Immune system IgGs

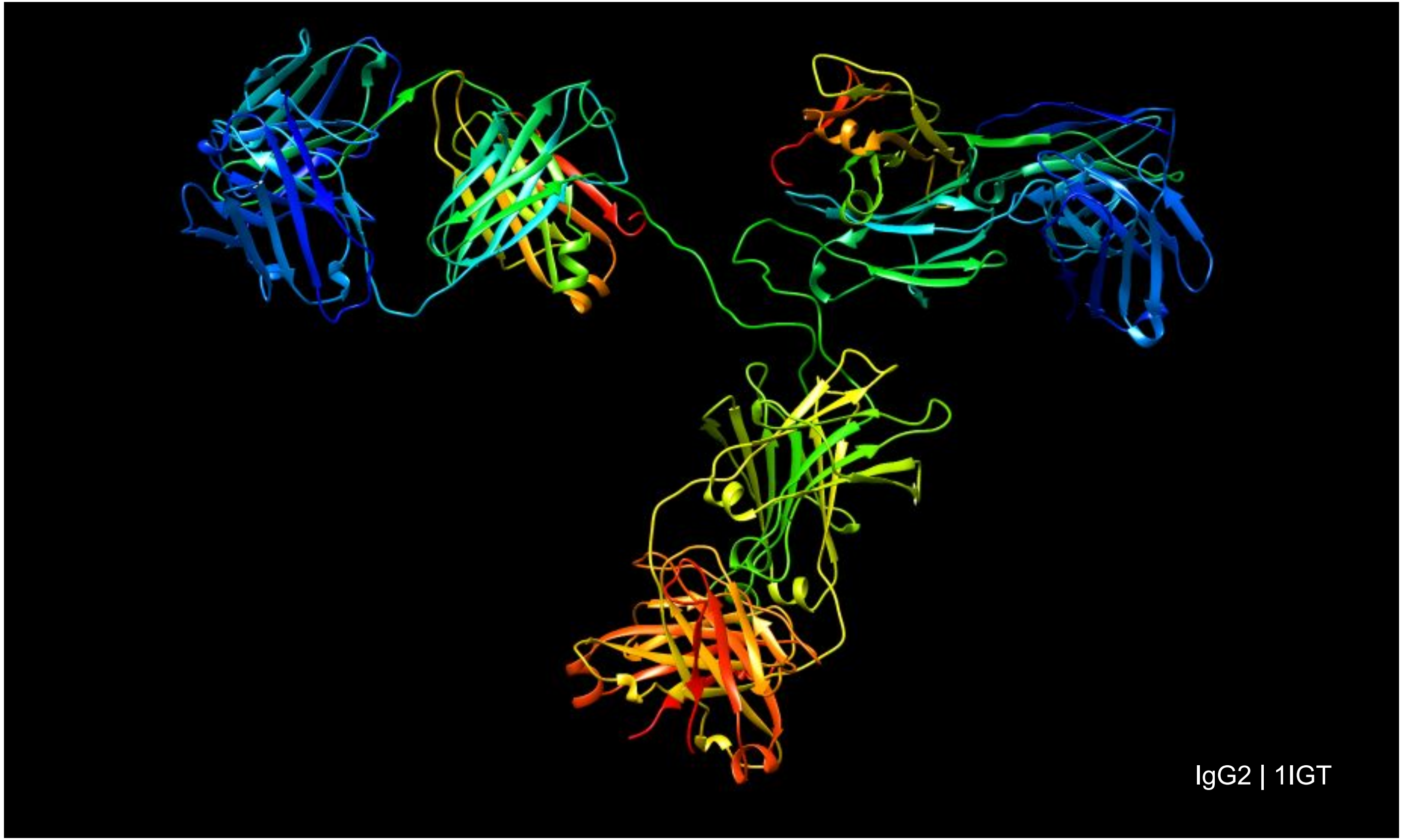
Carla Cortinas, Eva Espigulé, Guillem Lopez-Grado, Margalida Roig, Valentina Salas

Group 2

Index

Introduction

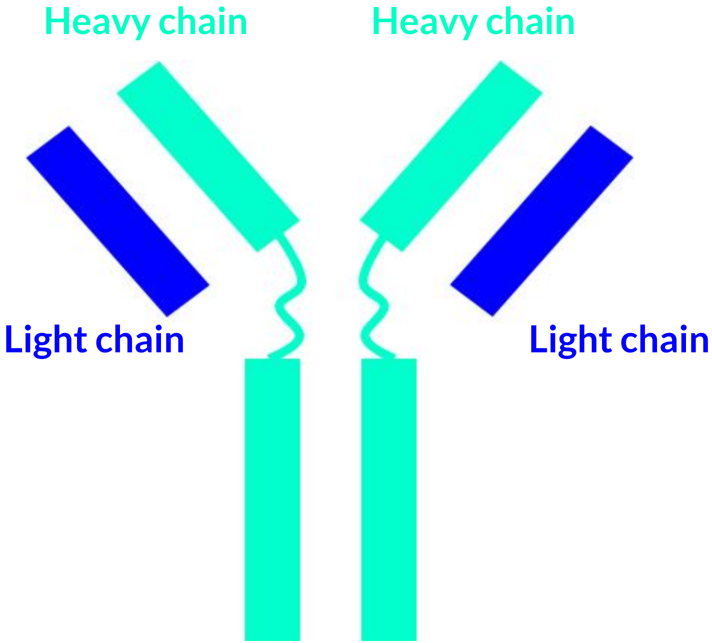
Introduction - Immunoglobulins



IgG2 | 1IGT

Introduction - Immunoglobulins

Ig are formed by 4 chains:

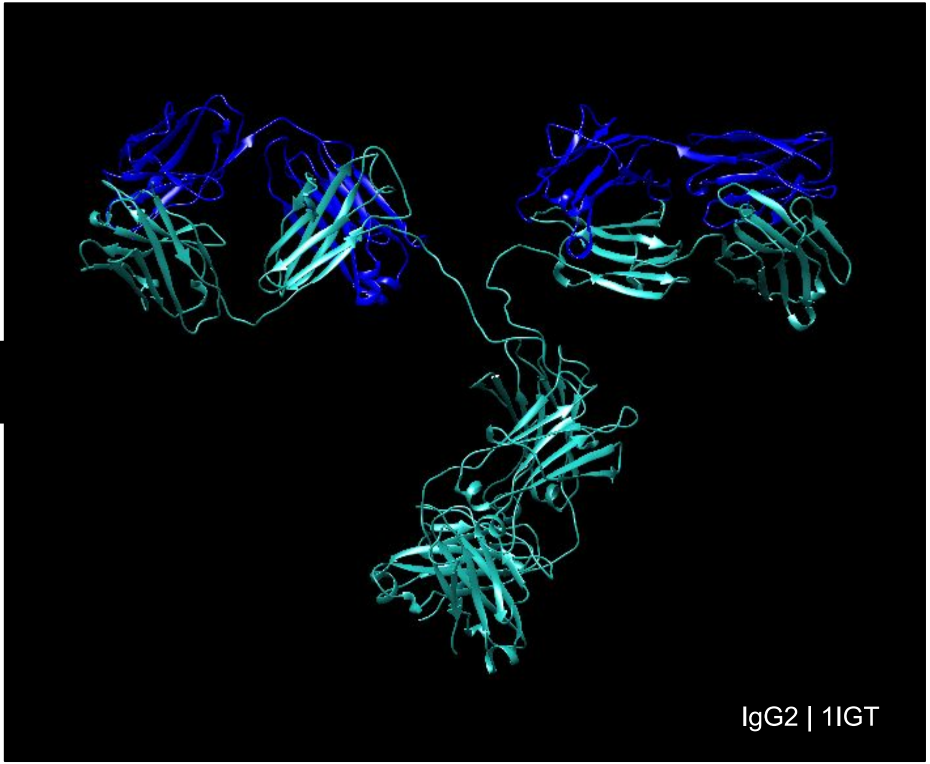


Heavy chain

Heavy chain

Light chain

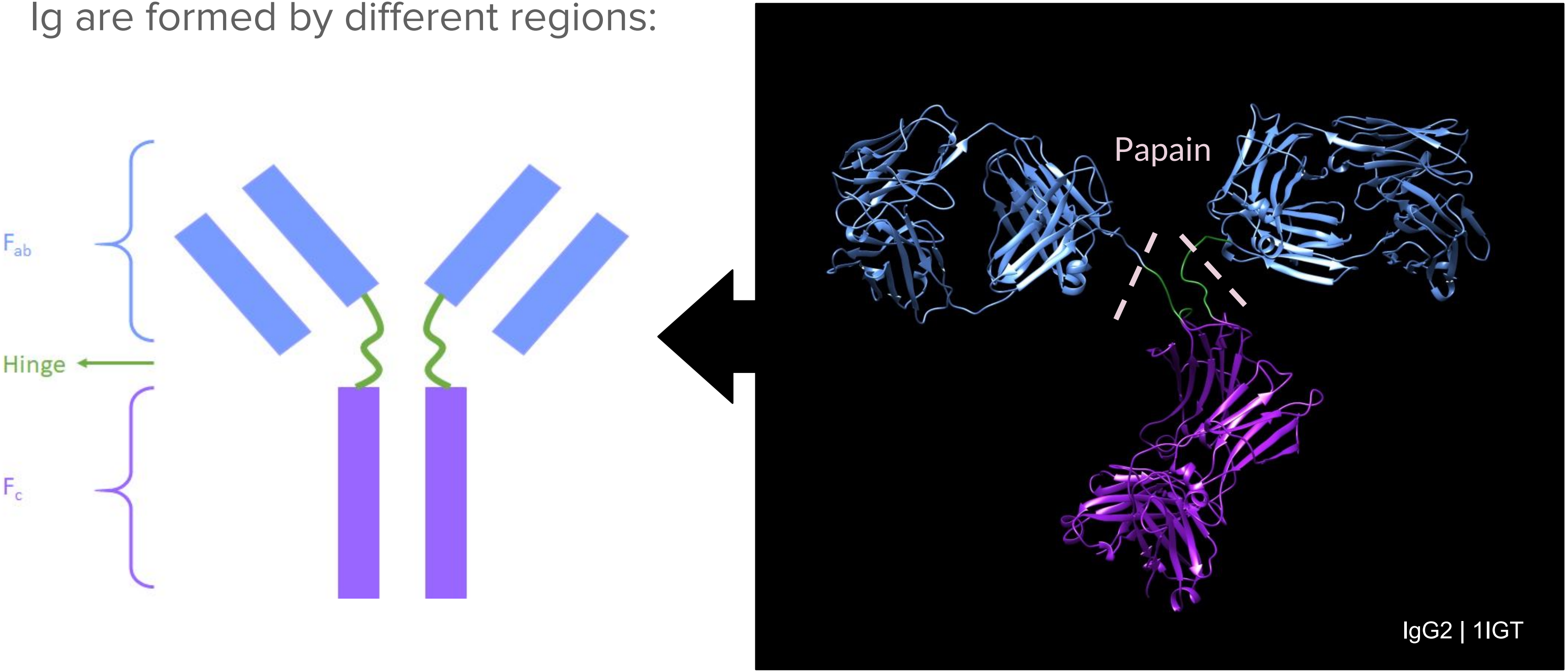
Light chain



IgG2 | 1IGT

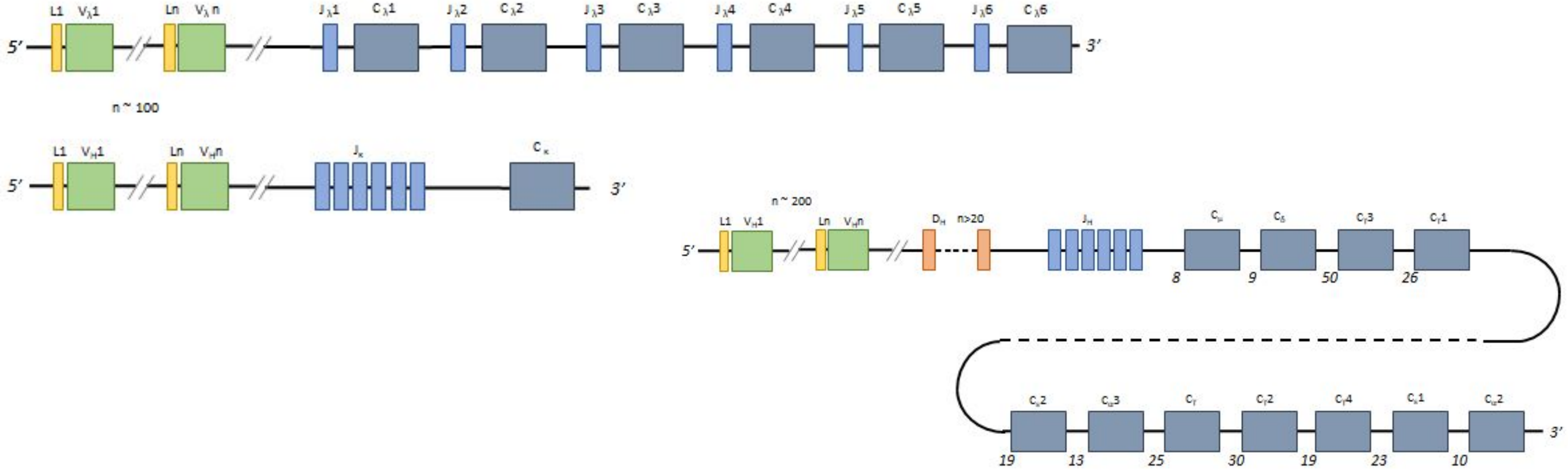
Introduction - Immunoglobulins

Ig are formed by different regions:



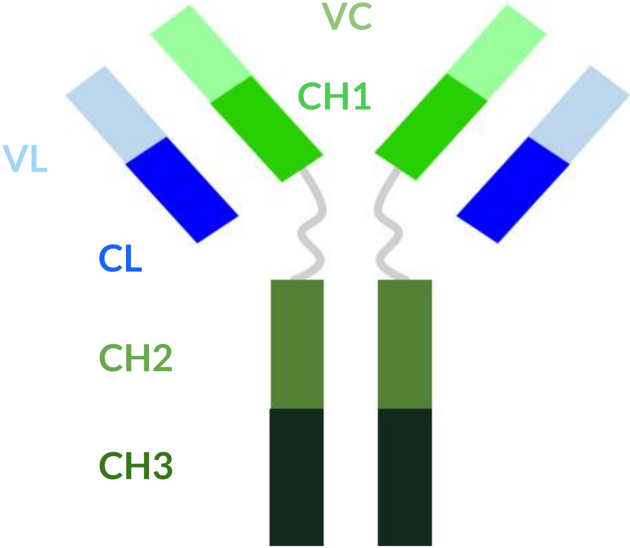
Introduction - IgG formation

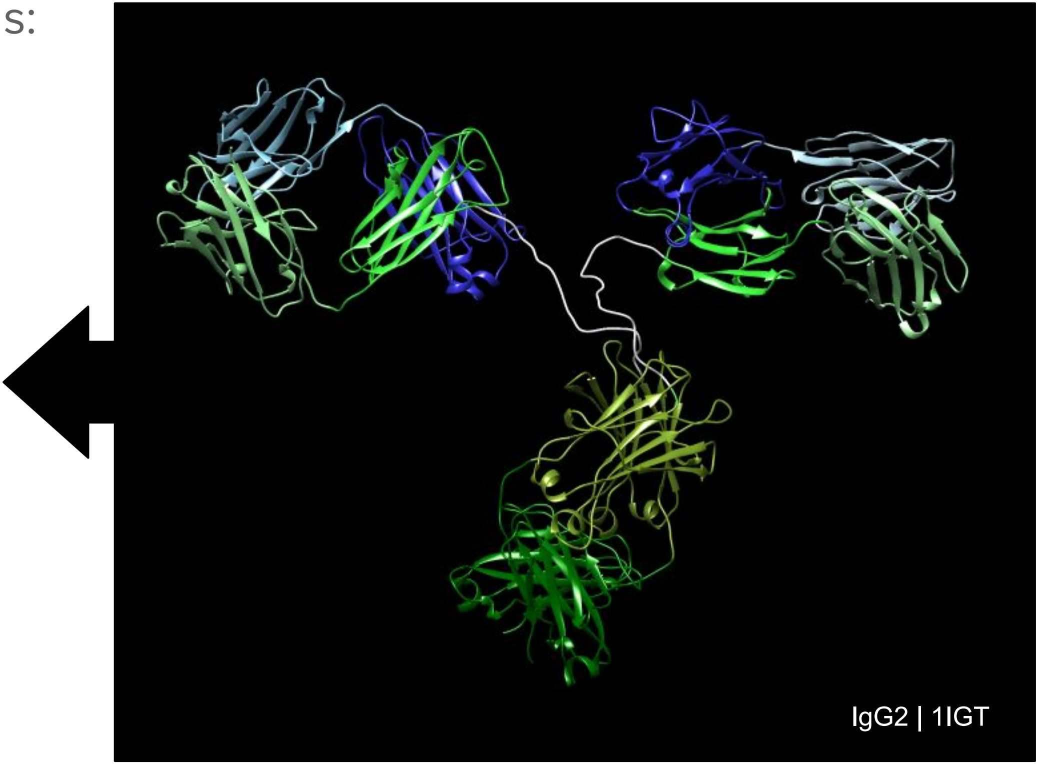
- Ig chains are encoded in: Chromosome 14 (HChains), Chromosome 2 (κ LC) and Chromosome 22 (λ LC).
- Ig variability is generated by somatic recombination.
- CDRs are encoded in the V Domain (HC) and in the DNA section between V and J (LC).



Introduction - IgG

IgG are formed by different regions:

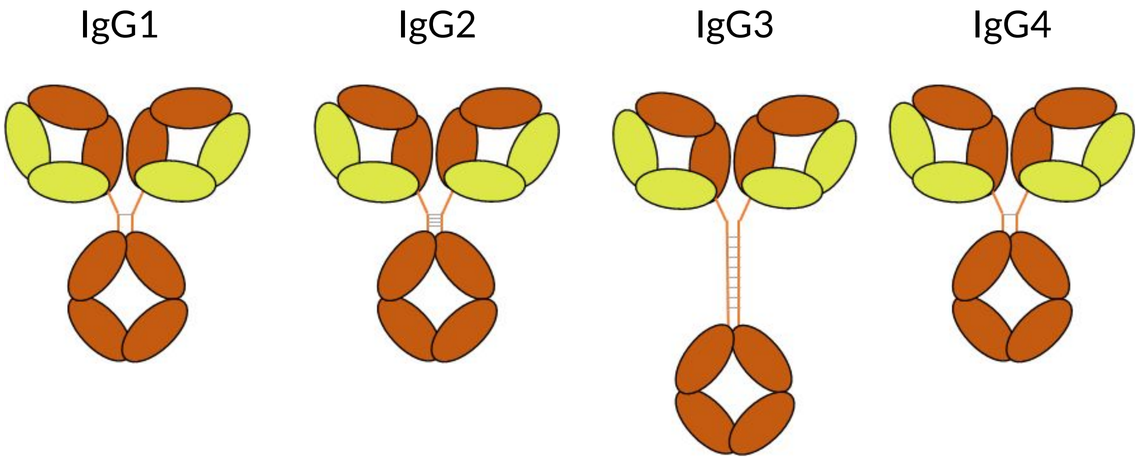




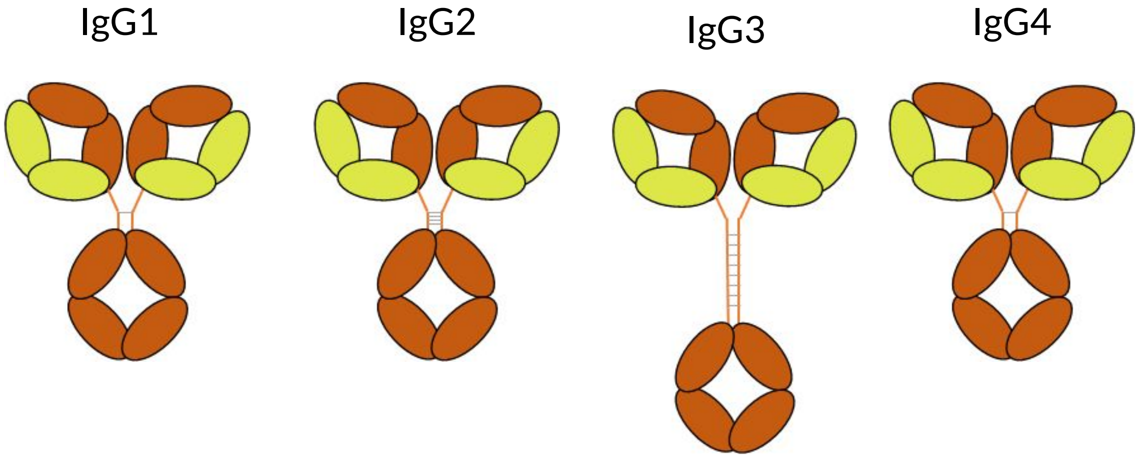
Introduction - IgG subclasses

IgG amino acidic identity: 90% → **Differences?**

- Function
- Response
- Structure



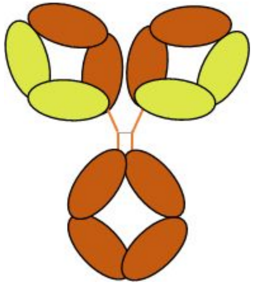
Introduction - IgG subclasses: *function*



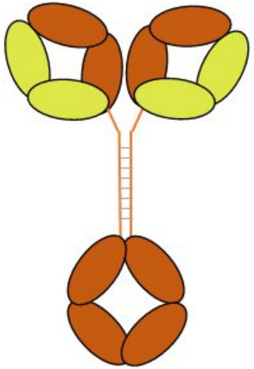
Proteins	+++	+/-	++	++*
Polysaccharides	+	+++	+/-	+/-
Allergens	+	-	(-)	-

Introduction - IgG subclasses: *response*

IgG1



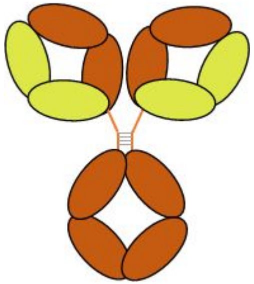
IgG3



- They can activate the complement response trough C1b
- In response to T-heplers through MHC-II in B-cells
- IgG1 the most abundant one
- IgG3 the 1st in viral infections

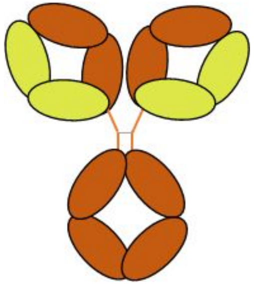
Introduction - IgG subclasses: *response*

IgG2



- Reacts to polysaccharides without T-helpers
- Most of bacterial capsular polysaccharides

IgG4



- Allergies after a peptide exposure repetition
- Modulated by IL-10
- Important against helminths and philaries

Introduction - IgG subclasses: *structure*

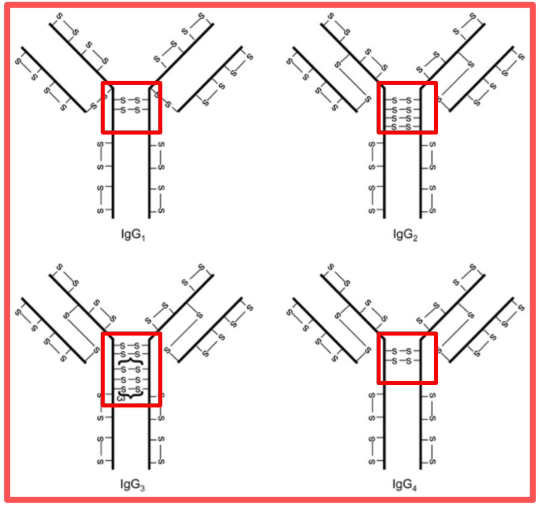
Flexibility affects antigen-binding capacity and immune complex formation.

The **hinge** has different flexibility in the different IgG subclasses.

IgG3 > IgG1 > IgG4 > IgG2

Factors that determine the hinge flexibility:

- Length of the molecule
- Poly-proline helix
- Amino Acids ➔ disulfide bonds



Introduction - Structural classification

SCOP Classification

- **Class: All beta protein**
- **Fold:** Immunoglobulin-like beta-sandwich
- **Superfamily:** Immunoglobulin
- **Family:**
  - V set domains
  - C1 set domains
  - C2 set domains
  - I set domains

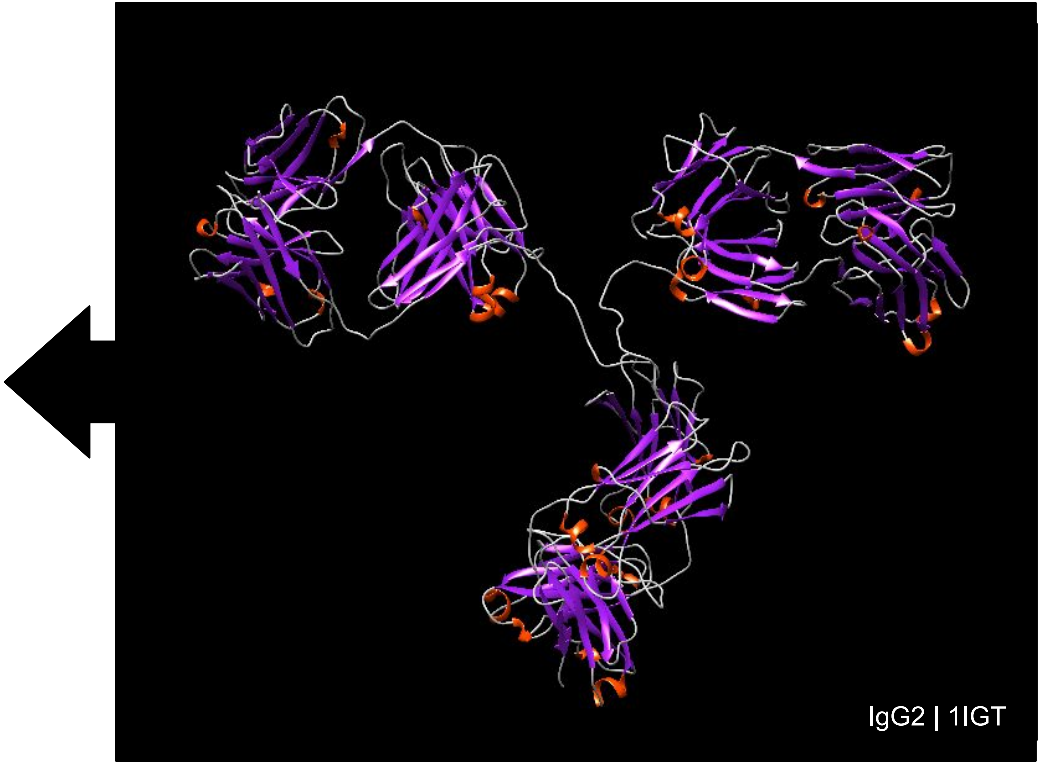
CATH Classification

- **Class: Mainly Beta**
- **Architecture:** Sandwich
- **Topology:** Immunoglobulin like
- **Homologous Superfamily:** Immunoglobulins

Introduction - Structural classification: *Class*

IgG have a typical structure:

- **Beta-sheet**
- **Helix**
- Loop



Introduction - Structural classification

SCOP Classification

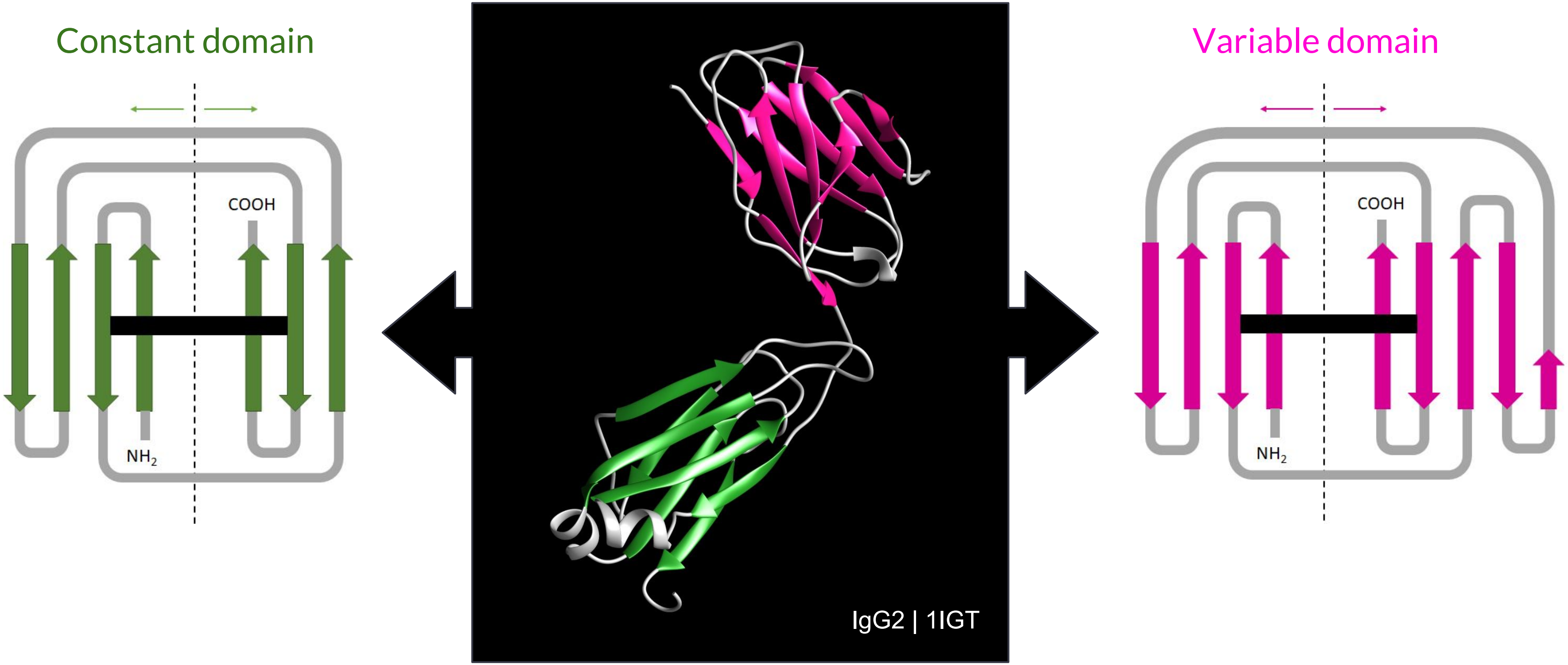
- **Class:** All beta protein
- **Fold: Immunoglobulin-like beta-sandwich**
- **Superfamily:** Immunoglobulin
- **Family:**
  - V set domains
  - C1 set domains
  - C2 set domains
  - I set domains

CATH Classification

- **Class:** Mainly Beta
- **Architecture: Sandwich**
- **Topology: Immunoglobulin like**
- **Homologous Superfamily:** Immunoglobulins

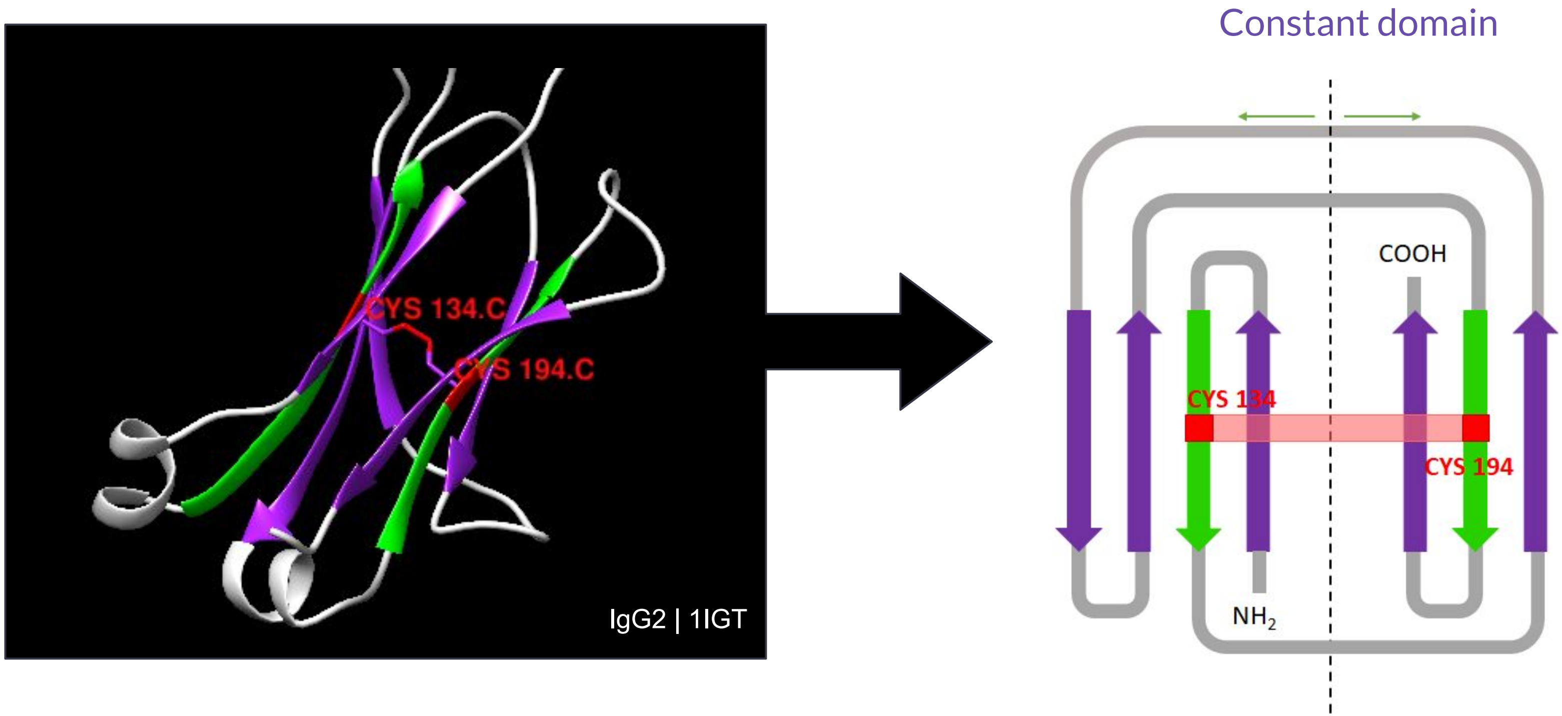
Introduction - Structural classification: *fold and architecture*

Diagram of the immunoglobulin sandwich structure in the light chain:



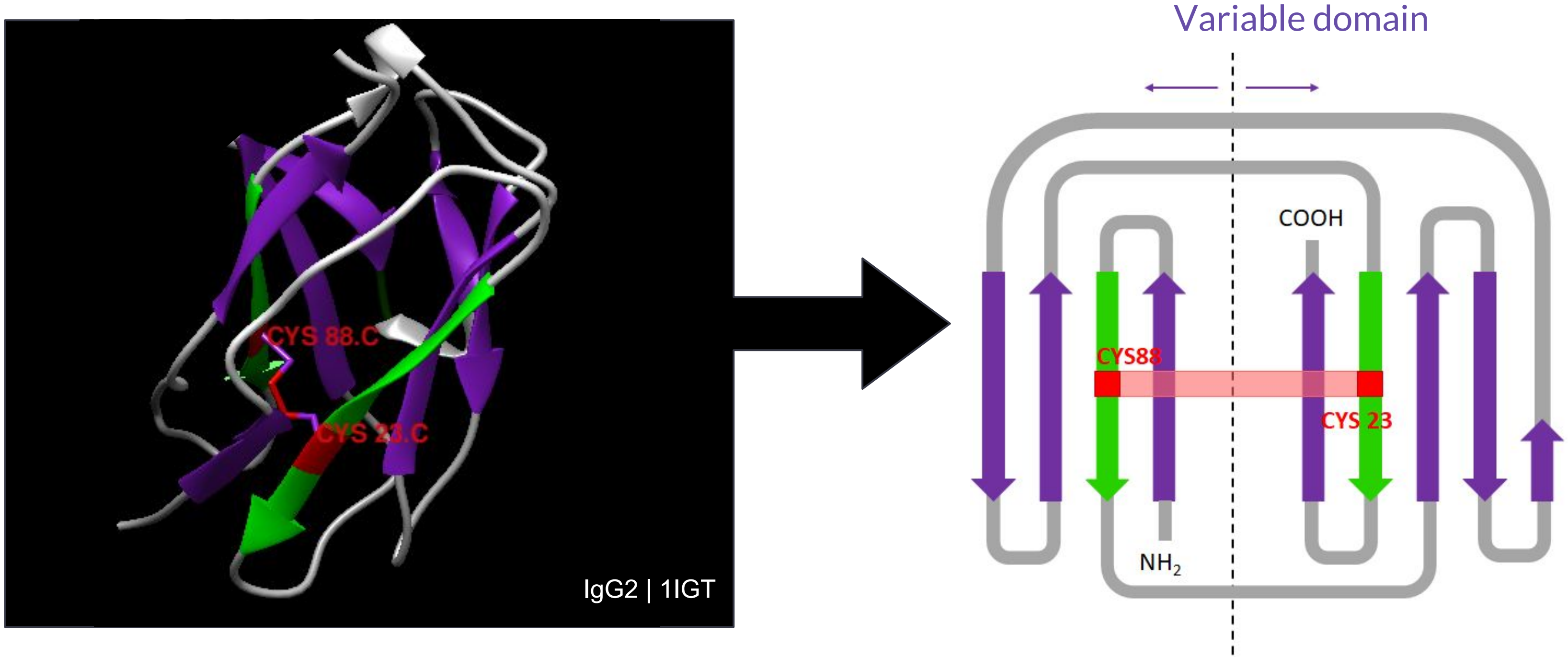
Introduction - Structural classification: *fold and architecture*

Diagram of the immunoglobulin fold structure in the light chain: **disulfide bond**



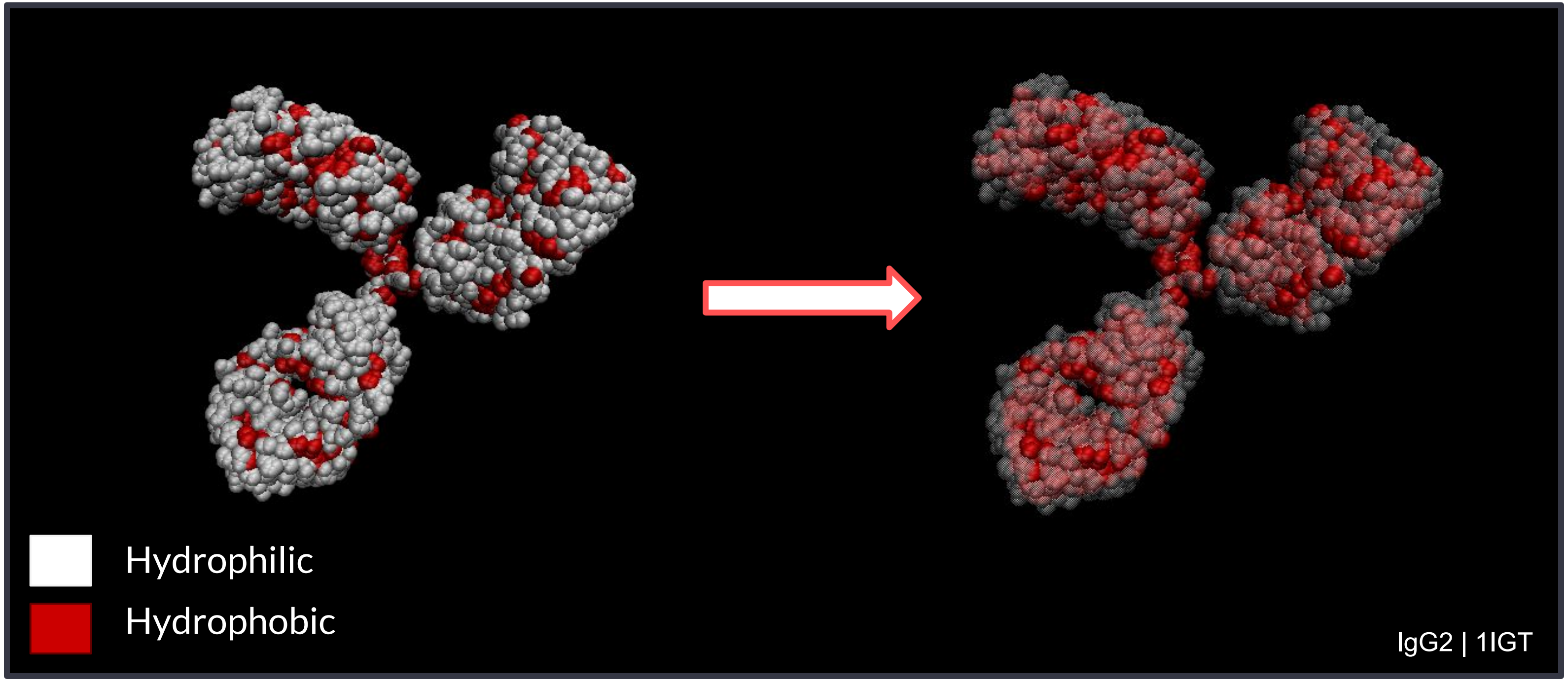
Introduction - Structural classification: *fold and architecture*

Diagram of the immunoglobulin fold structure in the light chain: **disulfide bond**



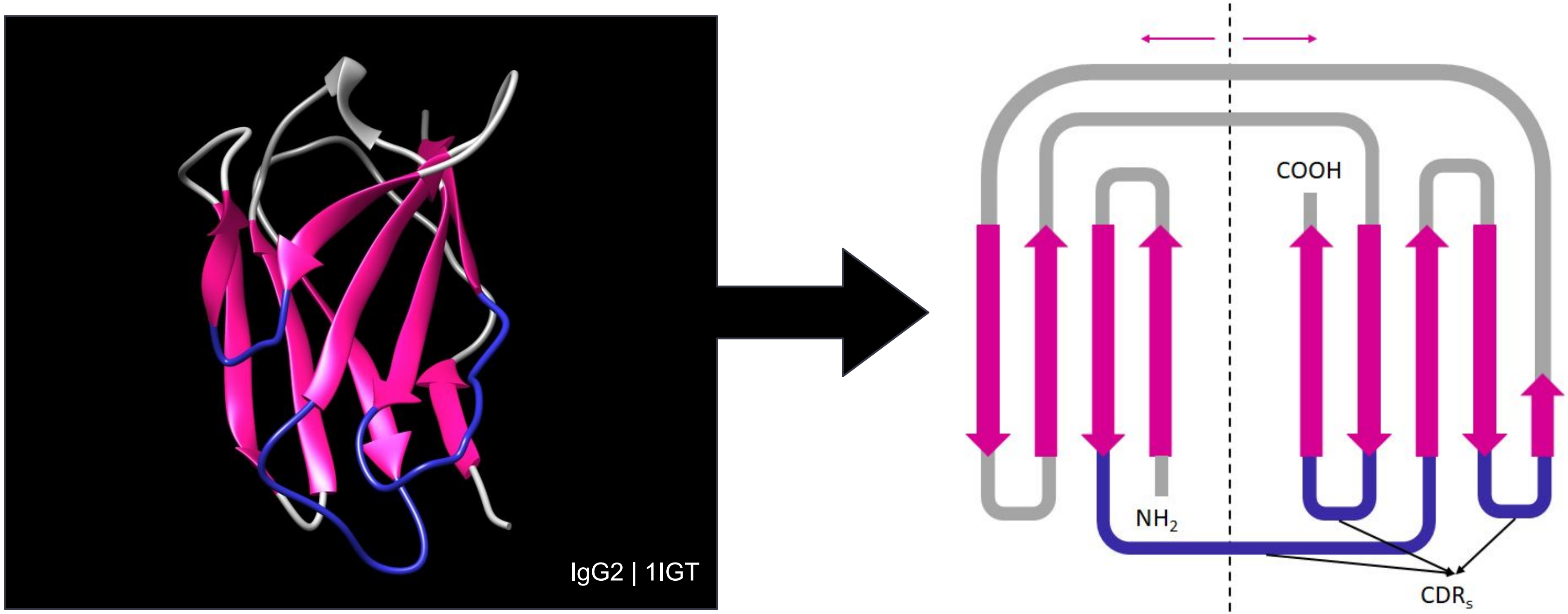
Introduction - Structural classification: *fold and architecture*

Diagram of the immunoglobulin fold structure light domain: **hydrophobic core**



Introduction - Structural classification: *fold and architecture*

Diagram of the immunoglobulin fold structure light chain:



Introduction - Structural classification

SCOP Classification

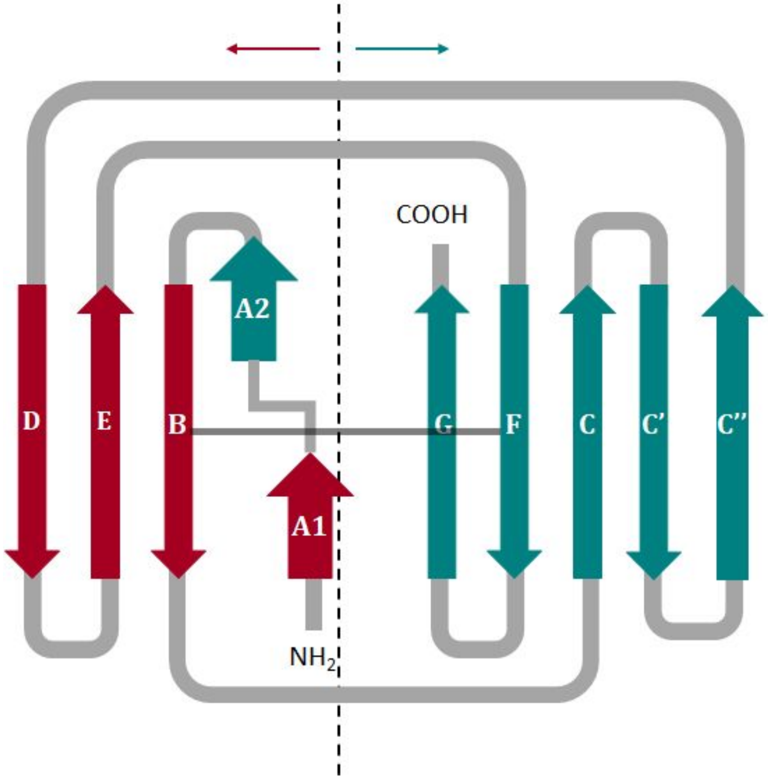
- **Class:** All beta protein
- **Fold:** Immunoglobulin-like beta-sandwich
- **Superfamily:** Immunoglobulin
- **Family:**
    - **V set domains**
    - **C1 set domains**
    - **C2 set domains**
    - **I set domains**

CATH Classification

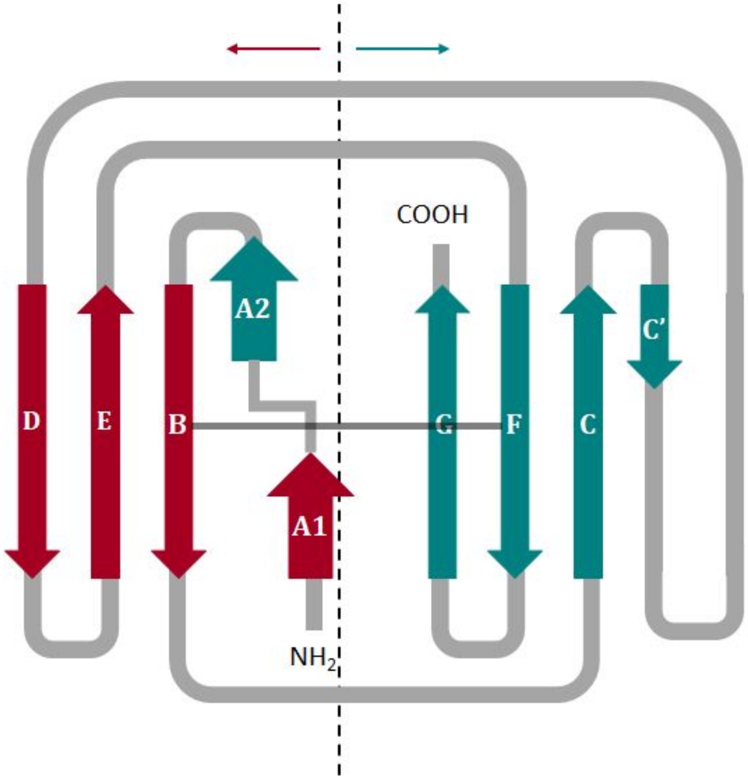
- **Class:** Mainly Beta
- **Architecture:** Sandwich
- **Topology:** Immunoglobulin like
- **Homologous Superfamily:** Immunoglobulins

Introduction - Structural classification: *family*

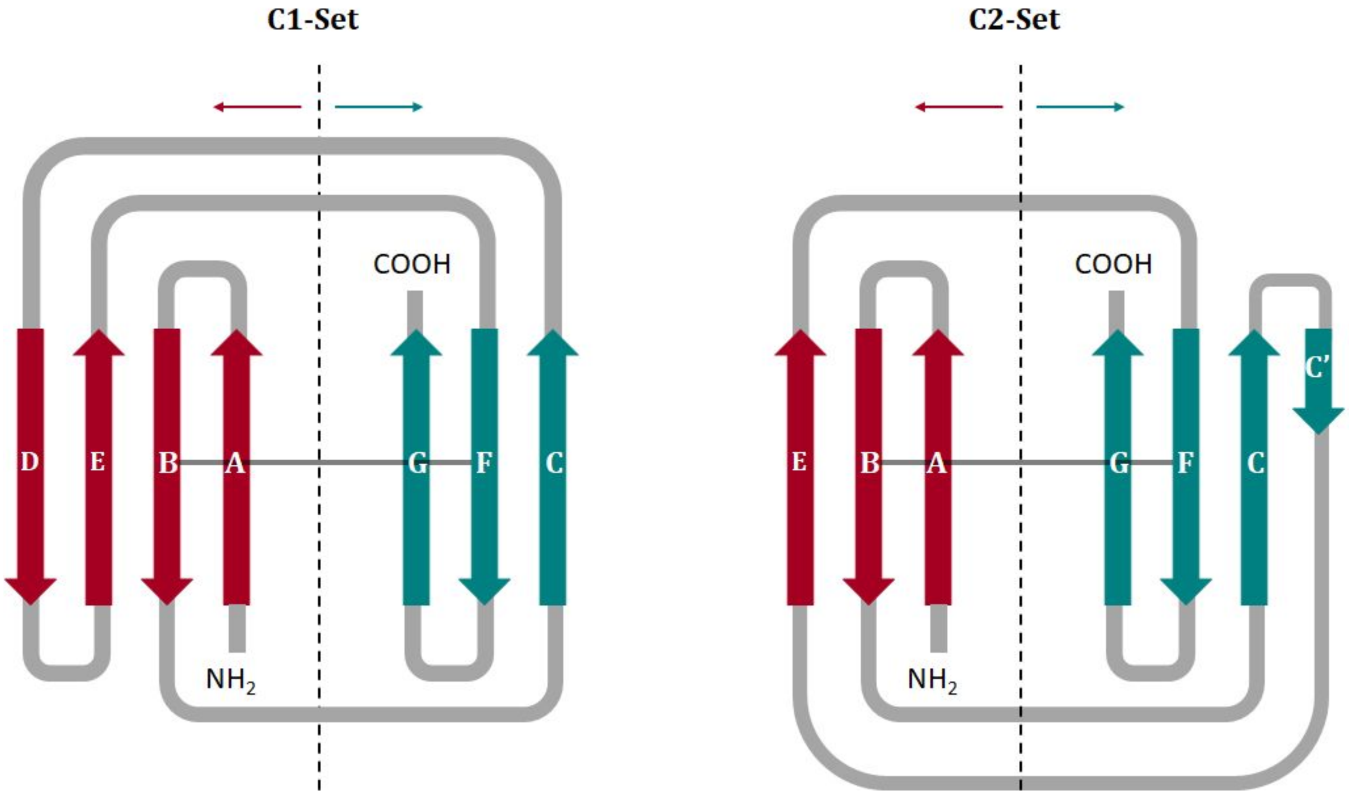
V-Set



I-Set



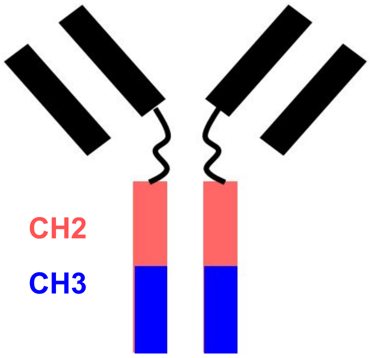
Introduction - Structural classification: *family*



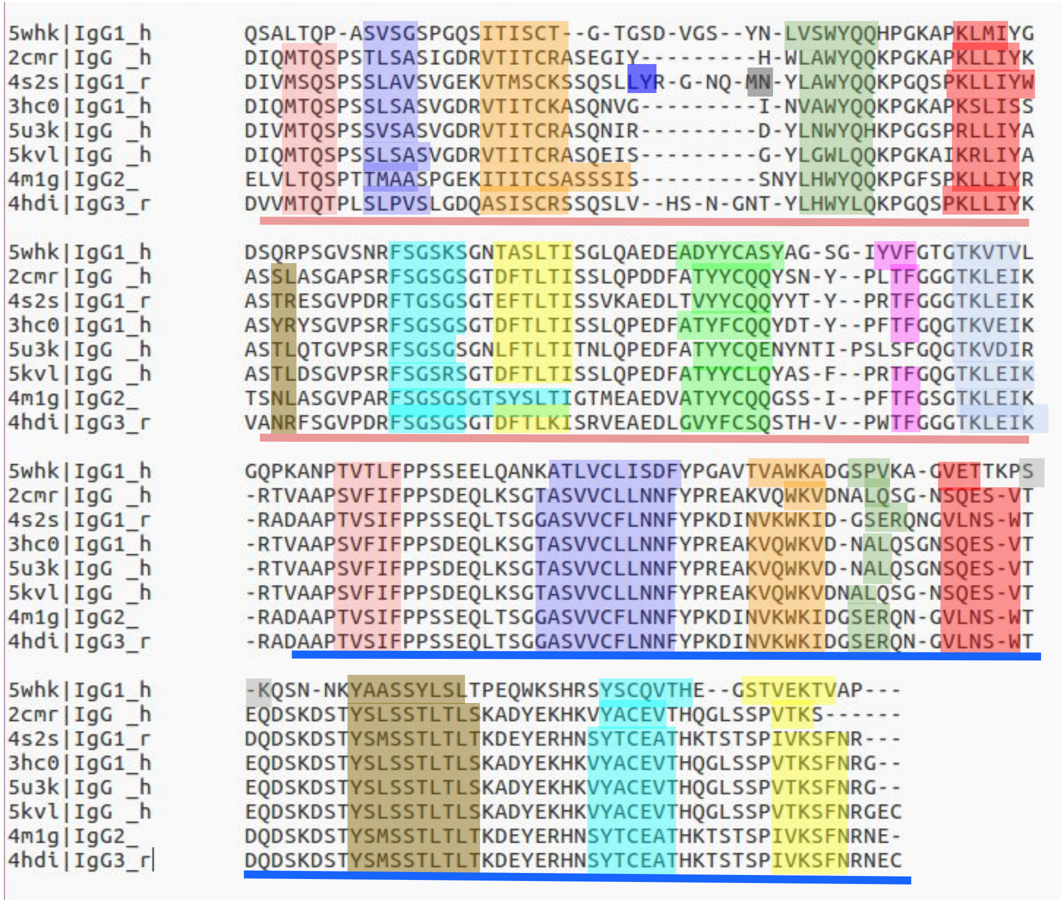
IgG structural analysis

IgG structural analysis: β - strands - *Fc Heavy chain*

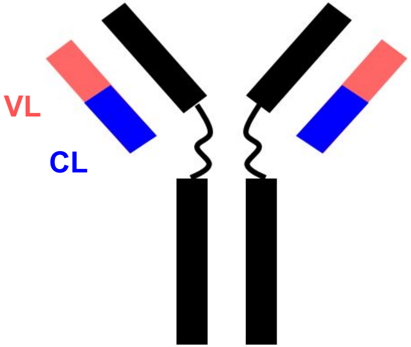
```
4haf|IgG2_h      ------AGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVV
4byh|IgG1_h      --------PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL
5w38|IgG3_h      -----LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVL
4c55|IgG4_h      -------GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVL
2vuo|IgG1_c      PPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQFTWYINNEQVRTARPPLREQQFNSTIRVVSTLPIA
5d4q|IgG1_h      -------GPDVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL

4haf|IgG2_h      HQDWLNGKEYKCKVSN-KGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE
4byh|IgG1_h      HQDWLNGKEYKCKVSN-KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE
5w38|IgG3_h      HQDWLNGKEYKCKVSN-KALPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSGQPE
4c55|IgG4_h      HQDWLNGKEYKCKVSNKGLP-SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE
2vuo|IgG1_c      HQDWLRGKEFKCKVHN-KALPAPIEKTISKARGQPLEPKVYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAE
5d4q|IgG1_h      HQDWLNGKEYKCKVSN-KALPLPEEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE

4haf|IgG2_h      NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL---------SS--VFLFPPKPKDTL
4byh|IgG1_h      NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSG--G------PSVFLFPPKPKDTL
5w38|IgG3_h      NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNIFSCSVMHEALHNRFTQKSLS----------LGPSVFLFPPKPKDTL
4c55|IgG4_h      NNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSL---------SP-SVFLFPPKPKDTL
2vuo|IgG1_c      DNYKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRS-PPELLGG--PSVFIFPPKPKDTL
5d4q|IgG1_h      NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL---------SGPDVFLFPPKPKDTL

4haf|IgG2_h      MISRTPEVTCVV-V-------V-QFNWYVDGVEVHN-AKTKPR-EN---STFRVVSVLTVVHQDWLNGKEYKCKVSA---
4byh|IgG1_h      MISRTPEVTCVVVDVS-HEDPEVKFNWYVDGVEVHN-AKTK-PREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV-SN-K
5w38|IgG3_h      MISRTPEVTCVVVDVSHE-DPEVQFKWYVDGVEVHN-AKTKPR-EEQFNSTFRVVSVLTVLHQDWLNGKEYKCKV-SN-K
4c55|IgG4_h      MISRTPEVTCVVVDVSQE-DPEVQFNWYVDGVEVHN-AKTKPR-EEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV-SNKG
2vuo|IgG1_c      MISRTPEVTCVVVDVSQD-DPEVQFTWYINNEQVRTARPPL-R-EQQFNSTIRVVSTLPIAHQDWLRGKEFKCKV-HN-K
5d4q|IgG1_h      MISRTPEVTCVVVDVSHE-DPEVKFNWYVDGVEVHN-AKTKPR-EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV-SN-K

4haf|IgG2_h      -----PIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFF
4byh|IgG1_h      -ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF
5w38|IgG3_h      ALP-APIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSGQPENNYKTTPPMLDSDGSFF
4c55|IgG4_h      LPS--SIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF
2vuo|IgG1_c      ALP-APIEKTISKARGQPLEPKVYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYF
5d4q|IgG1_h      ALP-LPEEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF

4haf|IgG2_h      LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS-
4byh|IgG1_h      LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS-
5w38|IgG3_h      LYSKLTVDKSRWQQGNIFSCSVMHEALHNRFTQKSLSLSP
4c55|IgG4_h      LYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSL--
2vuo|IgG1_c      LYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRS-
5d4q|IgG1_h      TLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS-
```



IgG structural analysis: β - strands **-** *Fab Light chain*

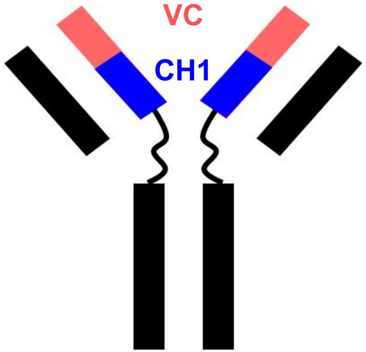


```
5whk|IgG1_h        QSALTQP-ASVSGSPGQSITISCT--G-TGSD-VGS--YN-LVSWYQQHPGKAPKLMIYG
2cmr|IgG _h        DIQMTQSPSTLSASIGDRVTITCRASEGIY---------H-WLAWYQQKPGKAPKLLIYK
4s2s|IgG1_r        DIVMSQSPSSLAVSVGEKVTMSCKSSQSLLYR-G-NQ-MN-YLAWYQQKPGQSPKLLIYW
3hc0|IgG1_h        DIQMTQSPSSLSASVGDRVTITCKASQNVG---------I-NVAWYQQKPGKAPKSLISS
5u3k|IgG _h        DIVMTQSPSSVSASVGDRVTITCRASQNIR---------D-YLNWYQHKPGGSPRLLIYA
5kvl|IgG _h        DIQMTQSPSSLSASVGDRVTITCRASQEIS---------G-YLGWLQQKPGKAIKRLIYA
4m1g|IgG2_         ELVLTQSPTTMAASPGEKITITCSASSSIS---------SNYLHWYQQKPGFSPKLLIYR
4hdi|IgG3_r        DVVMTQTPLSLPVSLGDQASISCRSSQSLV--HS-N-GNT-YLHWYLQKPGQSPKLLIYK

5whk|IgG1_h        DSQRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCASYAG-SG-IYVFGTGTKVTVL
2cmr|IgG _h        ASSLASGAPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYSN-Y--PLTFGGGTKLEIK
4s2s|IgG1_r        ASTRESGVPDRFTGSGSGTEFTLTISSVKAEDLTVYYCQQYYT-Y--PRTFGGGTKLEIK
3hc0|IgG1_h        ASYRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYFCQQYDT-Y--PFTFGQGTKVEIK
5u3k|IgG _h        ASTLQTGVPSRFSGSGSGNLFTLTITNLQPEDFATYYCQENYNTI-PSLSFGQGTKVDIR
5kvl|IgG _h        ASTLDSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCLQYAS-F--PRTFGQGTKLEIK
4m1g|IgG2_         TSNLASGVPARFSGSGSGTSYSLTIGTMEAEDVATYYCQQGSS-I--PFTFGSGTKLEIK
4hdi|IgG3_r        VANRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTH-V--PWTFGGGTKLEIK

5whk|IgG1_h        GQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKA-GVETTKPS
2cmr|IgG _h        -RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG-NSQES-VT
4s2s|IgG1_r        -RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKID-GSERQNGVLNS-WT
3hc0|IgG1_h        -RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD-NALQSGNSQES-VT
5u3k|IgG _h        -RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD-NALQSGNSQES-VT
5kvl|IgG _h        -RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG-NSQES-VT
4m1g|IgG2_         -RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQN-GVLNS-WT
4hdi|IgG3_r        -RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQN-GVLNS-WT

5whk|IgG1_h        -KQSN-NKYAASSYLSLTPEQWKSHRSYSCQVTHE--GSTVEKTVAP---
2cmr|IgG _h        EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS------
4s2s|IgG1_r        DQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNR---
3hc0|IgG1_h        EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG--
5u3k|IgG _h        EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG--
5kvl|IgG _h        EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
4m1g|IgG2_         DQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNE-
4hdi|IgG3_r        DQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC
```

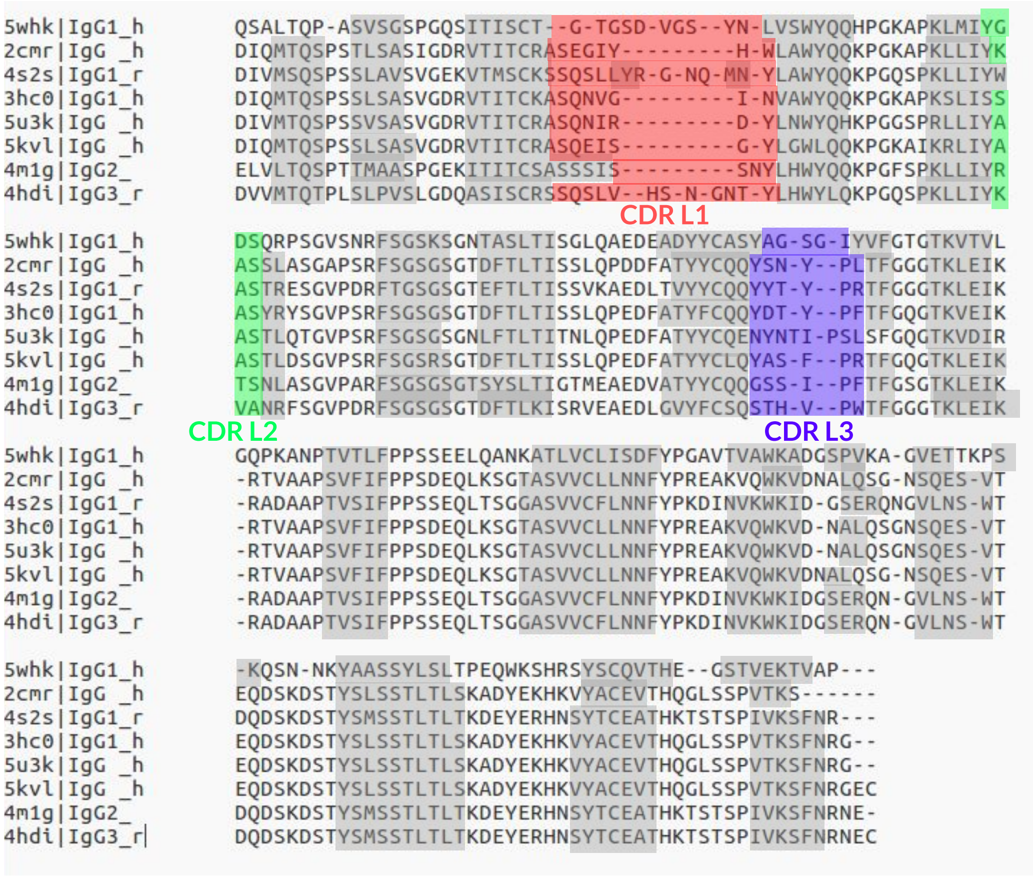


IgG structural analysis: β - strands - *Fab Heavy chain*

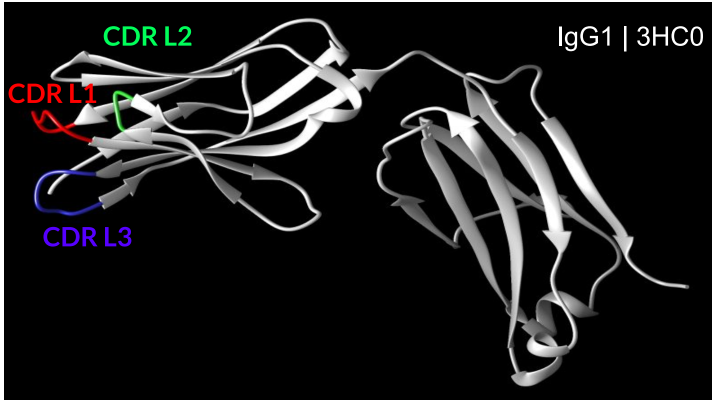
```
4m1g|IgG2_        QVQLKESGPGLVAPSQSLSITCTVS-GFSLTD-YGVSWIRQPPGK-GLEWLGVTWGG---
5kvl|IgG _h       QVQLQESGPGLVKPSETLSVTCTVS-GYSITSSYSWNWIRQFPGK-GLEWIGNIYYS---
5whk|IgG1_h       EVQLLESGGGLVQPGGSLRLSCAAS-GFTFSE-YAMGWVRQAPGK-GLEWVSSIGSS---
4hdi|IgG3_r       DVKLVESGGGLVKLGGSLKLSCAAS-GFTFSN-YFMSWVRQTPEK-RLELVAVITSN---
5u3k|IgG _h       QVQLVQSGGGLVKPGGSLTLSCSAS-GFFFDN-SWMGWVRQAPGK-GLEWVGRIRRLKDG
4s2s|IgG1_r       EVQLQESGGGLVKPGGSLKLSCAAS-GFTFST-YAMSWVRQTPEK-RLEWVASIS-T-G-
3hc0|IgG1_h       QVQLVQSGAEVKKPGSSVKVSCKAS-GYTFTT-YYLHWVRQA-PGQGLEWMGWIYPG-N-
2cmr|IgG _h       --QLVQSGAEVRKPGASVKVSCKASGDT-FSS-YAISWVRQAPGQ-GLEWMGGIIPI-F-

4m1g|IgG2_        G-TTYYNSALKSRLSISKDNSKSQVFLKMNSLQTDDTAMYYCAKHKAS------------
5kvl|IgG _h       G-STNYNPSLKSRISISRDTSKNQFSLKLSSVTAADTAVYYCANP---------------
5whk|IgG1_h       GGQTKYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARLA-I------------
4hdi|IgG3_r       GDNTYYPDTVKGRFTISRDNAQNTLYLQMSSLKSEDTALYYCARRDSSA-----------
5u3k|IgG _h       A-TGEYGAAVKDRFTISRDDSRNMLYLHMRTLKTEDSGTYYCTMDE-GTPVTRFLEWGYF
4s2s|IgG1_r       D-NTYYTDSVRGRFTISRDNARNILYLQMSSLRSEDTAMYFCTRGR-GDR----------
3hc0|IgG1_h       V-HAQYNEKFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARS--W------------
2cmr|IgG _h       G-TANYAQAFQGRVTITANESTSTAYMELSSLRSEDTAIYYCARDN-PT-----------

4m1g|IgG2_        -YNGLDYWGQGTTLTVSSAKTTAPSVYPLAPV--C--G--SSVTLGCLVKGYFPEPVTLT
5kvl|IgG _h       ----R-VWGQGTTVTVSSASTKGPSVFPLAPS--SKSTSGGTAALGCLVKDYFPEPVTVS
5whk|IgG1_h       -G-DS-YWGQGTMVTVSSASTKGPSVFPLAP------SG--TAALGCLVKDYFPEPVTVS
4hdi|IgG3_r       -SLYFDYWGQGTTLTVSSATTTAPSVYPLVPGC-SDTSG-SSVTLGCLVKGYFPEPVTVK
5u3k|IgG _h       -YYYMAVWGRGTTVIVSSASTKGPSVFPLAP---S--A-----ALGCLVKDYFPEPVTVS
4s2s|IgG1_r       -GDLFGYWGQGTLVTVSSAKTTAPSVYPLAP--VC--G--SSVTLGCLVKGYFPEPVTLT
3hc0|IgG1_h       -E-GFPYWGQGTTVTVSSASTKGPSVFPLAP--SS--G--GTAALGCLVKDYFPEPVTVS
2cmr|IgG _h       LL-GSDYWGAGTLVTVSSASTKGPSVFPL-A------G---TAALGCLVKDYFPEPVTVS

4m1g|IgG2_        WNSGSLSSGVHTFPAVLQ-SDLYTLSSSVTVTSST---WPSQSITCNVAHPASSTKVDKK
5kvl|IgG _h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS---LGTQTYICNVNHKPSNTKVDKR
5whk|IgG1_h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS---LGTQTYICNVNHKPSNTKVDKR
4hdi|IgG3_r       WNYGALSSGVRTVSSVLQ-SGFYSLSSLVTVPSST---WPSQTVICNVAHPASKTELIKR
5u3k|IgG _h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVT-PSSSLGTQT-YICNVNHK--P--SNTKVD
4s2s|IgG1_r       WNSGSLSSGVHTFPAVLQ-SDLYTLSSSVTVTSSTWPSQS-ITCNVAHP--A--SSTKVD
3hc0|IgG1_h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT-YICNVNHK--P--SNTKVD
2cmr|IgG _h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS--T-QT-YICNVNHK--P--SNTKVD

4m1g|IgG2_        IEPRGP-----
5kvl|IgG _h       VEPKSC-----
5whk|IgG1_h       VEPK-------
4hdi|IgG3_r       IEPR-------
5u3k|IgG _h       KRVE-------
4s2s|IgG1_r       KKIEPRGPTIK
3hc0|IgG1_h       KKVEPK-----
2cmr|IgG _h       KRV--------
```



IgG structural analysis: CDRs - *Fab light chain*

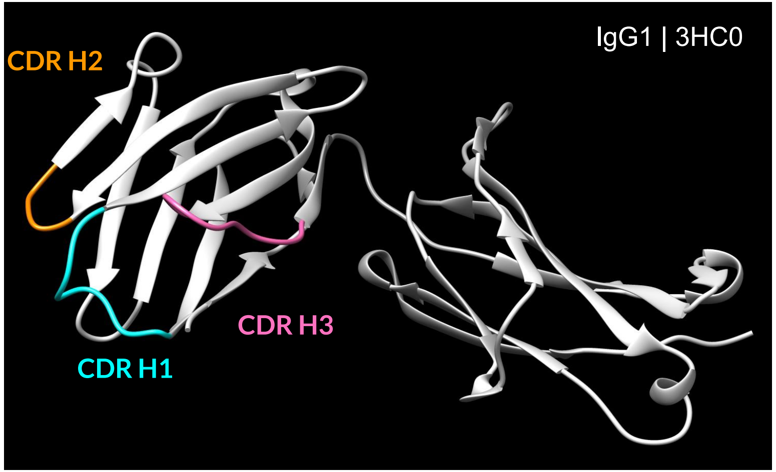


```
5whk|IgG1_h      QSALTQP-ASVSGSPGQSITISCT--G-TGSD-VGS--YN-LVSWYQQHPGKAPKLMIYG
2cmr|IgG _h      DIQMTQSPSTLSASIGDRVTITCRASEGIY---------H-WLAWYQQKPGKAPKLLIYK
4s2s|IgG1_r      DIVMSQSPSSLAVSVGEKVTMSCKSSQSLLYR-G-NQ-MN-YLAWYQQKPGQSPKLLIYW
3hc0|IgG1_h      DIQMTQSPSSLSASVGDRVTITCKASQNVG---------I-NVAWYQQKPGKAPKSLISS
5u3k|IgG _h      DIVMTQSPSSVSASVGDRVTITCRASQNIR---------D-YLNWYQHKPGGSPRLLIYA
5kvl|IgG _h      DIQMTQSPSSLSASVGDRVTITCRASQEIS---------G-YLGWLQQKPGKAIKRLIYA
4m1g|IgG2_       ELVLTQSPTTMAASPGEKITITCSASSSIS---------SNYLHWYQQKPGFSPKLLIYR
4hdi|IgG3_r      DVVMTQTPLSLPVSLGDQASISCRSSQSLV--HS-N-GNT-YLHWYLQKPGQSPKLLIYK

5whk|IgG1_h      DSQRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCASYAG-SG-IYVFGTGTKVTVL
2cmr|IgG _h      ASSLASGAPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYSN-Y--PLTFGGGTKLEIK
4s2s|IgG1_r      ASTRESGVPDRFTGSGSGTEFTLTISSVKAEDLTVYYCQQYYT-Y--PRTFGGGTKLEIK
3hc0|IgG1_h      ASYRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYFCQQYDT-Y--PFTFGQGTKVEIK
5u3k|IgG _h      ASTLQTGVPSRFSGSGSGNLFTLTITNLQPEDFATYYCQENYNTI-PSLSFGQGTKVDIR
5kvl|IgG _h      ASTLDSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCLQYAS-F--PRTFGQGTKLEIK
4m1g|IgG2_       TSNLASGVPARFSGSGSGTSYSLTIGTMEAEDVATYYCQQGSS-I--PFTFGSGTKLEIK
4hdi|IgG3_r      VANRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTH-V--PWTFGGGTKLEIK

5whk|IgG1_h      GQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKA-GVETTKPS
2cmr|IgG _h      -RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG-NSQES-VT
4s2s|IgG1_r      -RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKID-GSERQNGVLNS-WT
3hc0|IgG1_h      -RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD-NALQSGNSQES-VT
5u3k|IgG _h      -RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD-NALQSGNSQES-VT
5kvl|IgG _h      -RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG-NSQES-VT
4m1g|IgG2_       -RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQN-GVLNS-WT
4hdi|IgG3_r      -RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQN-GVLNS-WT

5whk|IgG1_h      -KQSN-NKYAASSYLSLTPEQWKSHRSYSCQVTHE--GSTVEKTVAP---
2cmr|IgG _h      EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS------
4s2s|IgG1_r      DQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNR---
3hc0|IgG1_h      EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG--
5u3k|IgG _h      EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG--
5kvl|IgG _h      EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
4m1g|IgG2_       DQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNE-
4hdi|IgG3_r      DQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC
```



IgG structural analysis: CDRs - *Fab heavy chain*

```
4m1g|IgG2_        QVQLKESGPGLVAPSQSLSITCTVS-GFSLTD-YGVSWIRQPPGK-GLEWLGVTWGG---
5kvl|IgG _h       QVQLQESGPGLVKPSETLSVTCTVS-GYSITSSYSWNWIRQFPGK-GLEWIGNIYYS---
5whk|IgG1_h       EVQLLESGGGLVQPGGSLRLSCAAS-GFTFSE-YAMGWVRQAPGK-GLEWVSSIGSS---
4hdi|IgG3_r       DVKLVESGGGLVKLGGSLKLSCAAS-GFTFSN-YFMSWVRQTPEK-RLELVAVITSN---
5u3k|IgG _h       QVQLVQSGGGLVKPGGSLTLSCSAS-GFFFDN-SWMGWVRQAPGK-GLEWVGRIRRLKDG
4s2s|IgG1_r       EVQLQESGGGLVKPGGSLKLSCAAS-GFTFST-YAMSWVRQTPEK-RLEWVASIS-T-G-
3hc0|IgG1_h       QVQLVQSGAEVKKPGSSVKVSCKAS-GYTFTT-YYLHWVRQA-PGQGLEWMGWIYPG-N-
2cmr|IgG _h       --QLVQSGAEVRKPGASVKVSCKASGDT-FSS-YAISWVRQAPGQ-GLEWMGGIIPI-F-

4m1g|IgG2_        G-TTYYNSALKSRLSISKDNSKSQVFLKMNSLQTDDTAMYYCAKHKAS------------
5kvl|IgG _h       G-STNYNPSLKSRISISRDTSKNQFSLKLSSVTAADTAVYYCANP---------------
5whk|IgG1_h       GGQTKYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARLA-I------------
4hdi|IgG3_r       GDNTYYPDTVKGRFTISRDNAQNTLYLQMSSLKSEDTALYYCARRDSSA-----------
5u3k|IgG _h       A-TGEYGAAVKDRFTISRDDSRNMLYLHMRTLKTEDSGTYYCTMDE-GTPVTRFLEWGYF
4s2s|IgG1_r       D-NTYYTDSVRGRFTISRDNARNILYLQMSSLRSEDTAMYFCTRGR-GDR----------
3hc0|IgG1_h       V-HAQYNEKFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARS--W------------
2cmr|IgG _h       G-TANYAQAFQGRVTITANESTSTAYMELSSLRSEDTAIYYCARDN-PT-----------

4m1g|IgG2_        -YNGLDYWGQGTTLTVSSAKTTAPSVYPLAPV--C--G--SSVTLGCLVKGYFPEPVTLT
5kvl|IgG _h       ----R-VWGQGTTVTVSSASTKGPSVFPLAPS--SKSTSGGTAALGCLVKDYFPEPVTVS
5whk|IgG1_h       -G-DS-YWGQGTMVTVSSASTKGPSVFPLAP------SG--TAALGCLVKDYFPEPVTVS
4hdi|IgG3_r       -SLYFDYWGQGTTLTVSSATTTAPSVYPLVPGC-SDTSG-SSVTLGCLVKGYFPEPVTVK
5u3k|IgG _h       -YYYMAVWGRGTTVIVSSASTKGPSVFPLAP---S--A-----ALGCLVKDYFPEPVTVS
4s2s|IgG1_r       -GDLFGYWGQGTLVTVSSAKTTAPSVYPLAP--VC--G--SSVTLGCLVKGYFPEPVTLT
3hc0|IgG1_h       -E-GFPYWGQGTTVTVSSASTKGPSVFPLAP--SS--G--GTAALGCLVKDYFPEPVTVS
2cmr|IgG _h       LL-GSDYWGAGTLVTVSSASTKGPSVFPL-A------G---TAALGCLVKDYFPEPVTVS

4m1g|IgG2_        WNSGSLSSGVHTFPAVLQ-SDLYTLSSSVTVTSST---WPSQSITCNVAHPASSTKVDKK
5kvl|IgG _h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS---LGTQTYICNVNHKPSNTKVDKR
5whk|IgG1_h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS---LGTQTYICNVNHKPSNTKVDKR
4hdi|IgG3_r       WNYGALSSGVRTVSSVLQ-SGFYSLSSLVTVPSST---WPSQTVICNVAHPASKTELIKR
5u3k|IgG _h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVT-PSSSLGTQT-YICNVNHK--P--SNTKVD
4s2s|IgG1_r       WNSGSLSSGVHTFPAVLQ-SDLYTLSSSVTVTSSTWPSQS-ITCNVAHP--A--SSTKVD
3hc0|IgG1_h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT-YICNVNHK--P--SNTKVD
2cmr|IgG _h       WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS--T-QT-YICNVNHK--P--SNTKVD

4m1g|IgG2_        IEPRGP-----
5kvl|IgG _h       VEPKSC-----
5whk|IgG1_h       VEPK-------
4hdi|IgG3_r       IEPR-------
5u3k|IgG _h       KRVE-------
4s2s|IgG1_r       KKIEPRGPTIK
3hc0|IgG1_h       KKVEPK-----
2cmr|IgG _h       KRV--------
```



IgG structural analysis: CDR and canonical structures

Canonical structures are determined by:

→ Residues at key sites

→ The length of the loop

}

Chothia et al. classification

Light chain

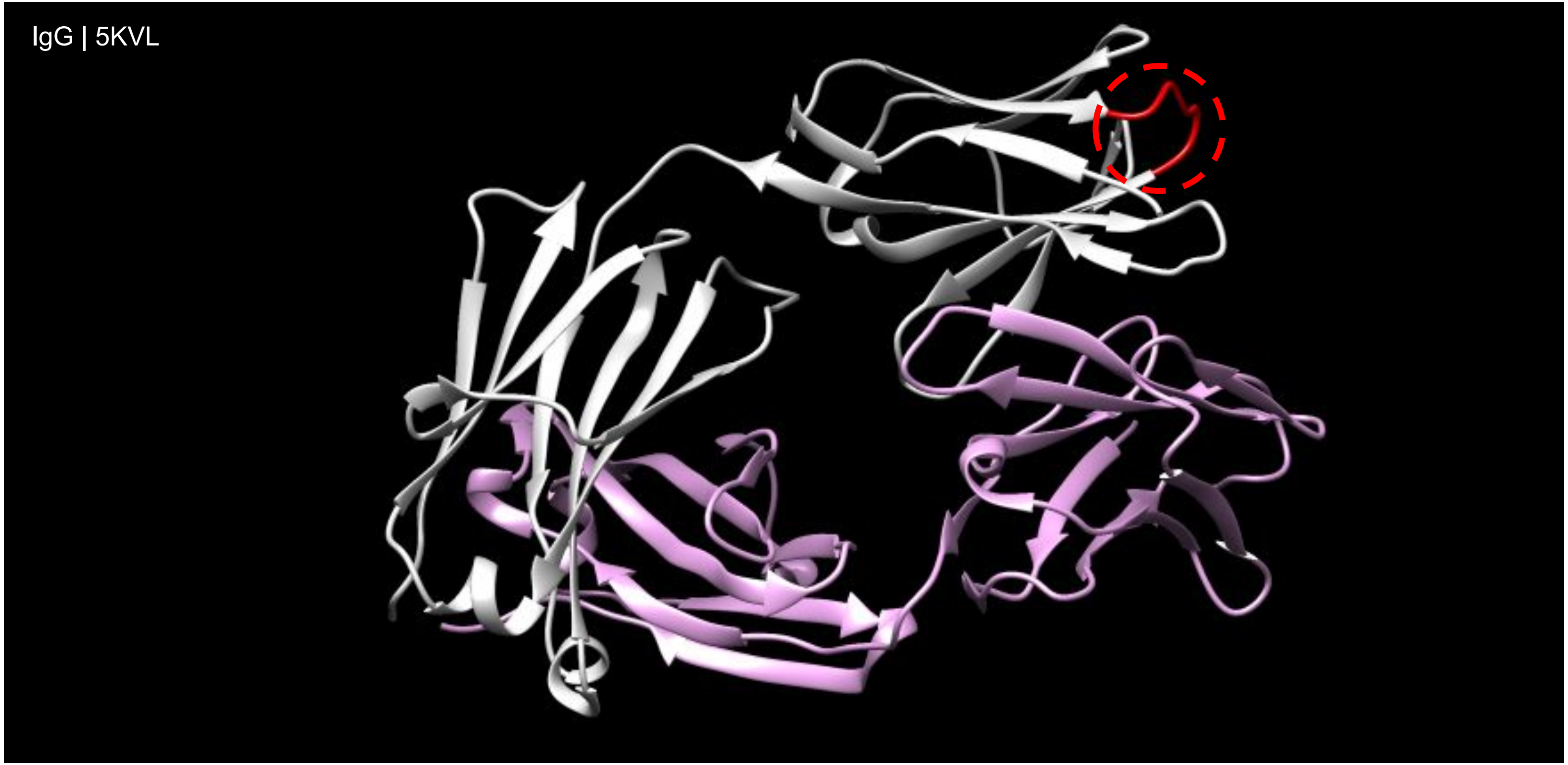
CDR		Canonical Structures
L1	→	κ1 - 6 λ1 - 4
L2	→	1
L3	→	κ1 - 6 λ1 - 2

Heavy chain

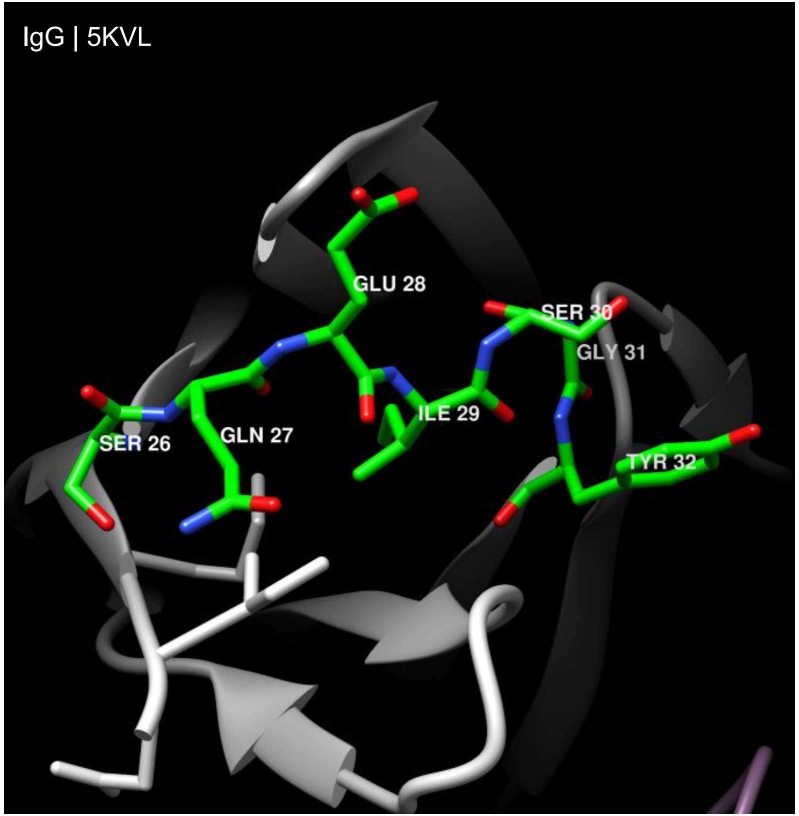
CDR		Canonical Structures
H1	→	3
H2	→	4
H3	→	NO

CDR ➳ L1

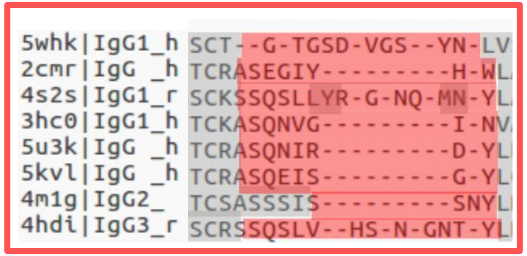
IgG structural analysis: CDR L1



IgG structural analysis: CDR L1

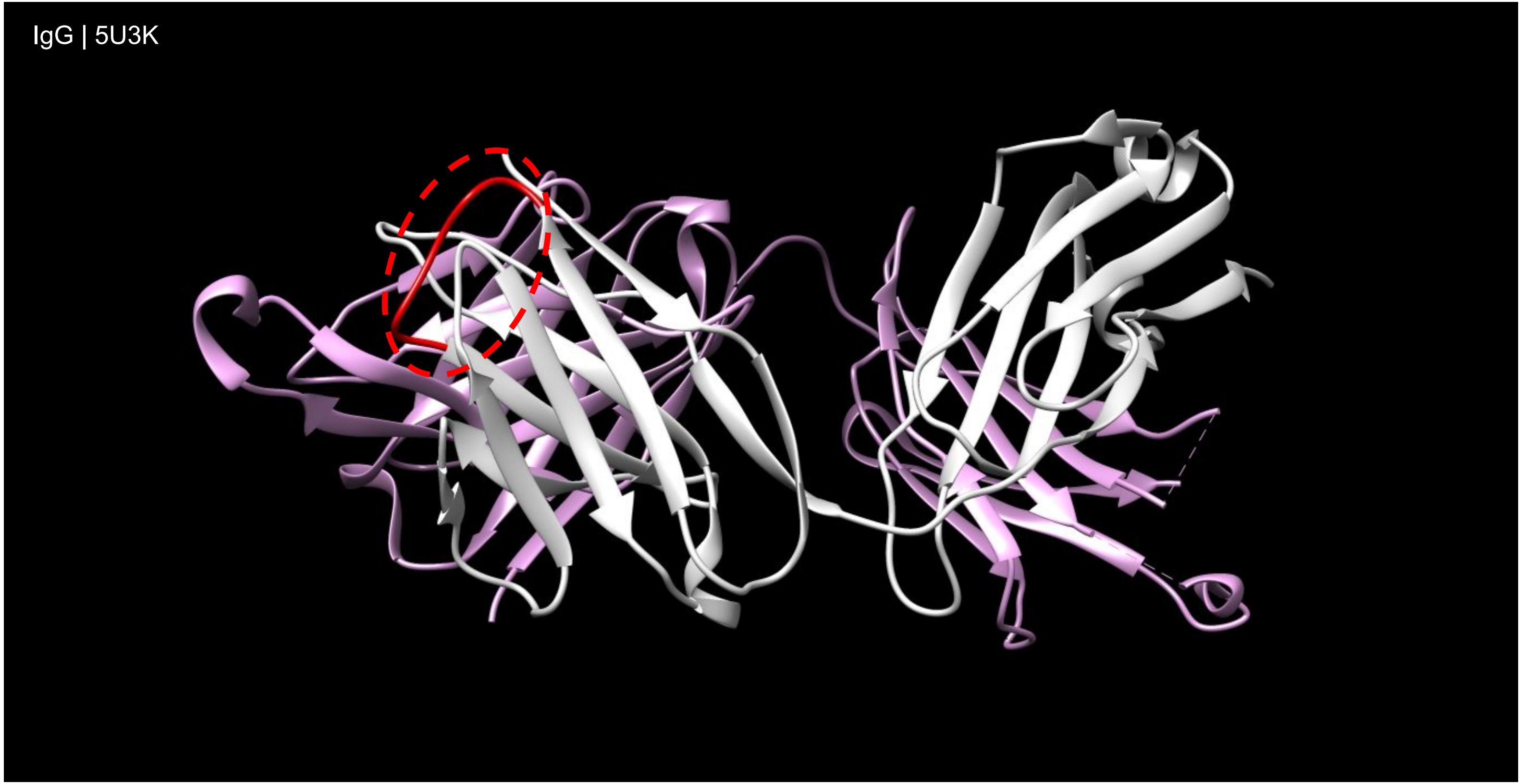


Canonical structure: K L1 1



```
5whk|IgG1_h SCT--G-TGSD-VGS--YN-LV
2cmr|IgG _h TCRASEGIY---------H-WL
4s2s|IgG1_r SCKSSQSLLYR-G-NQ-MN-YL
3hc0|IgG1_h TCKASQNVG---------I-NV
5u3k|IgG _h TCRASQNIR---------D-YL
5kvl|IgG _h TCRASQEIS---------G-YL
4m1g|IgG2_  TCSASSSIS---------SNYL
4hdi|IgG3_r SCRSSQSLV--HS-N-GNT-YL
```

IgG structural analysis: CDR L1

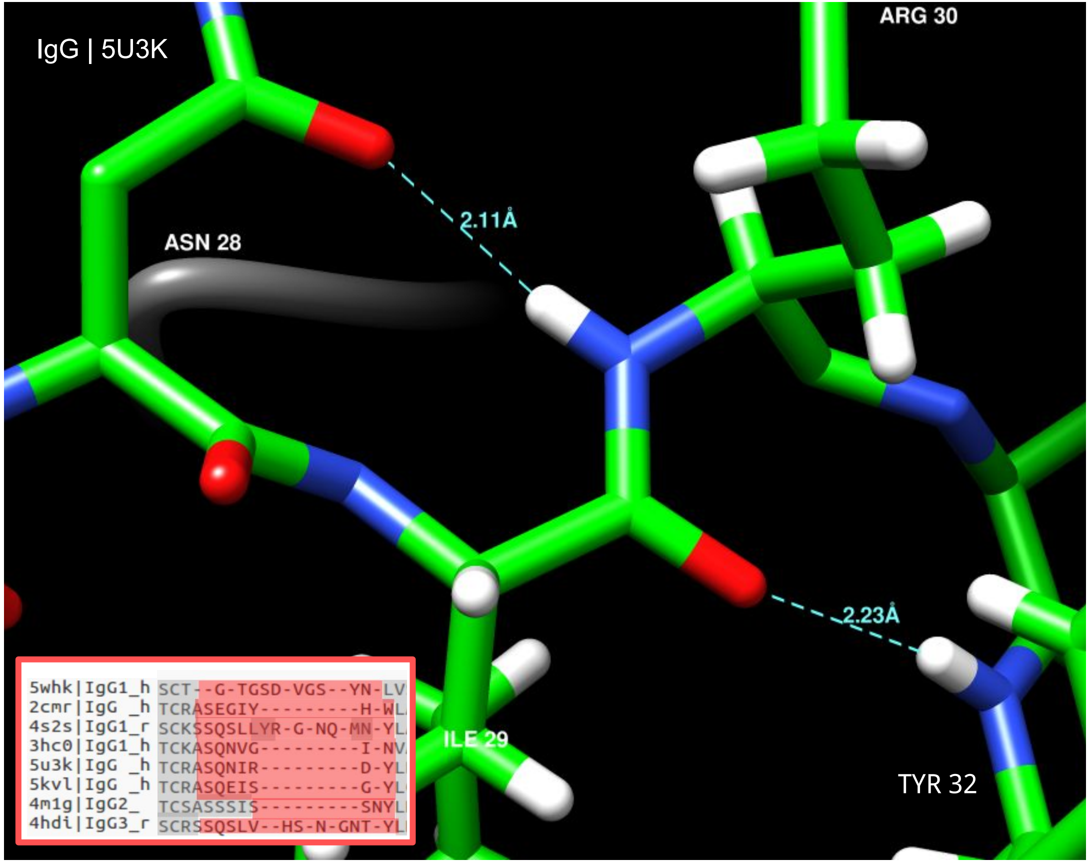


IgG structural analysis: CDR L1

Hydrogen Bonds

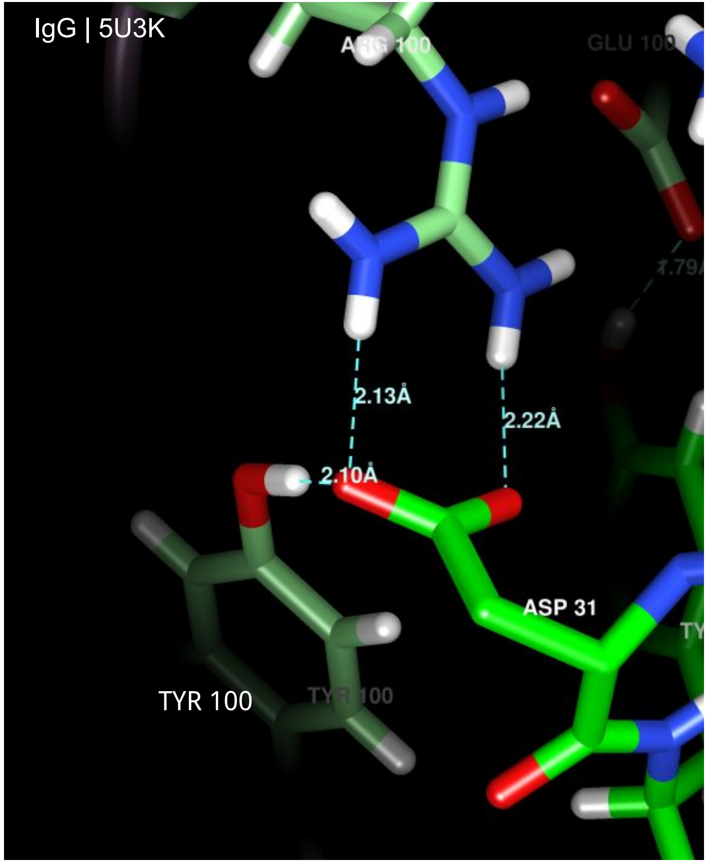
ILE 29 O . . . . . N TYR 32
ASN 28 O. . . . . . N ARG 30

Canonical structure: K L1 2a



```
5whk|IgG1_h SCT--G-TGSD-VGS--YN-LV
2cmr|IgG _h TCRASEGIY---------H-WL
4s2s|IgG1_r SCKSSQSLLYR-G-NQ-MN-YL
3hc0|IgG1_h TCKASQNVG---------I-NV
5u3k|IgG _h TCRASQNIR---------D-YL
5kvl|IgG _h TCRASQEIS---------G-YL
4m1g|IgG2_  TCSASSSIS---------SNYL
4hdi|IgG3_r SCRSSQSLV--HS-N-GNT-YL
```

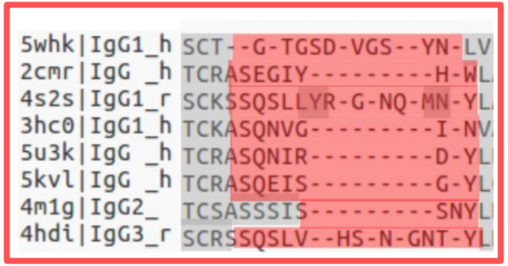
IgG structural analysis: CDR L1



Hydrogen Bonds

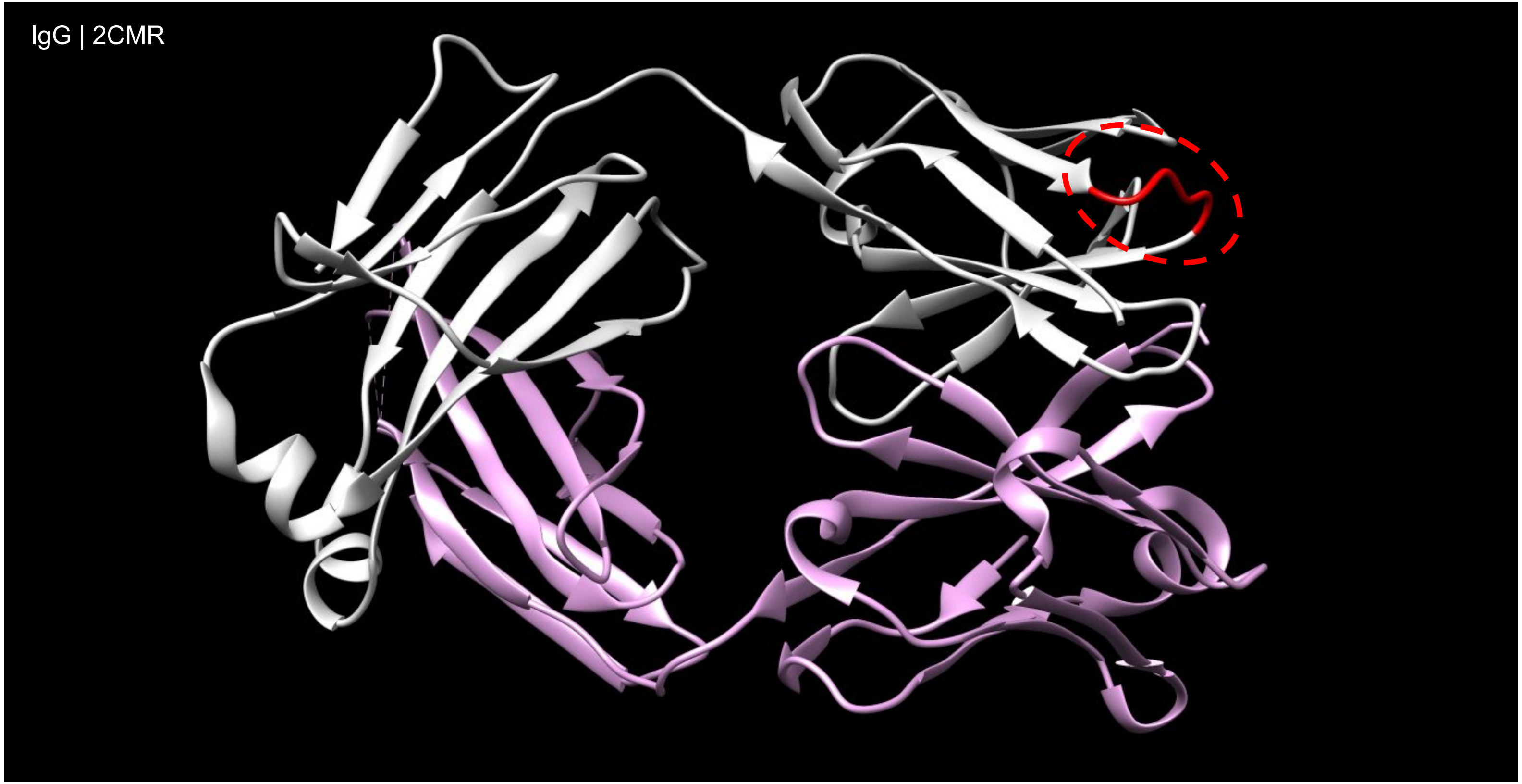
ASP 31 O . . . . . N ARG 100B
ASP 31 O . . . . . N ARG 100B
ASP 31 O . . . . . O TYR 100J

H3 - interaction

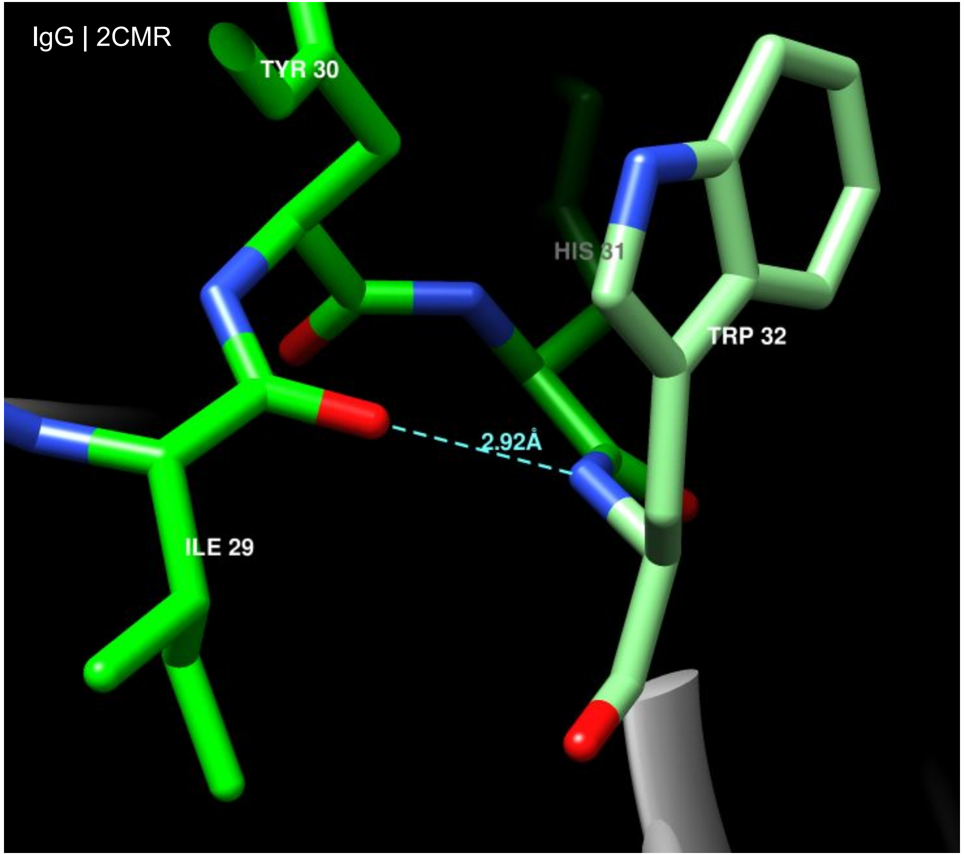


```
5whk|IgG1_h SCT--G-TGSD-VGS--YN-LV
2cmr|IgG _h TCRASEGIY---------H-WL
4s2s|IgG1_r SCKSSQSLLYR-G-NQ-MN-YL
3hc0|IgG1_h TCKASQNVG---------I-NV
5u3k|IgG _h TCRASQNIR---------D-YL
5kvl|IgG _h TCRASQEIS---------G-YL
4m1g|IgG2_  TCSASSSIS---------SNYL
4hdi|IgG3_r SCRSSQSLV--HS-N-GNT-YL
```

IgG structural analysis: CDR L1



IgG structural analysis: CDR L1

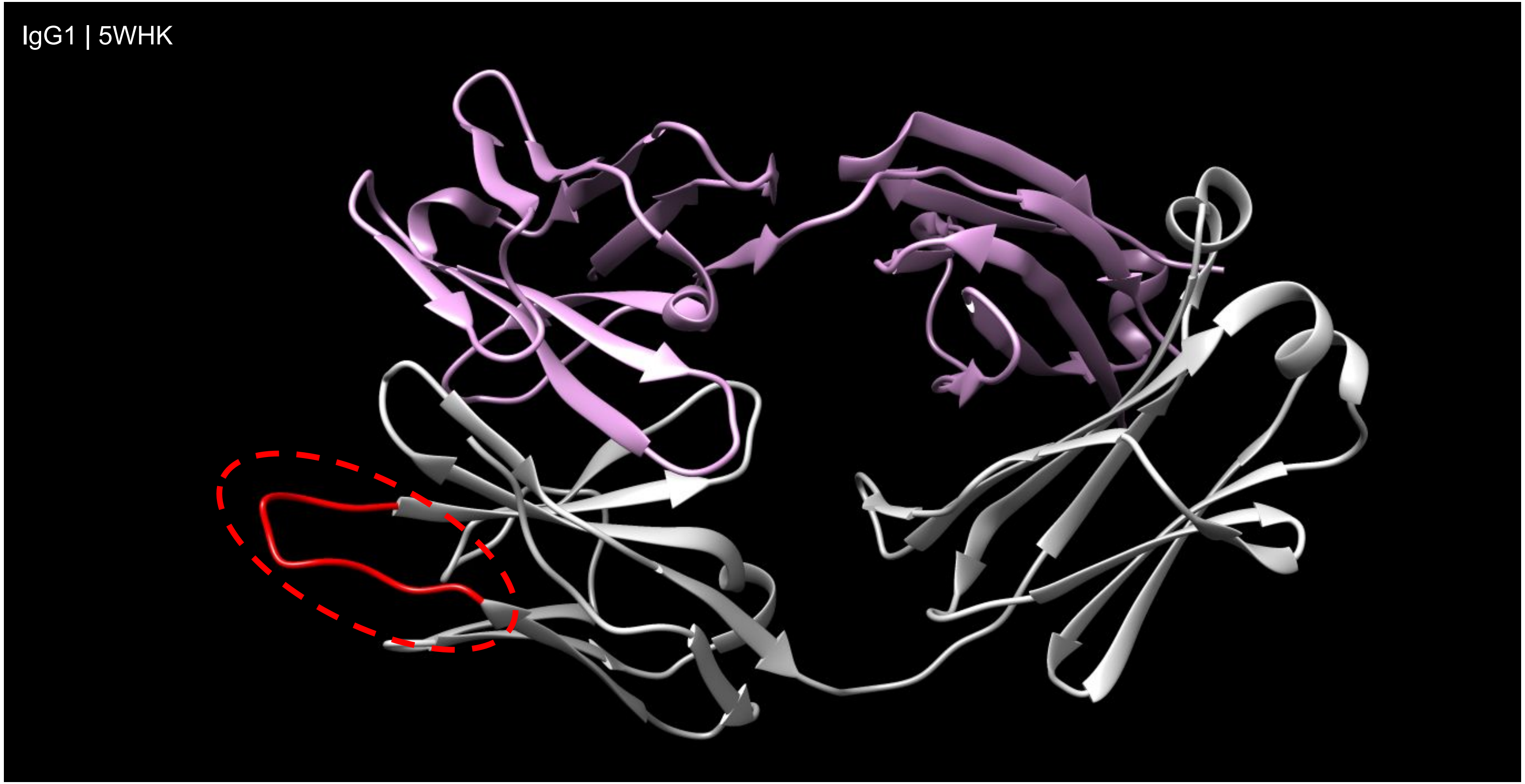


Hydrogen Bonds

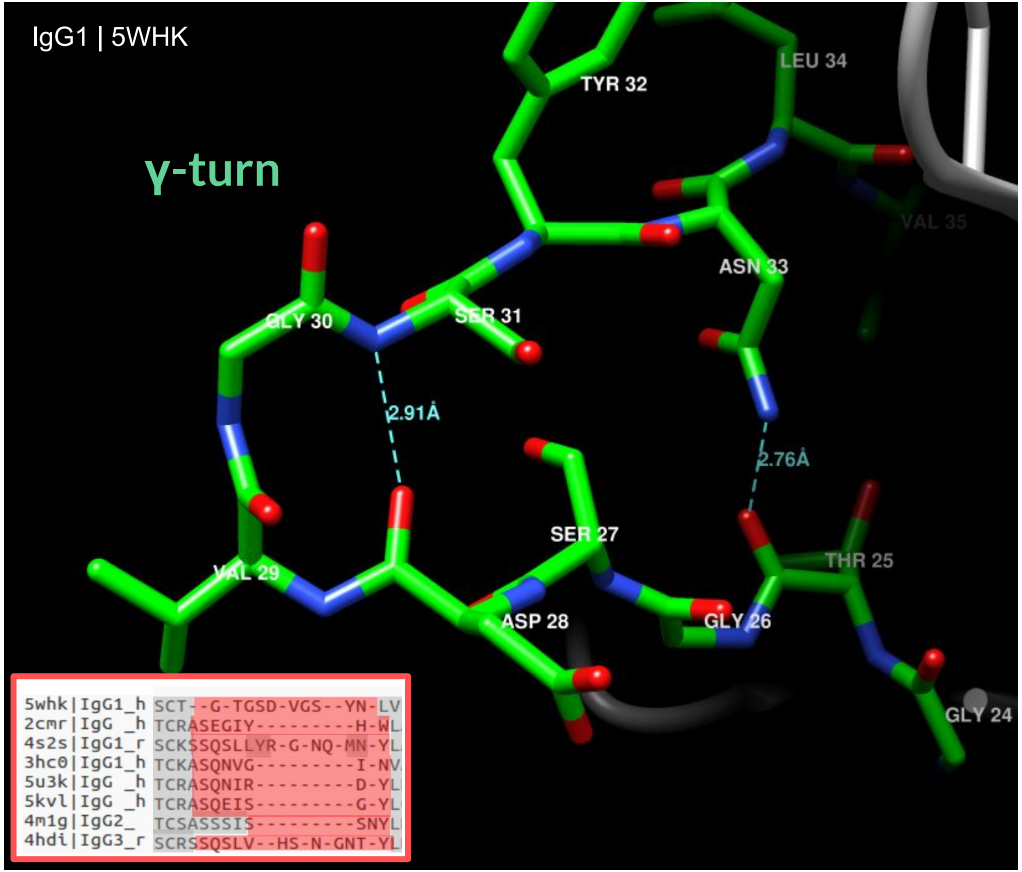
ILE 29 O . . . . . . N TRP 32

Canonical structure: K L1 2a

IgG structural analysis: CDR L1



IgG structural analysis: CDR L1



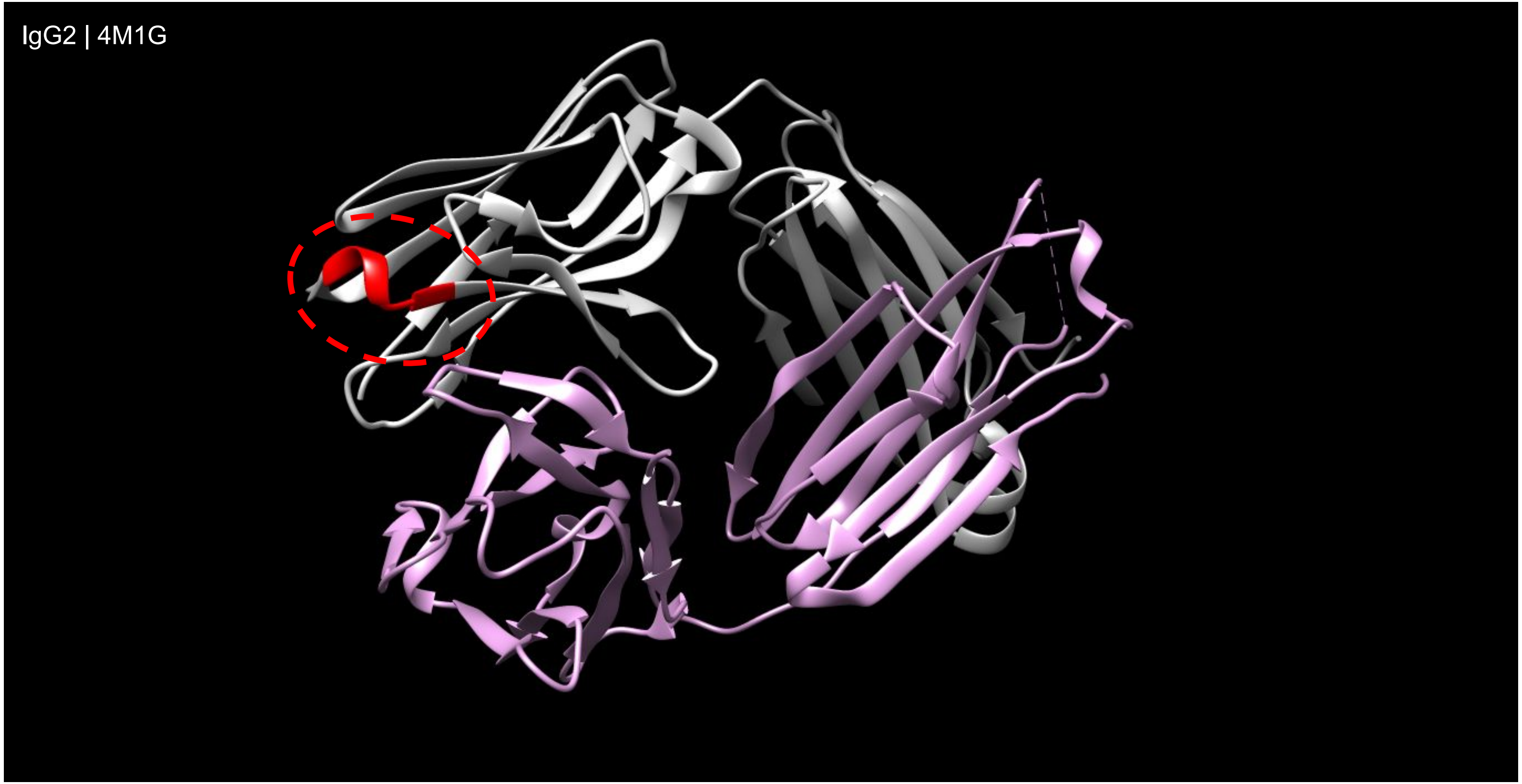
```
5whk|IgG1_h SCT--G-TGSD-VGS--YN-LV
2cmr|IgG _h TCRASEGIY---------H-WL
4s2s|IgG1_r SCKSSQSLLYR-G-NQ-MN-YL
3hc0|IgG1_h TCKASQNVG---------I-NV
5u3k|IgG _h TCRASQNIR---------D-YL
5kvl|IgG _h TCRASQEIS---------G-YL
4m1g|IgG2_  TCSASSSIS---------SNYL
4hdi|IgG3_r SCRSSQSLV--HS-N-GNT-YL
```

Hydrogen Bonds

VAL 29 O . . . . . N TYR 32
THR 25 N . . . . . O ASN 33

Canonical structure: ---

IgG structural analysis: CDR L1

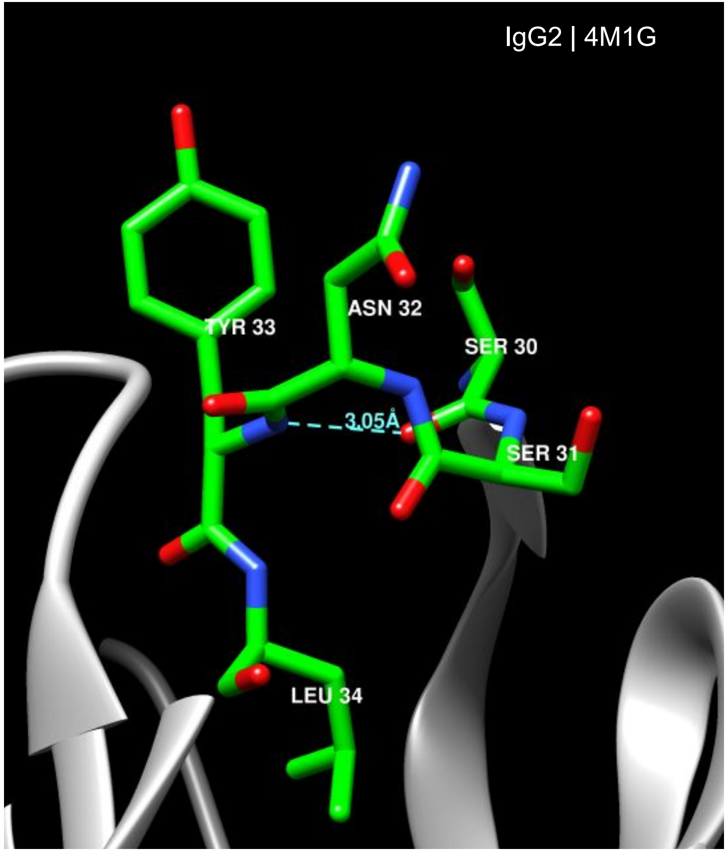


IgG structural analysis: CDR L1

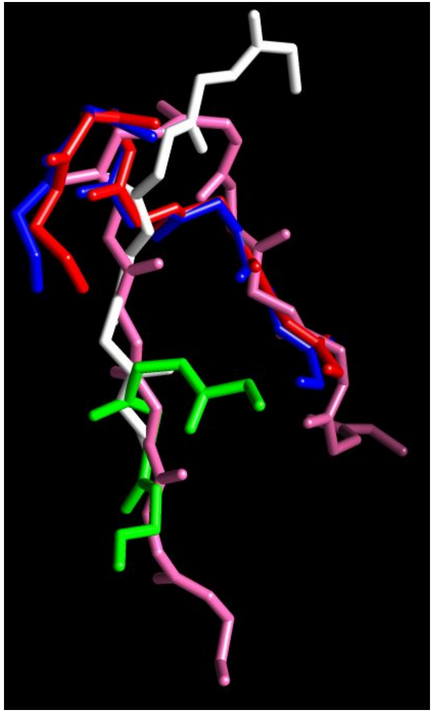
Hydrogen Bonds

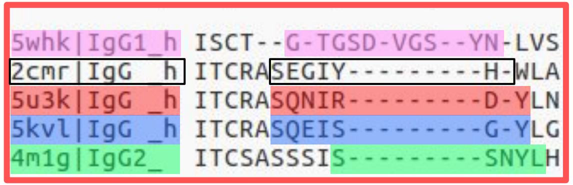
SER 30 O . . . . . . N TYR 33

Canonical structure: K L1 2a



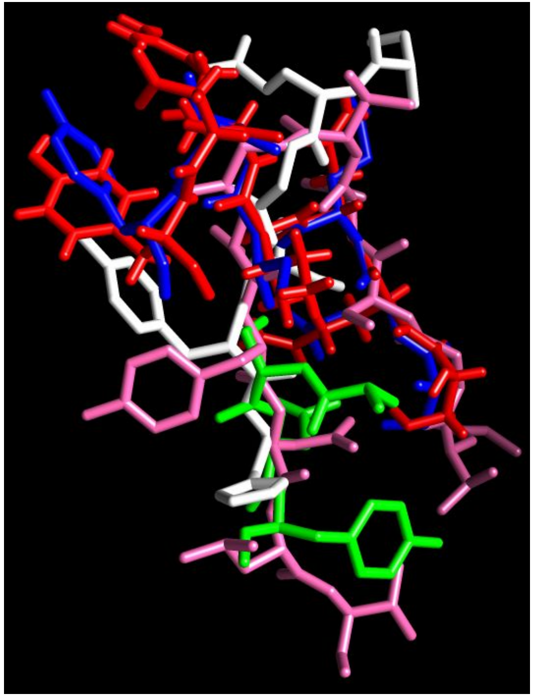
IgG structural analysis: CDR L1 - *superimposition*





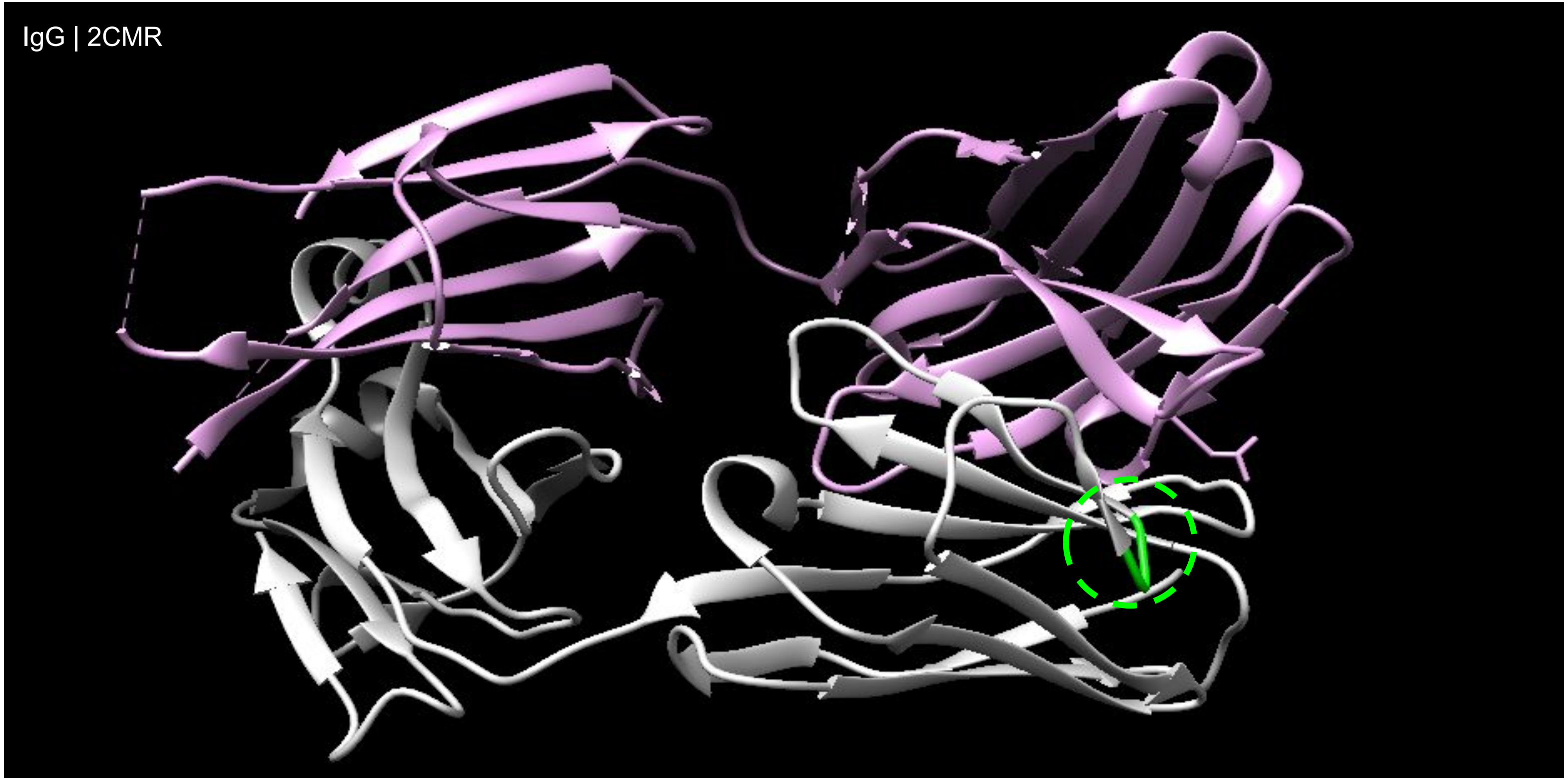
```
5whk|IgG1_h  ISCT--G-TGSD-VGS--YN-LVS
2cmr|IgG  _h ITCRASEGIY---------H-WLA
5u3k|IgG  _h ITCRASQNIR---------D-YLN
5kvl|IgG  _h ITCRASQEIS---------G-YLG
4m1g|IgG2_   ITCSASSSIS---------SNYLH
```

RMSD: 4.23

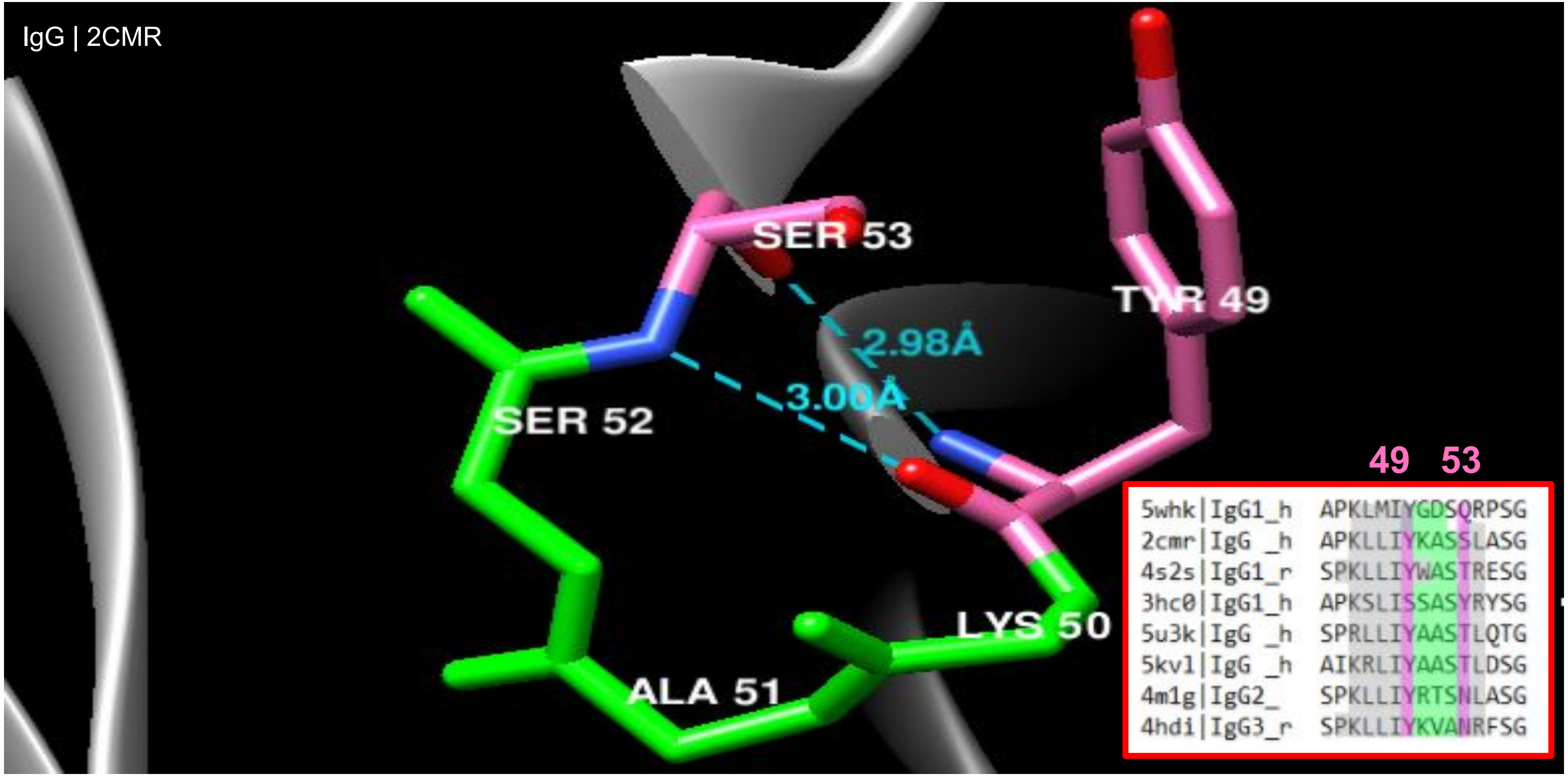


CDR ➳ L2

IgG structural analysis: CDR L2

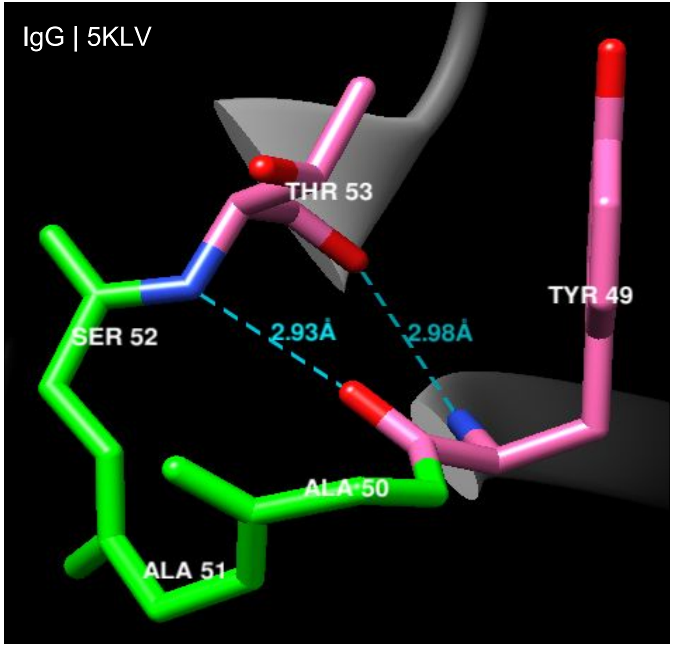


IgG structural analysis: CDR L2

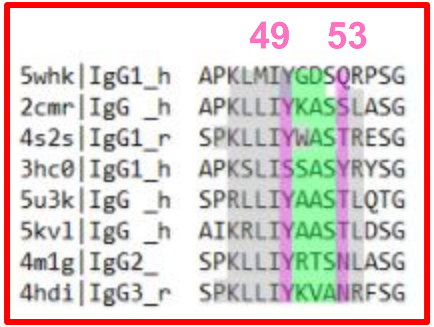


```
5whk|IgG1_h  APKLMIYGDSQRPSG
2cmr|IgG _h  APKLLIYKASSLASG
4s2s|IgG1_r  SPKLLIYWASTRESG
3hc0|IgG1_h  APKSLISSASYRYSG
5u3k|IgG _h  SPRLLIYAASTLQTG
5kvl|IgG _h  AIKRLIYAASTLDSG
4m1g|IgG2_   SPKLLIYRTSNLASG
4hdi|IgG3_r  SPKLLIYKVANRFSG
```

IgG structural analysis: CDR L2



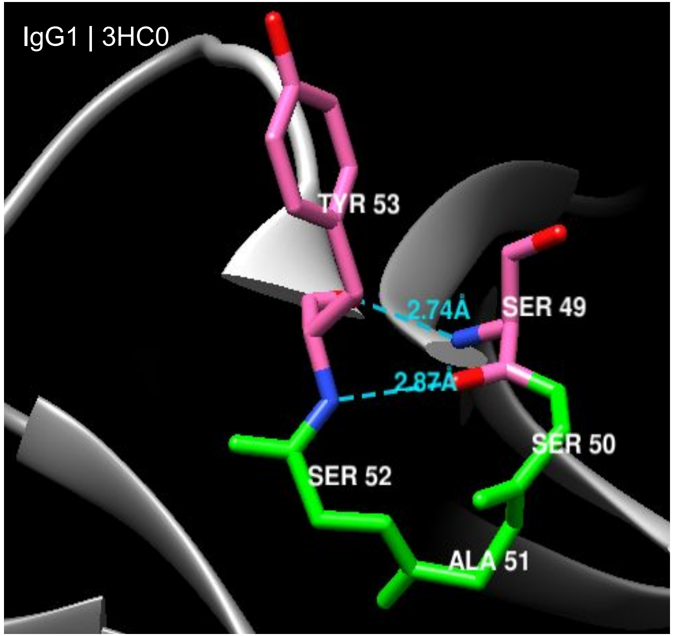
Length of the loop 50-56



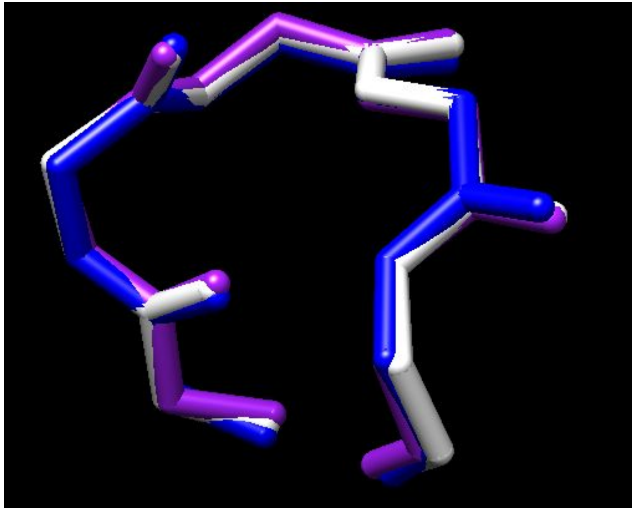
```
5whk|IgG1_h   APKLMIYGDSQRPSG
2cmr|IgG _h   APKLLIYKASSLASG
4s2s|IgG1_r   SPKLLIYWASTRESG
3hc0|IgG1_h   APKSLISSASYRYSG
5u3k|IgG _h   SPRLLIYAASTLQTG
5kvl|IgG _h   AIKRLIYAASTLDSG
4m1g|IgG2_    SPKLLIYRTSNLASG
4hdi|IgG3_r   SPKLLIYKVANRFSG
```

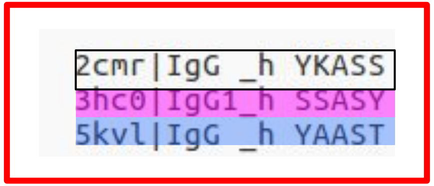
Hydrogen Bonds

TYR 49 N . . . . . . O 53
TYR 49 O . . . . . . N 53



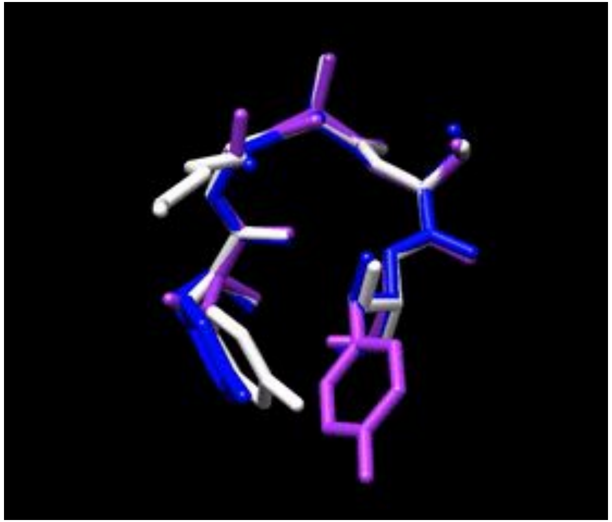
IgG structural analysis: CDR L2- *superimposition*





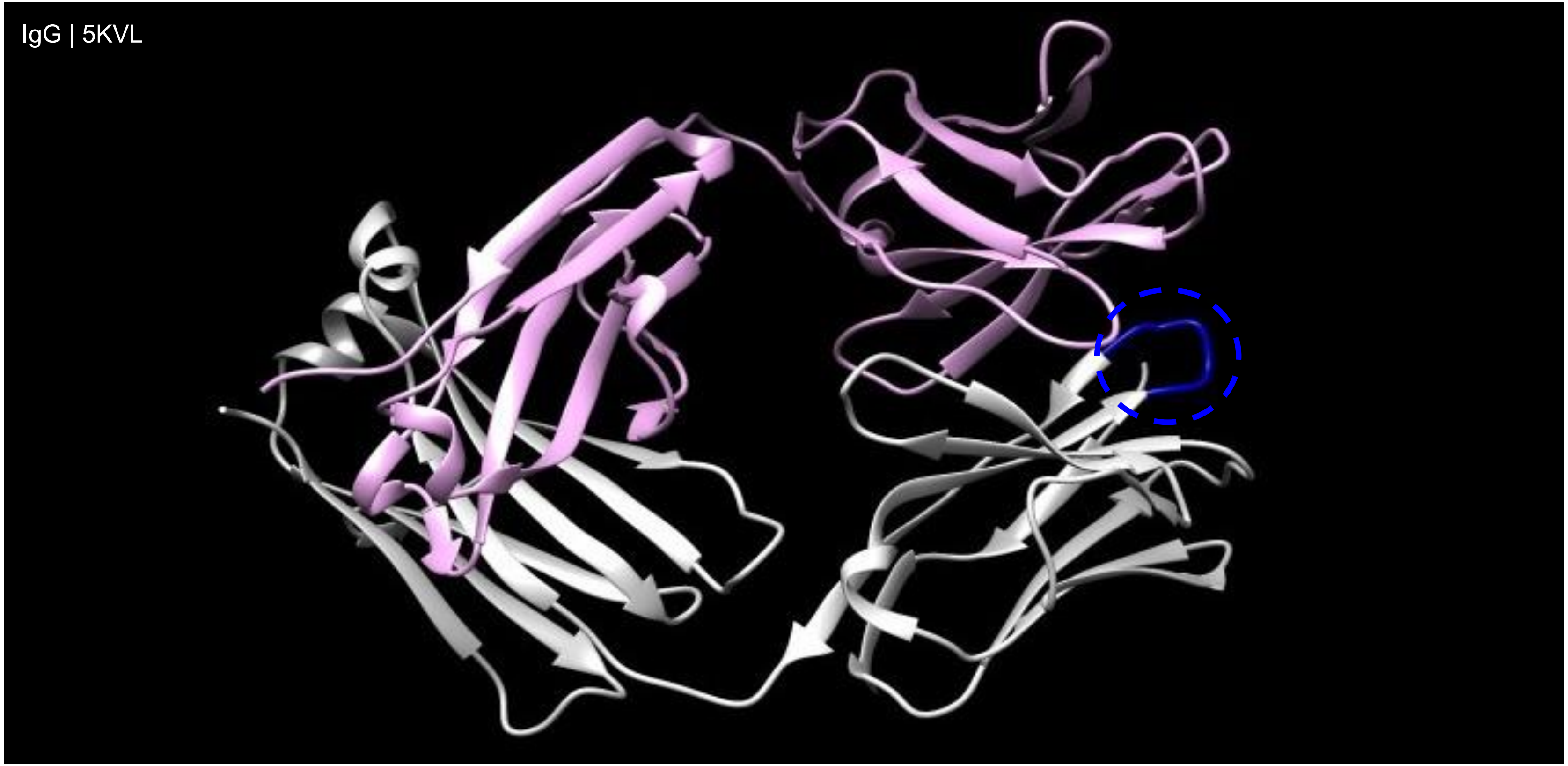
```
2cmr|IgG _h YKASS
3hc0|IgG1_h SSASY
5kvl|IgG _h YAAST
```

RSMD: 0.13

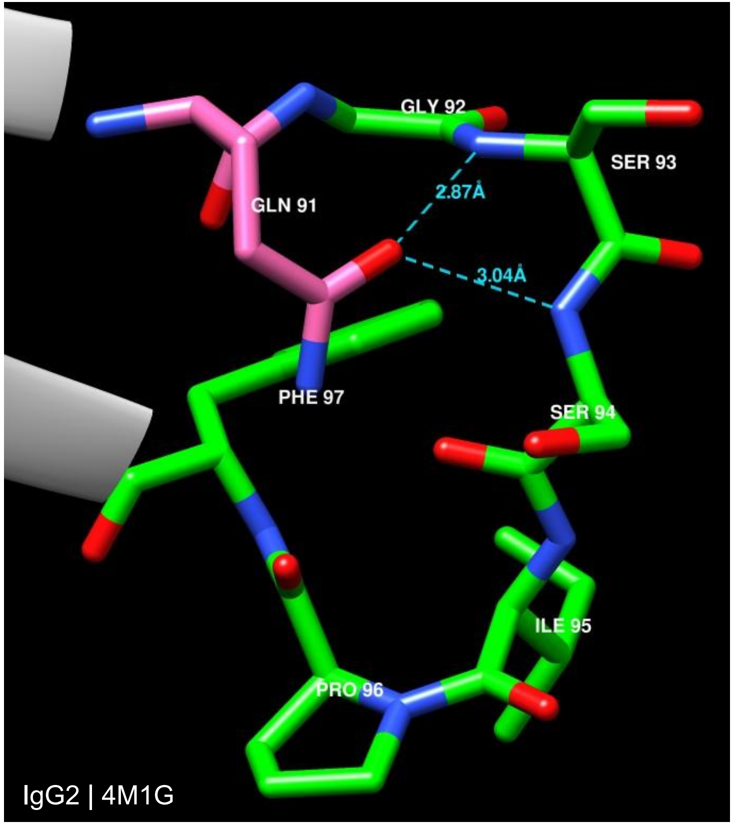


CDR ➳ L3

IgG structural analysis: CDR L3



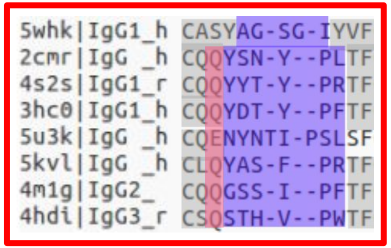
IgG structural analysis: CDR L3



Canonical structure: K L3 1

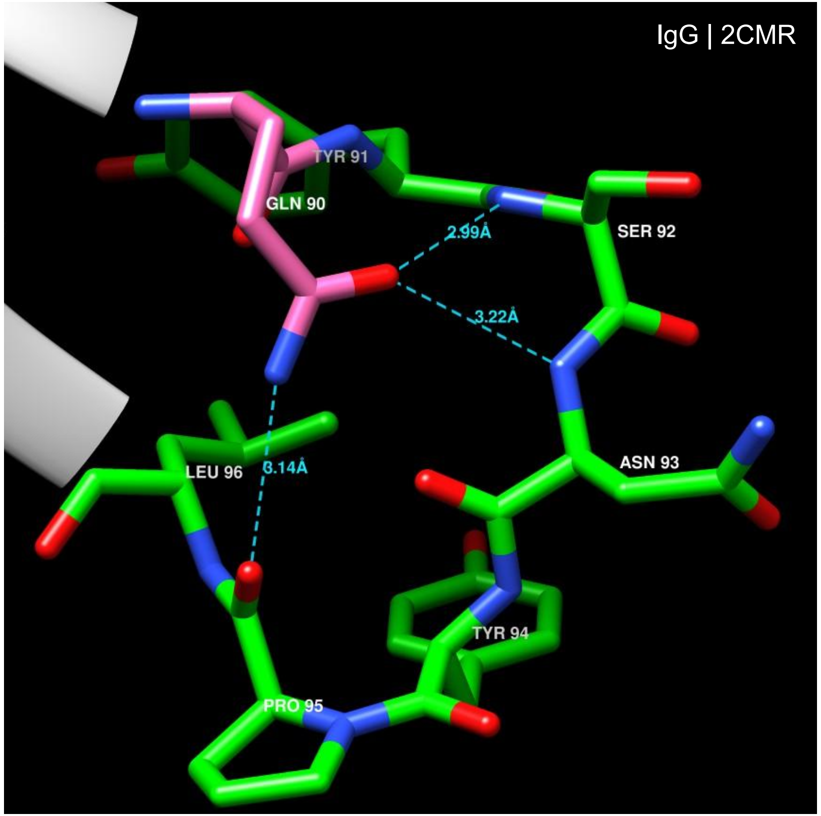
Hydrogen bonds:

GLN 91 O...N SER 93
GLN 91 O...N SER 94



```
5whk|IgG1_h CASYAG-SG-IYVF
2cmr|IgG _h CQQYSN-Y--PLTF
4s2s|IgG1_r CQQYYT-Y--PRTF
3hc0|IgG1_h CQQYDT-Y--PFTF
5u3k|IgG _h CQENYNTI-PSLSF
5kvl|IgG _h CLQYAS-F--PRTF
4m1g|IgG2_  CQQGSS-I--PFTF
4hdi|IgG3_r CSQSTH-V--PWTF
```

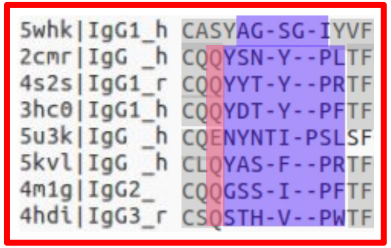
IgG structural analysis: CDR L3



Canonical structure: K L3 1

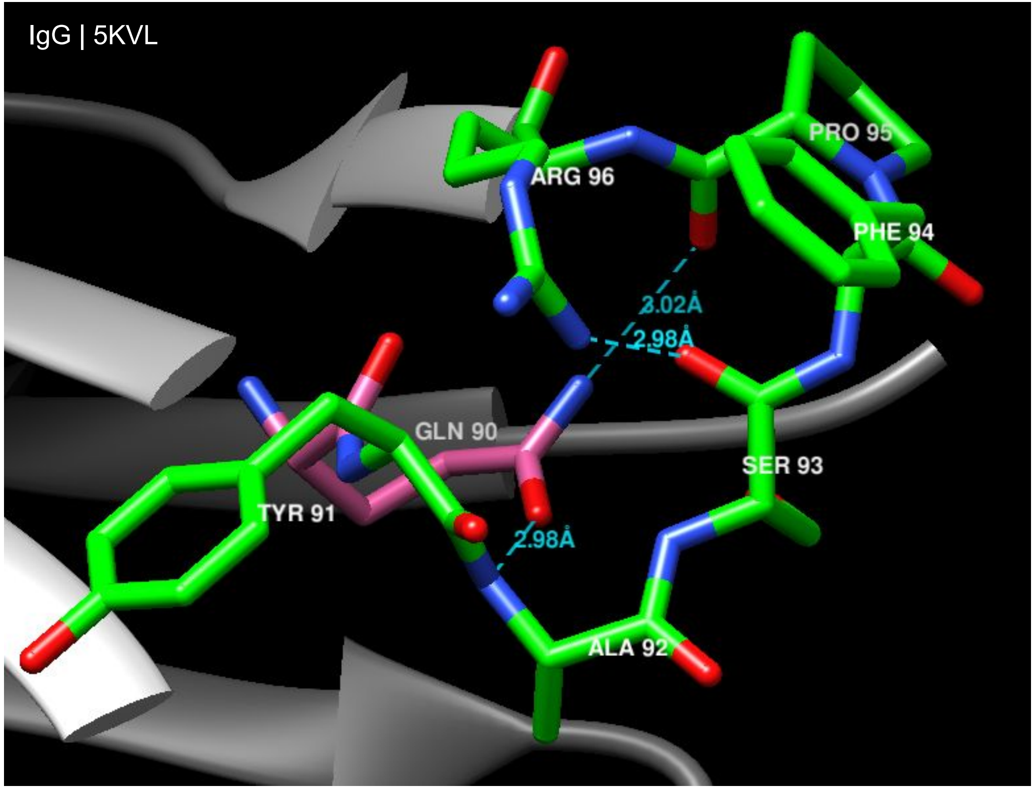
Hydrogen bonds:

GLN 90 O...N SER 92
GLN 90 O...N ASN 93
GLN 90 N...O PRO 95



```
5whk|IgG1_h  CASYAG-SG-IYVF
2cmr|IgG _h  CQQYSN-Y--PLTF
4s2s|IgG1_r  CQQYYT-Y--PRTF
3hc0|IgG1_h  CQQYDT-Y--PFTF
5u3k|IgG _h  CQENYNTI-PSLSF
5kvl|IgG _h  CLQYAS-F--PRTF
4m1g|IgG2_   CQQGSS-I--PFTF
4hdi|IgG3_r  CSQSTH-V--PWTF
```

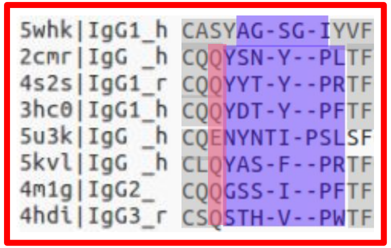
IgG structural analysis: CDR L3



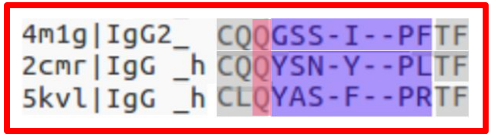
Canonical structure: K L3 1

Hydrogen bonds:

GLN 90 O...N ALA 92
GLN 90 N...O PRO 95
SER 93 O...N ARG 96

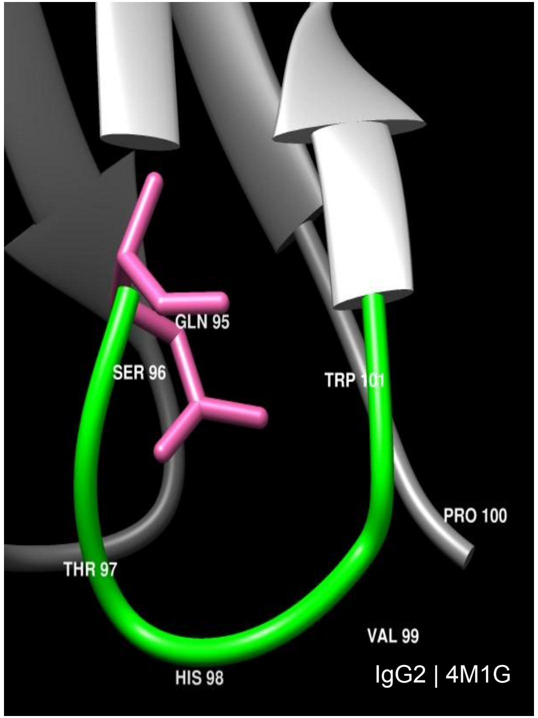

```
5whk|IgG1_h  CASYAG-SG-IYVF
2cmr|IgG _h  CQQYSN-Y--PLTF
4s2s|IgG1_r  CQQYYT-Y--PRTF
3hc0|IgG1_h  CQQYDT-Y--PFTF
5u3k|IgG _h  CQENYNTI-PSLSF
5kvl|IgG _h  CLQYAS-F--PRTF
4m1g|IgG2_   CQQGSS-I--PFTF
4hdi|IgG3_r  CSQSTH-V--PWTF
```

IgG structural analysis: CDR L3

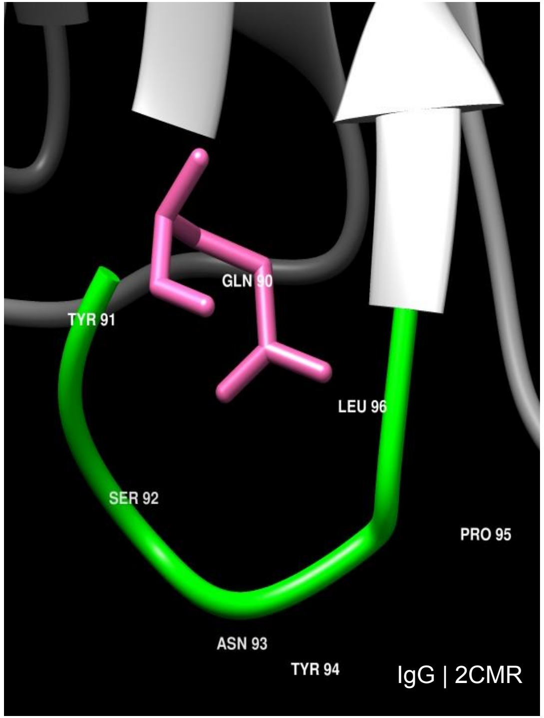


```
4m1g|IgG2_  CQQGSS-I--PFTF
2cmr|IgG _h CQQYSN-Y--PLTF
5kvl|IgG _h CLQYAS-F--PRTF
```

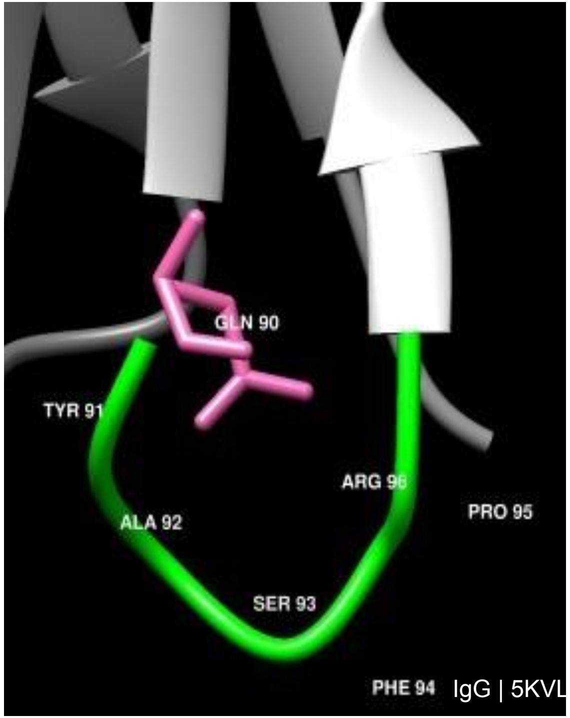
Canonical structure: K L3 1



IgG2 | 4M1G

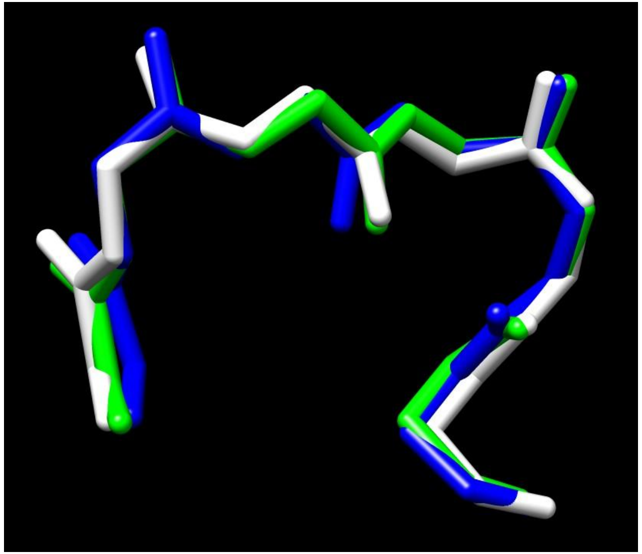


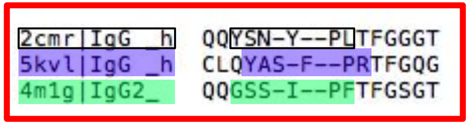
IgG | 2CMR



IgG | 5KVL

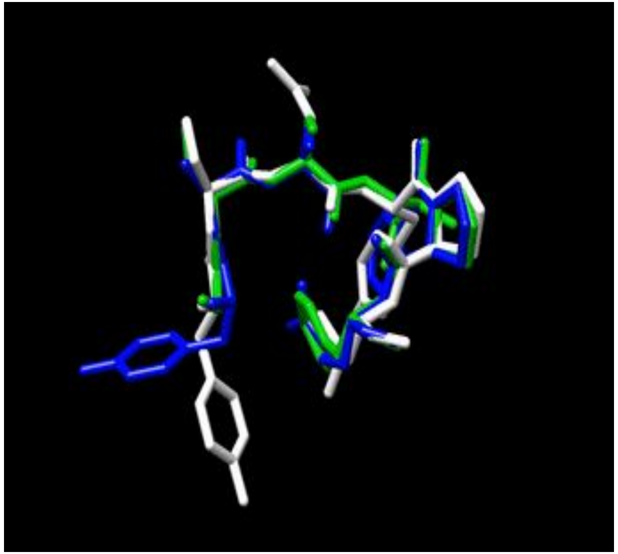
IgG structural analysis: CDR L3 - *superimposition*





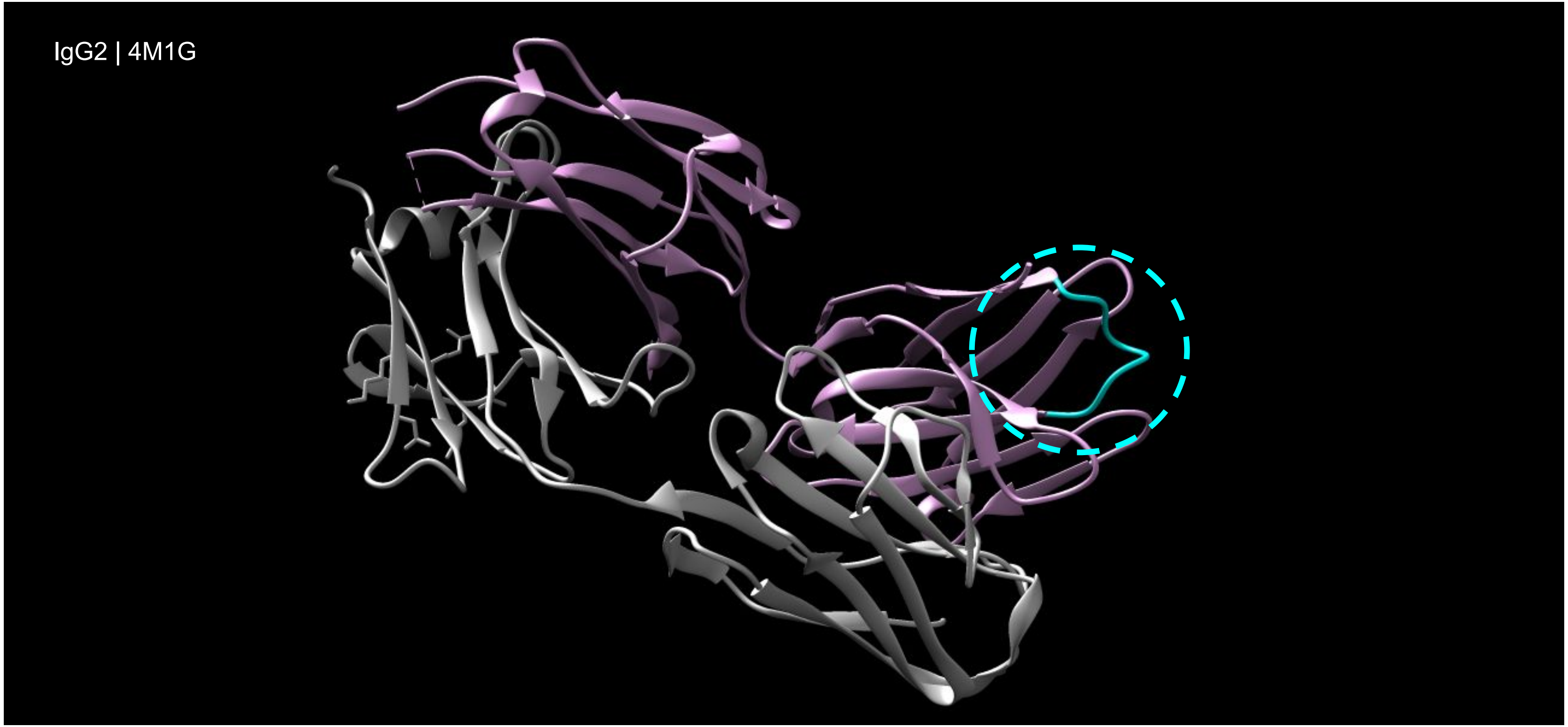
```
2cmr|IgG _h   QQYSN-Y--PLTFGGGT
5kvl|IgG _h   CLQYAS-F--PRTFGQG
4m1g|IgG2_    QQGSS-I--PFTFGSGT
```

RMSD: 0.306



CDR ➳ H1

IgG structural analysis: CDR H1



IgG structural analysis: CDR H1

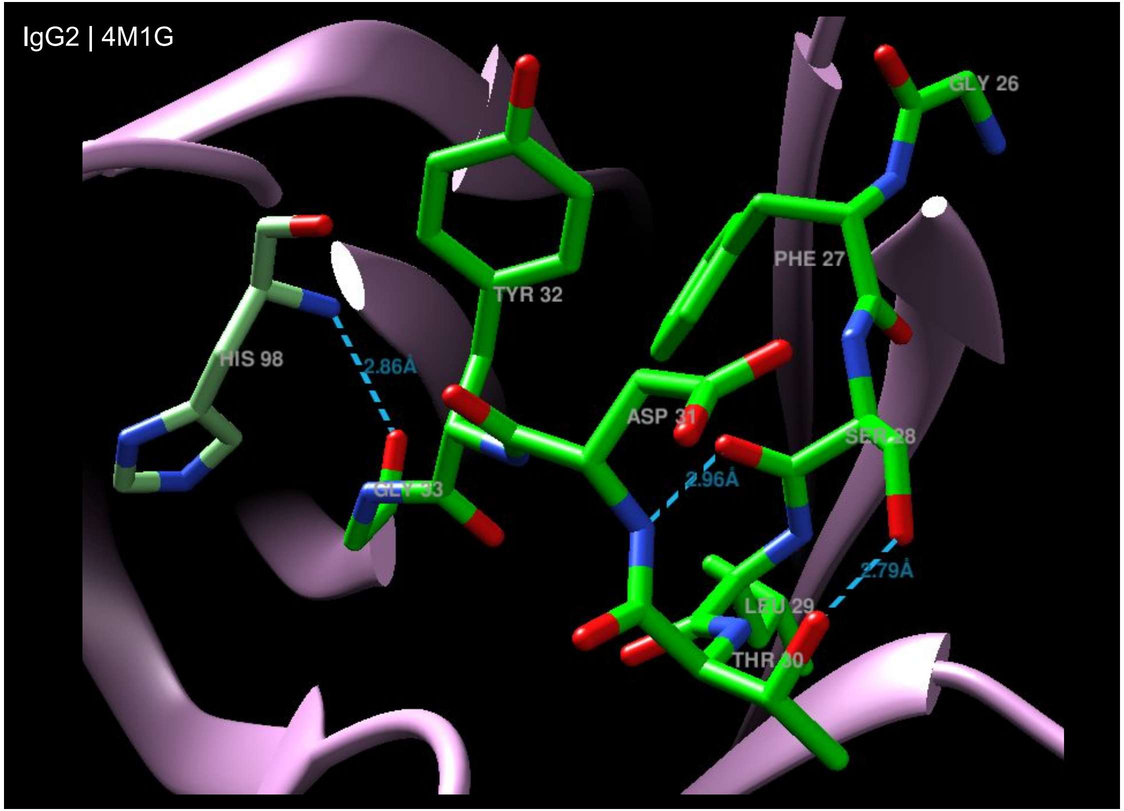
Hydrogen bonds

SER 28 O …… N ASP 31
SER 28 O …… O THR 30

GLY 33 O …… N HIS 98

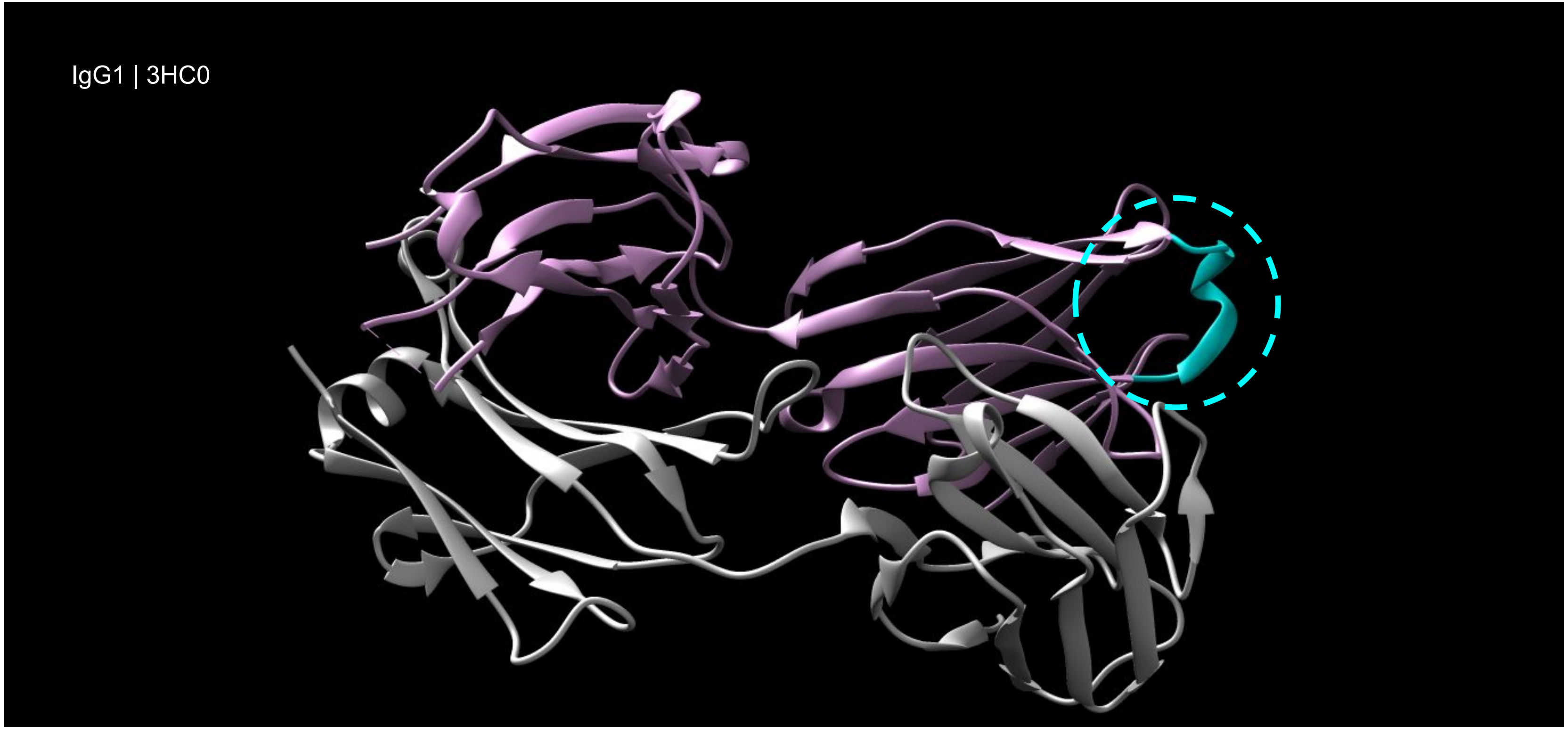
Interaction with H3

```
4m1g|IgG2_   SLSITCTVS-GFSLTD-YGVSWIRQP
5kvl|IgG _h  TLSVTCTVS-GYSITSSYSWNWIRQF
5whk|IgG1_h  SLRLSCAAS-GFTFSE-YAMGWVRQA
4hdi|IgG3_r  SLKLSCAAS-GFTFSN-YFMSWVRQT
5u3k|IgG _h  SLTLSCSAS-GFFFDN-SWMGWVRQA
4s2s|IgG1_r  SLKLSCAAS-GFTFST-YAMSWVRQT
3hc0|IgG1_h  SVKVSCKAS-GYTFTT-YYLHWVRQA-
2cmr|IgG _h  SVKVSCKASGDT-FSS-YAISWVRQA
```



IgG2 | 4M1G

IgG structural analysis: CDR H1



IgG structural analysis: CDR H1

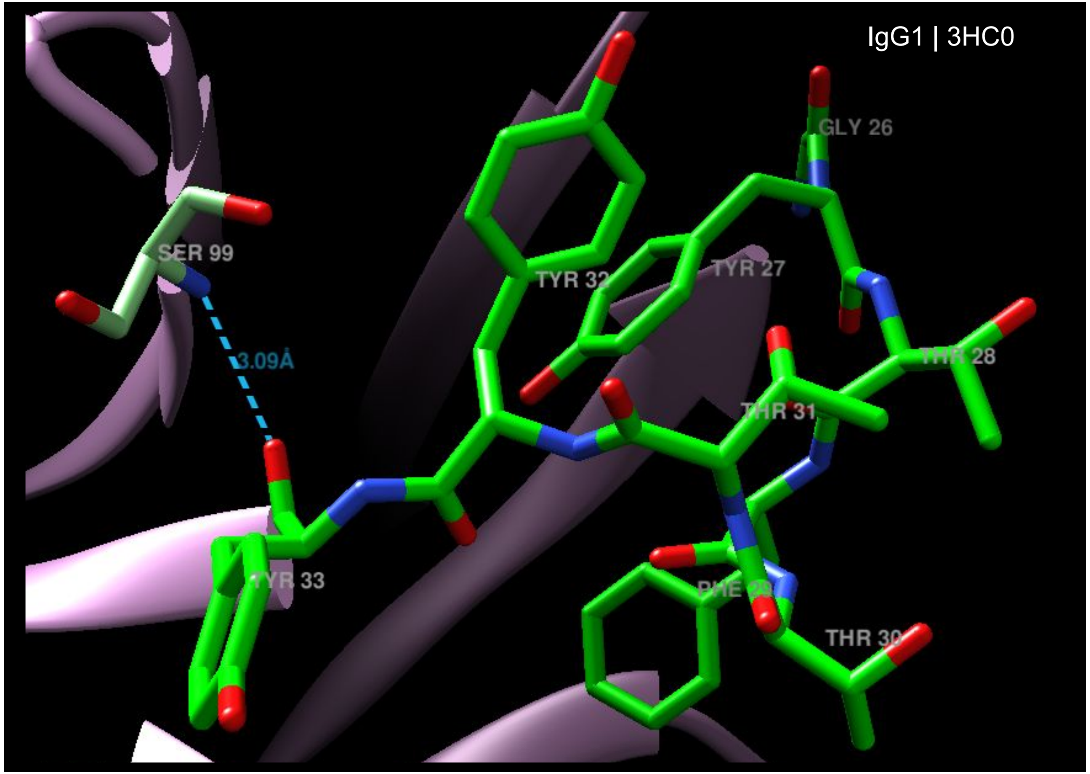
Hydrogen bonds

No internal interactions

TYR 33 O……. N SER 99

Interaction with H3

```
4m1g|IgG2_   SLSITCTVS-GFSLTD-YGVSWIRQP
5kvl|IgG _h  TLSVTCTVS-GYSITSSYSWNWIRQF
5whk|IgG1_h  SLRLSCAAS-GFTFSE-YAMGWVRQA
4hdi|IgG3_r  SLKLSCAAS-GFTFSN-YFMSWVRQT
5u3k|IgG _h  SLTLSCSAS-GFFFDN-SWMGWVRQA
4s2s|IgG1_r  SLKLSCAAS-GFTFST-YAMSWVRQT
3hc0|IgG1_h  SVKVSCKAS-GYTFTT-YYLHWVRQA-
2cmr|IgG _h  SVKVSCKASGDT-FSS-YAISWVRQA
```



IgG structural analysis: CDR H1

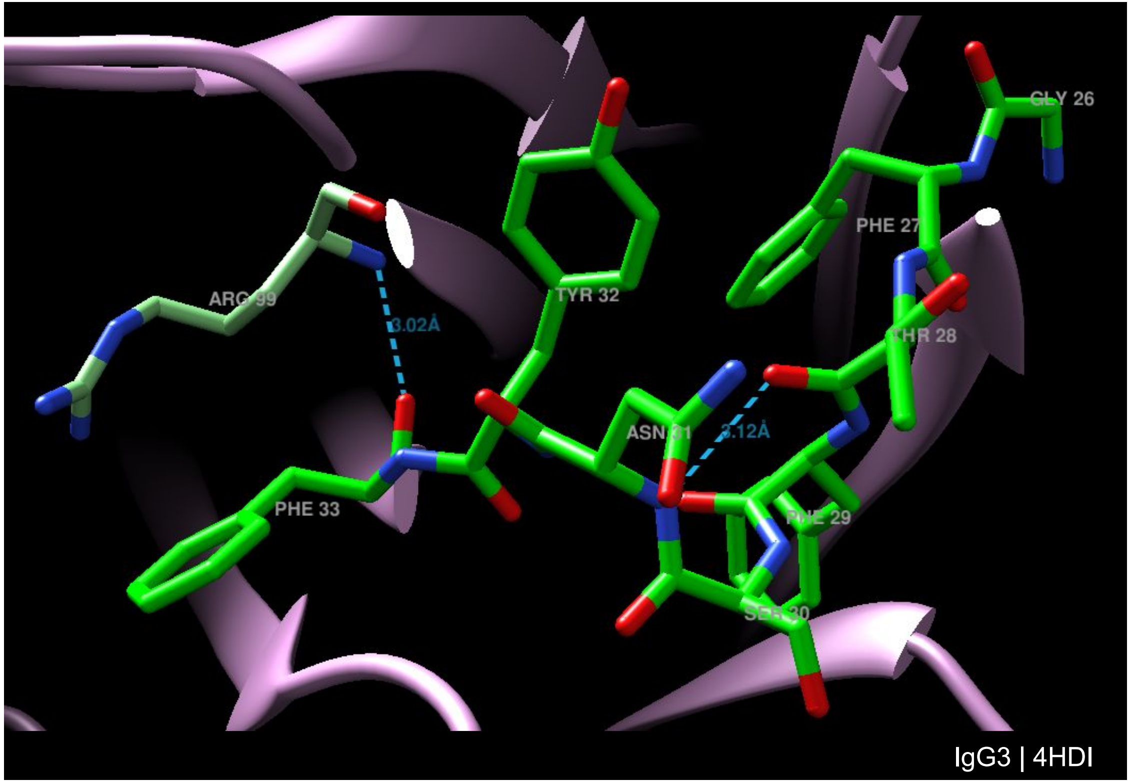
Hydrogen bonds

THR 28 O … ASN 31 N

PHE 33 O … N ARG 99

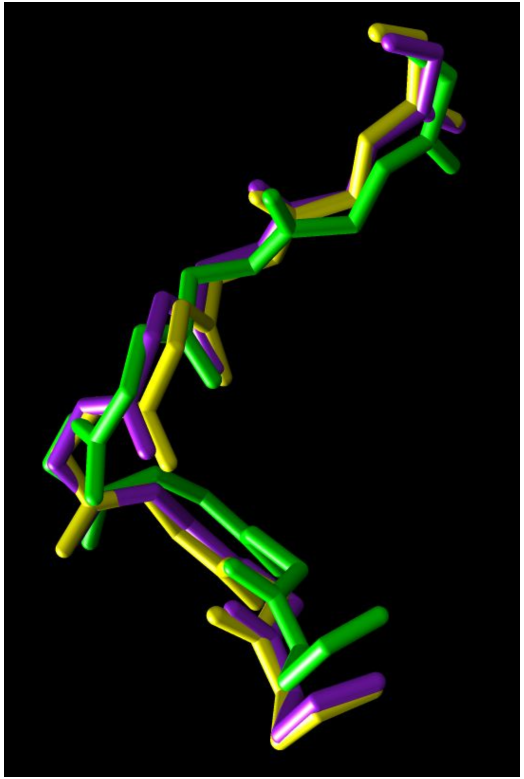
Interaction with H3

```
4m1g|IgG2_   SLSITCTVS-GFSLTD-YGVSWIRQP
5kvl|IgG _h  TLSVTCTVS-GYSITSSYSWNWIRQF
5whk|IgG1_h  SLRLSCAAS-GFTFSE-YAMGWVRQA
4hdi|IgG3_r  SLKLSCAAS-GFTFSN-YFMSWVRQT
5u3k|IgG _h  SLTLSCSAS-GFFFDN-SWMGWVRQA
4s2s|IgG1_r  SLKLSCAAS-GFTFST-YAMSWVRQT
3hc0|IgG1_h  SVKVSCKAS-GYTFTT-YYLHWVRQA-
2cmr|IgG _h  SVKVSCKASGDT-FSS-YAISWVRQA
```



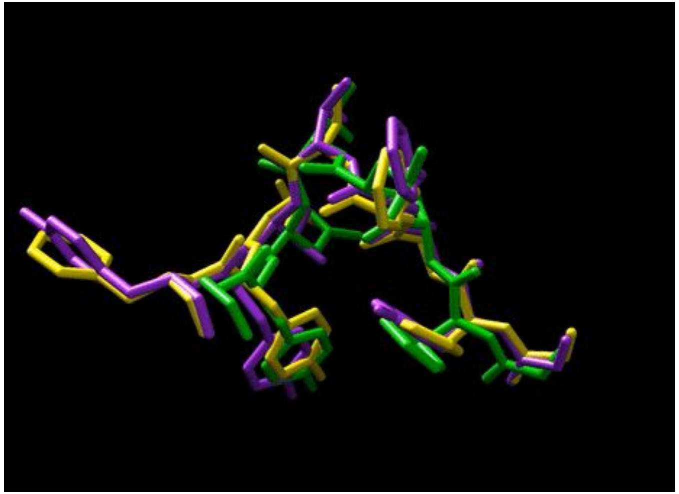
IgG3 | 4HDI

IgG structural analysis: CDR H1 - *superimposition*



```
4m1g|IgG2_   TVS-GFSLTD-YGVSW
4hdi|IgG3_r  AAS-GFTFSN-YFMSW
3hc0|IgG1_h  KAS-GYTFTT-YYLHW
```

RMSD: 0.356



CDR → H_2

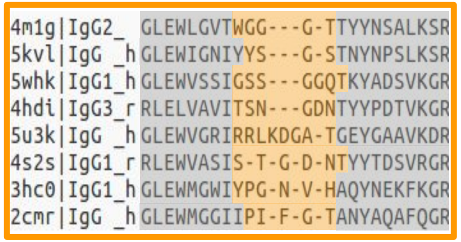
IgG structural analysis: CDR H2

IgG structural analysis: CDR H2

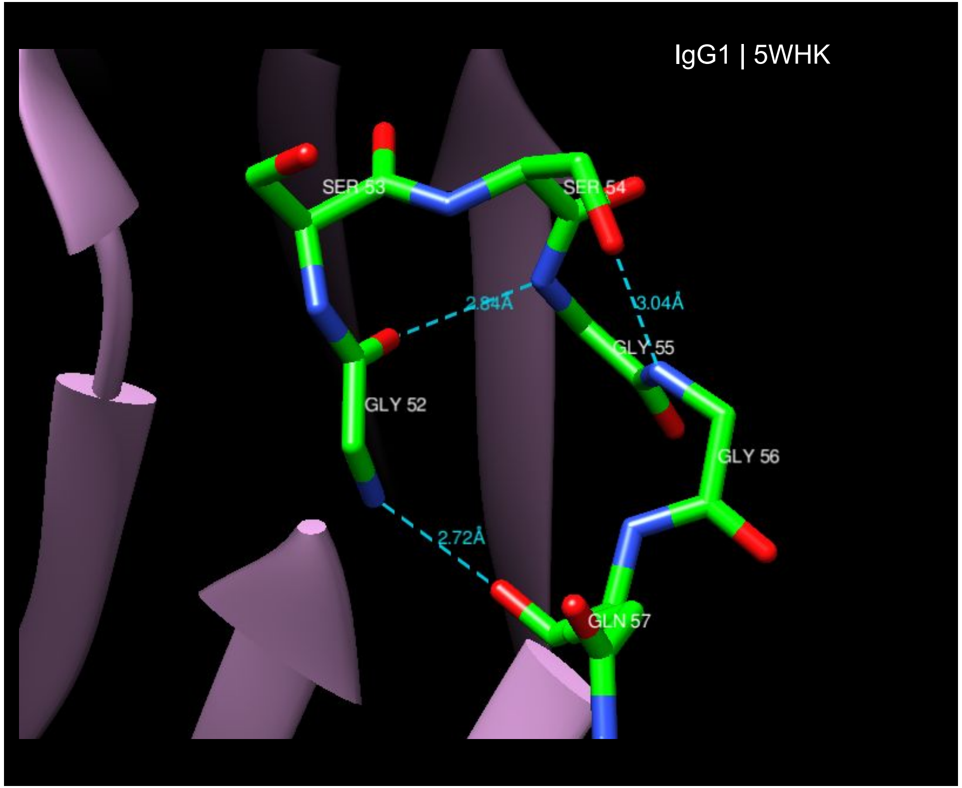
Canonical structure: H2 3A

Hydrogen bonds
GLY 52 O …… N GLY 55

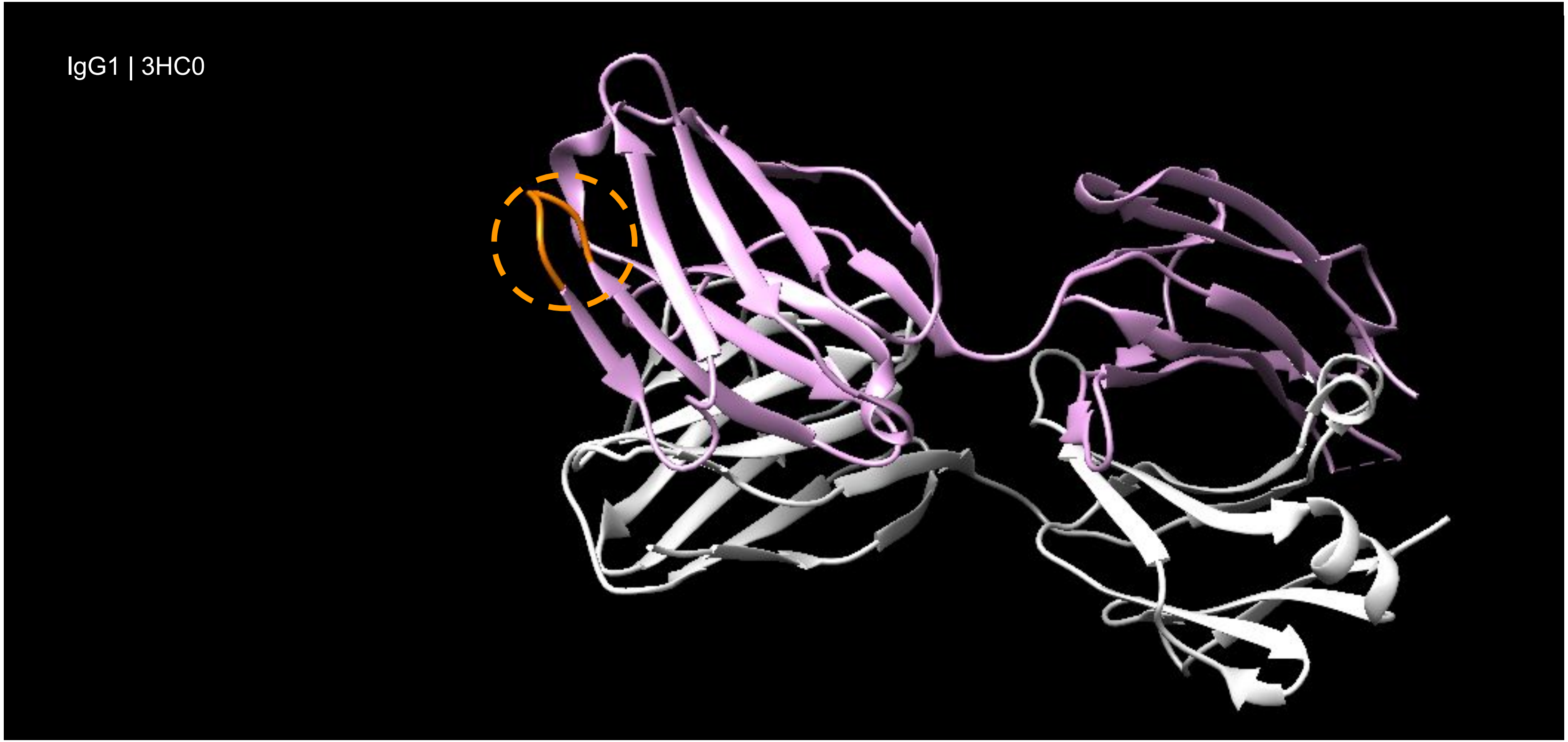
SER 53 O …… N GLY 56
GLY 52 N …… O GLY 57



```
4m1g|IgG2_  GLEWLGVTWGG---G-TTYYNSALKSR
5kvl|IgG _h GLEWIGNIYYS---G-STNYNPSLKSR
5whk|IgG1_h GLEWVSSIGSS---GGQTKYADSVKGR
4hdi|IgG3_r RLELVAVITSN---GDNTYYPDTVKGR
5u3k|IgG _h GLEWVGRIRRLKDGA-TGEYGAAVKDR
4s2s|IgG1_r RLEWVASIS-T-G-D-NTYYTDSVRGR
3hc0|IgG1_h GLEWMGWIYPG-N-V-HAQYNEKFKGR
2cmr|IgG _h GLEWMGGIIPI-F-G-TANYAQAFQGR
```



IgG structural analysis: CDR H2



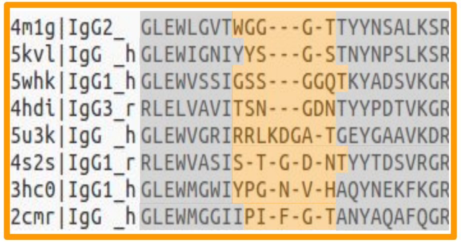
IgG structural analysis: CDR H2

Canonical structure: H2 2A

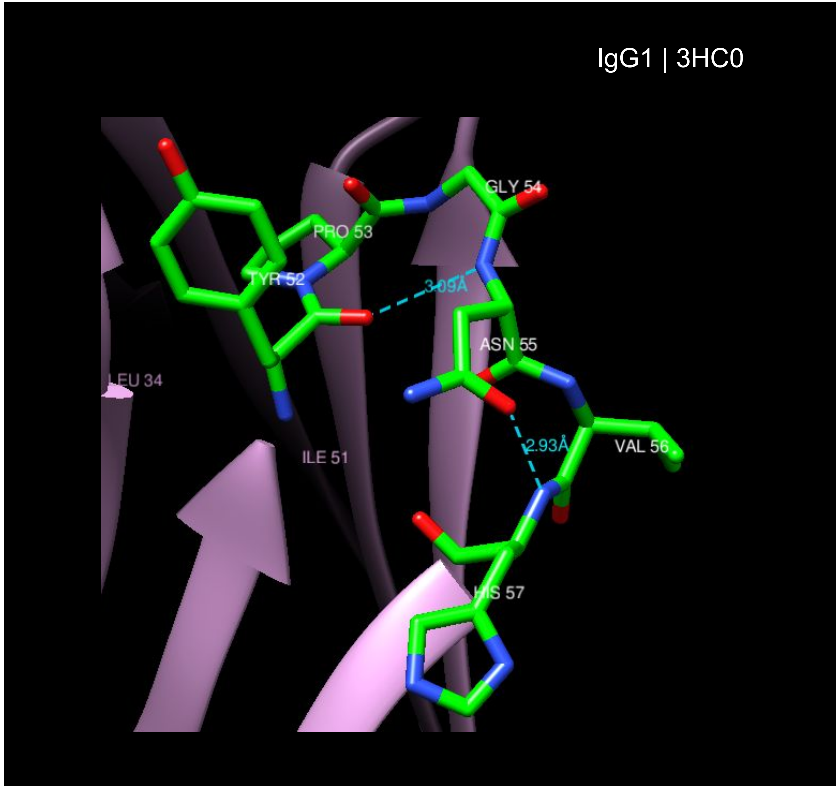
Hydrogen bonds

TYR 52 O …… N 55 ASN

ASN 55 O …… N HIS 57

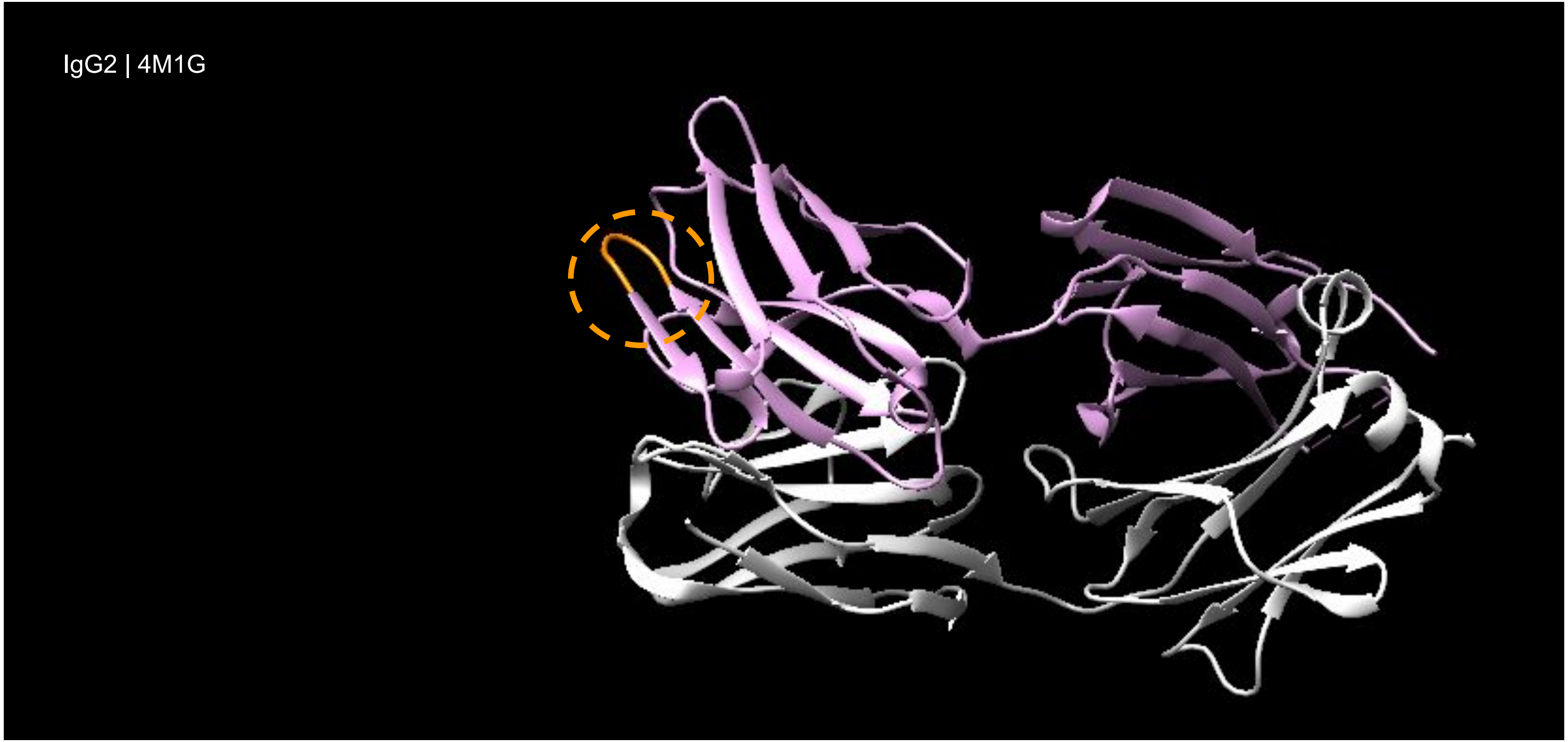


```
4m1g|IgG2_  GLEWLGVTWGG---G-TTYYNSALKSR
5kvl|IgG _h GLEWIGNIYYS---G-STNYNPSLKSR
5whk|IgG1_h GLEWVSSIGSS---GGQTKYADSVKGR
4hdi|IgG3_r RLELVAVITSN---GDNTYYPDTVKGR
5u3k|IgG _h GLEWVGRIRRLKDGA-TGEYGAAVKDR
4s2s|IgG1_r RLEWVASIS-T-G-D-NTYYTDSVRGR
3hc0|IgG1_h GLEWMGWIYPG-N-V-HAQYNEKFKGR
2cmr|IgG _h GLEWMGGIIPI-F-G-TANYAQAFQGR
```



IgG1 | 3HC0

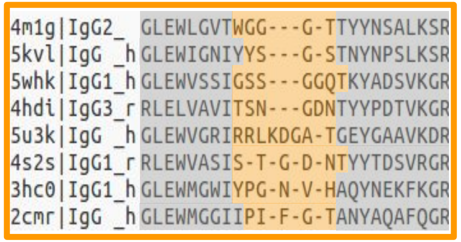
IgG structural analysis: CDR H2



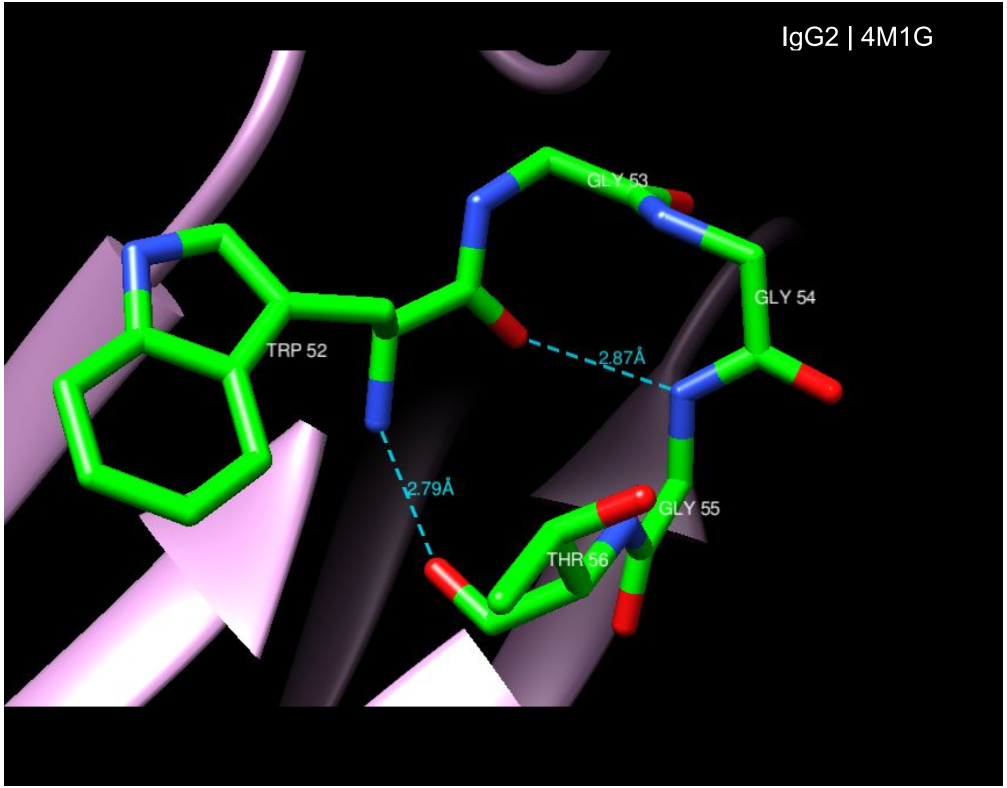
IgG structural analysis: CDR H2

Canonical structure: H2 1

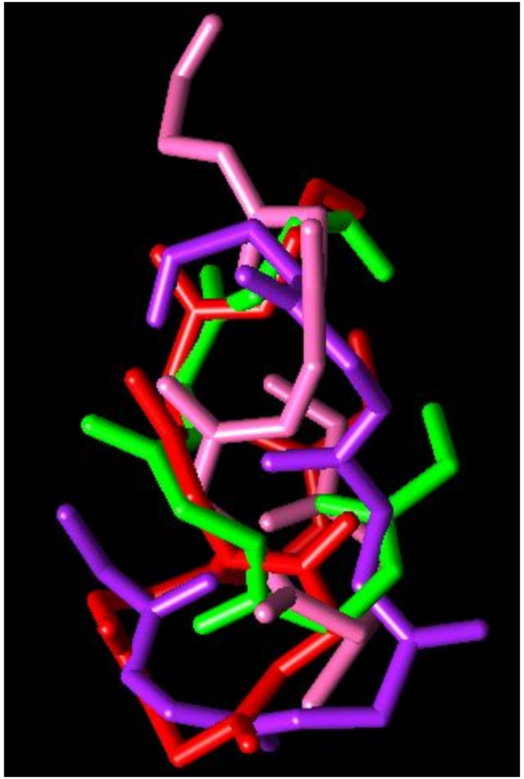
Hydrogen bonds
TRP 52 N …… O 56 THR
TRP 52 O …… N 55 GLY



```
4m1g|IgG2_  GLEWLGVTWGG---G-TTYYNSALKSR
5kvl|IgG _h GLEWIGNIYYS---G-STNYNPSLKSR
5whk|IgG1_h GLEWVSSIGSS---GGQTKYADSVKGR
4hdi|IgG3_r RLELVAVITSN---GDNTYYPDTVKGR
5u3k|IgG _h GLEWVGRIRRLKDGA-TGEYGAAVKDR
4s2s|IgG1_r RLEWVASIS-T-G-D-NTYYTDSVRGR
3hc0|IgG1_h GLEWMGWIYPG-N-V-HAQYNEKFKGR
2cmr|IgG _h GLEWMGGIIPI-F-G-TANYAQAFQGR
```

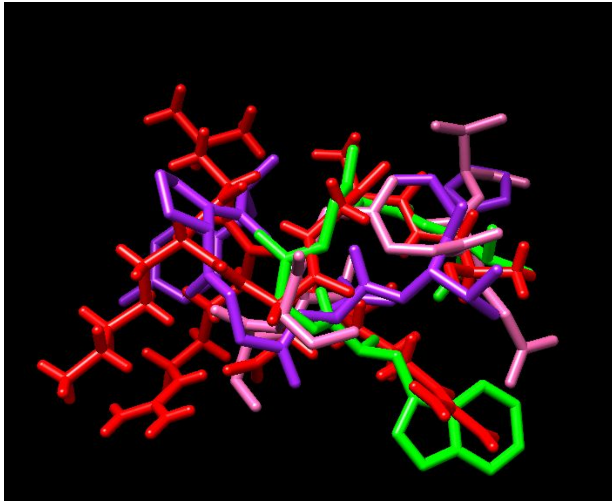


IgG structural analysis: CDR H2 - *superimposition*



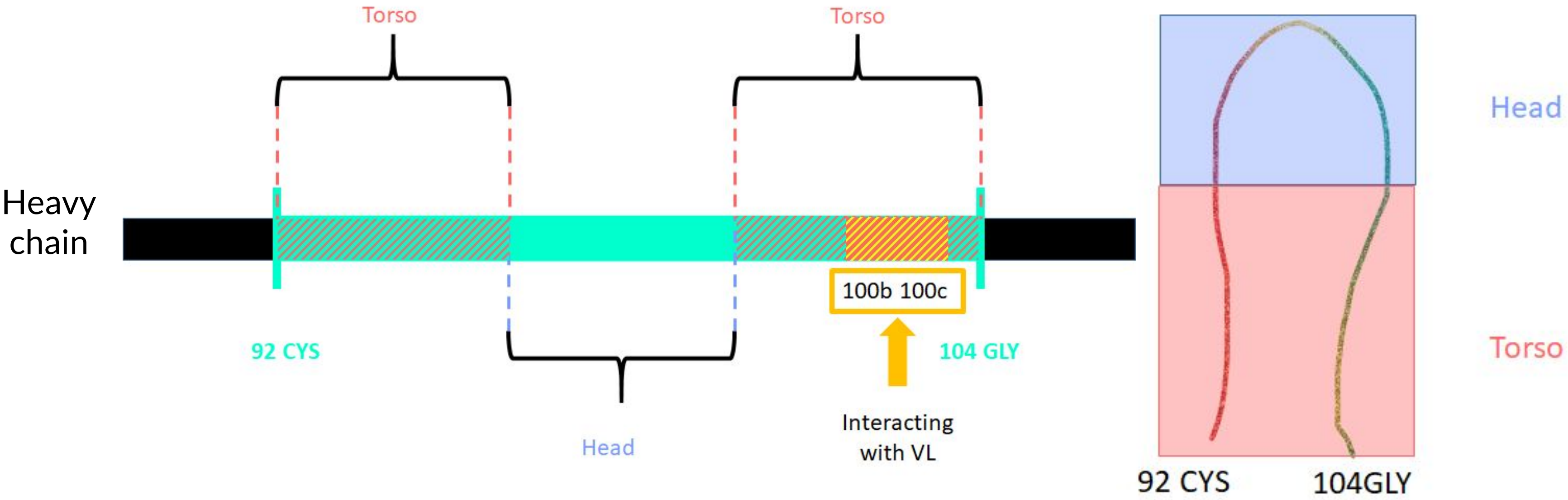
```
4m1g|IgG2_   GLEWLGVTWGG---G-TTYYNSALKSR
3hc0|IgG1_h GLEWIGNIYYS---G-STNYNPSLKSR
5whk|IgG1_h GLEWVSSIGSS---GGQTKYADSVKGR
5u3k|IgG_ _h GLEWVGRIRRLKDGA-TGEYGAAVKDR
```

RMSD: 2.416

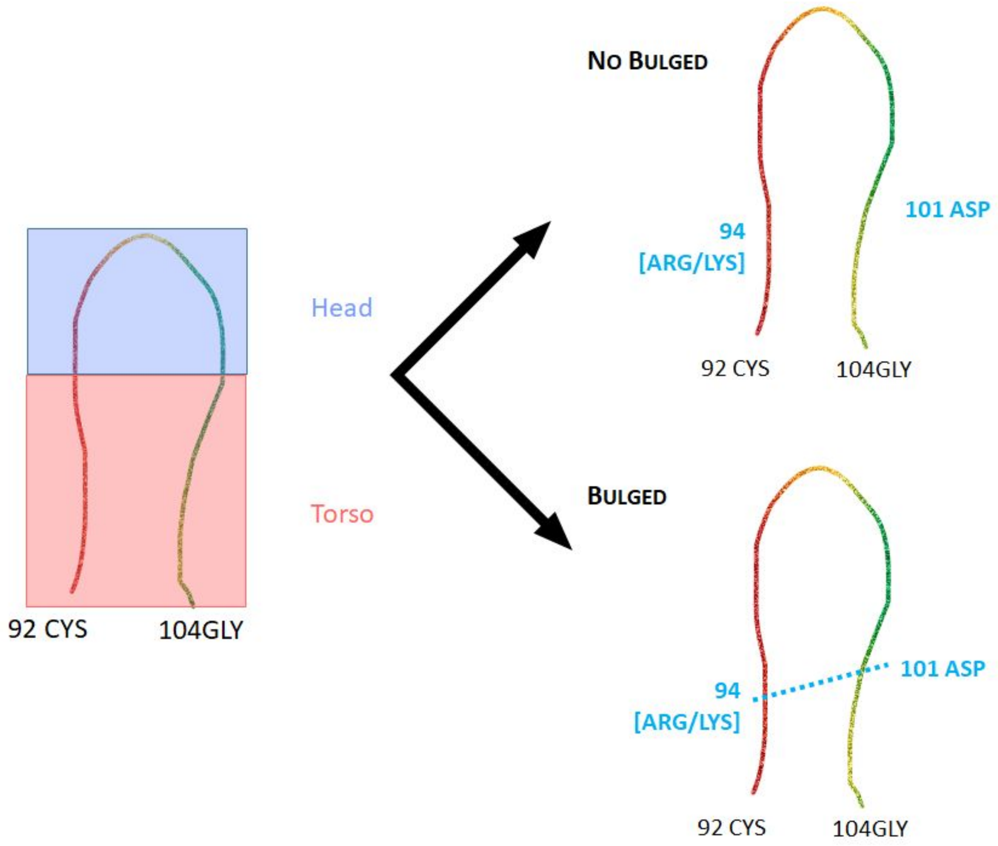


CDR➳ H3

IgG structural analysis: CDR H3

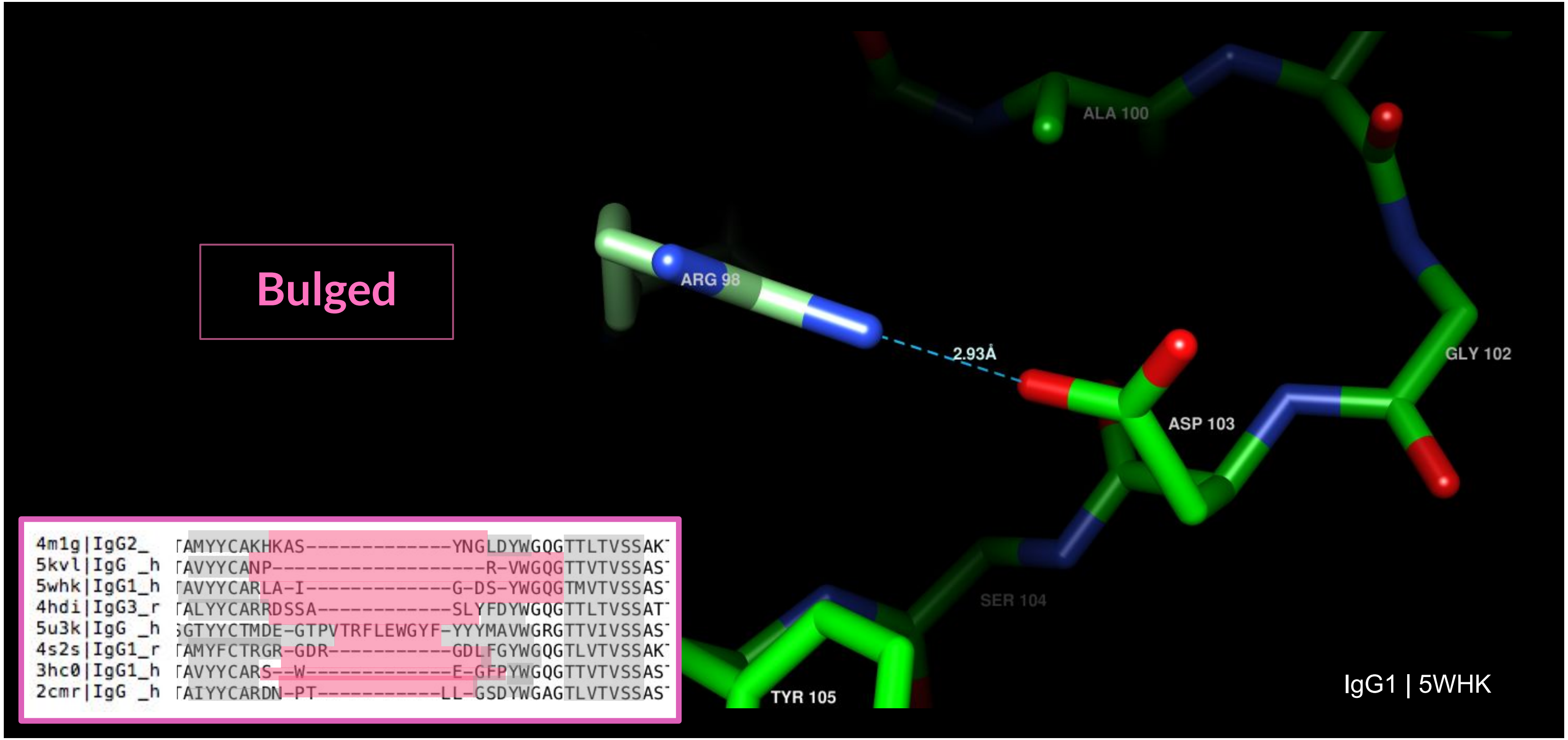


IgG structural analysis: CDR H3



IgG structural analysis: CDR H3

IgG structural analysis: CDR H3



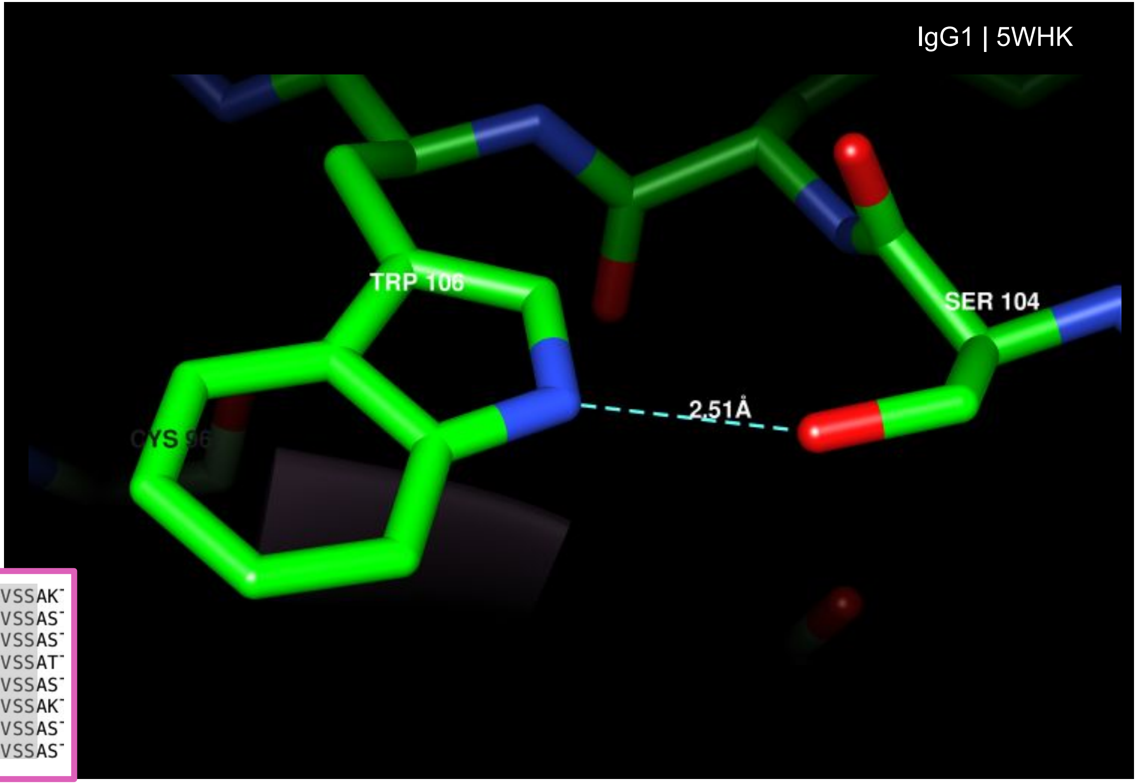
```
4m1g|IgG2_   TAMYYCAKHKAS-------------YNGLDYWGQGTTLTVSSAK
5kvl|IgG _h  TAVYYCANP-------------------R-VWGQGTTVTVSSAS
5whk|IgG1_h  TAVYYCARLA-I-------------G-DS-YWGQGTMVTVSSAS
4hdi|IgG3_r  TALYYCARRDSSA------------SLYFDYWGQGTTLTVSSAT
5u3k|IgG _h  SGTYYCTMDE-GTPVTRFLEWGYF-YYYMAVWGRGTTVIVSSAS
4s2s|IgG1_r  TAMYFCTRGR-GDR-----------GDLFGYWGQGTLVTVSSAK
3hc0|IgG1_h  TAVYYCARS--W-------------E-GFPYWGQGTTVTVSSAS
2cmr|IgG _h  TAIYYCARDN-PT-----------LL-GSDYWGAGTLVTVSSAS
```

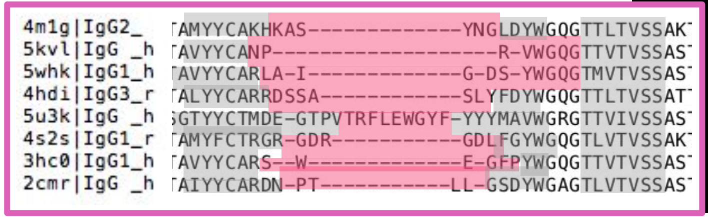
IgG structural analysis: CDR H3

Hydrogen bonds

TRP 106 N …… O SER 104

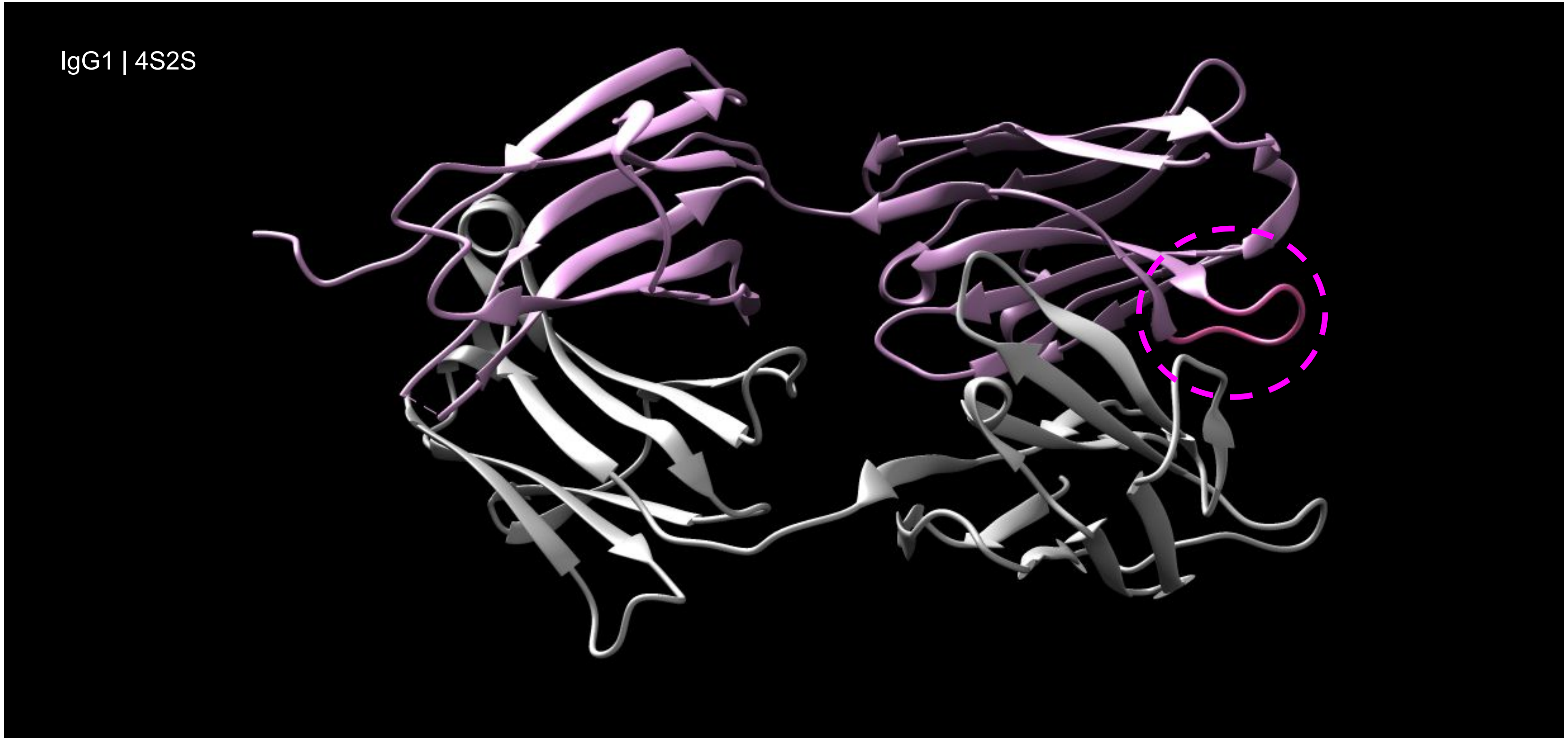
Conserved





```
4m1g|IgG2_   TAMYYCAKHKAS-------------YNGLDYWGQGTTLTVSSAK
5kvl|IgG _h  TAVYYCANP-------------------R-VWGQGTTVTVSSAS
5whk|IgG1_h  TAVYYCARLA-I--------------G-DS-YWGQGTMVTVSSAS
4hdi|IgG3_r  TALYYCARRDSSA------------SLYFDYWGQGTTLTVSSAT
5u3k|IgG _h  SGTYYCTMDE-GTPVTRFLEWGYF-YYYMAVWGRGTTVIVSSAS
4s2s|IgG1_r  TAMYFCTRGR-GDR-----------GDLFGYWGQGTLVTVSSAK
3hc0|IgG1_h  TAVYYCARS--W-------------E-GFPYWGQGTTVTVSSAS
2cmr|IgG _h  TAIYYCARDN-PT-----------LL-GSDYWGAGTLVTVSSAS
```

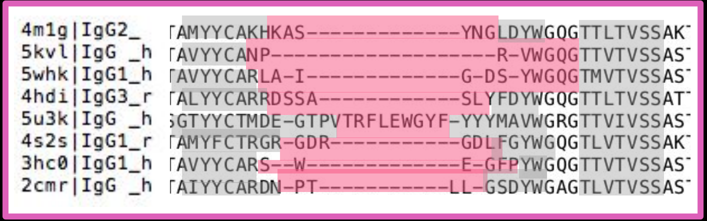
IgG structural analysis: CDR H3



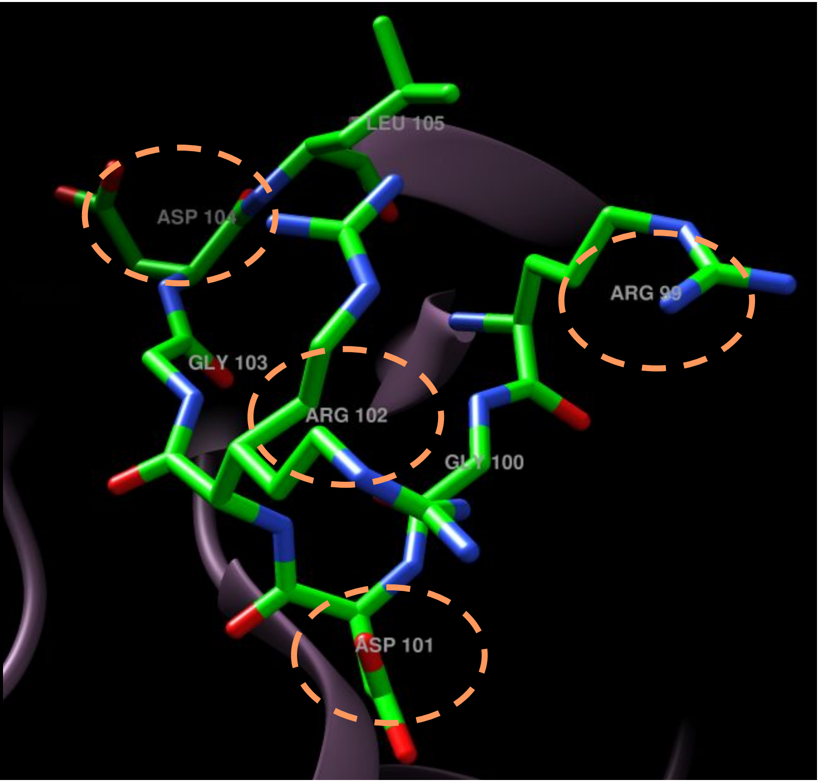
IgG structural analysis: CDR H3

IgG1 | 4S2S

No bulged



```
4m1g|IgG2_   AMYYCAKHKAS-------------YNGLDYWGQGTTLTVSSAK
5kvl|IgG _h  AVYYCANP-------------------R-VWGQGTTVTVSSAS
5whk|IgG1_h  AVYYCARLA-I-------------G-DS-YWGQGTMVTVSSAS
4hdi|IgG3_r  ALYYCARRDSSA------------SLYFDYWGQGTTLTVSSAT
5u3k|IgG _h  GTYYCTMDE-GTPVTRFLEWGYF-YYYMAVWGRGTTVIVSSAS
4s2s|IgG1_r  AMYFCTRGR-GDR-----------GDLFGYWGQGTLVTVSSAK
3hc0|IgG1_h  AVYYCARS--W-------------E-GFPYWGQGTTVTVSSAS
2cmr|IgG _h  AIYYCARDN-PT-----------LL-GSDYWGAGTLVTVSSAS
```



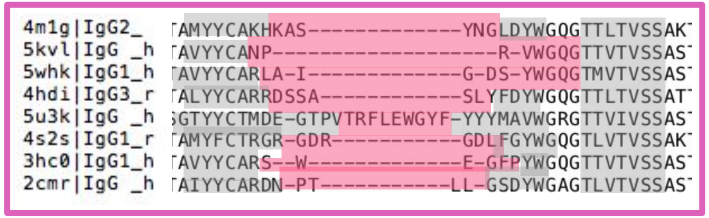
IgG structural analysis: CDR H3

Hydrogen bonds

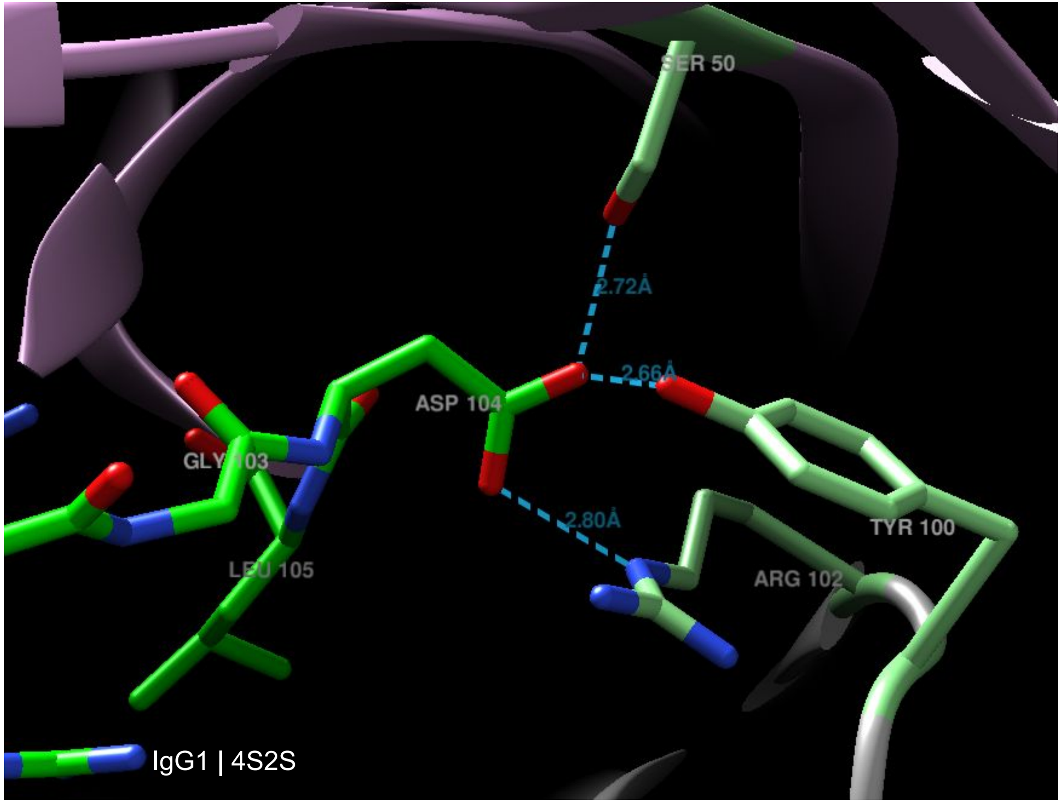
ARG 102 N …… O ASP 104
TYR 100 O …….O ASP 104

Interaction with L3

SER 50 O …… O ASP 104



```
4m1g|IgG2_   TAMYYCAKHKAS-------------YNGLDYWGQGTTLTVSSAK
5kvl|IgG _h  TAVYYCANP-------------------R-VWGQGTTVTVSSAS
5whk|IgG1_h  TAVYYCARLA-I-------------G-DS-YWGQGTMVTVSSAS
4hdi|IgG3_r  TALYYCARRDSSA------------SLYFDYWGQGTTLTVSSAT
5u3k|IgG _h  SGTYYCTMDE-GTPVTRFLEWGYF-YYYMAVWGRGTTVIVSSAS
4s2s|IgG1_r  TAMYFCTRGR-GDR-----------GDLFGYWGQGTLVTVSSAK
3hc0|IgG1_h  TAVYYCARS--W-------------E-GFPYWGQGTTVTVSSAS
2cmr|IgG _h  TAIYYCARDN-PT-----------LL-GSDYWGAGTLVTVSSAS
```

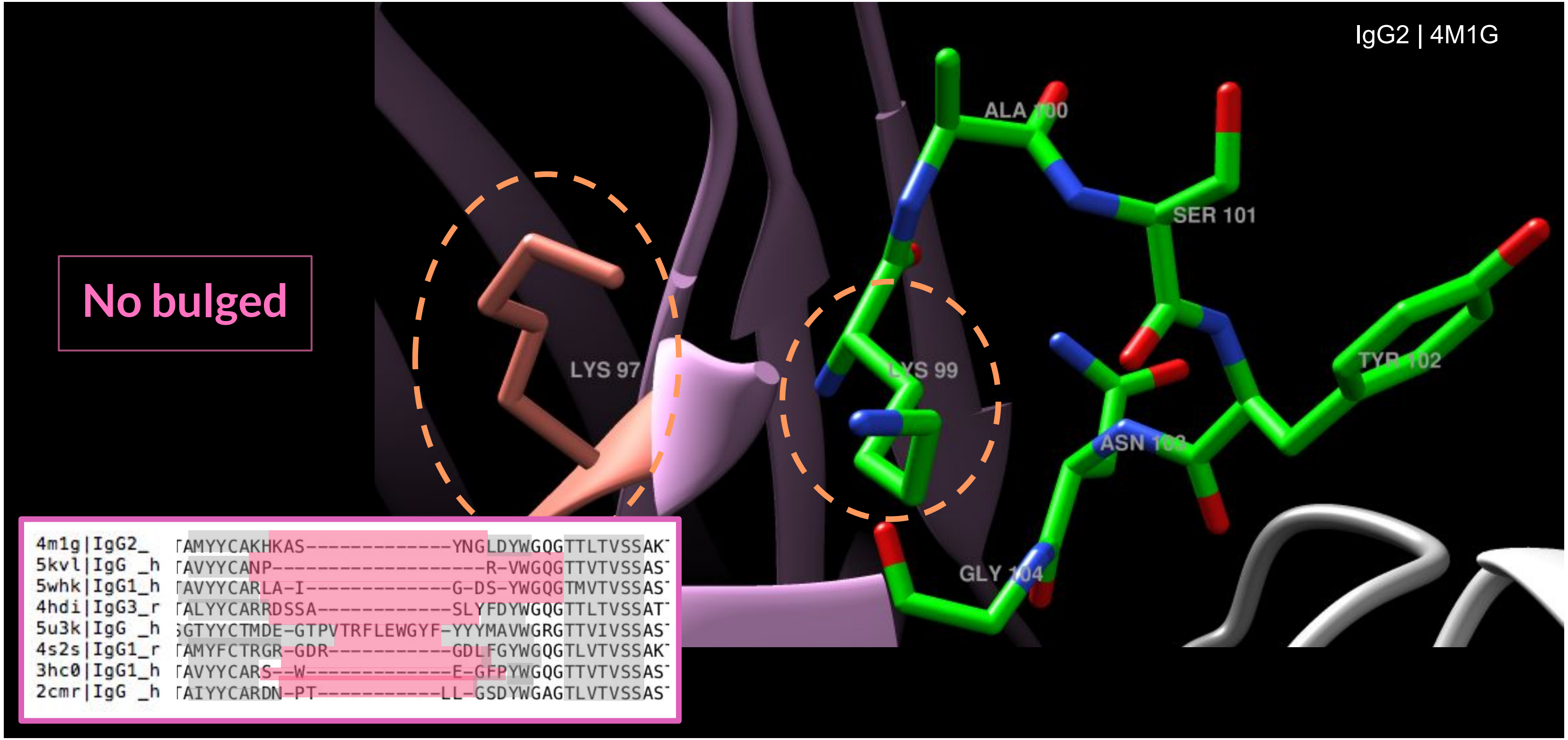


IgG1 | 4S2S

IgG structural analysis: CDR H3

IgG structural analysis: CDR H3

No bulged

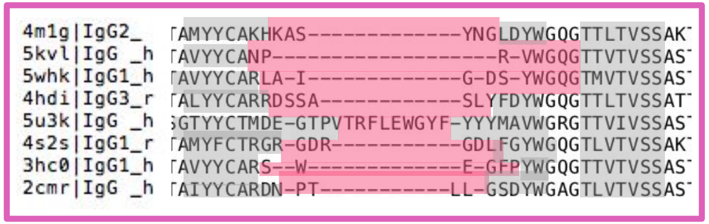


```
4m1g|IgG2_   TAMYYCAKHKAS--------------YNGLDYWGQGTTLTVSSAK
5kvl|IgG _h  TAVYYCANP--------------------R-VWGQGTTVTVSSAS
5whk|IgG1_h  TAVYYCARLA-I--------------G-DS-YWGQGTMVTVSSAS
4hdi|IgG3_r  TALYYCARRDSSA-------------SLYFDYWGQGTTLTVSSAT
5u3k|IgG _h  SGTYYCTMDE-GTPVTRFLEWGYF-YYYMAVWGRGTTVIVSSAS
4s2s|IgG1_r  TAMYFCTRGR-GDR------------GDLFGYWGQGTLVTVSSAK
3hc0|IgG1_h  TAVYYCARS--W--------------E-GFPYWGQGTTVTVSSAS
2cmr|IgG _h  TAIYYCARDN-PT------------LL-GSDYWGAGTLVTVSSAS
```

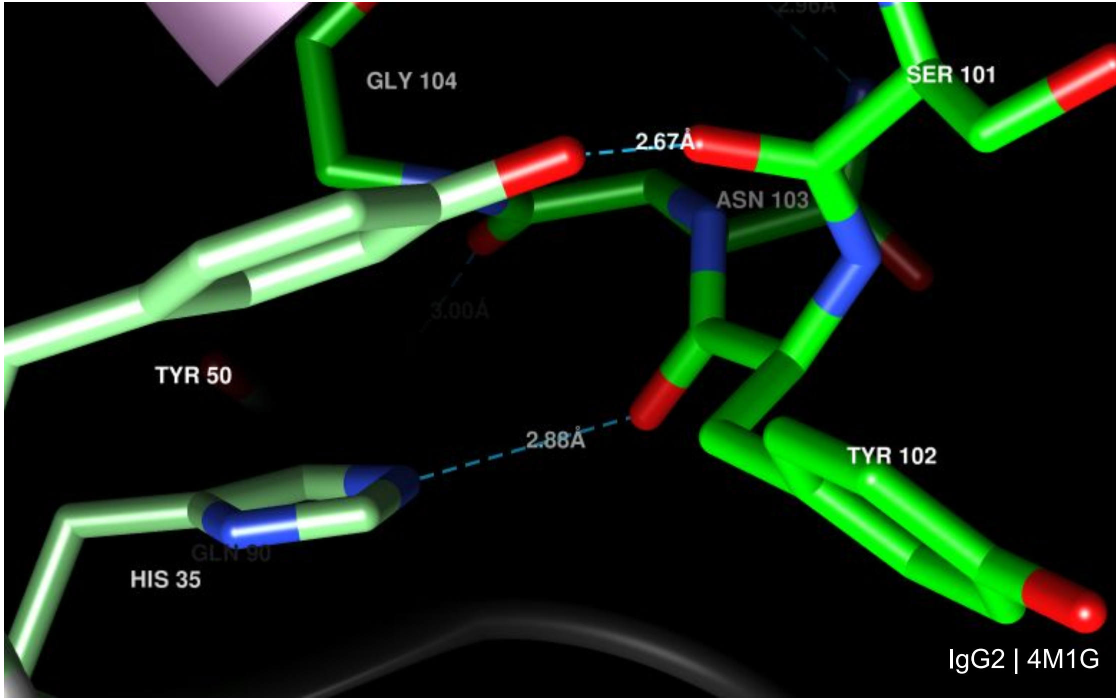
IgG structural analysis: CDR H3

Interactions with light chain:

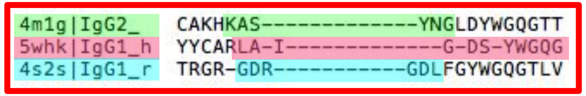
- HIS 35 N . . . . O TYR 102 → Near L1
- TYR 50 O . . . .O ASN 103 → Near L2



```
4m1g|IgG2_   TAMYYCAKHKAS-------------YNGLDYWGQGTTLTVSSAKT
5kvl|IgG _h  TAVYYCANP-------------------R-VWGQGTTVTVSSAST
5whk|IgG1_h  TAVYYCARLA-I-------------G-DS-YWGQGTMVTVSSAST
4hdi|IgG3_r  TALYYCARRDSSA------------SLYFDYWGQGTTLTVSSATT
5u3k|IgG _h  SGTYYCTMDE-GTPVTRFLEWGYF-YYYMAVWGRGTTVIVSSAST
4s2s|IgG1_r  TAMYFCTRGR-GDR-----------GDLFGYWGQGTLVTVSSAKT
3hc0|IgG1_h  TAVYYCARS--W-------------E-GFPYWGQGTTVTVSSAST
2cmr|IgG _h  TAIYYCARDN-PT-----------LL-GSDYWGAGTLVTVSSAST
```

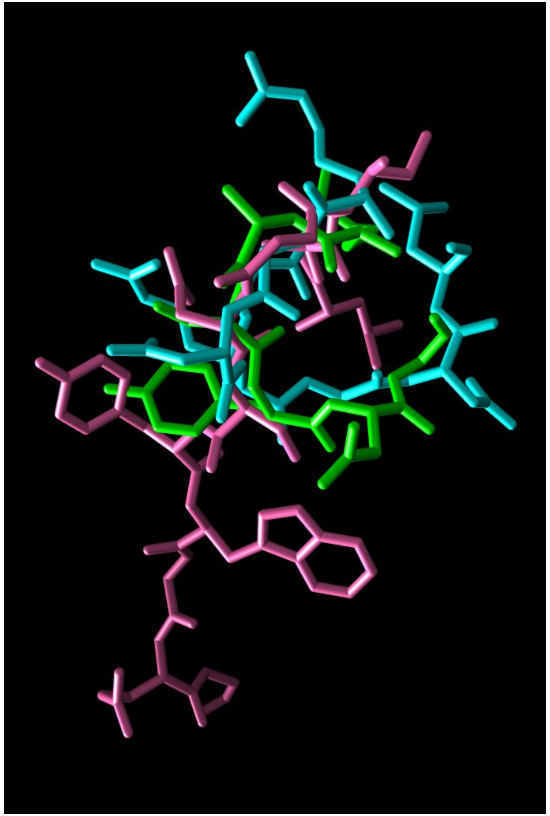


IgG structural analysis: CDR H3 - *superimposition*



```
4m1g|IgG2_   CAKHKAS-------------YNGLDYWGQGTT
5whk|IgG1_h  YYCARLA-I-------------G-DS-YWGQG
4s2s|IgG1_r  TRGR-GDR-----------GDLFGYWGQGTLV
```

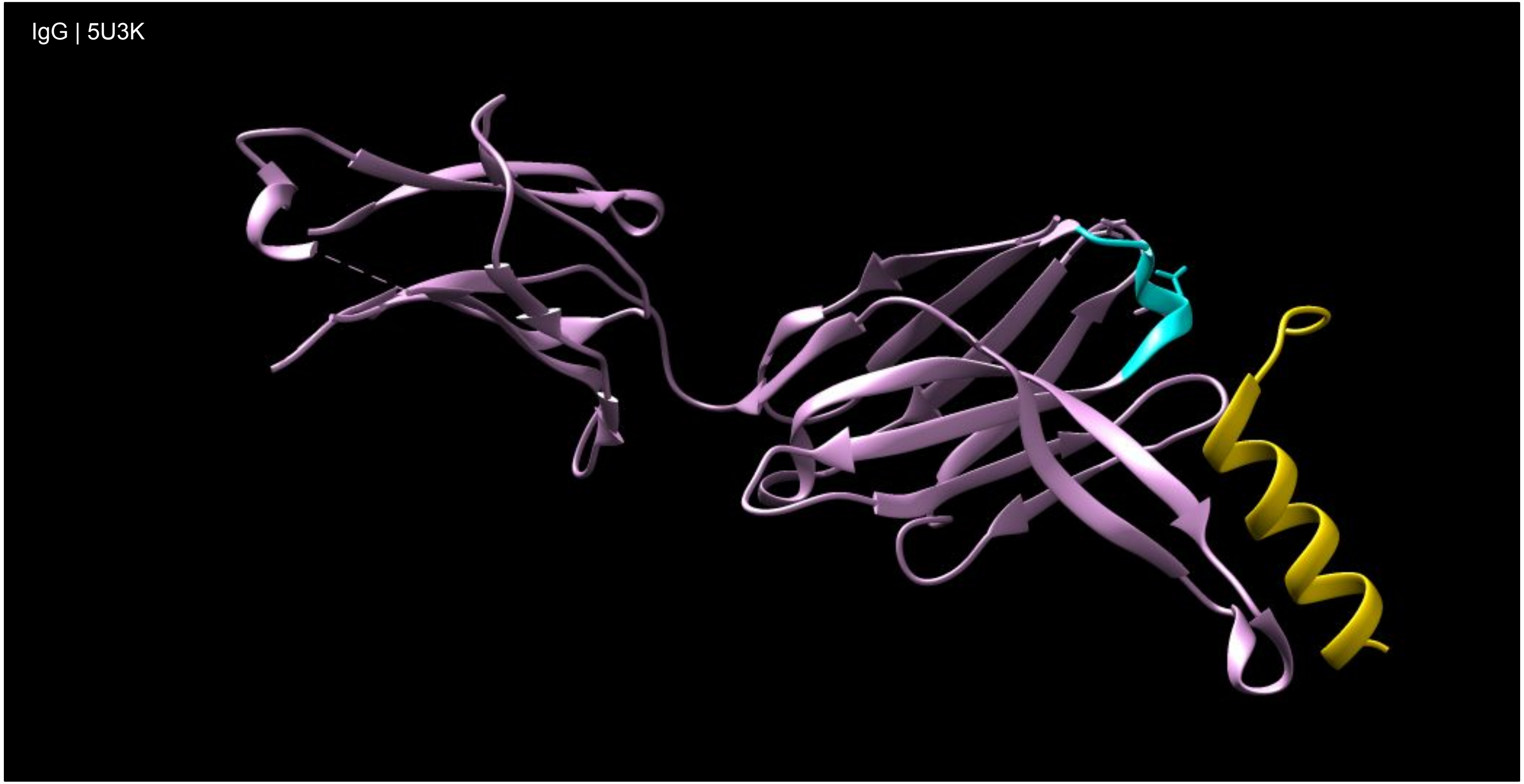
RMSD: 1,42



IgG-Antigen interaction

HIV

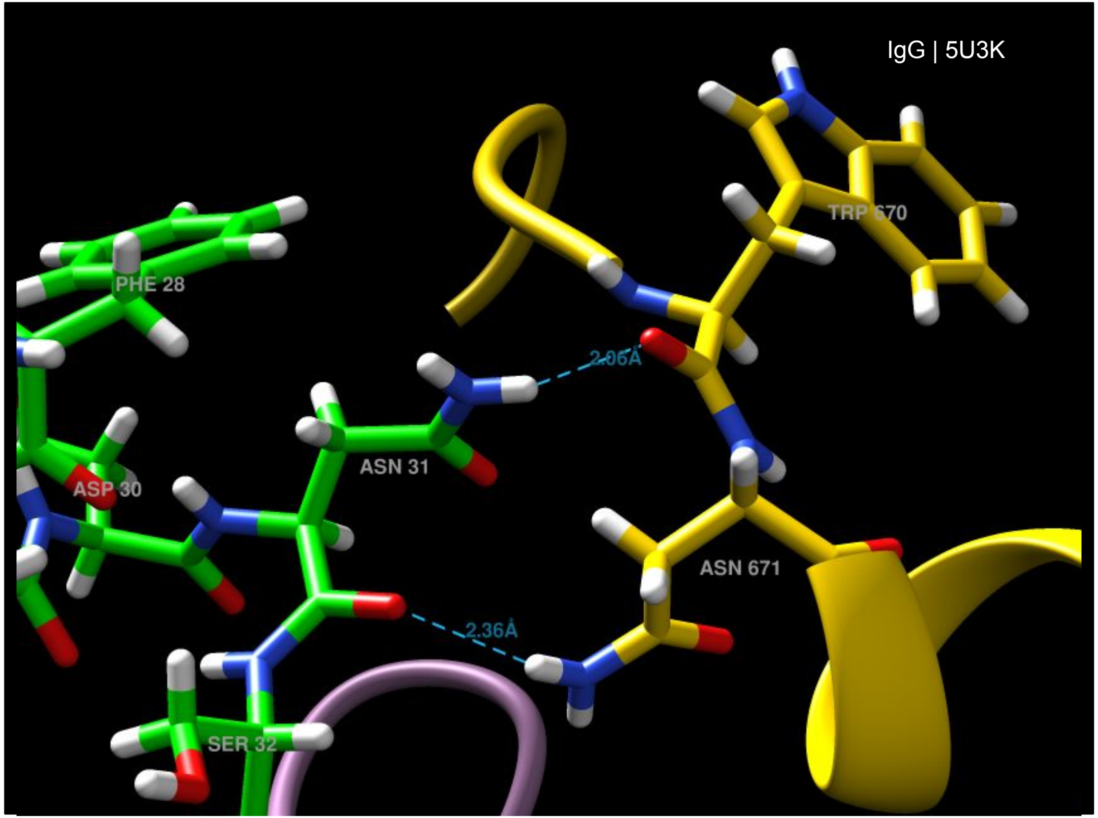
IgG-Antigen interaction: HIV - *H1 interaction*



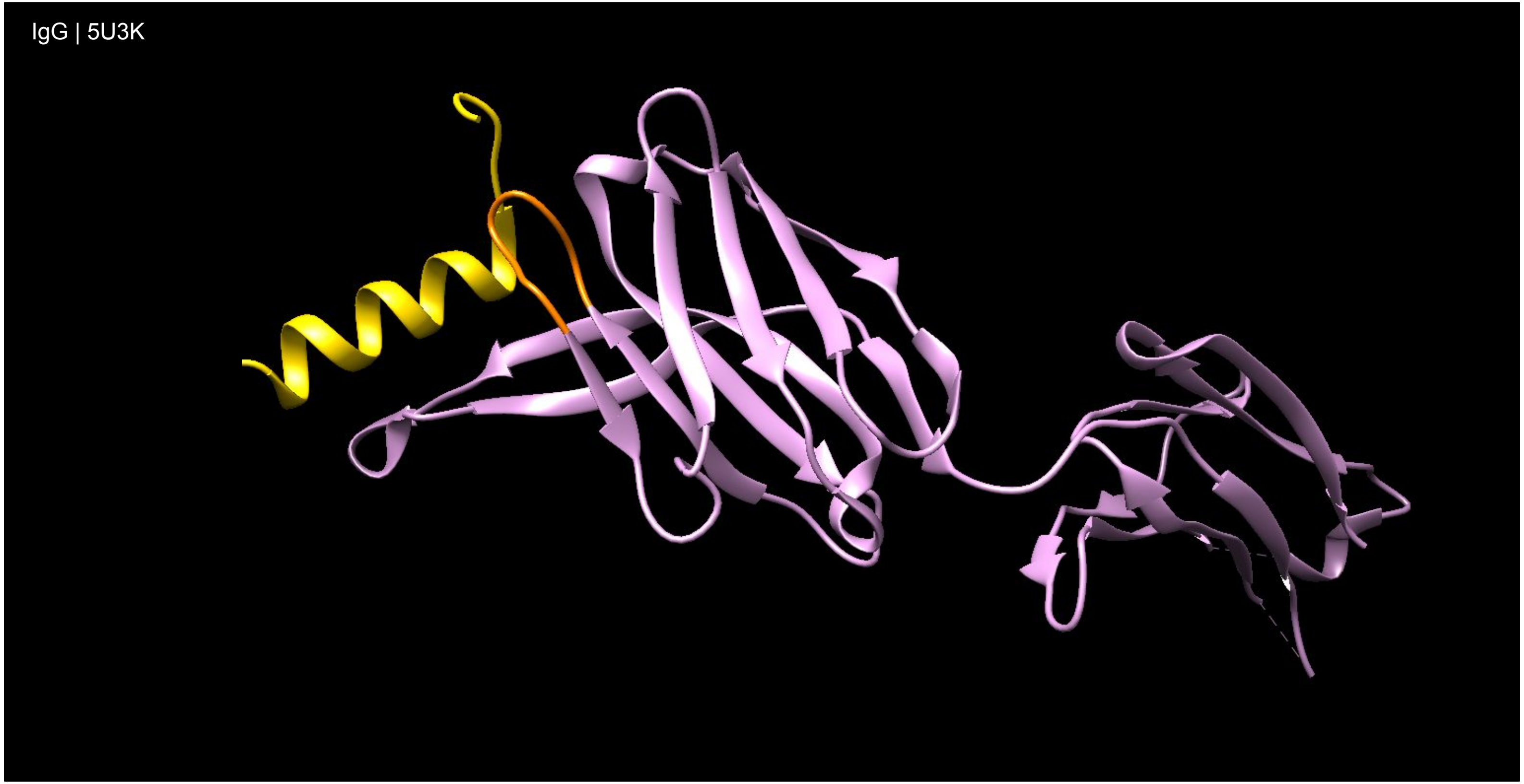
IgG-Antigen interaction: HIV - *H1 interaction*

Interactions with H1:

- ASN 31 O ... N ASN 671
- ASN 31 N ... O TRP 670



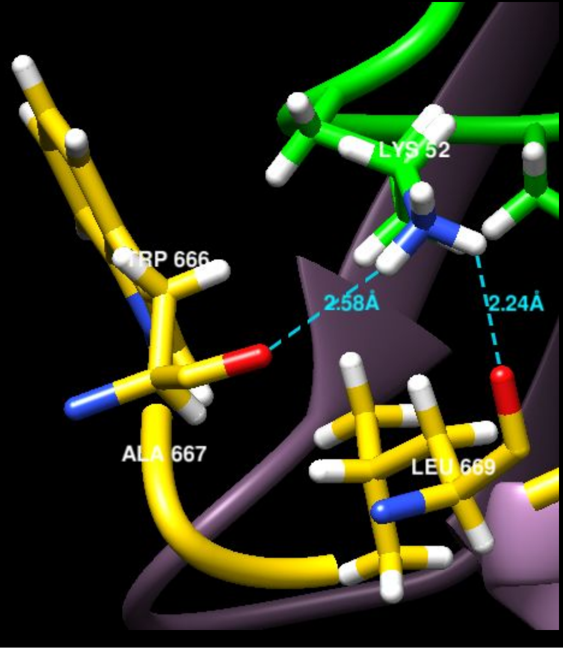
IgG-Antigen interaction: HIV - *H2 interaction*



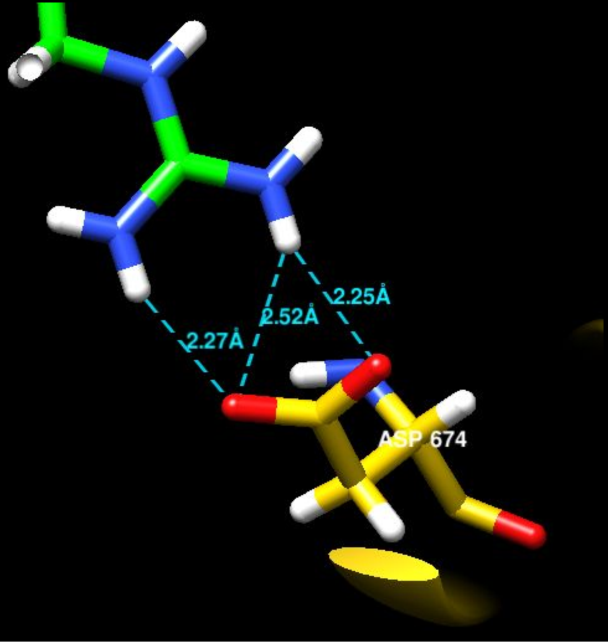
IgG-Antigen interaction: HIV - *H2 interaction*

IgG | 5U3K

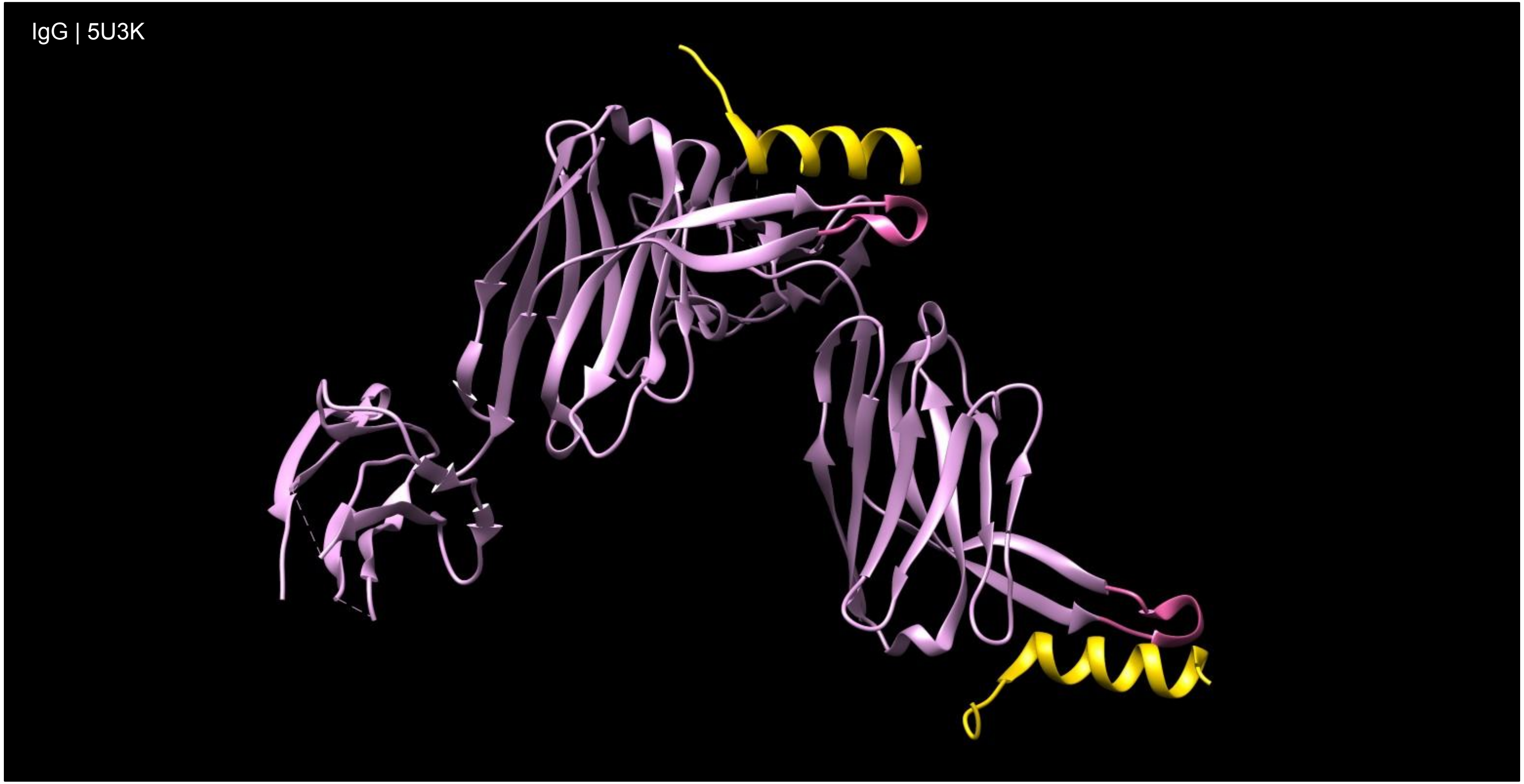
Hydrogen bonds:
LYS 52C N…O TRP 666
LYS 52C N…O LEU 669



Salt Bridge:
ARG 52A N…O ASP 674
ARG 52A N…O ASP 674



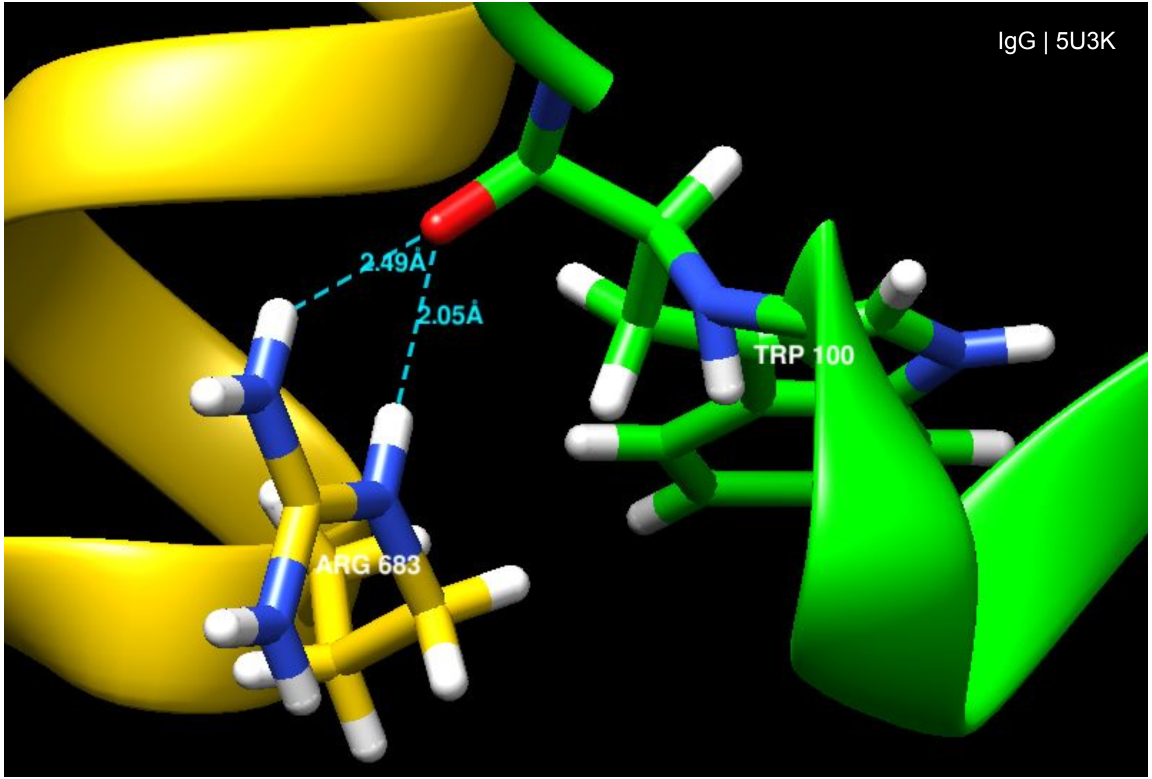
IgG-Antigen interaction: HIV - *H3 interaction*



IgG-Antigen interaction: HIV - *H3 interaction*

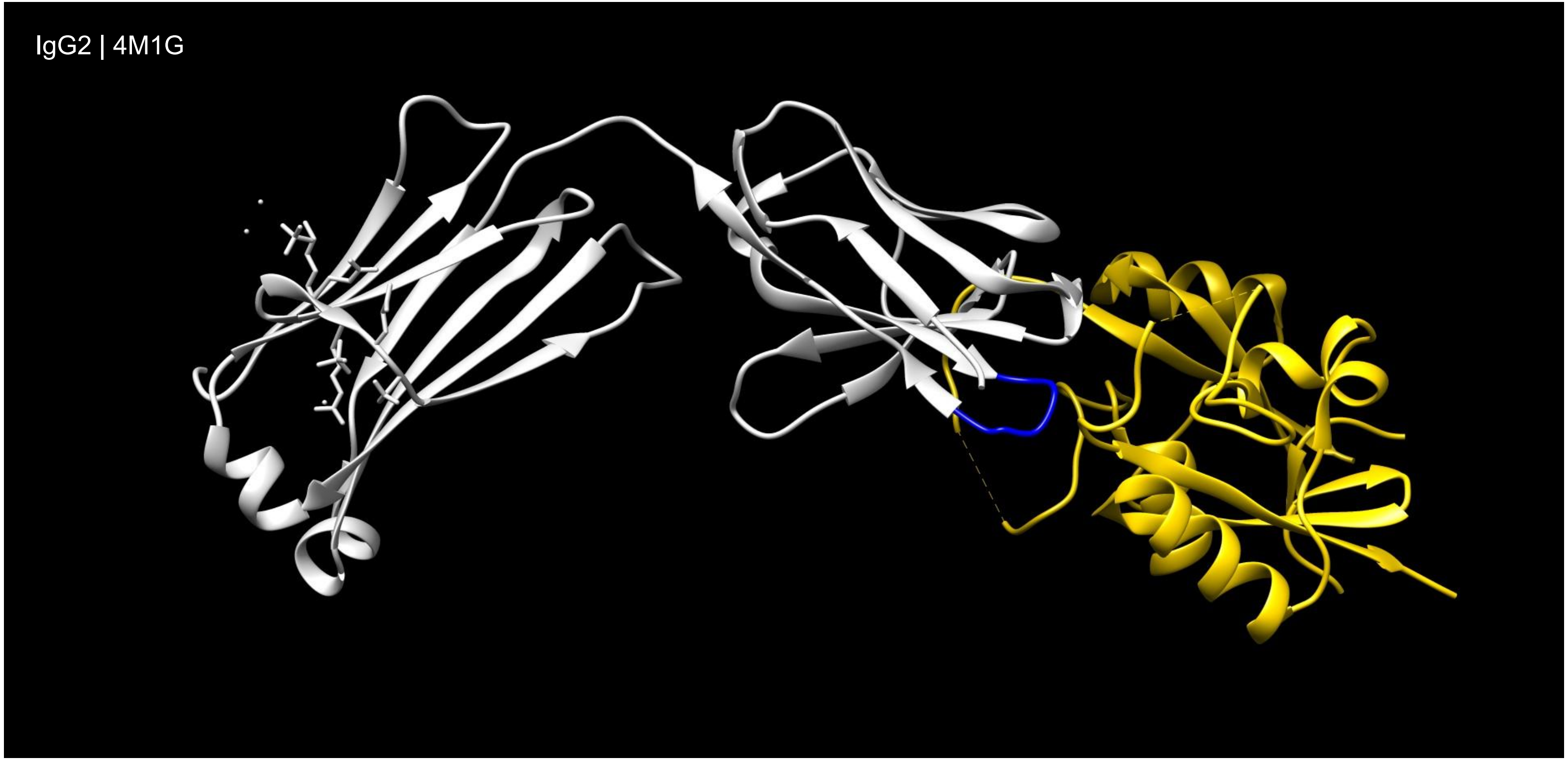
Interactions with H3:

- ARG 683 N...O TRP 100
- ARG 683 N...O TRP 100



Vaccinia virus

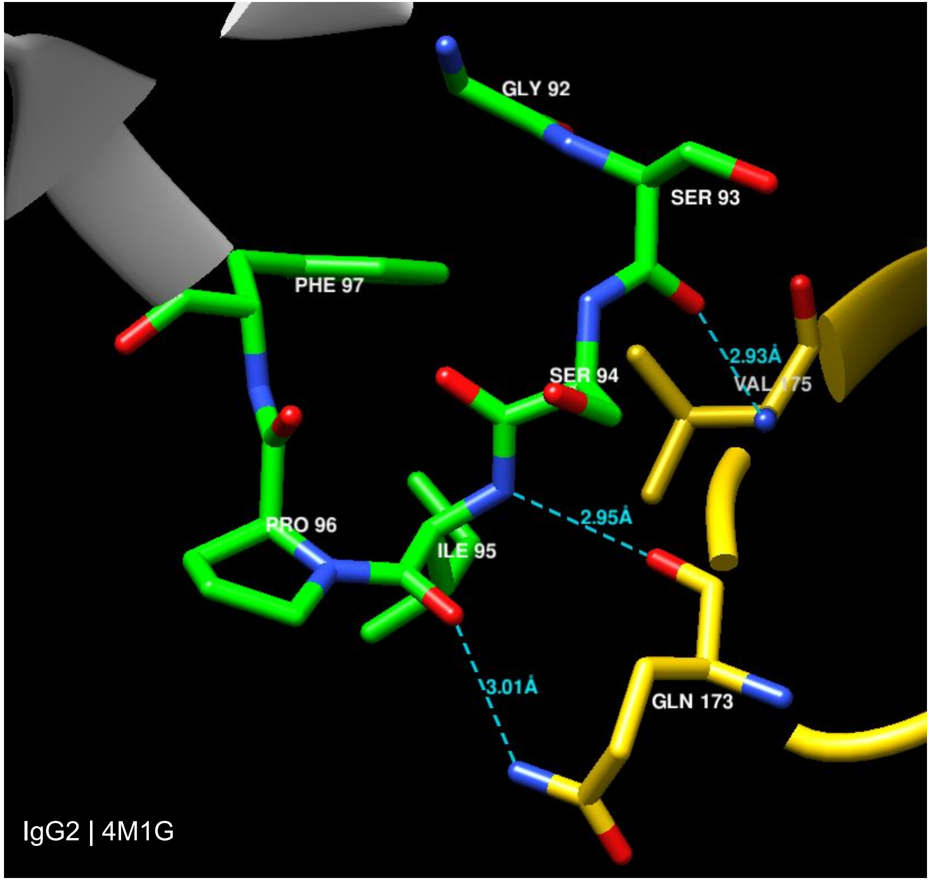
IgG-Antigen interaction: Vaccinia virus - *L3 interaction*



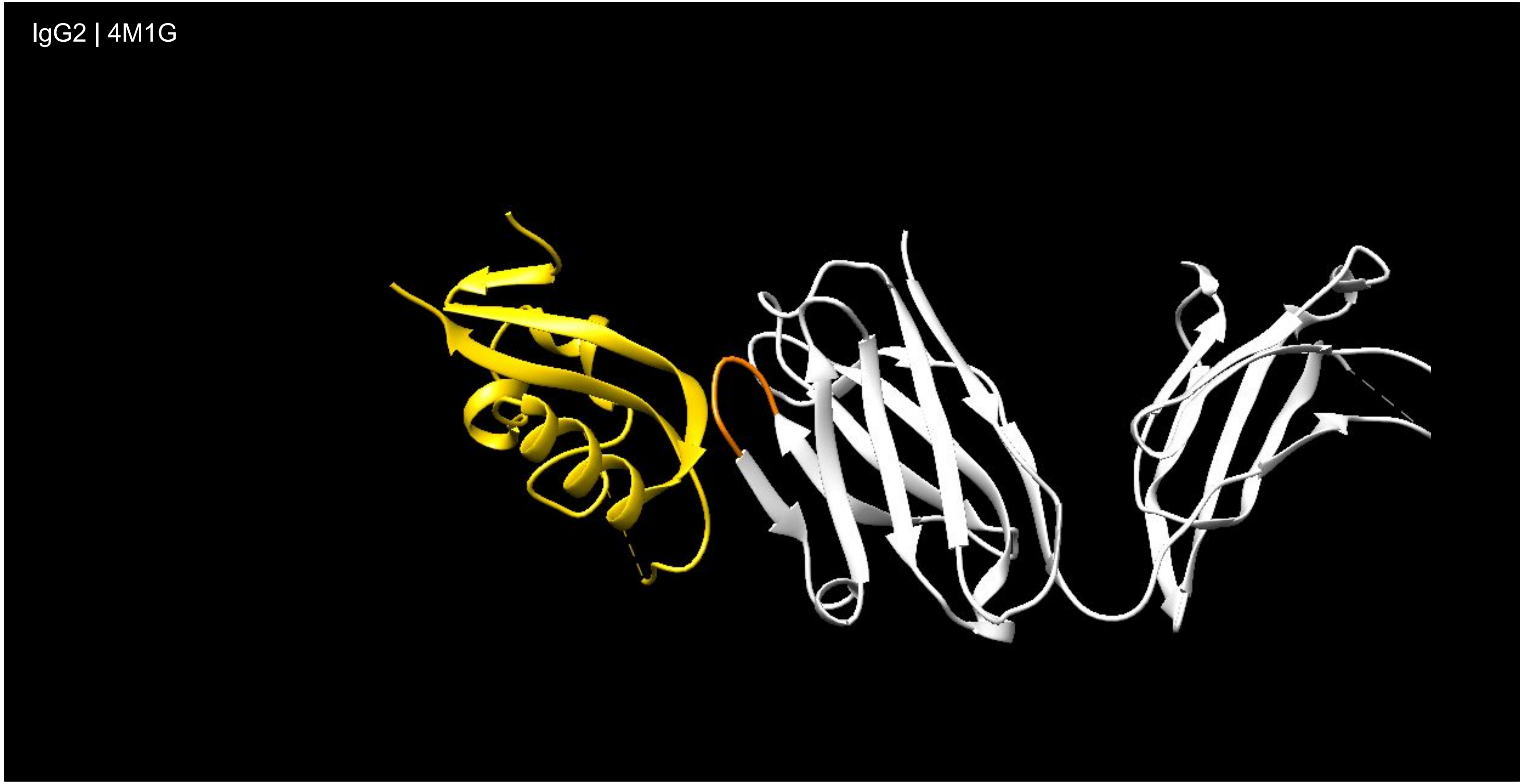
IgG-Antigen interaction: Vaccinia virus - *L3 interaction*

Interactions with L3:

- GLN 173 N...ILE 95 O
- GLN 173 O...ILE 95 N
- VAL 175 N...SER 93 O



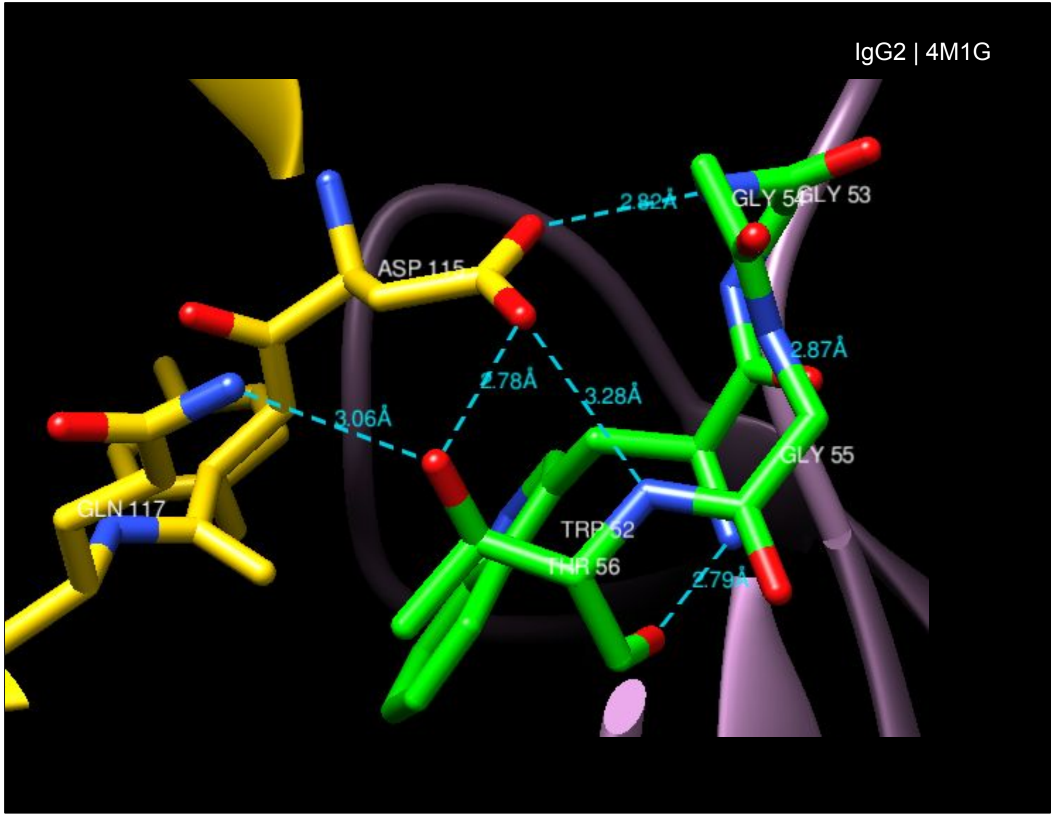
IgG-Antigen interaction: Vaccinia virus - *H2 interaction*



IgG-Antigen interaction: Vaccinia virus - *H2 interaction*

Interactions with H2:

Gly 54 N…O Asp 115
Thr 56 N…O Asp 115
Thr 56 O...N Asp 115
Thr 56 O…N Gln 117



Conclusions

Conclusions

- Comparing the amino acid sequences from many different immunoglobulins we can observe that beta strands are conserved while loops are variable.
- Five of the six CDRs usually have a small number of main chain conformations, called canonical structures.
- Following with CDRs, although they have a big amount of possible canonical structure classes, only a few of them appear with a high prevalence in the nature.
- Although CDRs are hypervariable regions, analyzing the amino acids sequence of the IgG we can predict what their structure/position in space will be.

Conclusions

- L2, L3 and H1 are the most conserved CDRs whereas L1 and H2 have more variability.
- Even though H3 is the most hypervariable CDR and no canonical structures have been identified in this region, it appears to have a limited repertoire of conformations.
- CDRs are important for antigen recognition. However, we have seen that in our case only H2 interacts with both Vaccinia and HIV.

Bibliography

Bibliography

- Al-Lazikani B, Lesk A, Chothia C. Standard conformations for the canonical structures of immunoglobulins. Edited by I. A. Wilson. Journal of Molecular Biology. 1997;273(4):927-948.
- Morea V, Tramontano A, Rustici M, Chothia C, Lesk A. Conformations of the third hypervariable region in the VH domain of immunoglobulins 1 1Edited by I. A. Wilson. Journal of Molecular Biology. 1998;275(2):269-294.
- North B, Lehmann A, Dunbrack R. A New Clustering of Antibody CDR Loop Conformations. Journal of Molecular Biology. 2011;406(2):228-256.
- Vargas-Madrazo, E., Lara-Ochoa, F. and Carlos Almagro, J. (1995). Canonical Structure Repertoire of the Antigen-binding Site of Immunoglobulins Suggests Strong Geometrical Restrictions Associated to the Mechanism of Immune Recognition. *Journal of Molecular Biology*, 254(3), pp.497-504.
- Brändén C, Tooze J. Introduction to protein structure. 2nd ed. New York, NY: Garland Pub.; 1999.
- Vidarsson G, Dekkers G, Rispens T. IgG Subclasses and Allotypes: From Structure to Effector Functions. Frontiers in Immunology. 2014;5.
- Owen, J., Punt, J., Stranford, S. and Jones, P. (2013). Kuby immunology. 7th ed. New York: W.H. Freeman.
- Cuesta Á, Sainz-Pastor N, Bonet J, Oliva B, Álvarez-Vallina L. Multivalent antibodies: when design surpasses evolution. Trends Biotechnol. 2010;28(7):355-362.
- Schroeder H, Cavacini L. Structure and function of immunoglobulins. J Allergy Clin Immunol. 2010;125(2):S41-S52.

Multiple choice questions

Multiple choice questions

1. **Canonical structures…**

a) Are located in the CDRs
b) Are determined by the loop length and by the presence of certain residues at key positions
c) The two previous ones are correct
d) Are located in both beta strands and loops
e) All the above are correct

2. **Which of the CDRs is the most hypervariable?**

a) L1
b) L3
c) H2
d) H3
e) H1

3. Following SCOP classification, immunoglobulins:

a) Belong to all alpha proteins
b) Belong to mainly beta class
c) The two previous ones are correct
d) Have four families: C2 set domain, C1 set domain, I set domain and V set domains
e) All the above are correct

Multiple choice questions

4. The beta strands from immunoglobulin domains:

a) Are not conserved in structure
b) Are as conserved as loops in structure
c) Are less conserved than loops in structure
d) Are more conserved than loops in structure
e) Are the less conserved in sequence

5. Which of the L3 CDR canonical structures is the most common?

a) 1
b) 2
c) The two previous ones are correct
d) All the L3 CDR canonical structures are presented equally
e) None of the above are correct

6. CDR canonical structures can be identified by:

a) The number of residues of the loop (length)
b) Residues at key sites
c) The two previous ones are correct
d) The number of Arginine residues
e) All the above are correct

Multiple choice questions

7. The correct statement about the immunoglobulins is…

a) Polar residues are located in the surface
b) Polar residues are located only around the core
c) The two previous ones are correct
d) Hydrophobic residues are located in the surface
e) None of the above are correct

8. The correct statement about the L2 is…

a) L2 has 4 canonical structures
b) L2 has 2 canonical structures
c) The two previous ones are correct
d) L2 has 1 canonical structure
e) None of the above are correct

9. CDRs are encoded...

a) In the DNA regions between the V and J sites in the genome
b) In the spacing DNA between the Variable and Constant coding regions of the light chain
c) The V regions of the light chain
d) Between the D and J regions coding for the heavy chain
e) In the Hypervariability coding region of the Immunoglobulin light chain

Multiple choice questions

10. The correct statement about CDRs is…

a) They are important for the antigen recognition.
b) H2 has more variability than L2 and can interact with different kinds of antigens.
c) The two previous are correct.
d) Only H1 is involved in antigen recognition.
e) None of the above are correct.

Thank you for your attention!