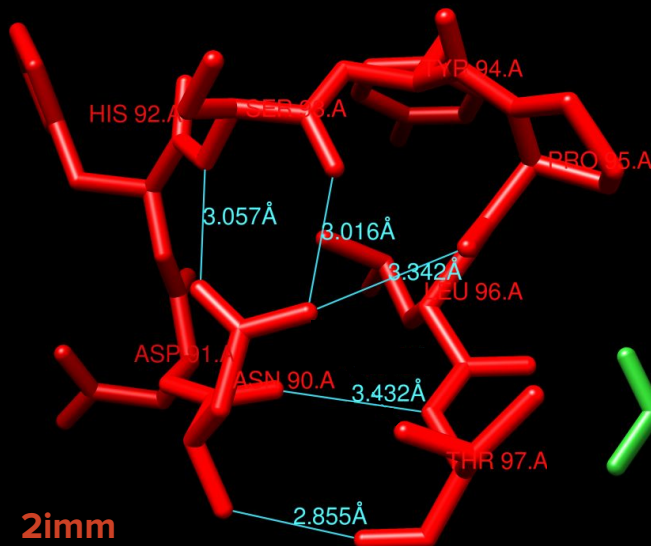
1igm

1fvc

CANONICAL STRUCTURES

L3

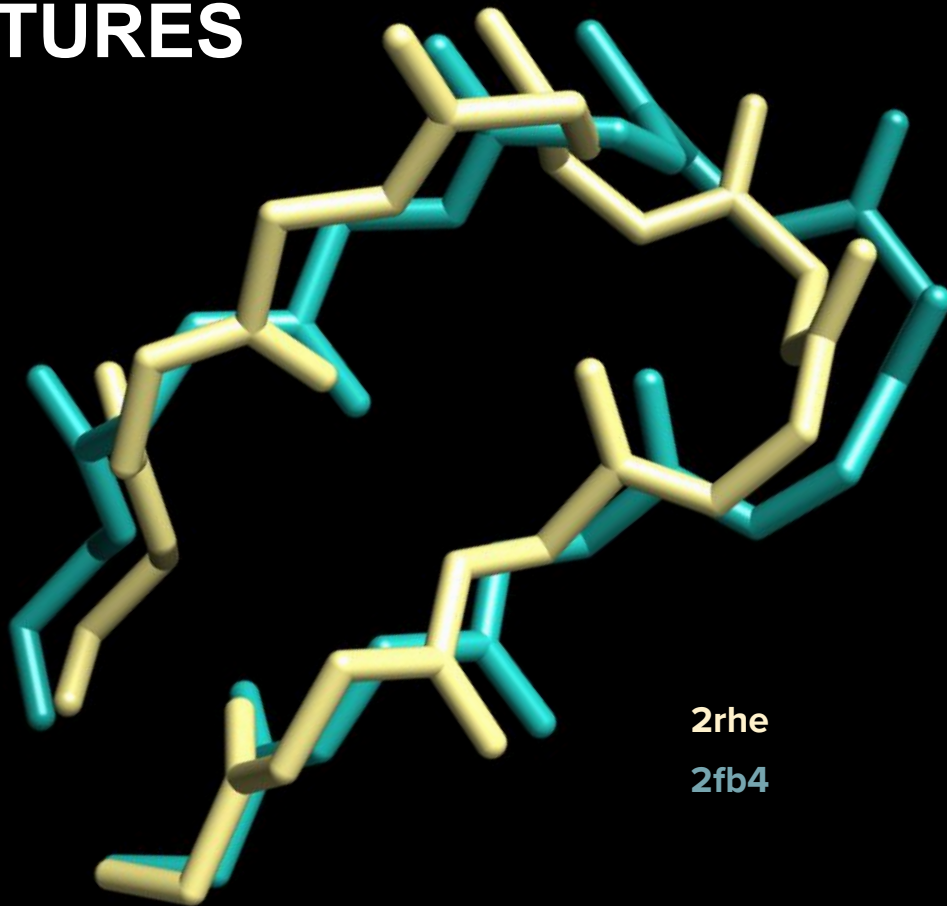
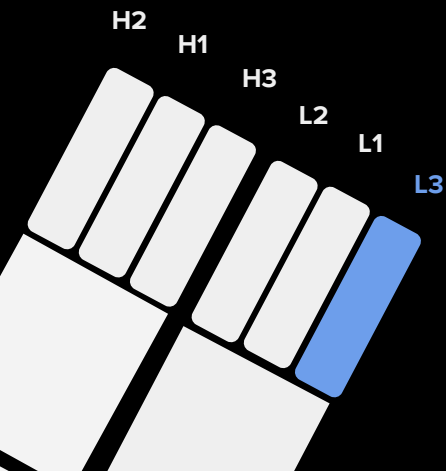
Kappa					
1	2	3	4	5	6
Lambda					
		1	2		



CANONICAL STRUCTURES

L3

Kappa					
1	2	3	4	5	6
Lambda					
		1	2		



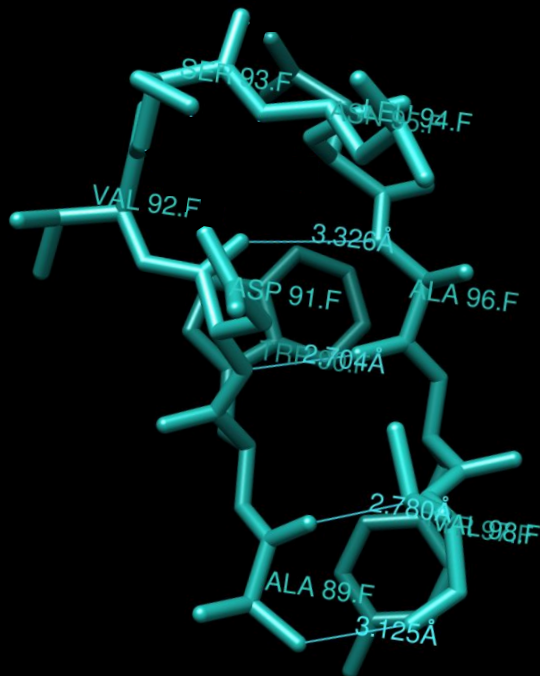
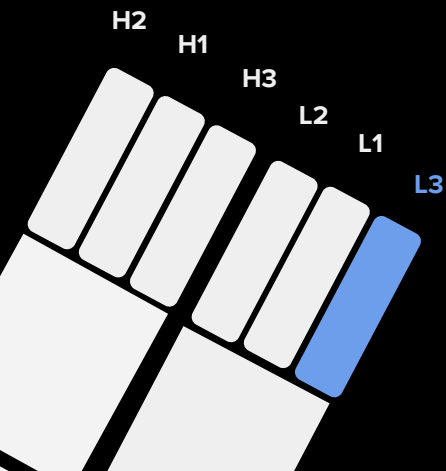
2rhe

2fb4

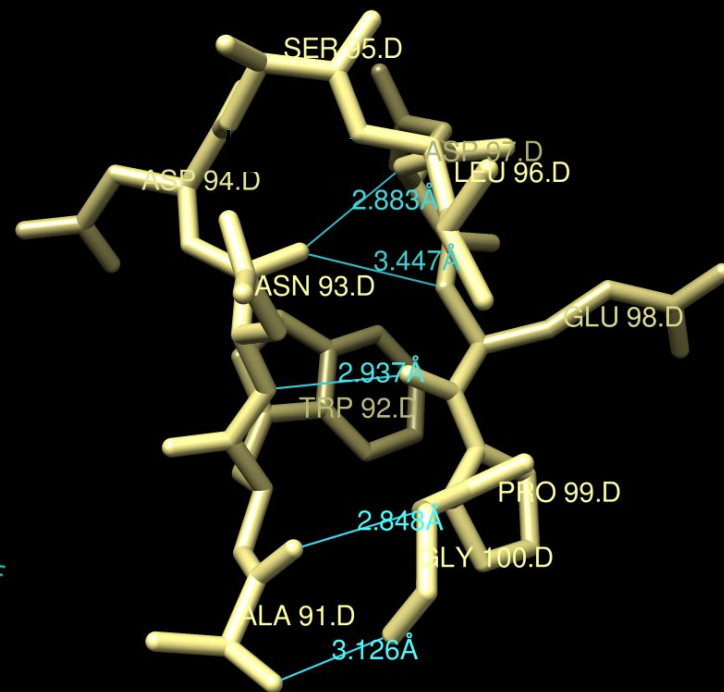
CANONICAL STRUCTURES

L3

Kappa					
1	2	3	4	5	6
Lambda					
1	2				



2fb4



2rhe

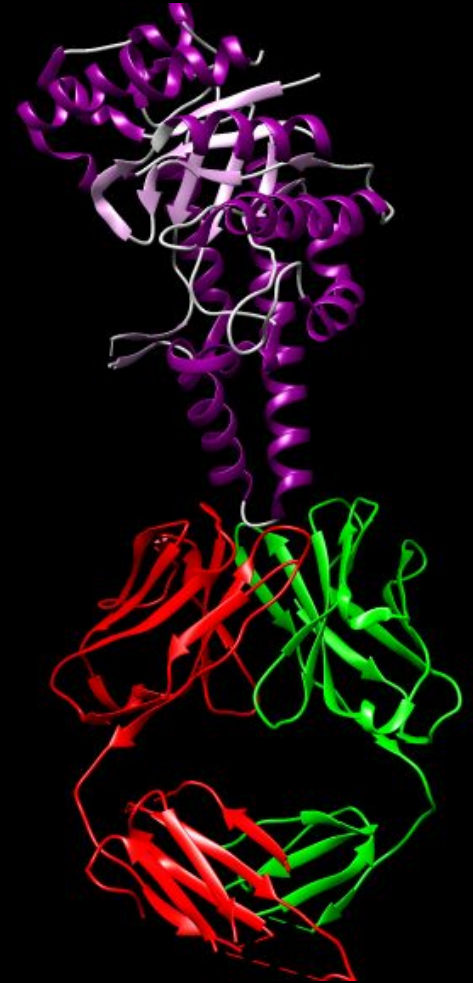
IgG - ANTIGEN INTERACTION

IgG-antigen

The forces involved in non covalent interactions are:

- Electrostatic forces
- Hydrogen bonds
- Van der Waals
- Hydrophobic forces
- Pi-cation interaction

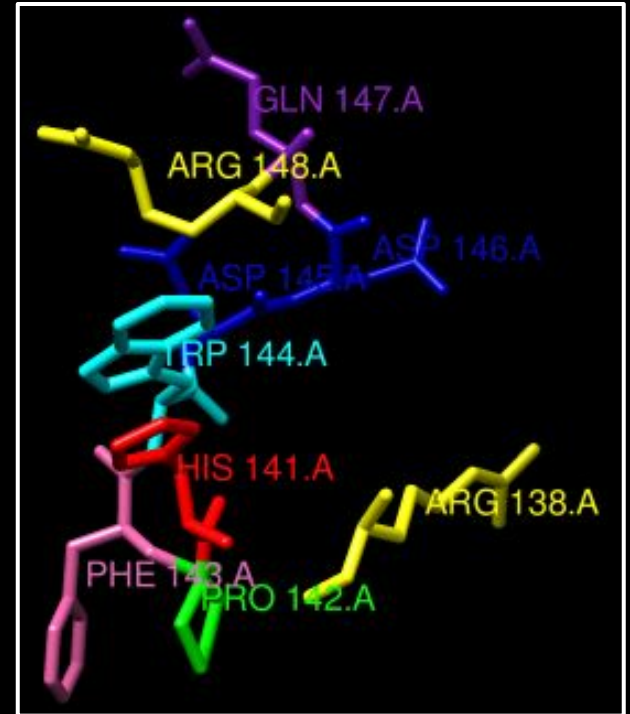
The immunoglobulins have many aromatic aminoacids in antigen binding site which participate mainly in Van der Waals and hydrophobic interactions.



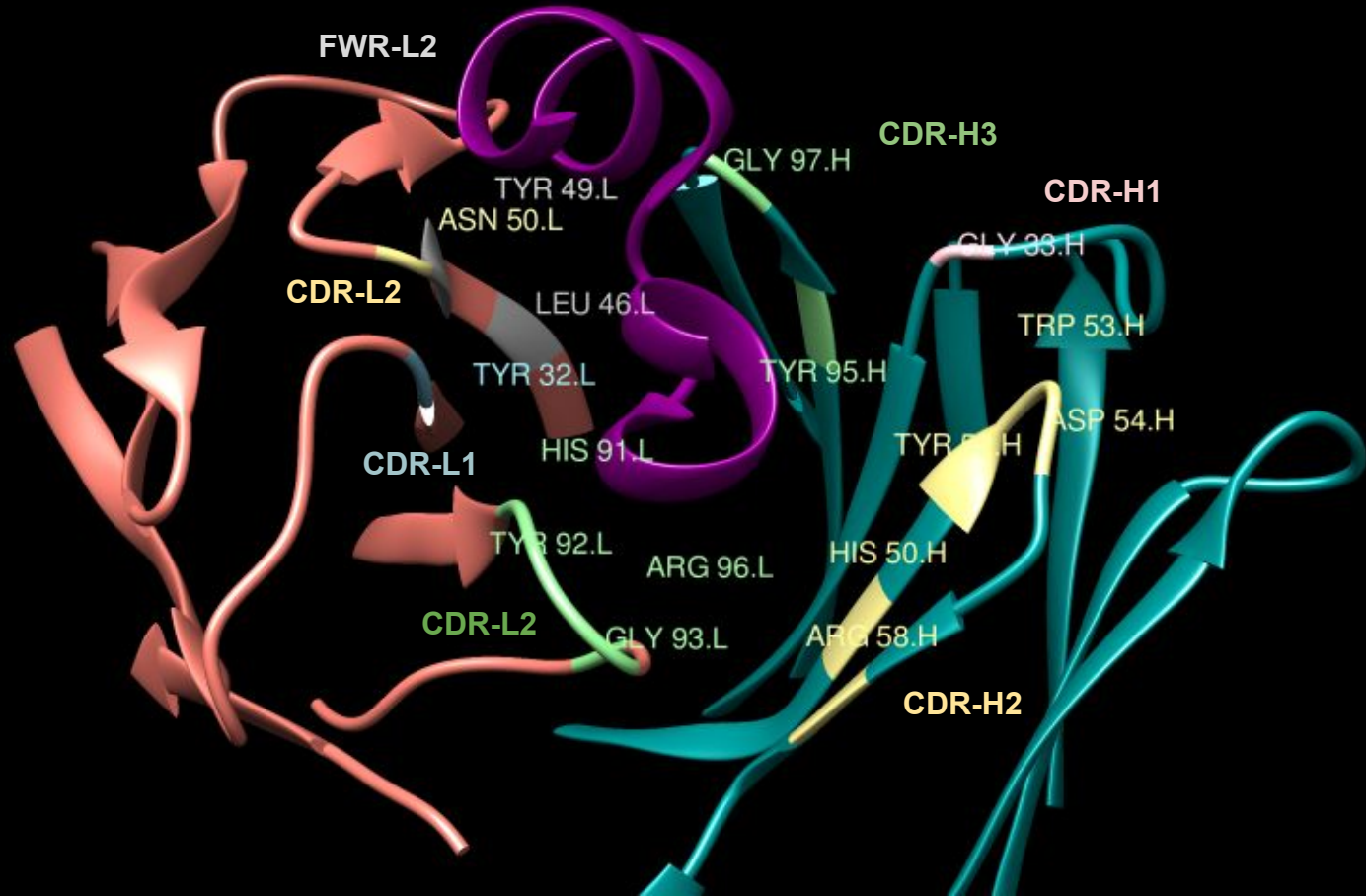
IgG-Hyaluronidase: Fold and Epitope



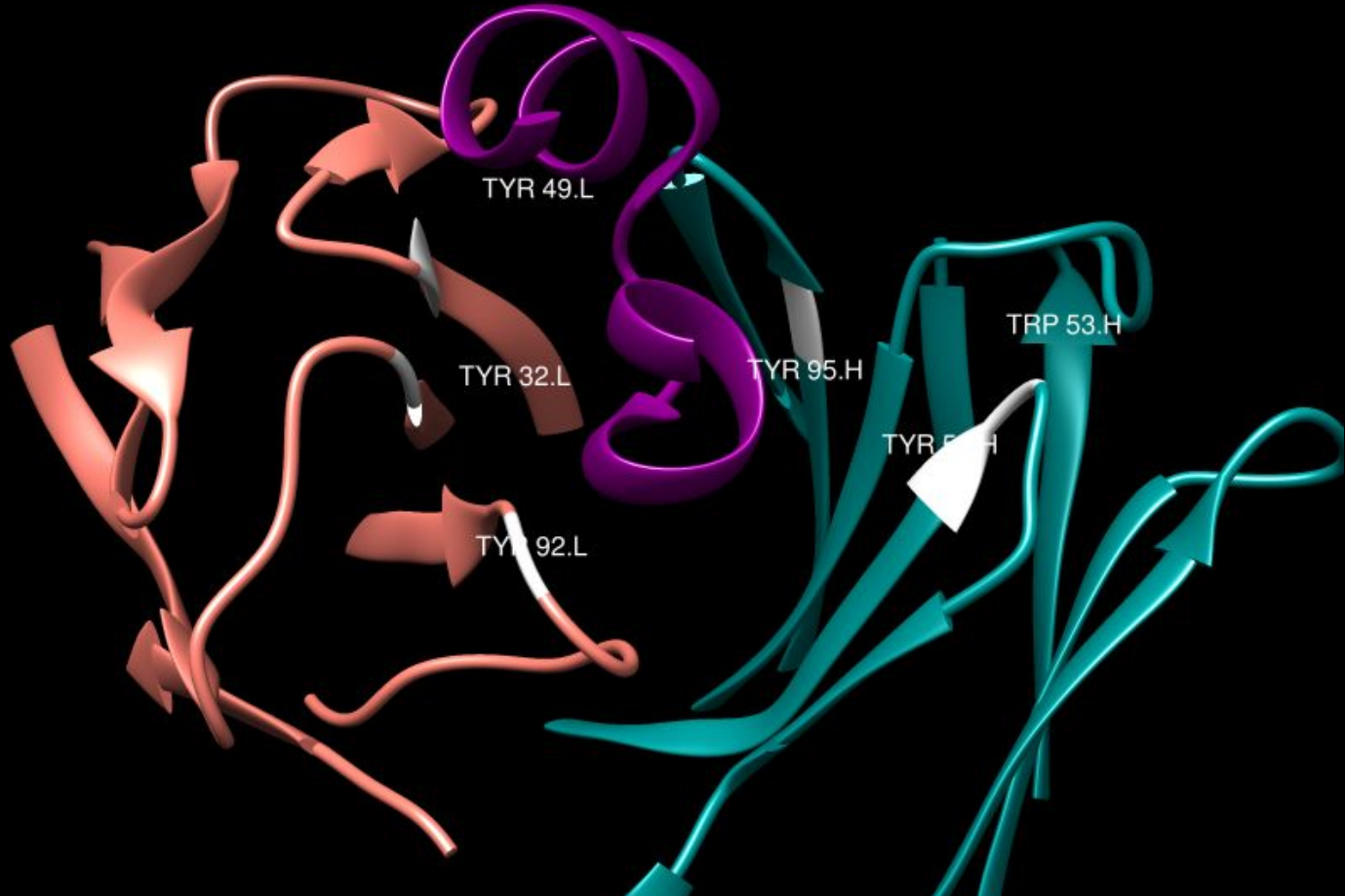
R+HPFWDDQR



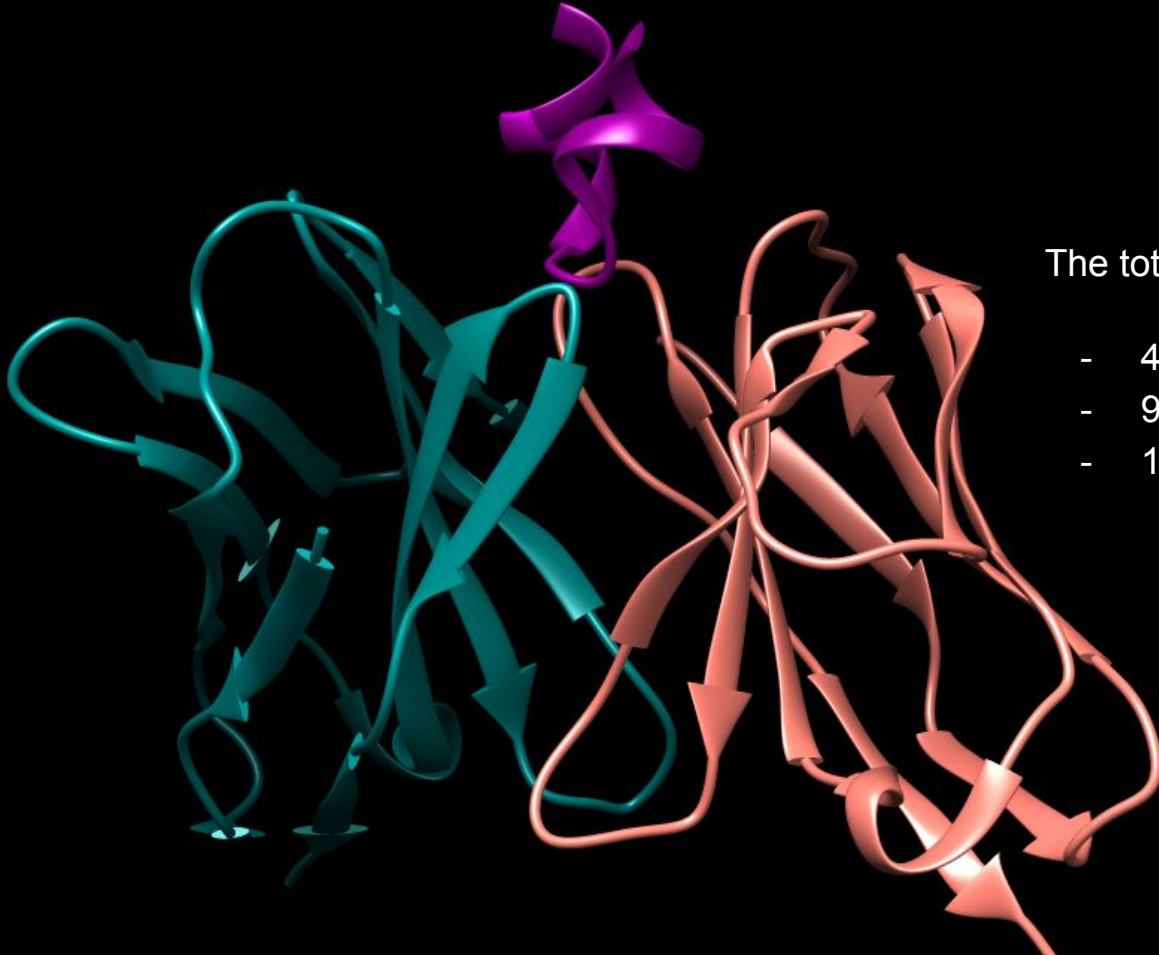
IgG-hyaluronidase: Fab-Hyal interaction



IgG-hyaluronidase: Aromatic amino acids



IgG-hyaluronidase: Fab-Hyal interaction

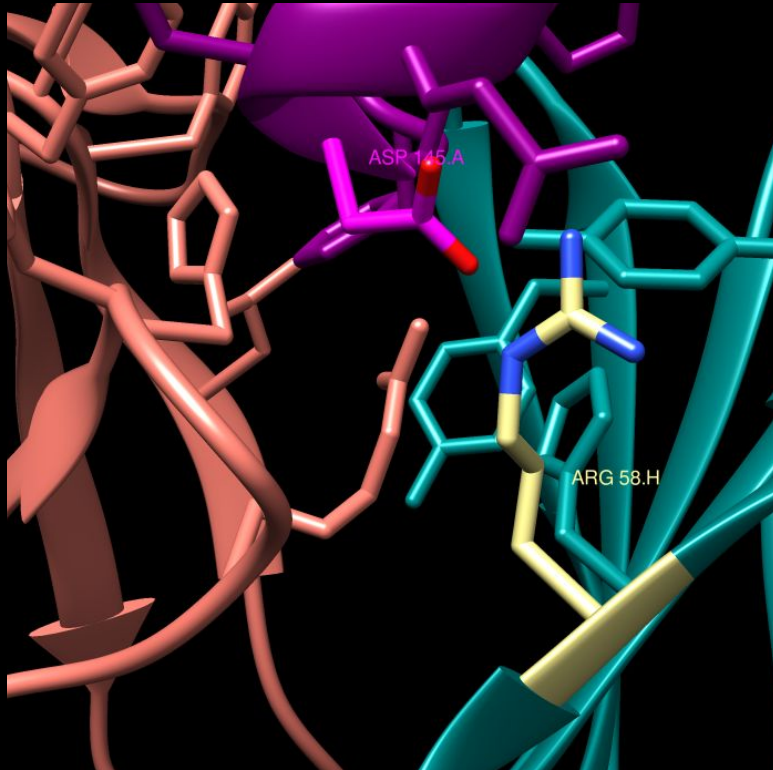


The total number of Hyal/Fab interactions:

- 4 salt bridges
- 9 hydrogen bonds
- 11 Van der Waals

IgG-hyaluronidase: Salt bridges

CDR-H2: ARG 58 - ASP 145, 3.2 Å

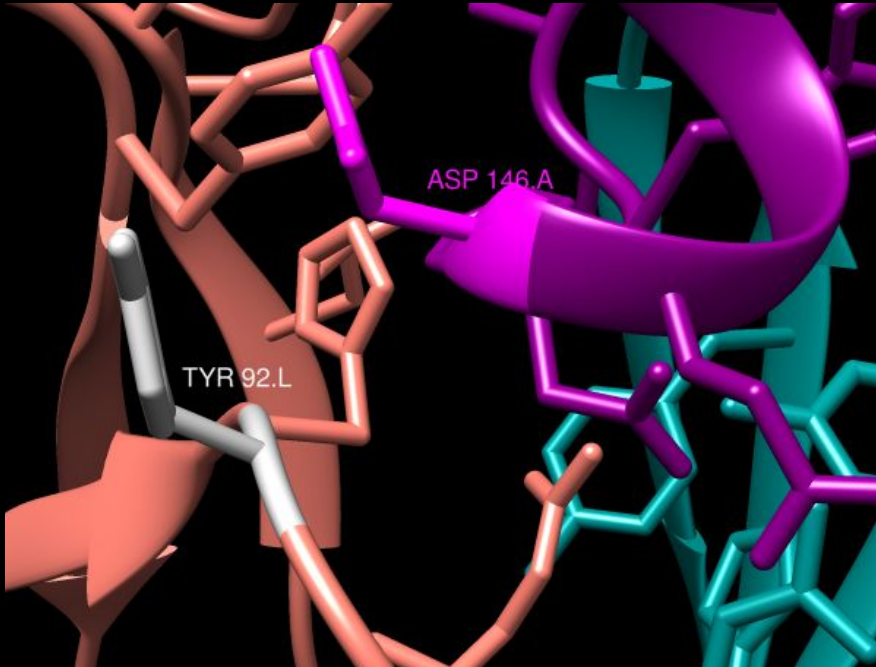


CDR-H2: ASP 54 - ARG 148, 3.2 Å

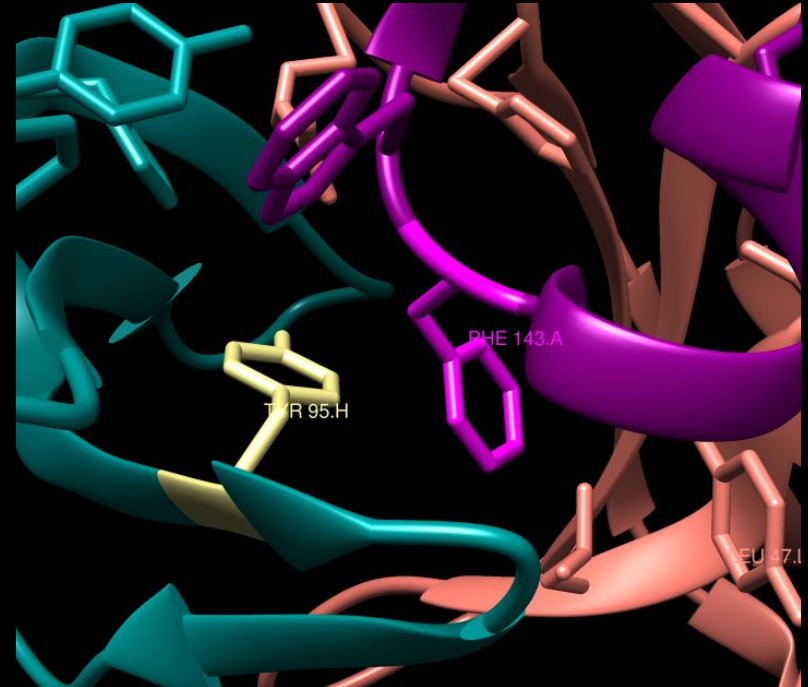


IgG-hyaluronidase: Van der Waals

CDR-L3: TYR 92 - ASP 146, 3.6 Å

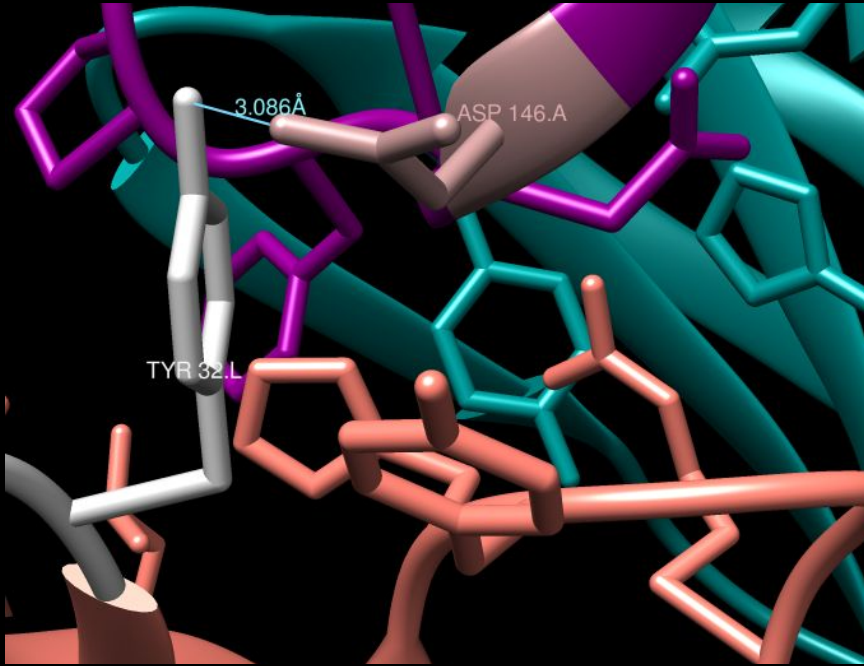


CDR-H3: TYR 95 - PHE 143, 3.5 Å

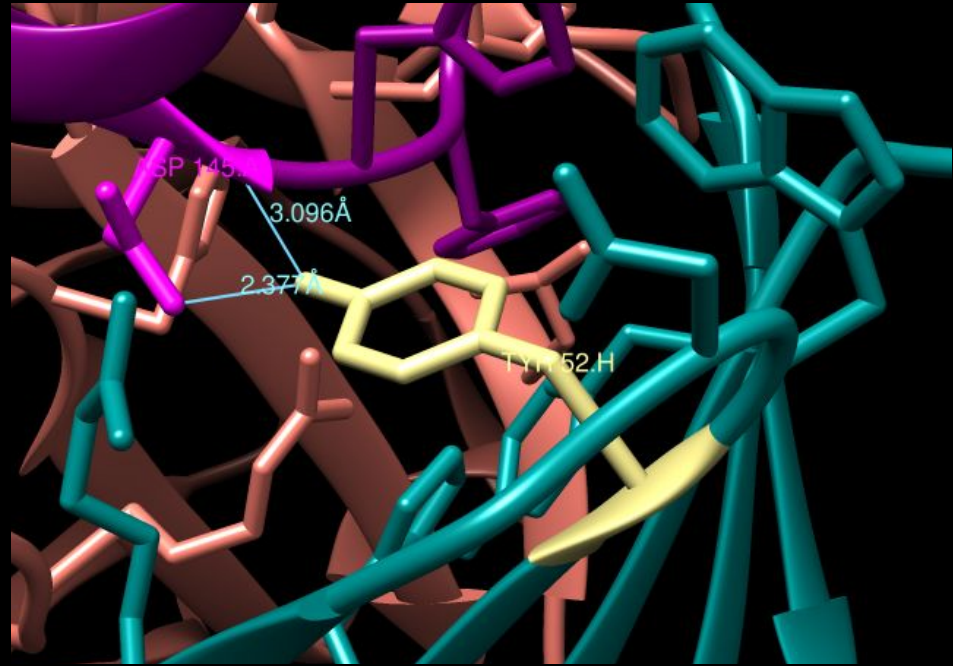


IgG-hyaluronidase: Hydrogen bonds

CDR-L1: TYR 32 - ASP 146, 3.1 Å



CDR-H2: TYR 52 - ASP 145, 3.1 Å

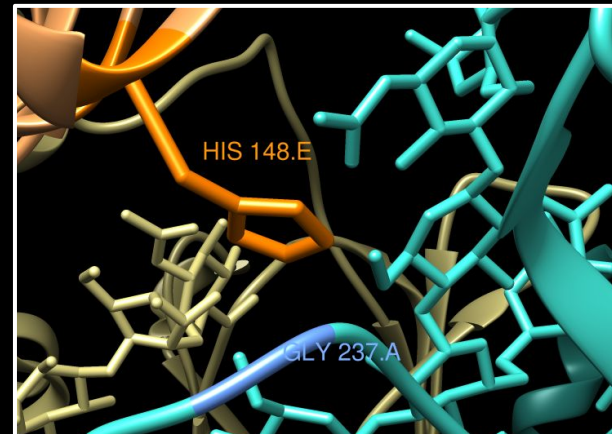
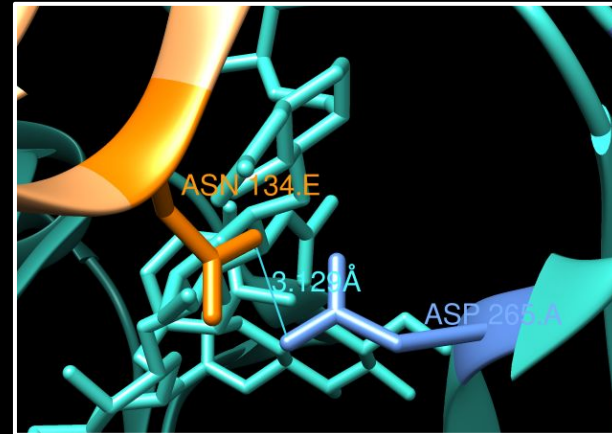


IgG - FcγRI INTERACTION

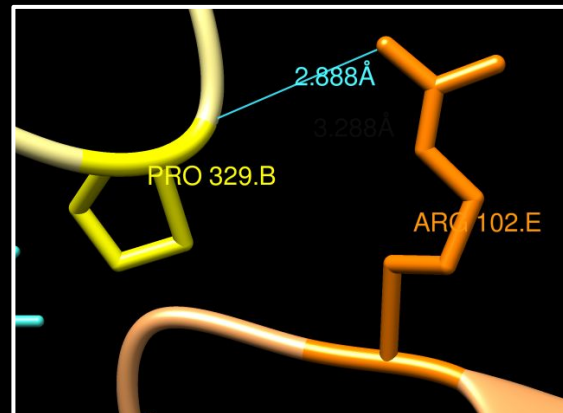
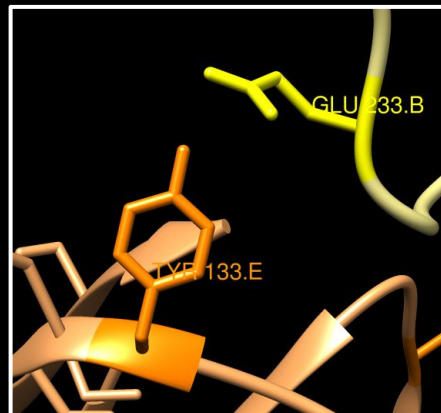
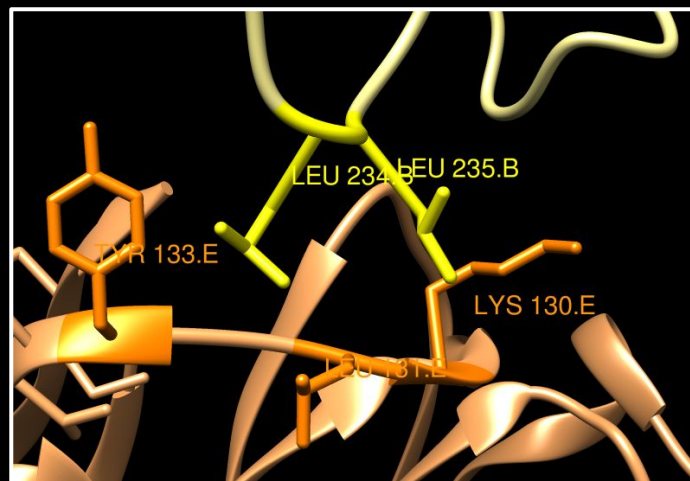
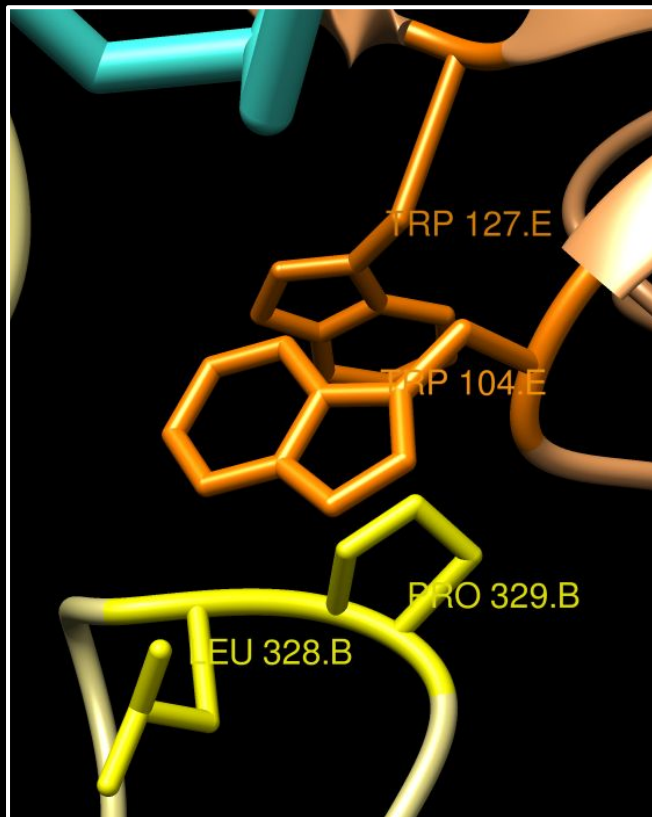
IgG-FcγRI



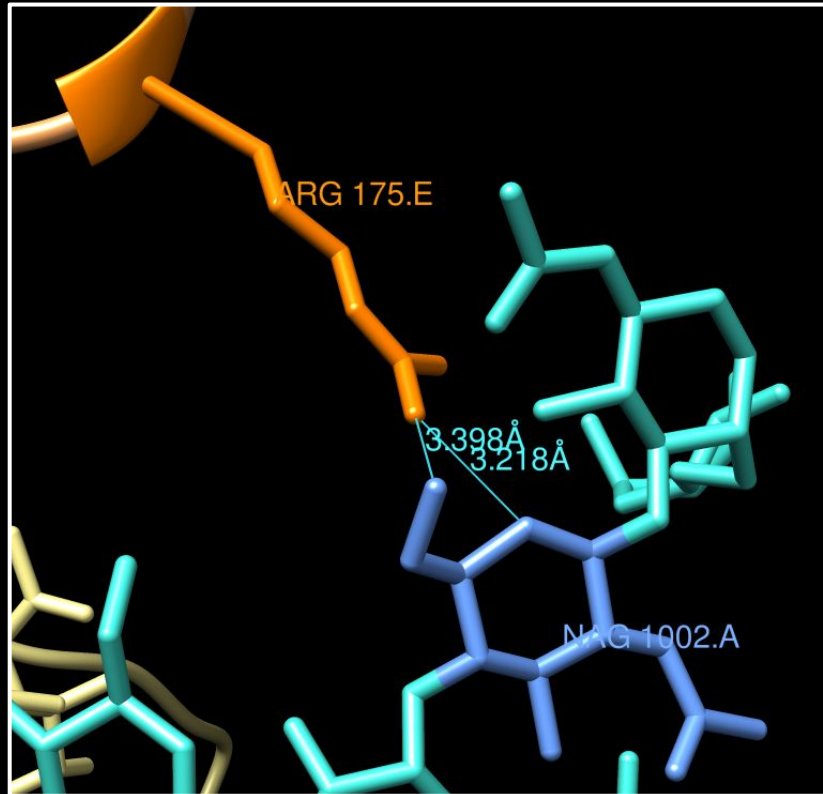
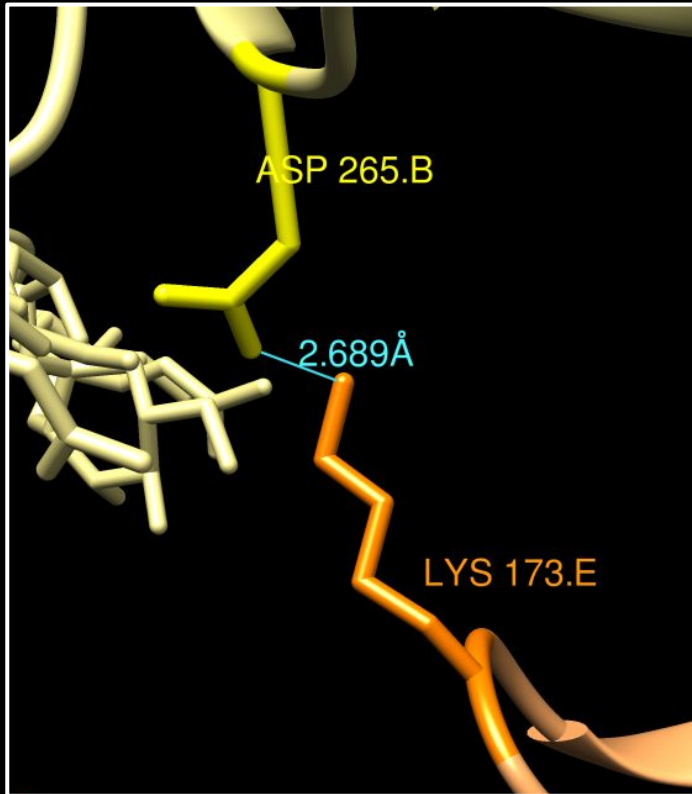
IgG-FcγRI: Region 1



IgG-FcγRI: Region 2



IgG-FcγRI: Region 3



CONCLUSIONS

- The immunoglobulins have an important function in the **immune system**.
- The **diversity** of immunoglobulins allows them to recognize specifically a great variety of **antigens**, as we have seen in hyaluronidase-IgG1 interaction.
- The Ig domain is formed by **two β -sheets** built up with several **antiparallel β -strands** with a **Greek key** topology. These β -sheets are covalently linked with a **disulfide bond**.
- The flexibility of the immunoglobulin is conferred, in large part, by the **hinge region**.

- The heavy chain can exist in two forms: a soluble one and a surface one.
- The Fc of immunoglobulins is majorly conserved in the IgG.
- N-glycosylation plays a key role in the interactions with the effector cells.
- The **CDRs** are the hypervariable regions of the immunoglobulin. They contribute to its specificity and form the **antigen binding site**. There are 3 in the light chain (**L1**, **L2** and **L3**) and 3 in the heavy chain (**H1**, **H2** and **H3**).
- Although the great variation of the CDRs, they have small main chain conformations that are called **canonical structures**.

Bibliography

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Questions

About the basic concepts of immunoglobulins:

- a) Structural differences in Fab fragment are the basis for five different isotypes classes of immunoglobulins.
- b) In immunoglobulin G the disulfide bonds are formed between cysteine residues of constant domain 2 close to the hinge.**
- c) The Fc fragment are formed by the association of variable and constant domains of light chain, and the variable and constant 1 domains of heavy chain.
- d) There are four different types of light chain.
- e) There are three loci that encode for heavy chain.

The difference between the fold of the variable domain and the constant domain is:

- a) The constant domain contains two extra β -strands called C' and C''
- b) The constant domains hasn't got a Greek Key topology
- c) a and b are true
- d) The variable domain contains two extra β -strands called C' and C''**
- e) There is no difference between them

About the Fab arm exchange, which of the following is false:

- a) **It is characteristic from IgG3**
- b) Involves that the core hinge forms intra- rather than inter heavy chain disulfide bonds
- c) It affects both, covalent and non covalent interaction
- d) Half molecules can recombine to create bispecific immunoglobulines
- e) All of them are true

The flexibility of the immunoglobulin is conferred in large part by:

- a) The constant domain
- b) The variable domain
- c) **The hinge**
- d) The light chain
- e) The heavy chain

About the Fc from immunoglobulin G:

- a) It is not mostly conserved between species
- b) The cysteines that form the disulphide bonds vary between IgGs
- c) There are two possible forms of the heavy chain that differ in the N-terminal end
- d) There are few possible glycosylation patterns
- e) **When the glycosylation is removed the effector functions are impaired**

Which determinant enables IgG4 to undergo Fab arm exchange?:

- a) The hinge
- b) CH3-CH3 domain interface
- c) a and b are true**
- d) CDR L1
- e) All of them are true

About the interaction between hyaluronidase and IgG1:

- a) The hyaluronidase fold is a Beta-alfa-Beta motif.
- b) The epitope is mostly continuous and composed of twenty consecutive residues.
- c) The apolar residues form most of the contacts with Ag.
- d) The hydrophobic residues are located predominantly at the periphery of Hyal binding surface.
- e) The total number of polar Hyal/Fab interactions comprises 4 salt bridges and 9 hydrogen bonds.**

About the Complementary Determining Regions (CDRs):

- a) They are only found in the light chain and its function is to bind with the antigen
- b) They are only found in the heavy chain and its function is to bind with the antigen
- c) They are only found in the light chain and its function is to stabilize the immunoglobuline
- d) They are found in both heavy and light chains and its function is to bind with the antigen**
- e) They are found in both heavy and light chains and its function is to stabilize the immunoglobuline

About the canonical structures of the Complementary Determining Regions (CDRs), mark the false sentence:

- a) All of the CDRs have canonical structures**
- b) The canonical structures are small number of main chain conformations
- c) L2 only have one canonical structure
- d) The H3-CDR is the one with more variability
- e) There are different canonical structures for the same CDR in lambda light chain and in kappa light chain

About the IgG1-FcγRI mark the correct answer:

1. There are no van der Waals interactions in any region
2. We can find three hydrophobic clusters
3. The interactions are with domains D1 and D2 from the receptor
4. The receptor also interacts with the glycan bound to the Fc of the immunoglobulin

- a) 1, 2, 3
- b) 1 i 3
- c) 2 i 4
- d) 4**
- e) 1, 2, 3, 4

