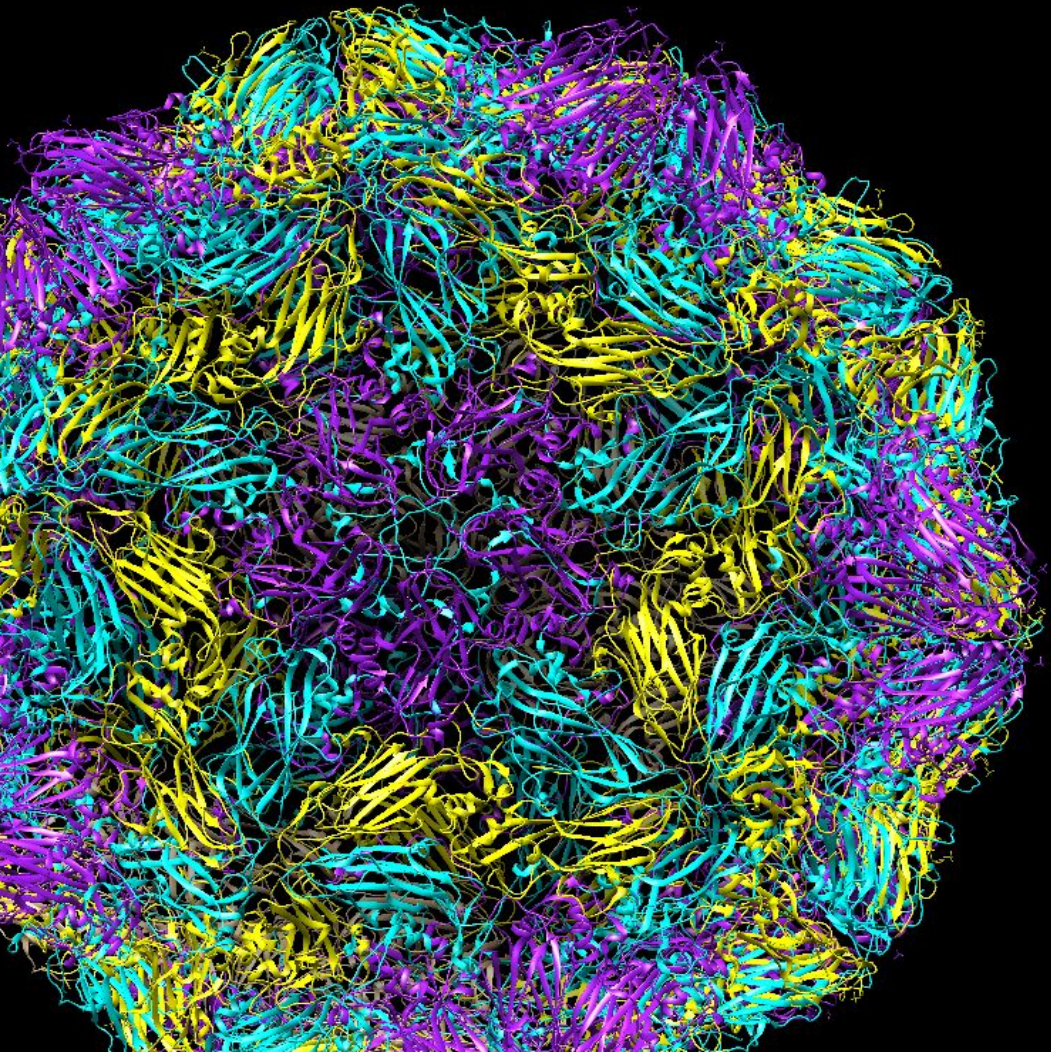

HEPATITIS A VIRUS CAPSID

Enric Aguilar
Neus Otero
Ona Piqué
Irene Vivancos

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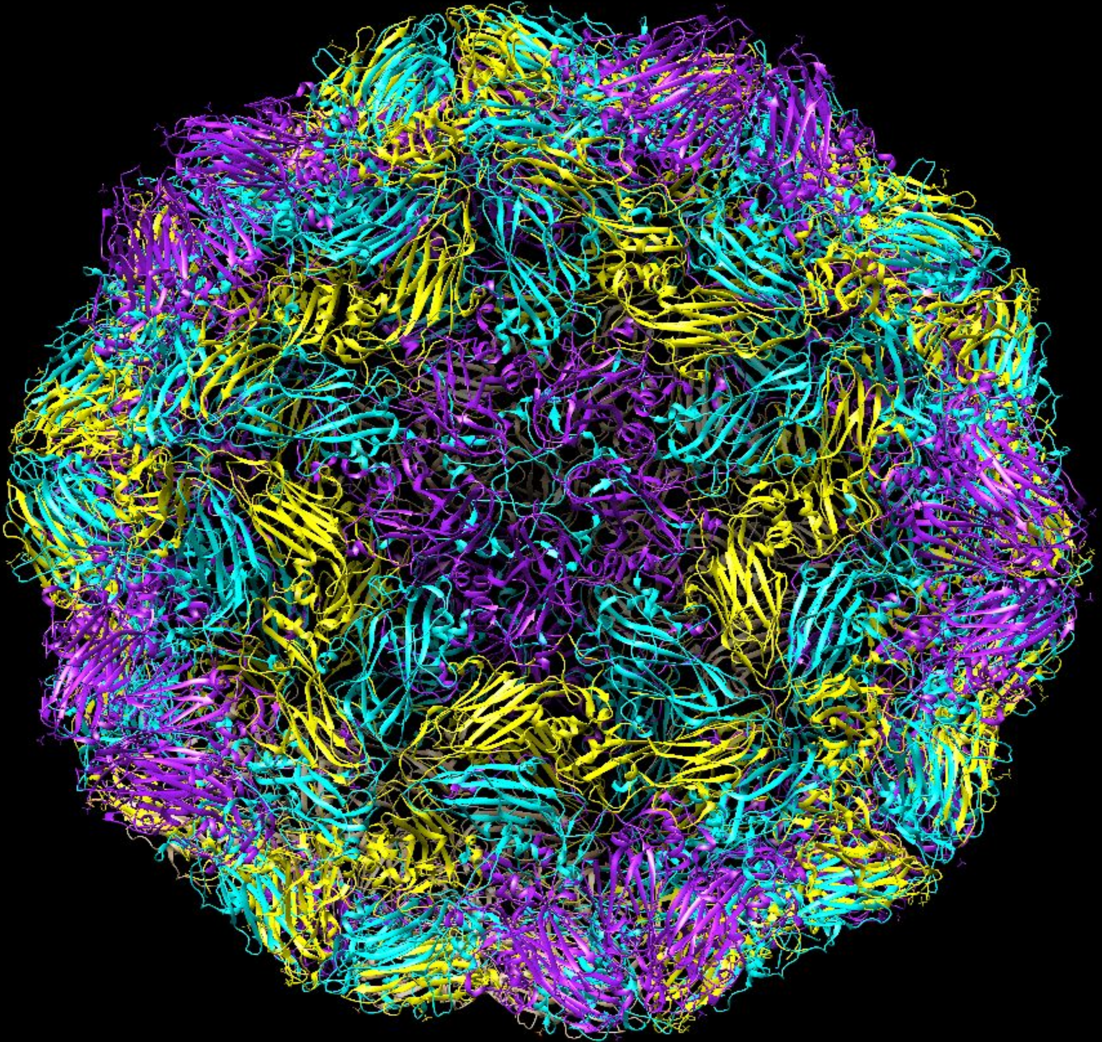
BACKGROUND

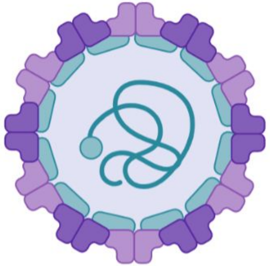


1.4

MILLION CASES WORLDWIDE

Picornavirus characteristics

- Small viruses
- Naked 30nm **icosahedral capsid** → 60 identical packed protomers
- Single-stranded RNA-positive viruses



Examples: poliovirus, rhinovirus, and hepatitis A virus

Reproductive cycle

Virus attachment (1)

Cell entry: Endocytosis (2)

Viral genome released into the cytoplasm (3)

Synthesis of viral proteins (4)

Capsid assembly (5) and maturation (6)

Virus release by cell lysis or budding (7)

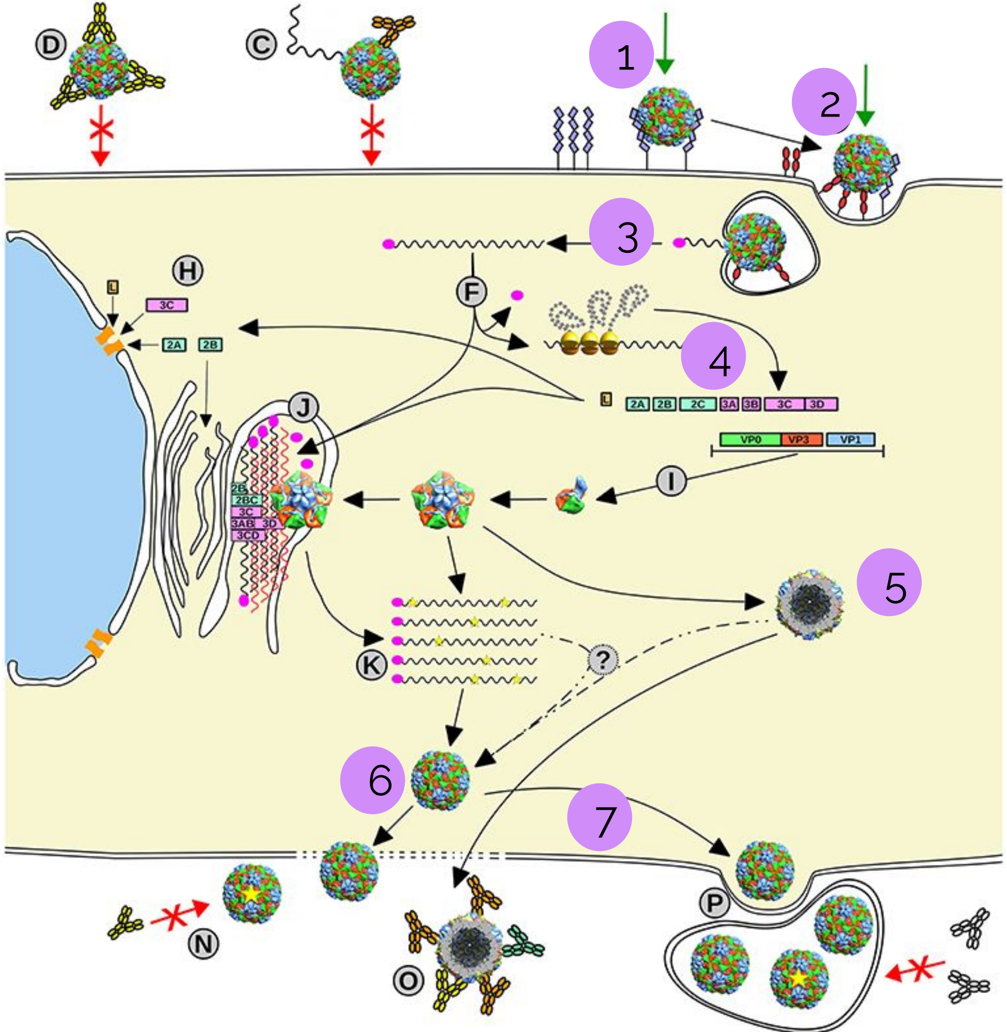
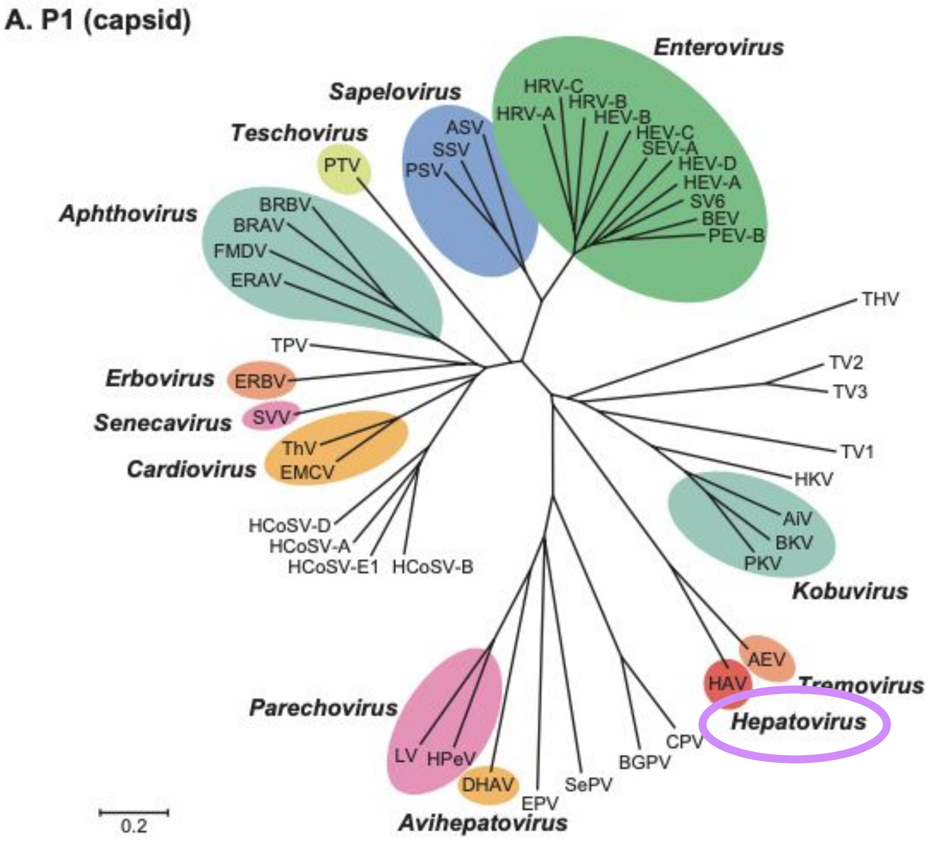


Figure 1. Life cycle of the Picornavirus life cycle. Adapted from Cifuente J, Moratorio G (2019).

Phylogeny

Family	*Picornaviridae*
Genus	*Enterovirus* *Cardiovirus* *Aphthovirus* ***Hepatovirus*** *Parechovirus* *Erbovirus* *Kobuvirus* *Teschovirus* *Senecavirus* *Tremovirus* *Avihepatovirus*

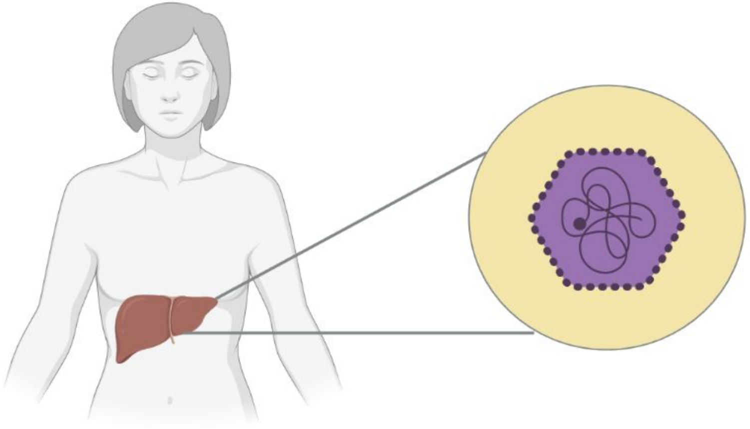


A. P1 (capsid)

Figure 2. Phylogenetic trees showing the relationships between the genera, species and unclassified members of the family Picornaviridae regarding protein P1. Adapted from King, Lefkowitz, Adams & Carstens, 2011.

Clinical manifestations of Hepatitis A

- Liver disease caused by HAV (hepatitis A virus).
- Symptoms include: fever, loss of appetite, diarrhea, jaundice...
- Not chronic, rarely fatal
- Transmitted by contaminated food and water (by faeces of an infected individual) or oral-anal sex.



Worldwide distribution of Hepatitis A

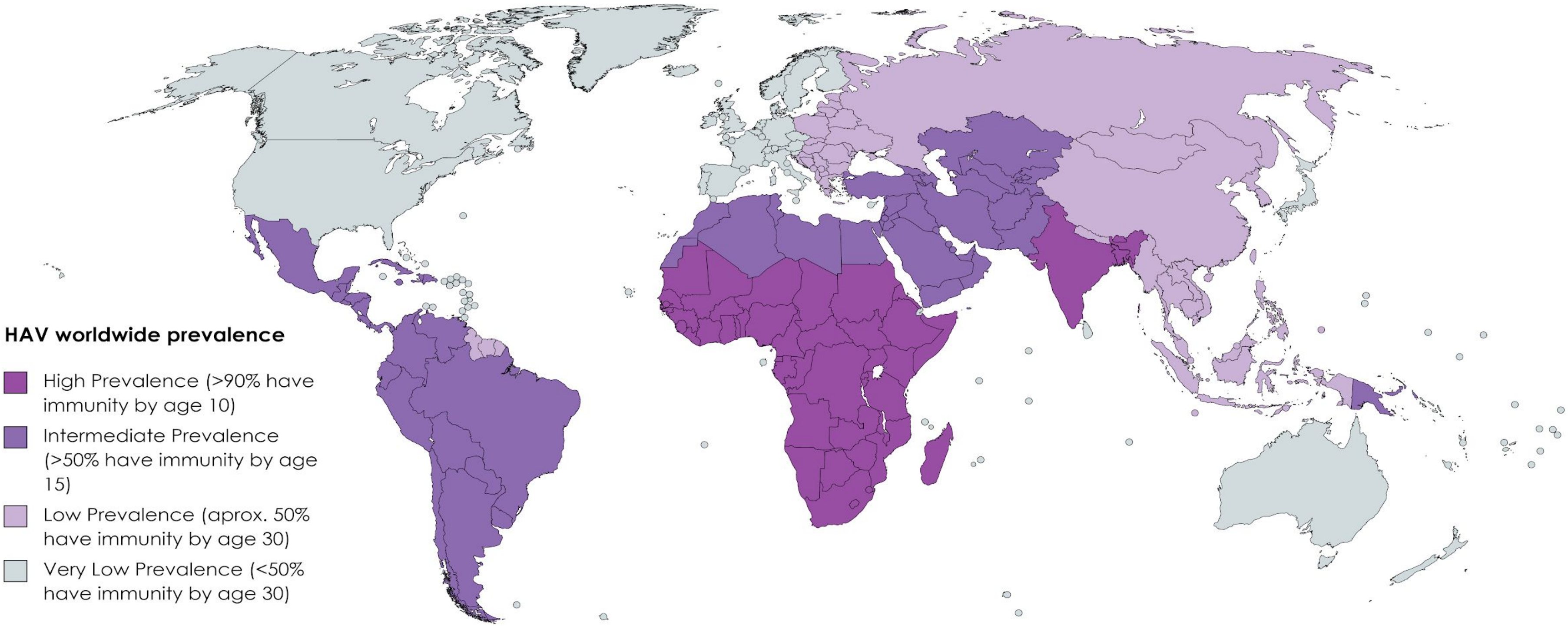
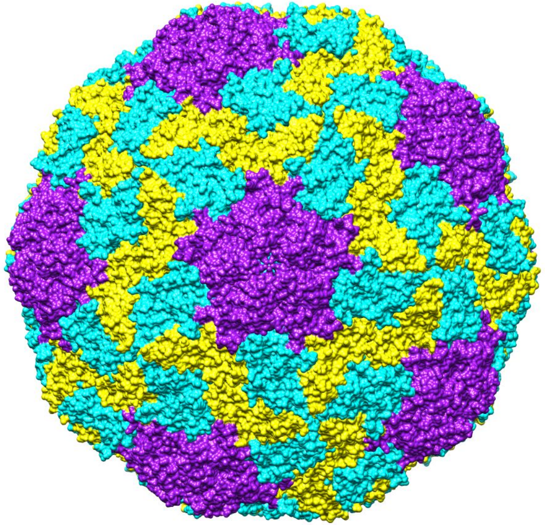


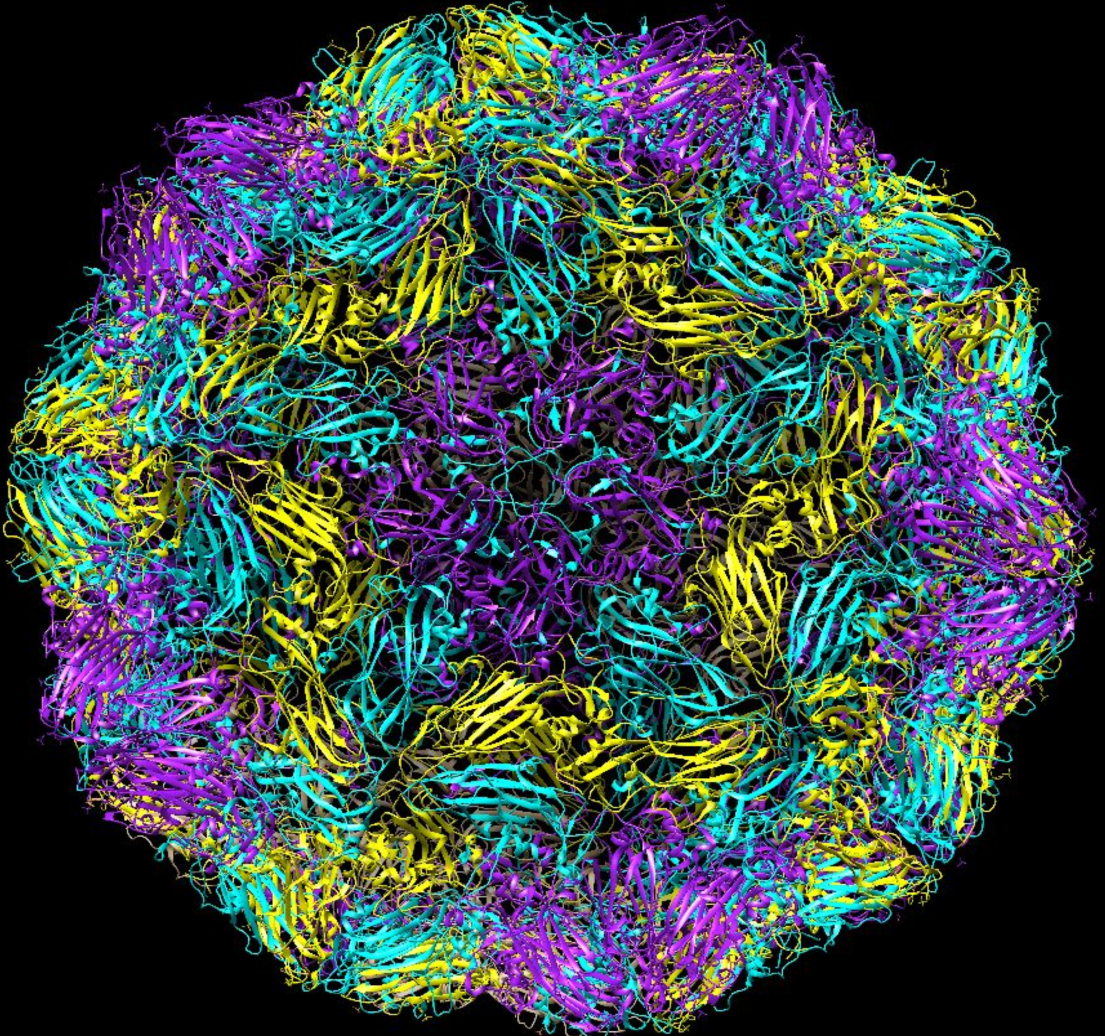
Figure 3. Hepatitis A (HAV) worldwide prevalence map. Adapted from Jacobsen K (2018) with MapChart.

HAV general characteristics

- Different properties than other picornaviruses
- It also exists in a quasi-enveloped form
- Can perform transcytosis (primitive-like)
- Highly stable
  - T = 80 ˚C
  - pH = as low as 2



CAPSID ASSEMBLY



Genomic organization of HAV

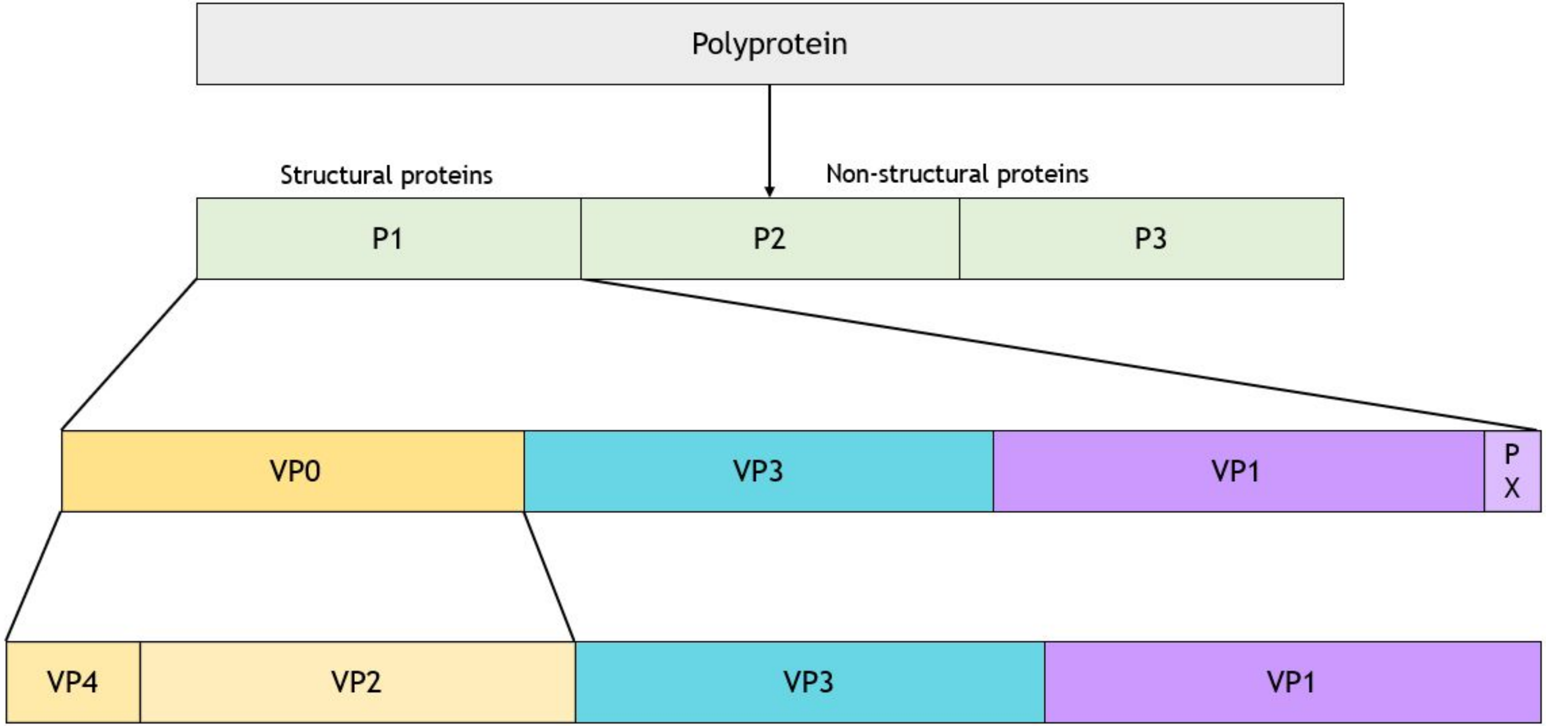
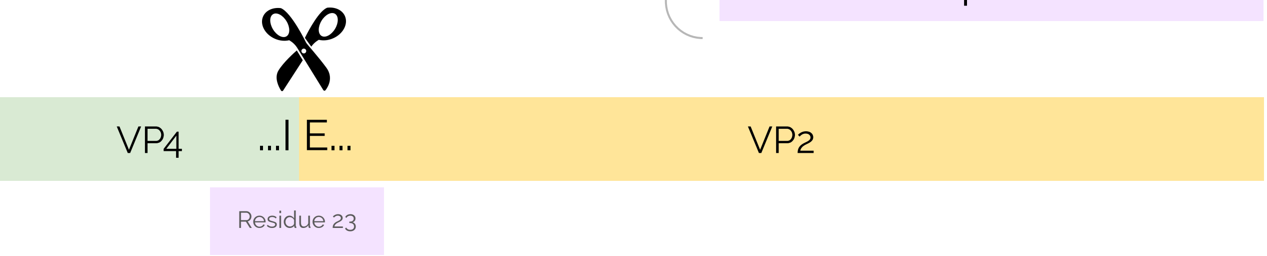


Figure 4. Organization of the hepatitis A virus (HAV) RNA genome and processing of the polyprotein. Adapted from McKnight et al, 2018.

VP0 cleavage → VP2, VP4

Autocatalytic cleavage

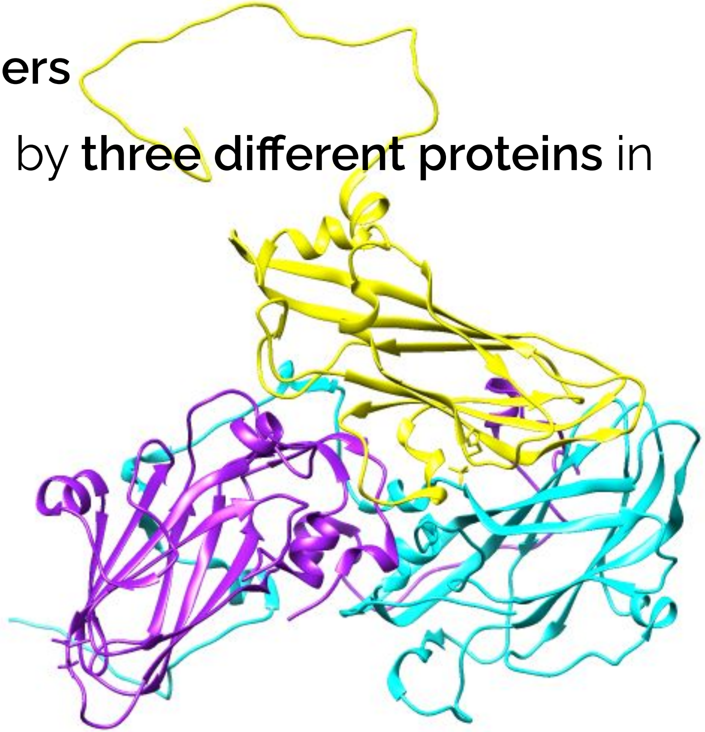
RNA-dependent (?)



```
1         11        21        31        41
GASYFTSVDQSSVHTAEVGSHQIEPLKTSVDKPGSKKTQGEKFFLIHSAR
51        61        71        81        91
WLTTHALFHEVAKLDVVKLLYNEQFAVQGLLRYHTYARFGIEIQVQINPT
101       111       121       131       141
PFQQGGLICAMVPGDQSYGSIASLTVYPHGLLNCNINNVVRIKVPFIYTR
151       161       171       181       191
GAYHFKDPQYPVWELTIRVWSELNIGTGTSAYTSLNVLARFTDLELHGLT
201
PLST
```

HAV Capsid

- Icosahedral capsid formed by **60 asymmetric units.**
- These units assemble forming **12 pentamers**
- The asymmetric unit (protomer) is formed by **three different proteins** in the mature capsid:
  - Viral protein 1: **VP1 (225 residues)**
  - Viral protein 2: **VP2 (204 residues)**
  - Viral protein 3: **VP3 (246 residues)**
- **Pseudo T** = 3 arrangement.



SCOP Classification

Class:
All beta proteins

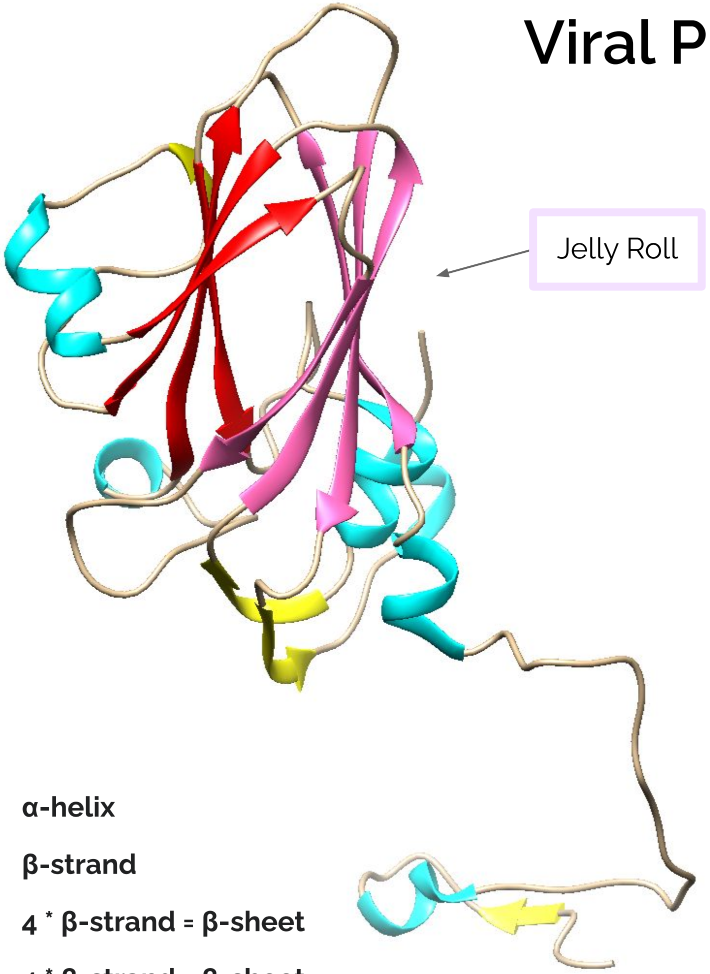
Fold:
Nucleoplasmin-like/VP (Viral coat and capsid proteins) sandwich; 8 strands in 2 sheets: jelly-roll

Interaction between folds (5-fold assemblies)

Superfamily:
Positive stranded ssRNA viruses

Family:
Picornaviridae-like VP (VP1, VP2, VP3 and VP4)

Viral Protein 1 (VP1)



🟦 α-helix

🟨 β-strand

🟪 4 * β-strand = β-sheet

🟥 4 * β-strand = β-sheet

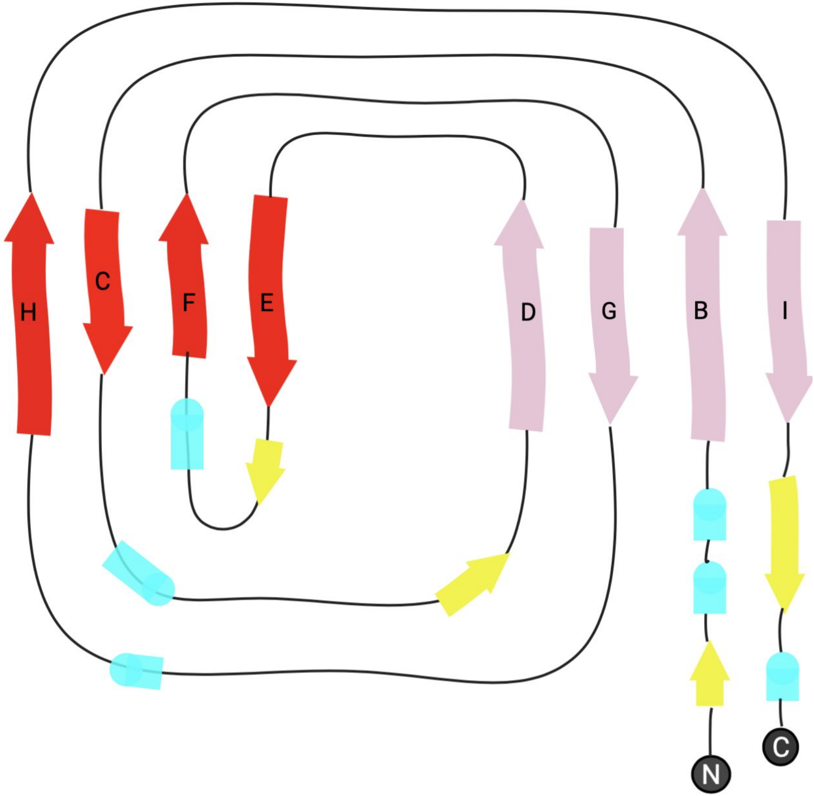
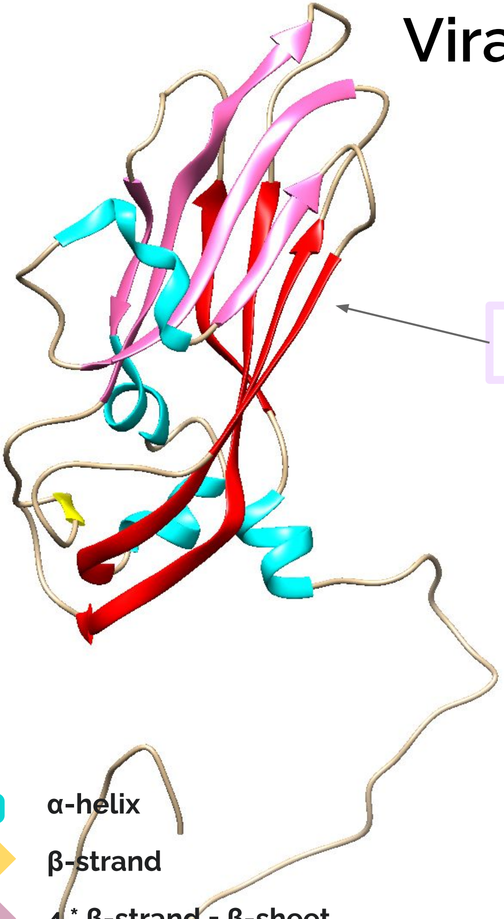


Figure 5. Topological diagram of VP1 from HAV.

Viral Protein 0 (VP0 = VP4+VP2)



▬ α-helix

➡ β-strand

➡ 4 * β-strand = β-sheet

➡ 4 * β-strand = β-sheet

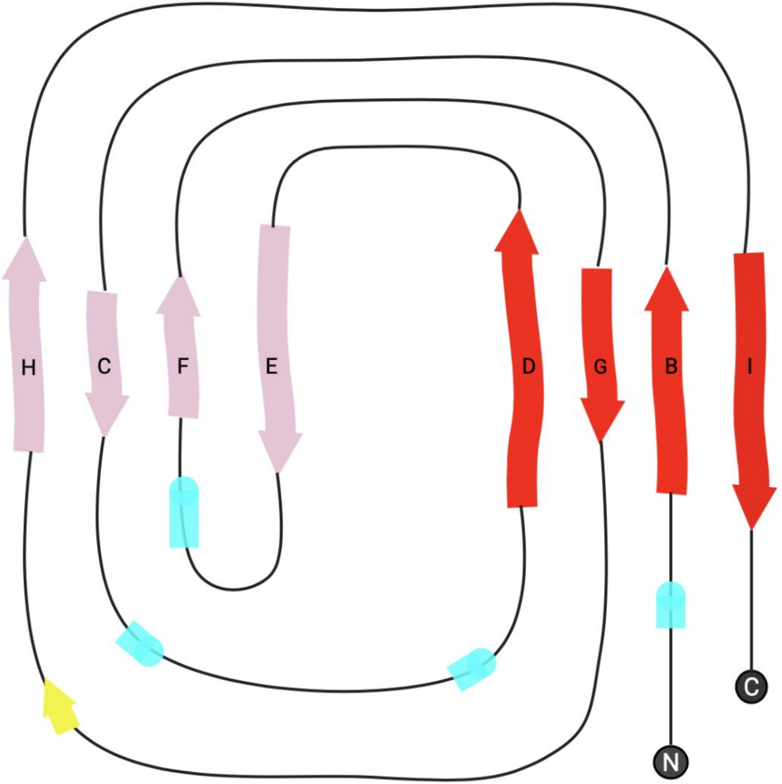
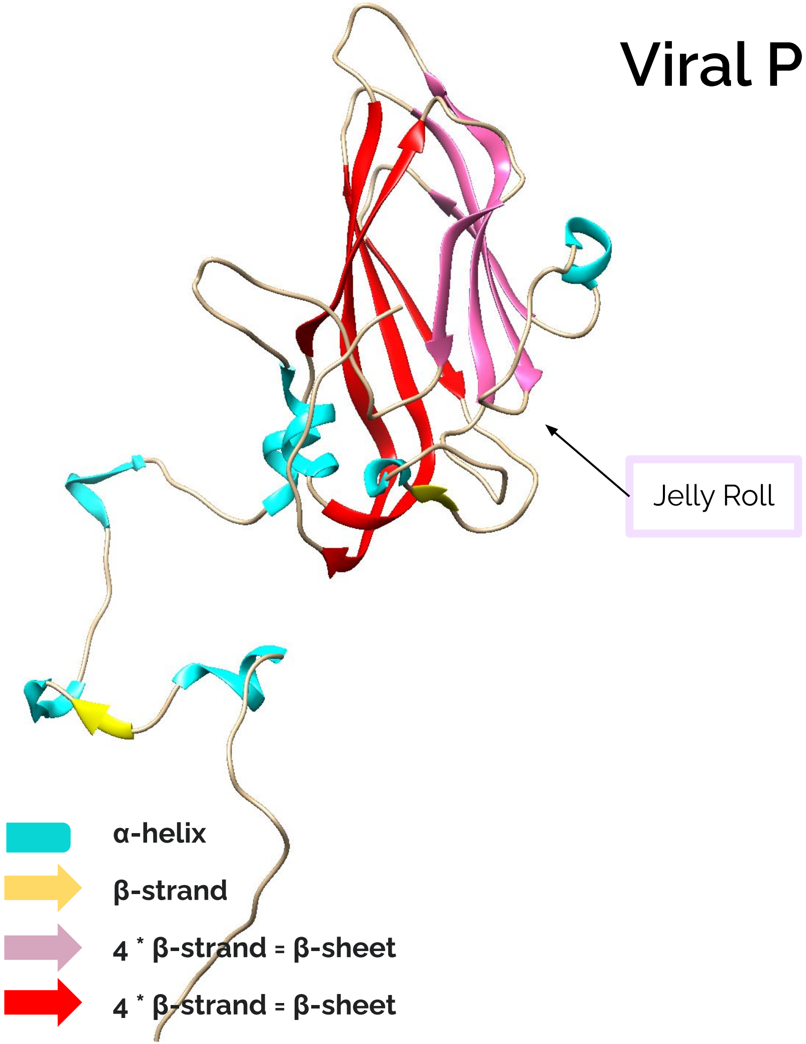


Figure 6. Topological diagram of VP0 from HAV.

Viral Protein 3 (VP3)



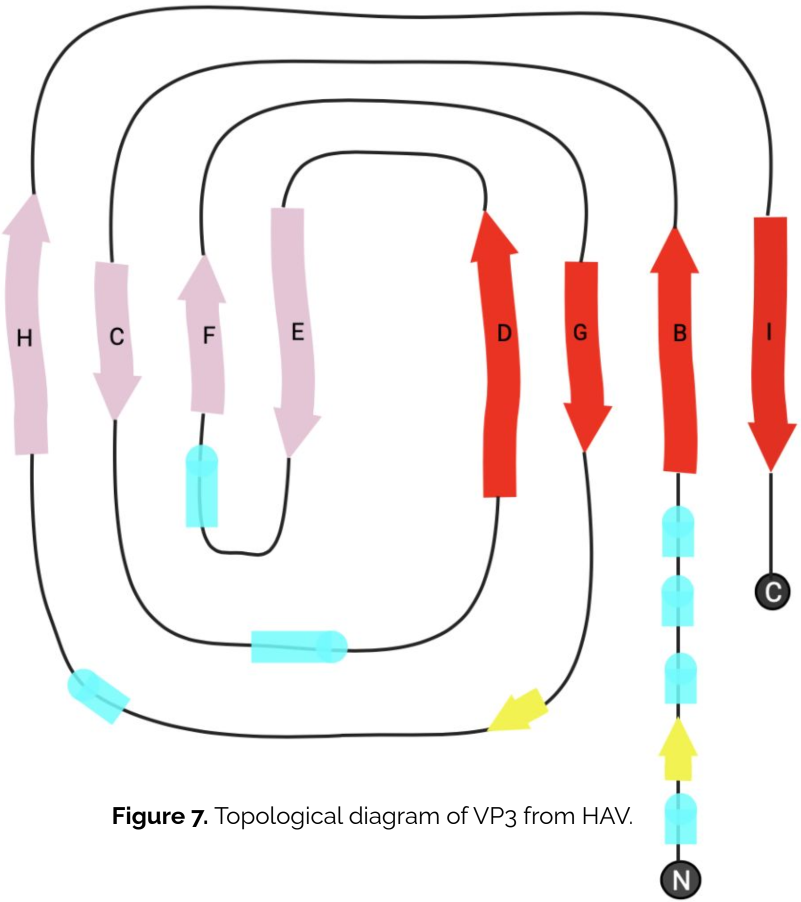
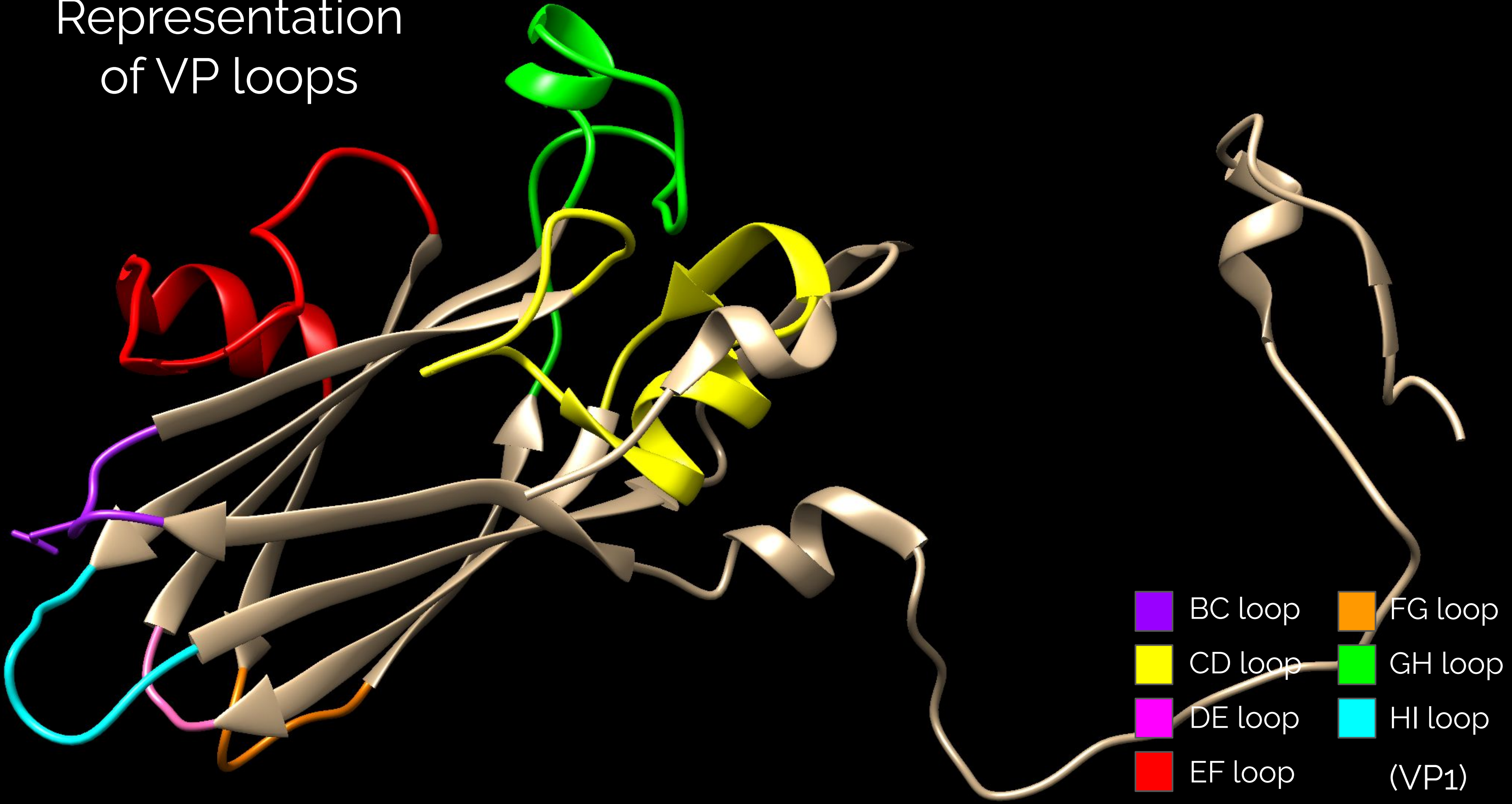


Figure 7. Topological diagram of VP3 from HAV.

Representation of VP loops



Viral Proteins Superimposition

RMSD: 2,13

HAV VP (4QPG)

🟪 VP1

🟨 VP0

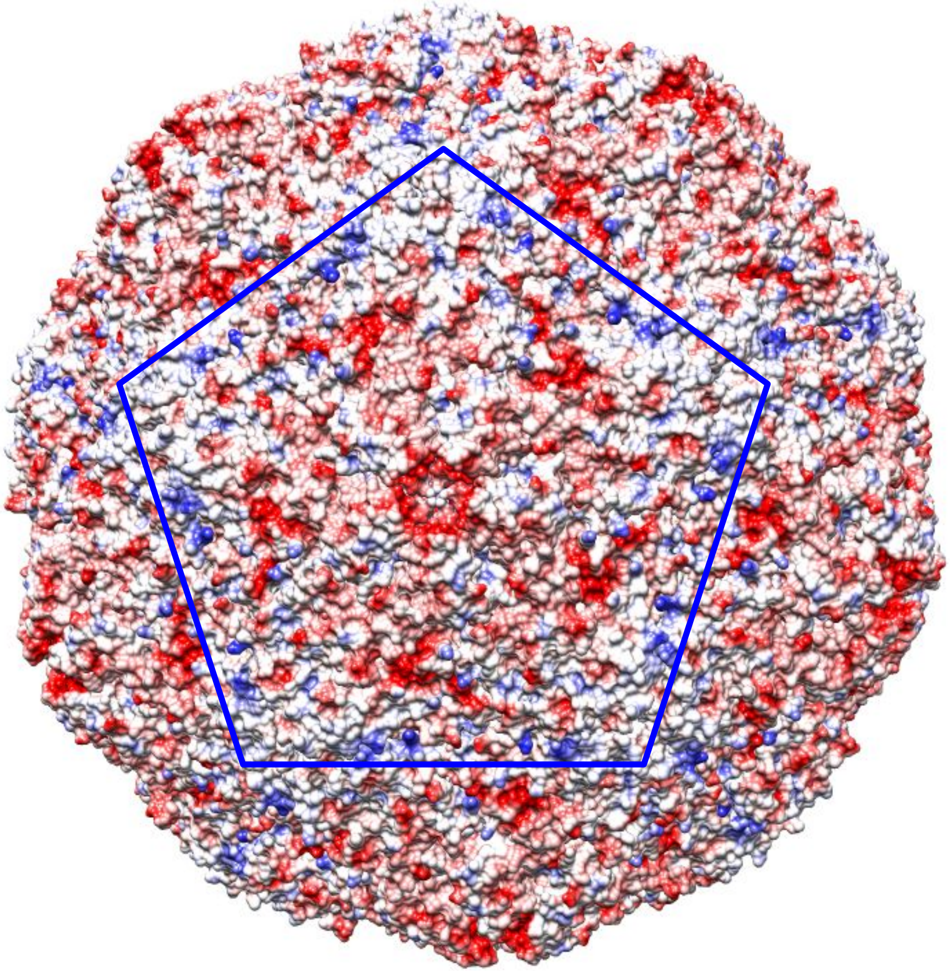
🟦 VP3

Electrostatic potential

HAV surface appears to be more negatively charge, but the fringes between pentamers have positive charge.

🟥 Negative charges

🟦 Positive charges



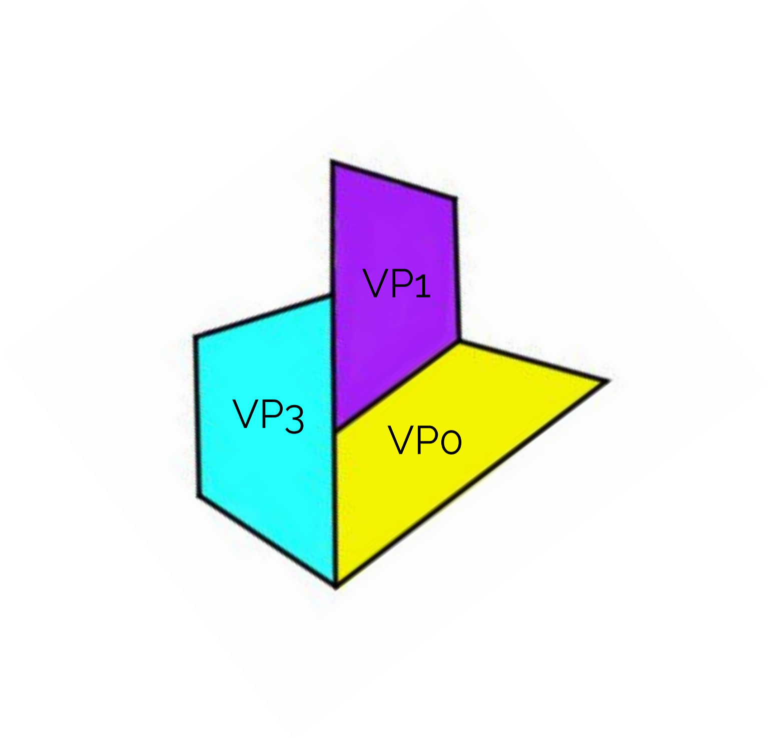
Electrostatic potential, Coulombic Surface Coloring

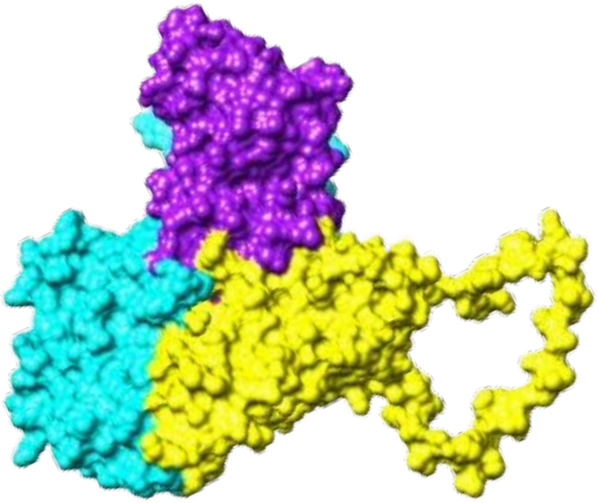
Capsid assembly: global vision

1) 5S Protomer: (VP0, **VP1**, VP3)
2) 14S Pentamer: (VP0, **VP1**, VP3)5
3) **75S Empty Capsid: [(VP0, VP1, VP3)5]12**
4) *Preprovirion* [(VP0, VP3,**VP1**-pX)5]12RNA
5) Provirion: [(VP0, **VP1**, VP3)5]12RNA
6) Mature Virions: [(*VP4,* VP2, VP3, **VP1**)5]12RNA

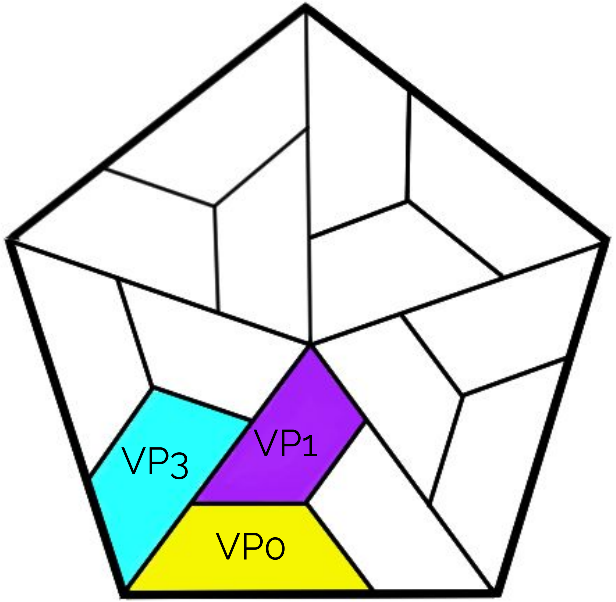
Capsid assembly likely follows a **dodecahedral pathway**

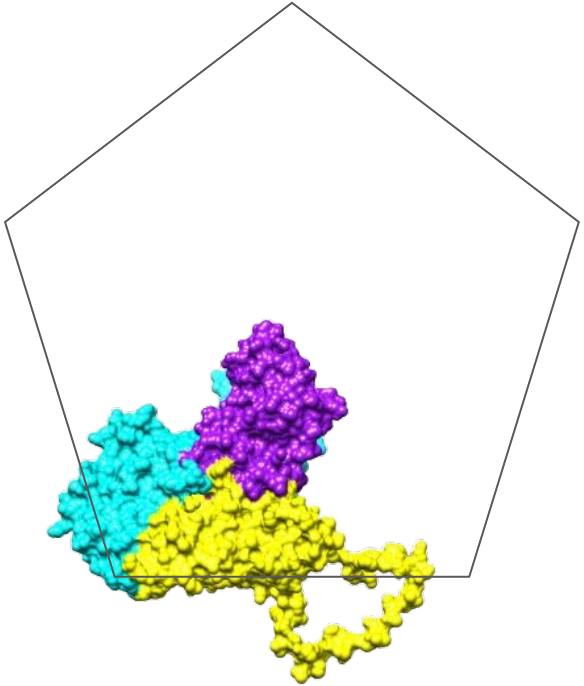
Capsid assembly: **5S Protomer:** (VP0, VP1, VP3)



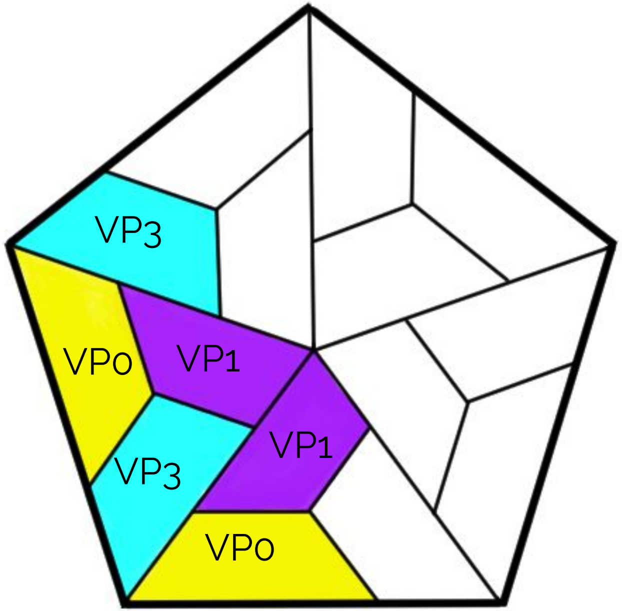


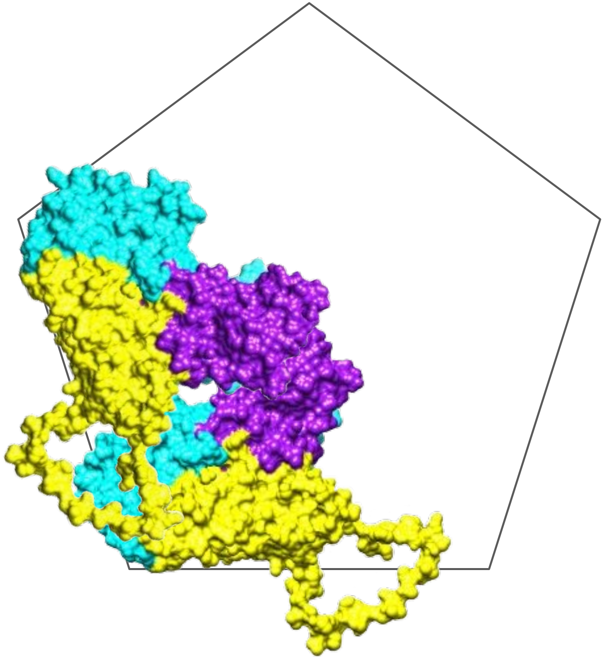
Capsid assembly: **14S Pentamer:** (VP0, VP1, VP3)5



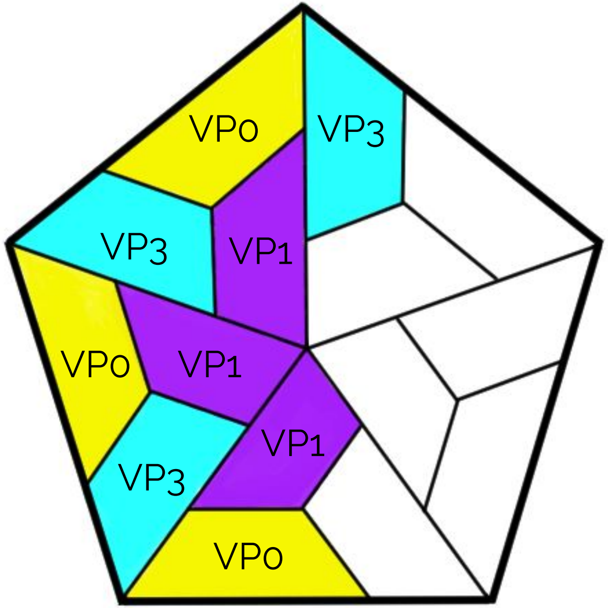


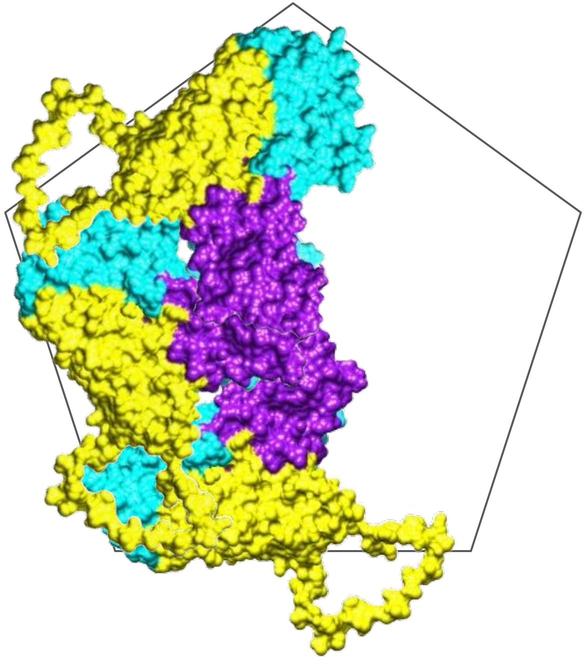
Capsid assembly: **14S Pentamer:** (VP0, VP1, VP3)5



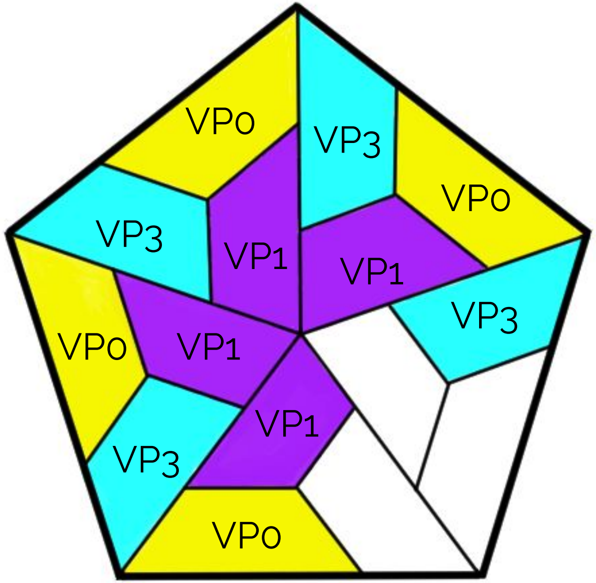


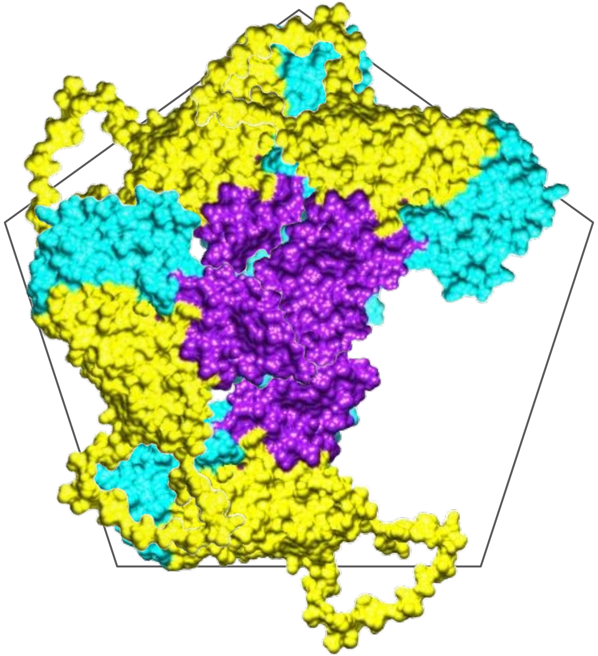
Capsid assembly: **14S Pentamer:** (VP0, VP1, VP3)5



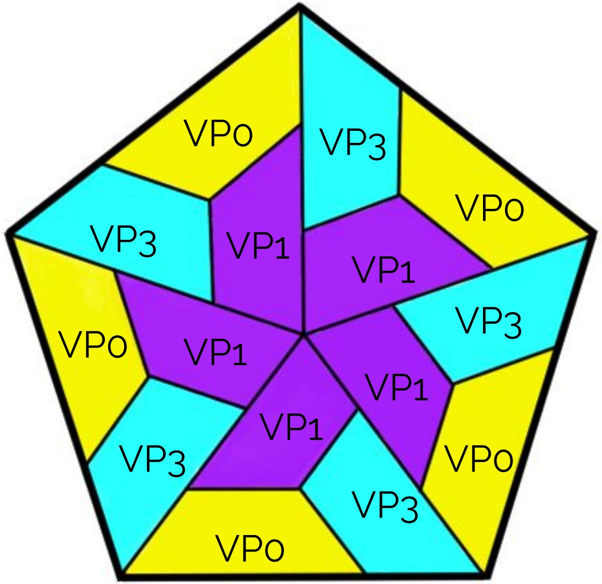


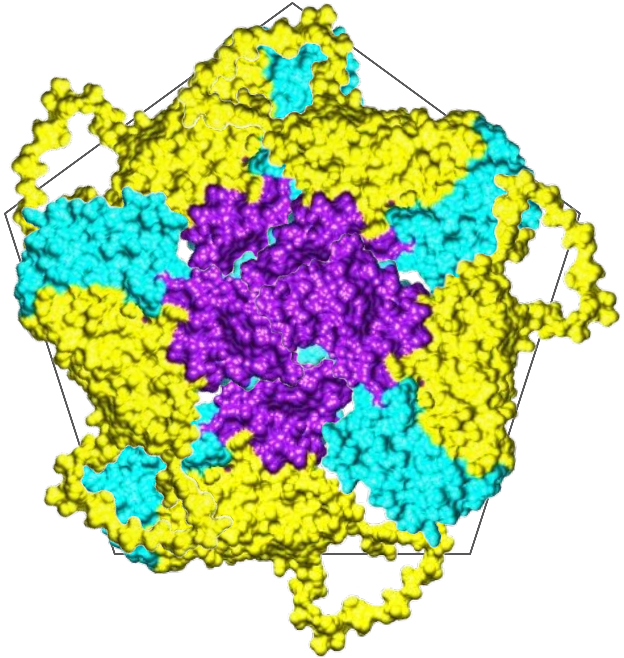
Capsid assembly: **14S Pentamer:** (VP0, VP1, VP3)5



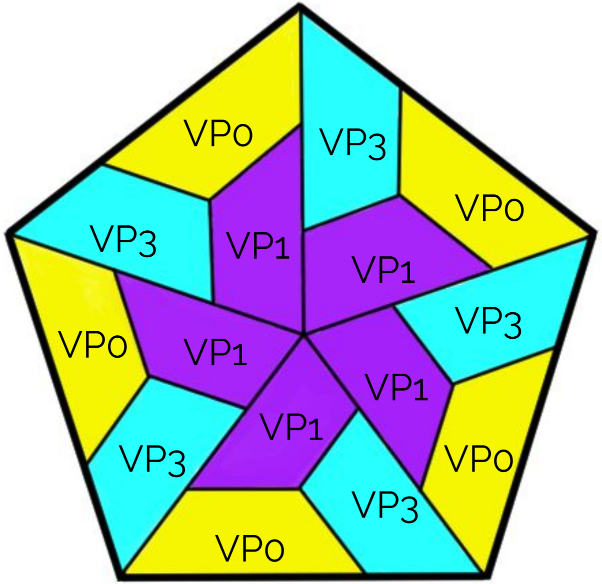


Capsid assembly: **14S Pentamer:** (VP0, VP1, VP3)5

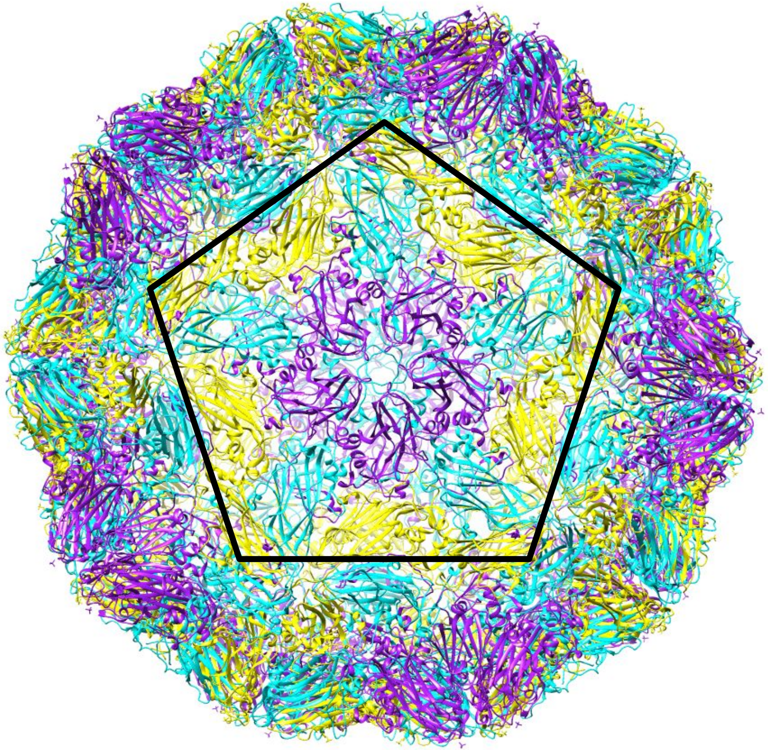




Capsid assembly: **75S Empty Capsid**: [(VP0, VP1, VP3)5]12



x12 =

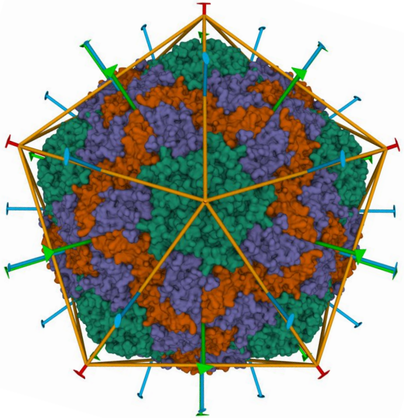


12 pentamers form the capsid

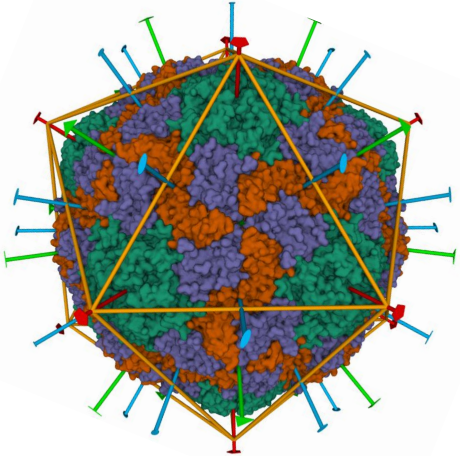
Capsid Symmetry

The association of protomers to form the icosahedral particle defines **3 symmetry axes**

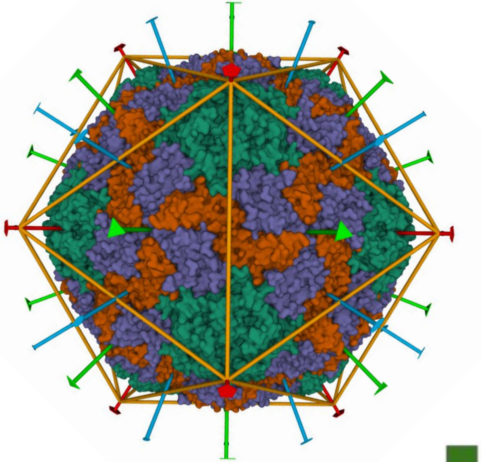
5-fold axis



3-fold axis



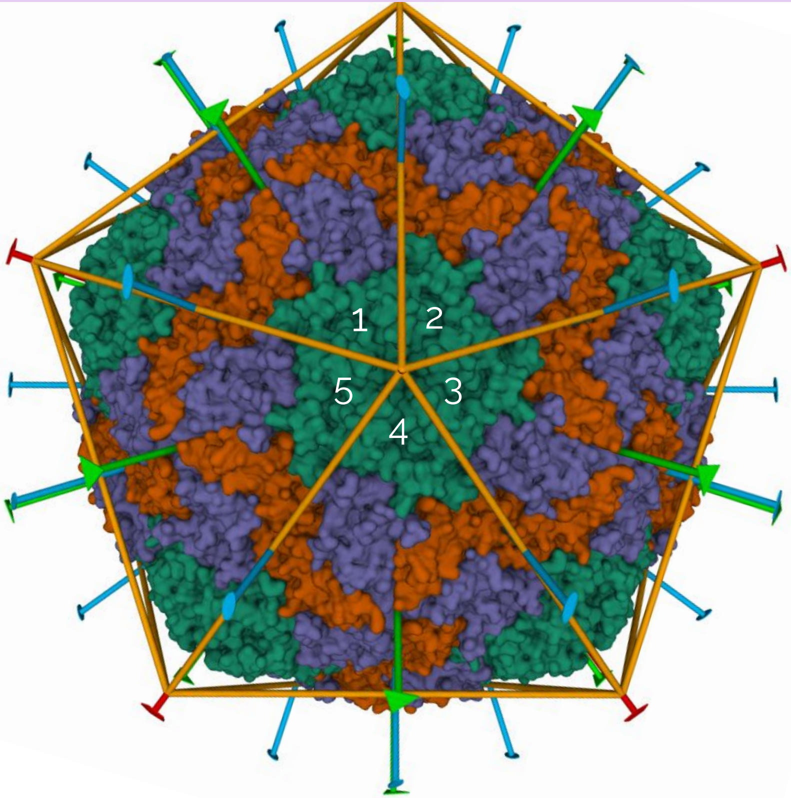
2-fold axis



🟩 VP1
🟥 VP0
🟪 VP3

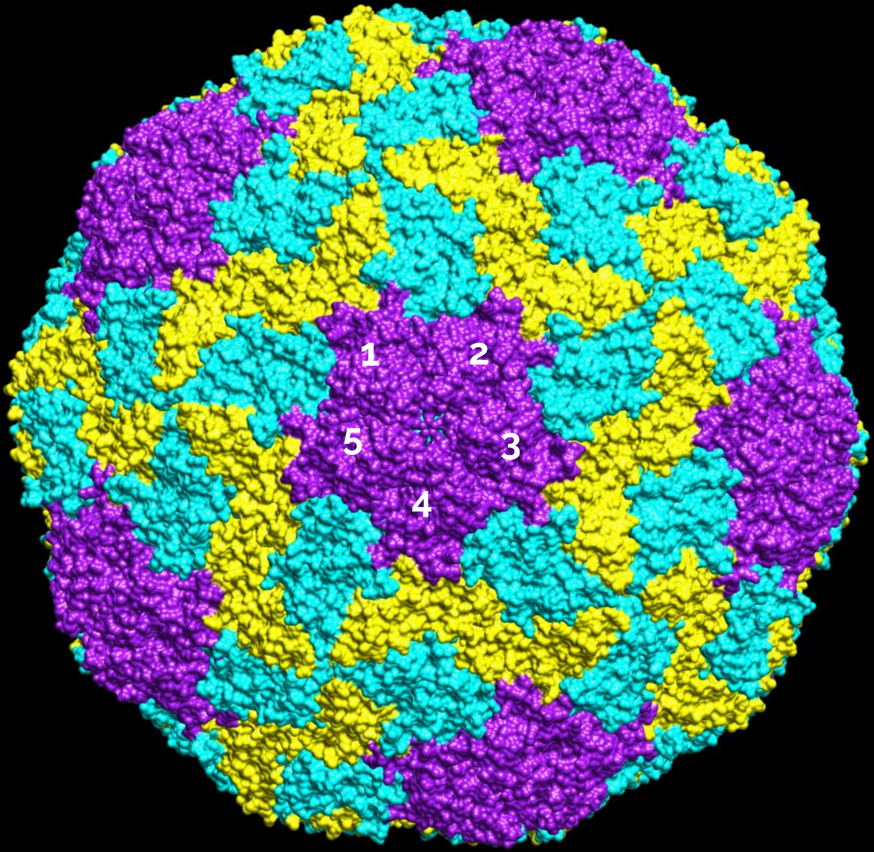
Capsid Symmetry: 5-fold axis

5 copies of VP1 assemble in the five-fold axis



🟩 VP1
🟥 VP0
🟪 VP3

5-fold axis



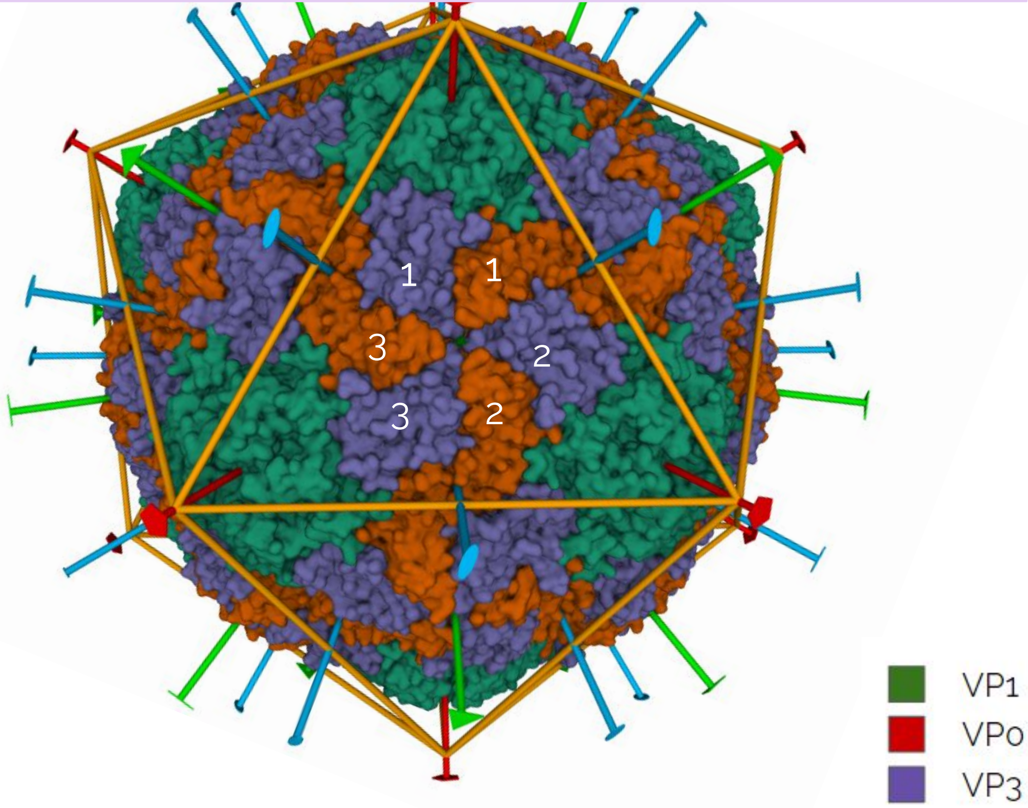
🟪 VP1

🟨 VP0

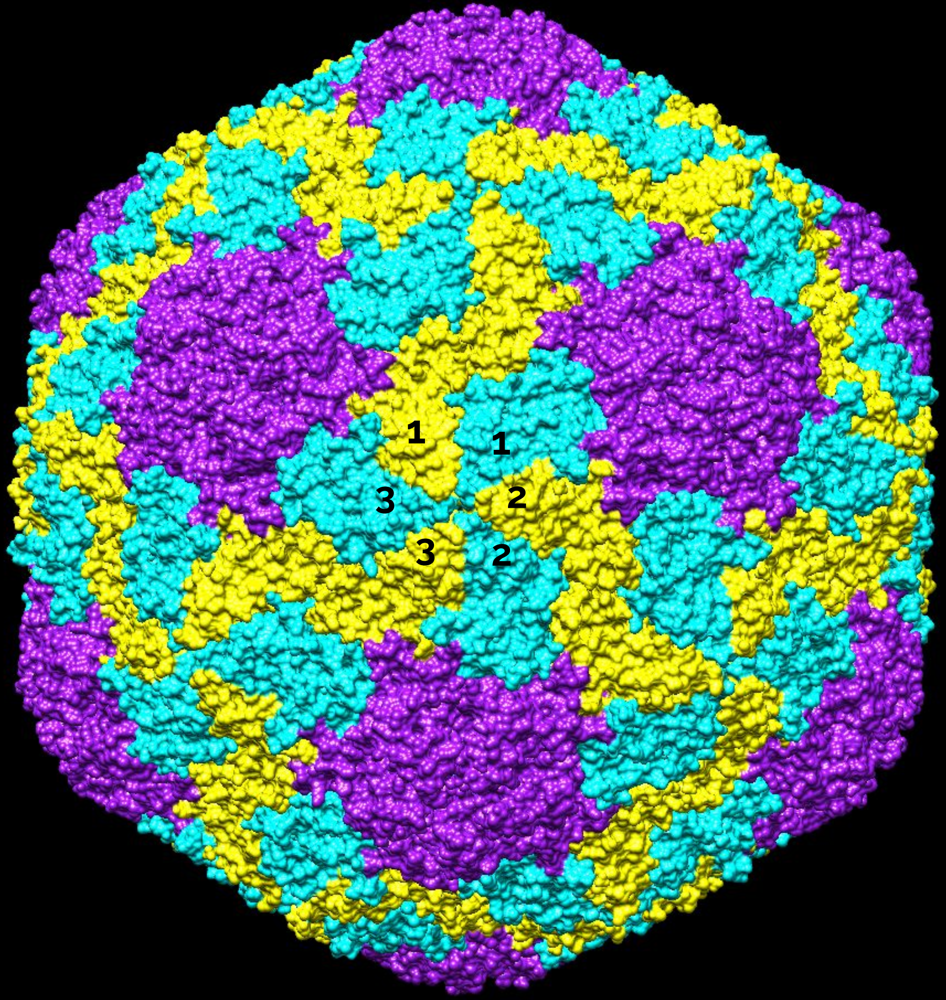
🟦 VP3

Capsid Symmetry: 3-fold axis

3 alternate copies of **VP0 (VP2)** and **VP3** assemble in the 3 fold axis



3-fold axis



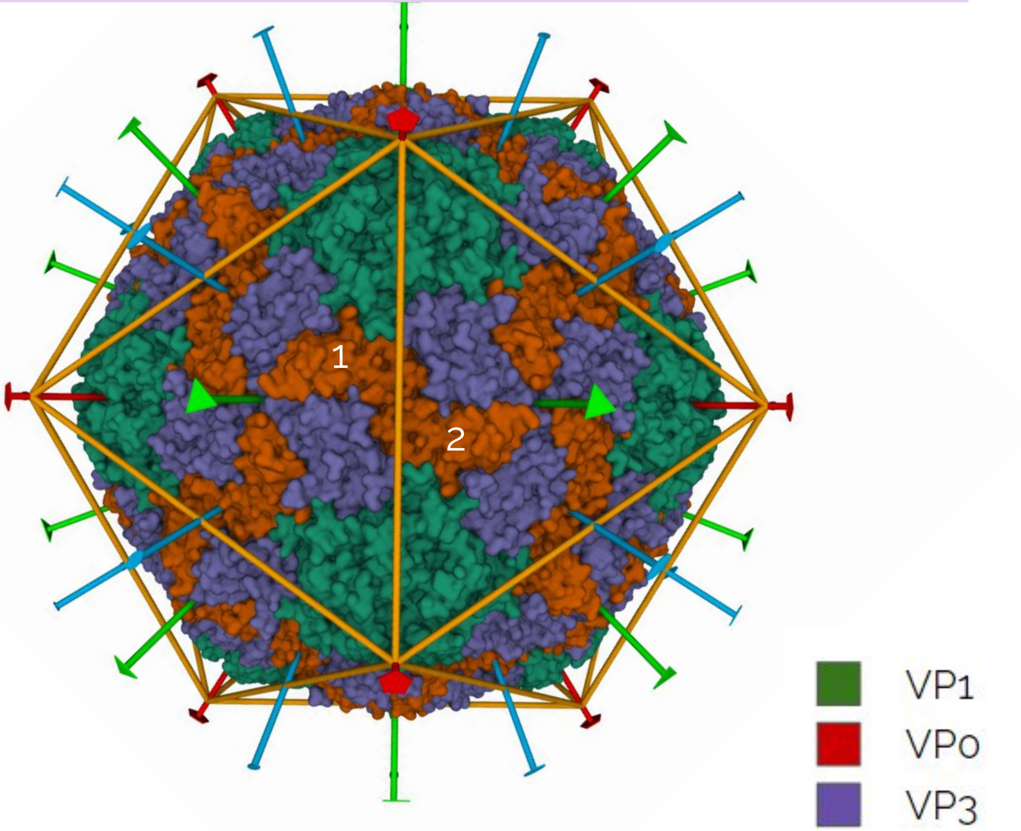
🟪 VP1

🟨 VP0

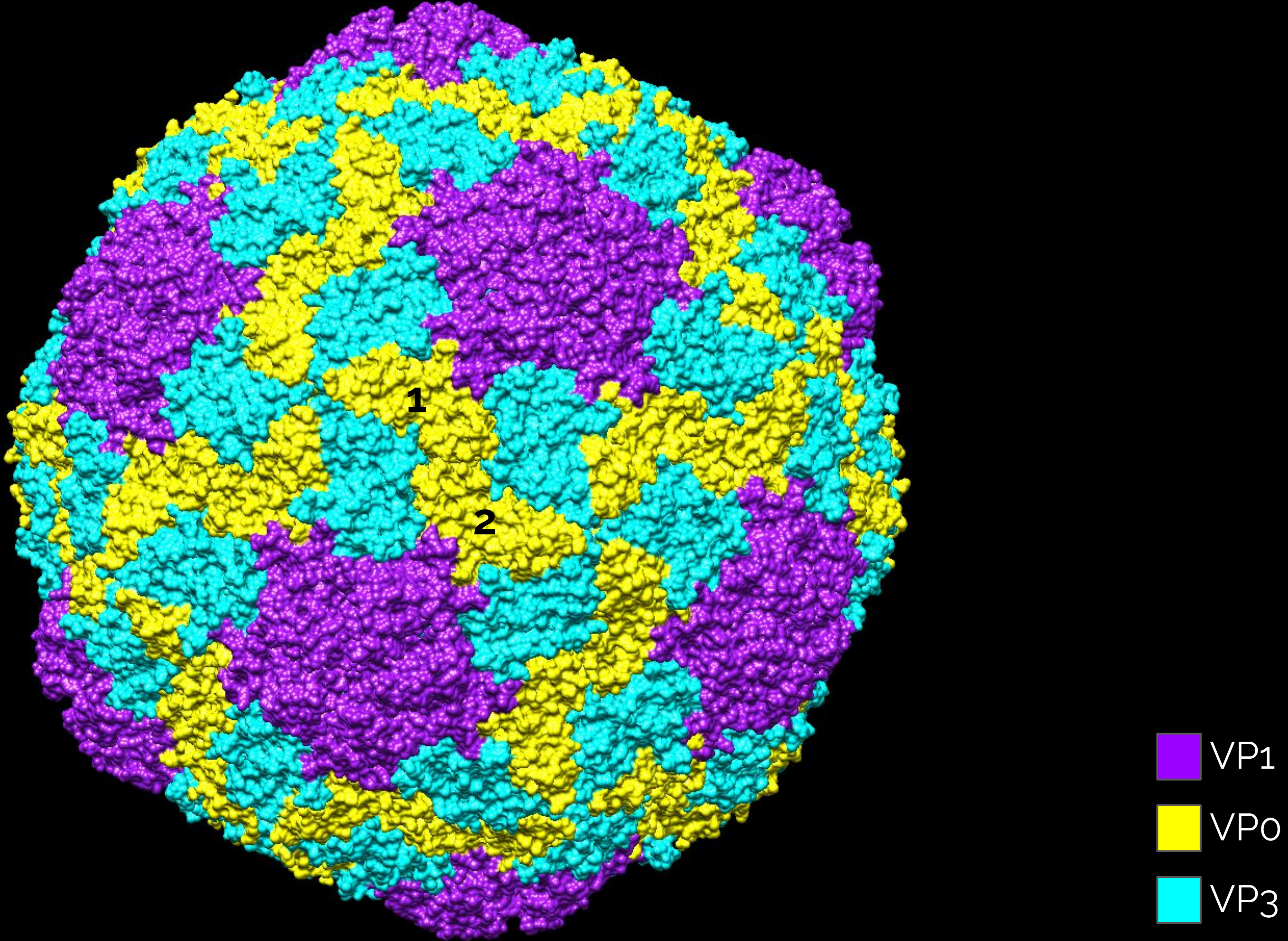
🟦 VP3

Capsid Symmetry: 2-fold axis

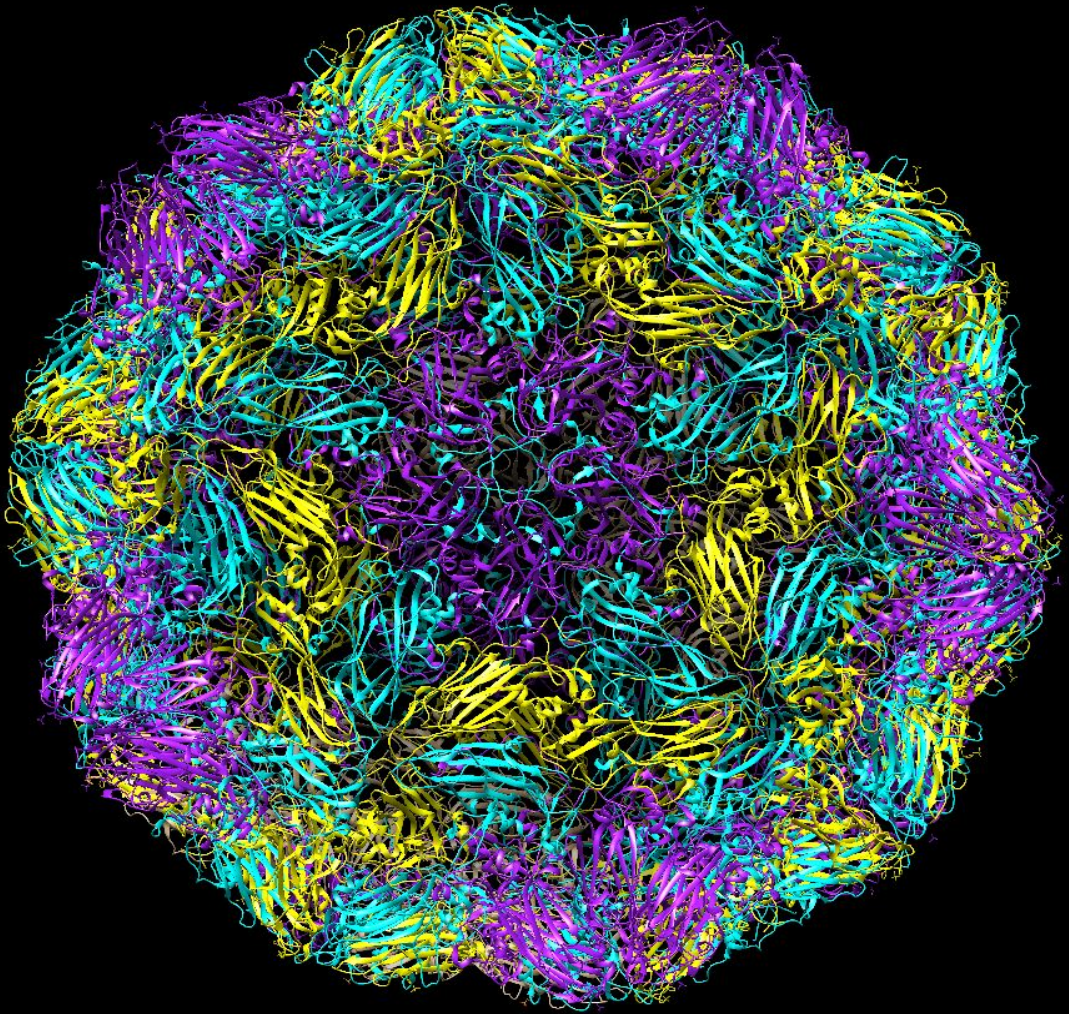
2 copies of **VP0 (VP2)** lean on each other in the 2-fold axis assembly



2-fold axis



CAPSID FEATURES



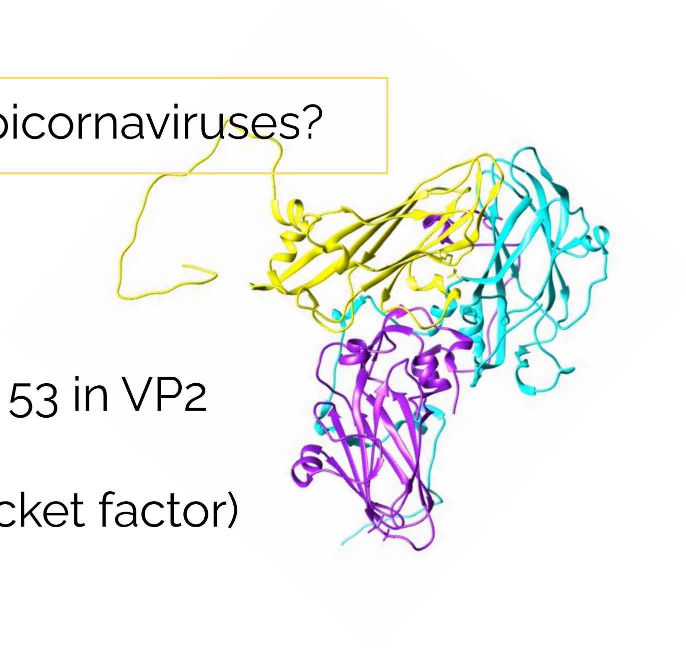
General features of picornavirus capsid

Main characteristics of picornavirus capsid	Does HAV share these characteristics?
VP1–3 adopt an eight-stranded antiparallel “β-barrel” fold.	✓
Some picornavirus have a depression called ‘canyon’	✗
Some picornavirus have a hydrophobic pocket in VP1.	✗
They present several loops in their structure	✓

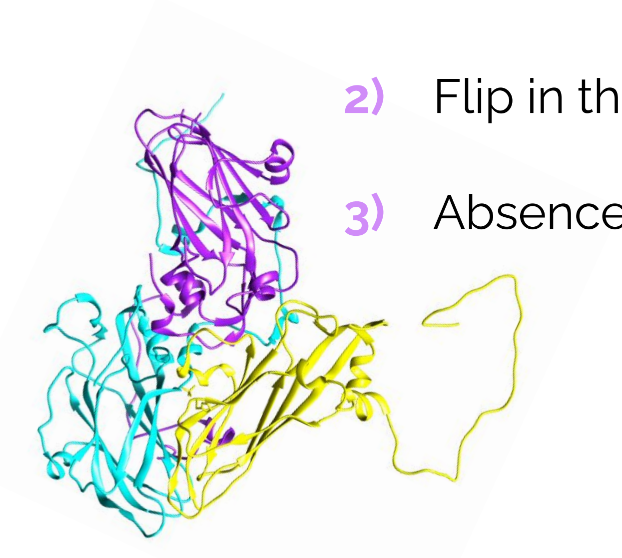
The differences in the loops are what distinguishes the several picornaviruses

Characteristic features of HAV

What distinguishes HAV from the other picornaviruses?



1) Absence of canyon
2) Flip in the ψ torsion angle of residue 53 in VP2
3) Absence of hydrophobic pocket (pocket factor)



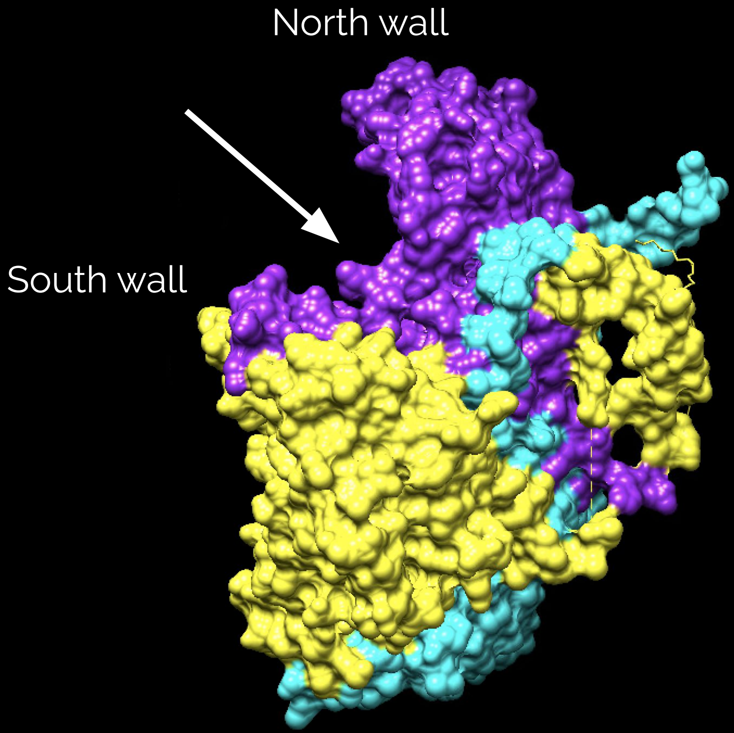
Absence of canyon

The surface of HAV capsid has **no canyon** compared with other picornavirus.

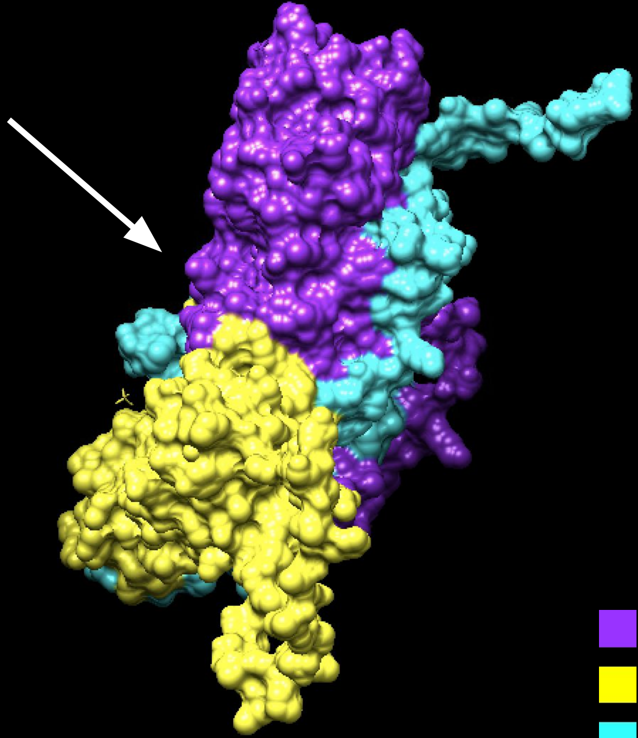
Why is that?

North wall lowers → BC loop of VP1 shortens
South wall disappears → EF VP2 loop and GH VP1 loop get reduced

HAV presents no canyon



Poliovirus (1POV)

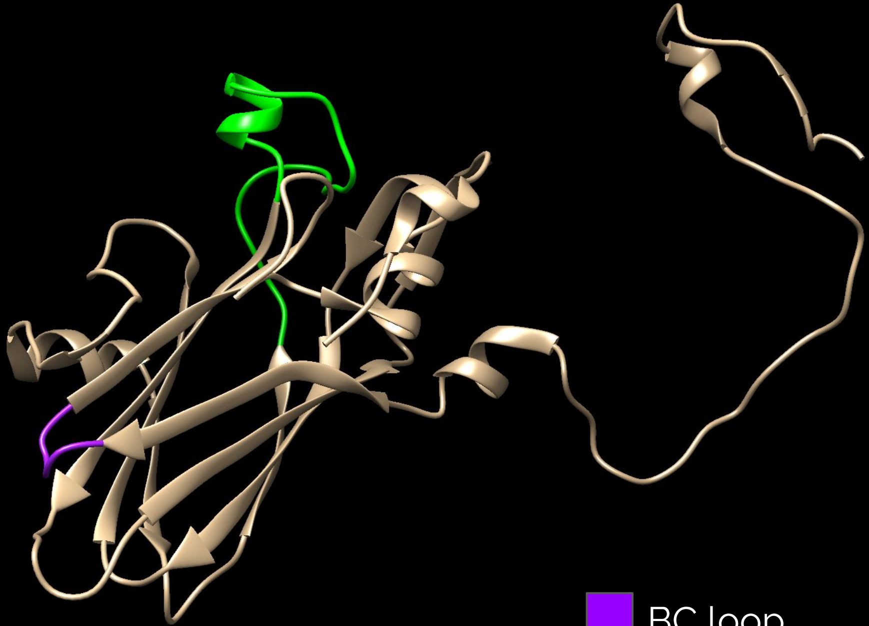


Hepatitis A virus (4QPG)

🟪 VP1
🟨 VP0/2
🟦 VP3

VP1 BC and GH loops

Poliovirus (1POV)



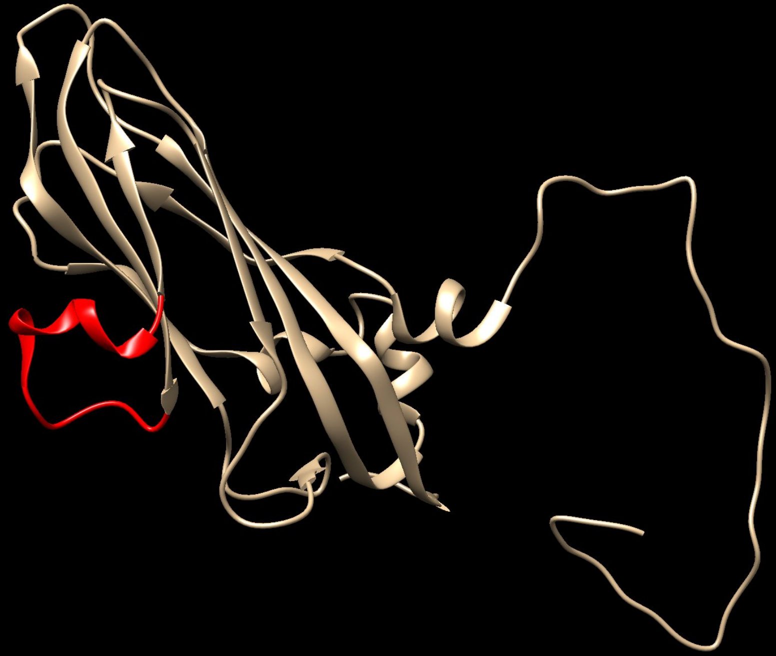
Hepatitis A virus (4QPG)

🟪 BC loop

🟩 GH loop

VP2 EF loop

Poliovirus (1POV)

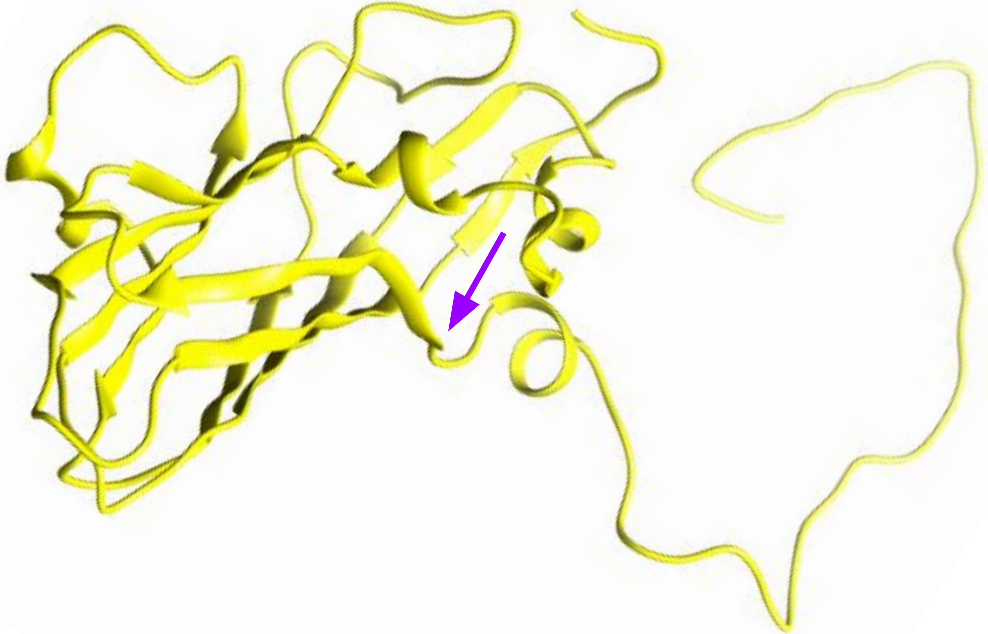


Hepatitis A virus (4QPG)

🟥 EF loop

VP2 ψ angle flip

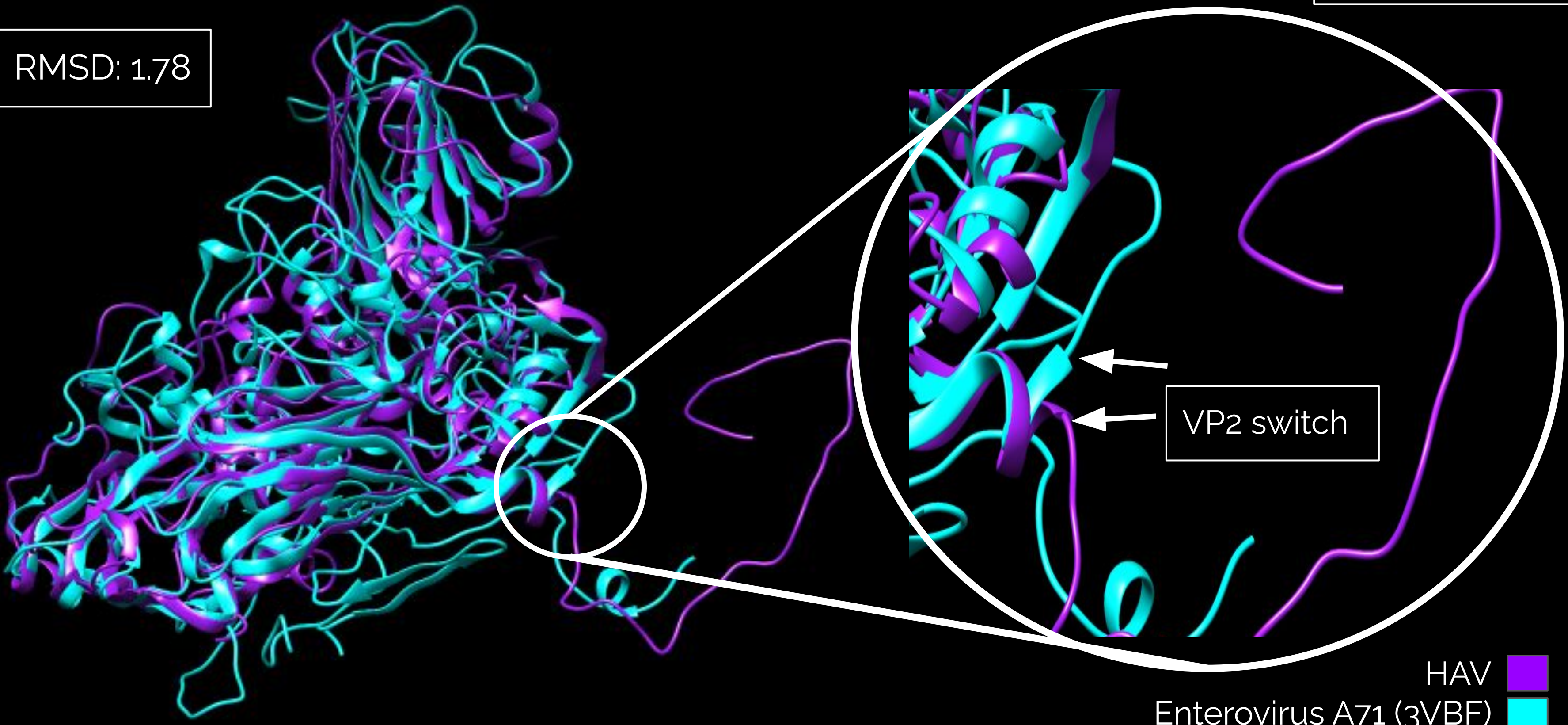
Flip in the ψ torsion angle of residue 53 (alanine) in VP2



EV-A71 and HAV superimposition

VP2 switch appears in HAV

RMSD: 1.78



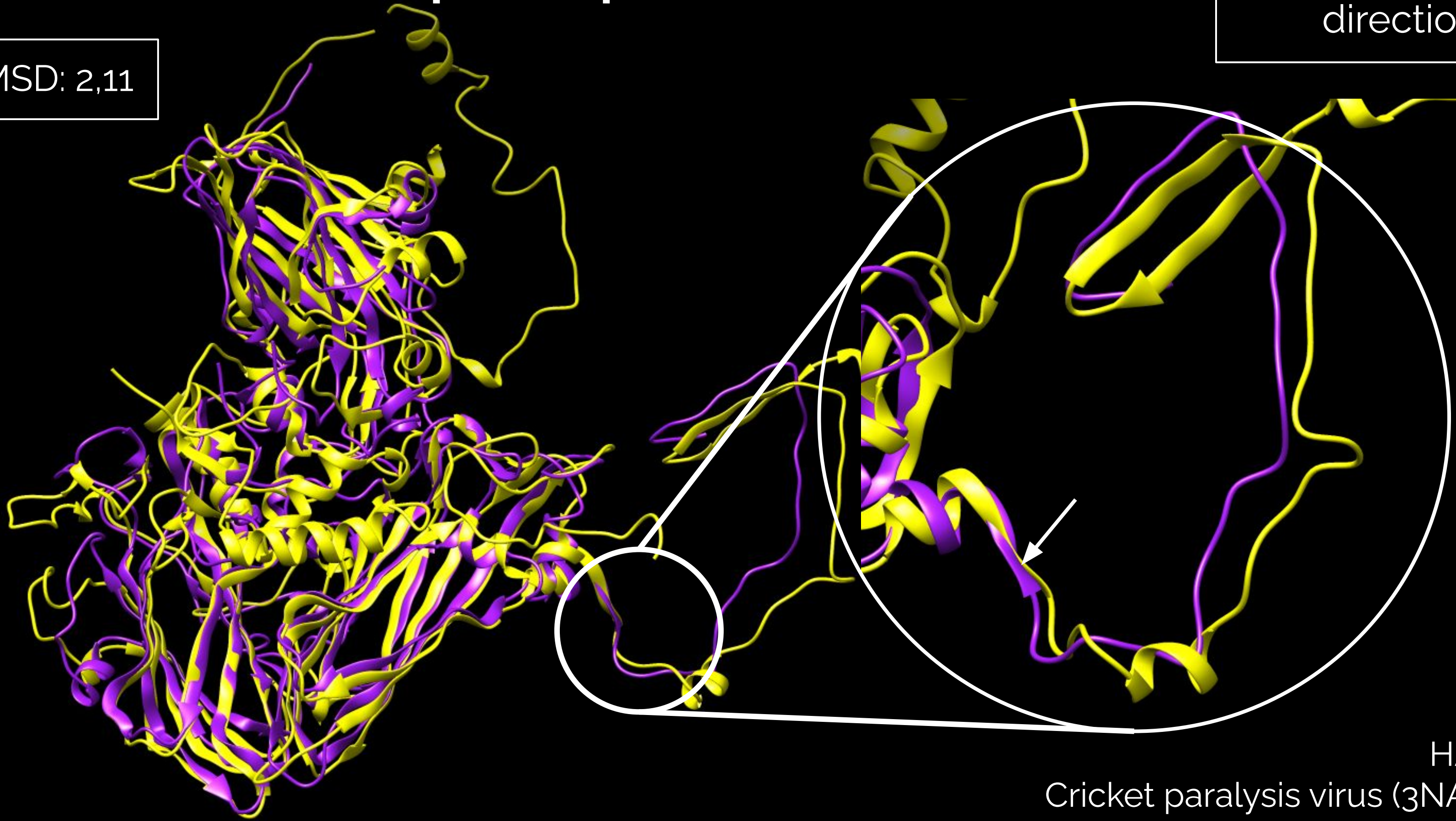
VP2 switch

HAV 🟪
Enterovirus A71 (3VBF) 🟦

CrPV and HAV superimposition

RMSD: 2,11

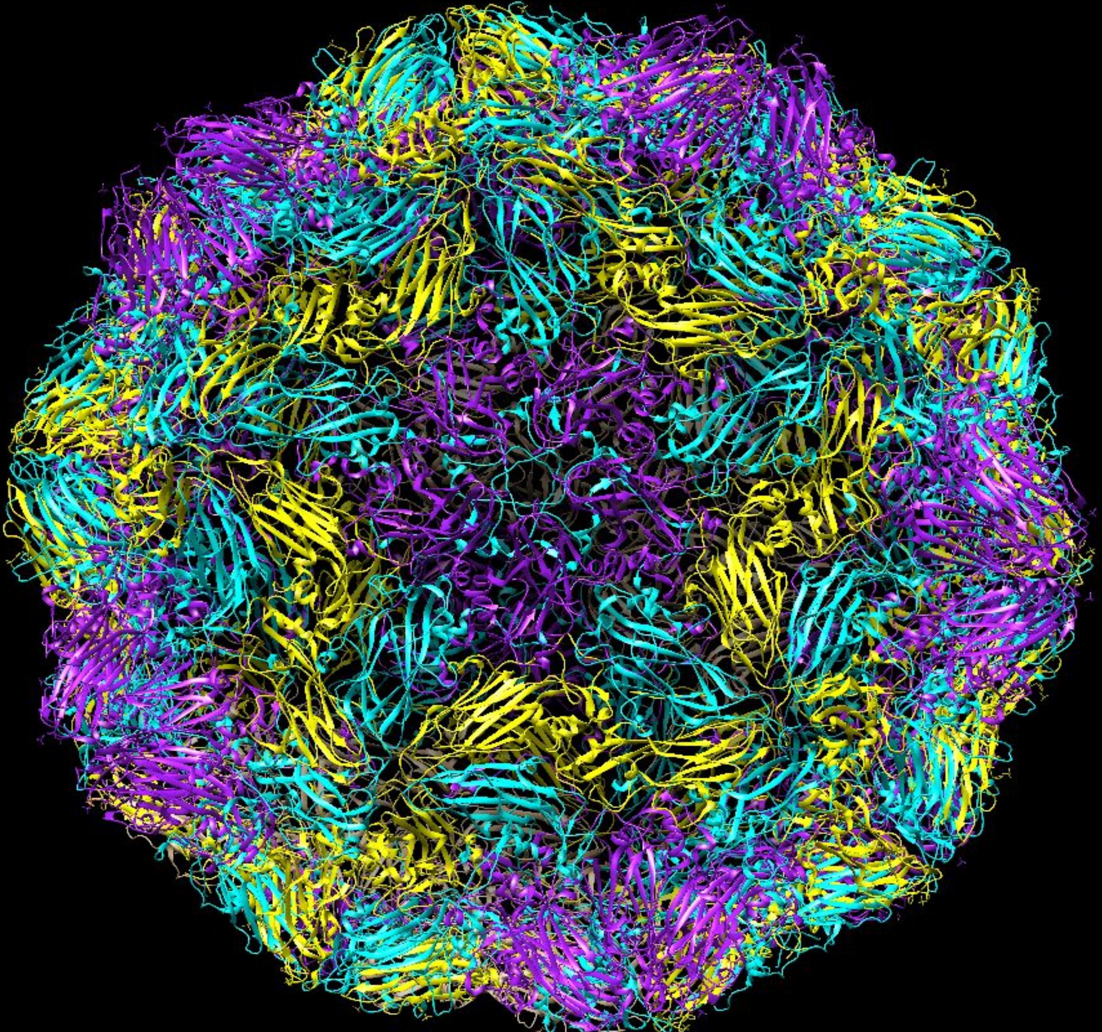
Both viruses “go” in the same direction



HAV 🟪

Cricket paralysis virus (3NAP) 🟨

CONSERVATION STUDY



Conservation Analysis (VP1, VP2 and VP3)

Hepatitis A Virus
(4QPG)

Insect picorna-like viruses

Cricket Paralysis Virus (1B35)

Triatoma Virus (3NAP)

Enteroviruses

Human Rhinovirus B 14 (4RHV)

Human Enterovirus A 71 (3VBF)

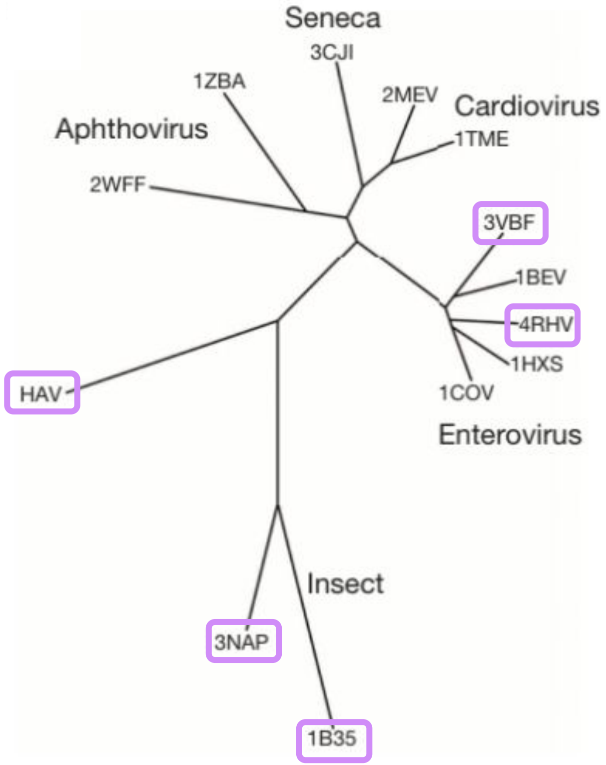
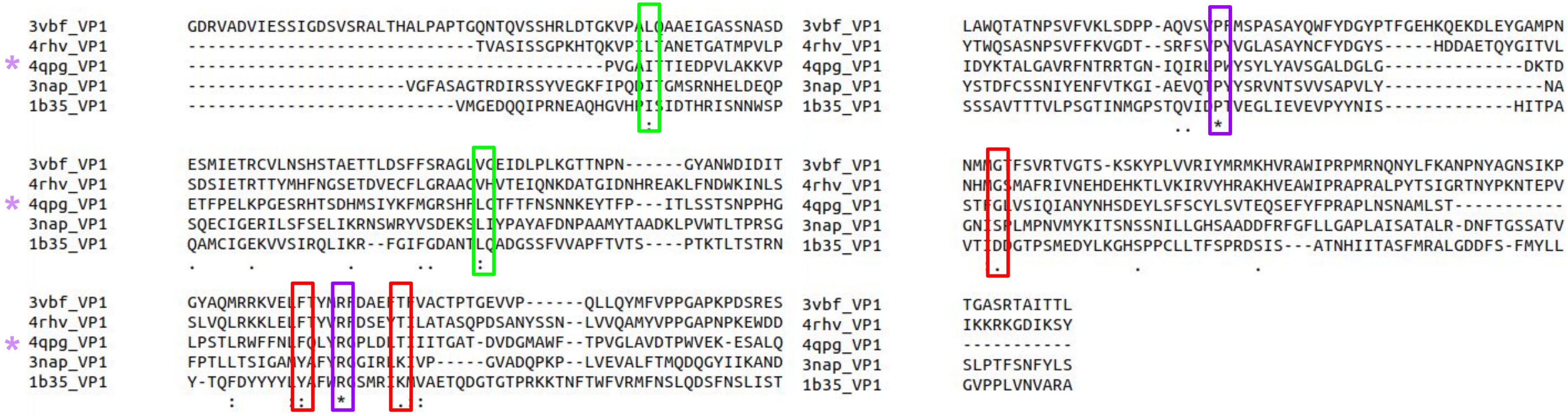


Figure 8. Structure-based phylogenetic tree of representative picornaviruses and cripaviruses (Adapted from Wang et al, 2014).

Conservation study: MSA of VP1



```
  3vbf_VP1      GDRVADVIESSIGDSVSRALTHALPAPTGQNTQVSSHRLDTGKVPALQAAEIGASSNASD
  4rhv_VP1      -----------------------------TVASISSGPKHTQKVPILTANETGATMPVLP
* 4qpg_VP1      ------------------------------------------PVGAITTIEDPVLAKKVP
  3nap_VP1      ----------------------VGFASAGTRDIRSSYVEGKFIPQDITGMSRNHELDEQP
  1b35_VP1      ---------------------------VMGEDQQIPRNEAQHGVHPISIDTHRISNNWSP
                                                              :

  3vbf_VP1      ESMIETRCVLNSHSTAETTLDSFFSRAGLVGEIDLPLKGTTNPN------GYANWDIDIT
  4rhv_VP1      SDSIETRTTYMHFNGSETDVECFLGRAACVHVTEIQNKDATGIDNHREAKLFNDWKINLS
* 4qpg_VP1      ETFPELKPGESRHTSDHMSIYKFMGRSHFLCTFTFNSNNKEYTFP---ITLSSTSNPPHG
  3nap_VP1      SQECIGERILSFSELIKRNSWRYVSDEKSLIYPAYAFDNPAAMYTAADKLPVWTLTPRSG
  1b35_VP1      QAMCIGEKVVSIRQLIKR--FGIFGDANTLQADGSSFVVAPFTVTS----PTKTLTSTRN
                .     .         .      ..    :

  3vbf_VP1      GYAQMRRKVELFTYMRFDAEFTFVACTPTGEVVP------QLLQYMFVPPGAPKPDSRES
  4rhv_VP1      SLVQLRKKLELFTYVRFDSEYTILATASQPDSANYSSN--LVVQAMYVPPGAPNPKEWDD
* 4qpg_VP1      LPSTLRWFFNLFQLYRGPLDLTIIITGAT-DVDGMAWF--TPVGLAVDTPWVEK-ESALQ
  3nap_VP1      FPTLLTSIGAMYAFYRGGIRLKIVP-----GVADQPKP--LVEVALFTMQDQGYIIKAND
  1b35_VP1      Y-TQFDYYYYLYAFWRGSMRIKMVAETQDGTGTPRKKTNFTWFVRMFNSLQDSFNSLIST
                    :      :   *     . :

  3vbf_VP1      LAWQTATNPSVFVKLSDPP-AQVSVPFMSPASAYQWFYDGYPTFGEHKQEKDLEYGAMPN
  4rhv_VP1      YTWQSASNPSVFFKVGDT--SRFSVPYVGLASAYNCFYDGYS-----HDDAETQYGITVL
  4qpg_VP1      IDYKTALGAVRFNTRRTGN-IQIRLPWYSYLYAVSGALDGLG--------------DKTD
  3nap_VP1      YSTDFCSSNIYENFVTKGI-AEVQTPYYSRVNTSVVSAPVLY----------------NA
  1b35_VP1      SSSAVTTTVLPSGTINMGPSTQVIDPTVEGLIEVEVPYYNIS-------------HITPA
                                     ..   *

  3vbf_VP1      NMMGTFSVRTVGTS-KSKYPLVVRIYMRMKHVRAWIPRPMRNQNYLFKANPNYAGNSIKP
  4rhv_VP1      NHMGSMAFRIVNEHDEHKTLVKIRVYHRAKHVEAWIPRAPRALPYTSIGRTNYPKNTEPV
  4qpg_VP1      STFGLVSIQIANYNHSDEYLSFSCYLSVTEQSEFYFPRAPLNSNAMLST-----------
  3nap_VP1      GNISPLMPNVMYKITSNSSNILLGHSAADDFRFGFLLGAPLAISATALR-DNFTGSSATV
  1b35_VP1      VTIDDGTPSMEDYLKGHSPPCLLTFSPRDSIS---ATNHIITASFMRALGDDFS-FMYLL
                   .             .           .

  3vbf_VP1      TGASRTAITTL
  4rhv_VP1      IKKRKGDIKSY
  4qpg_VP1      -----------
  3nap_VP1      SLPTFSNFYLS
  1b35_VP1      GVPPLVNVARA
```

🟪 Examples of residues conserved among all picornavirus

🟥 Examples of residues conserved among enteroviruses

🟩 Examples of residues conserved among insect picorna-like virus

3VBF: Human Enterovirus A71
4RHV: Human Rhinovirus B14
4QPG: Human Hepatitis A Virus
3NAP: Triatoma Virus
1B35: Cricket Paralysis Virus

VP1 Sequence identity

	3VBF (Enterovirus A71)	**4RHV (Rhinovirus B14)**	**4QPG (Hepatitis A virus)**	**3NAP (Triatoma Virus)**	**1B35 (Cricket paralysis virus)**
3VBF (Enterovirus A71)	100%				
4RHV (Rhinovirus B14)	**34,8%**	100%			
4QPG (Hepatitis A virus)	**15,11%**	**15,56%**	100%		
3NAP (Triatoma virus)	6,44%	9,47%	**12,98%**	100%	
1B35 (Cricket paralysis virus)	10,77%	6,92%	**9,78%**	**19,62%**	100%

Superimposition: VP1

RMSD: 2.24

🟦 Human Hepatitis A Virus

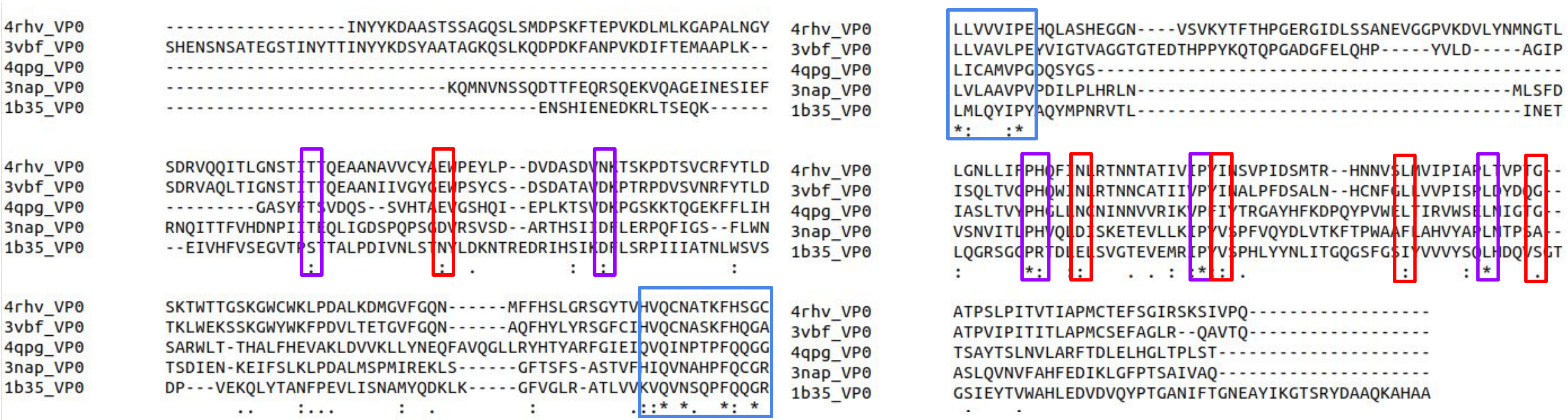
🟪 Human Enterovirus A71

🟩 Human Rhinovirus B14

🟧 Cricket Paralysis Virus

⬜ Triatoma Virus

Conservation study, MSA: VP0 (VP4 + VP2)



```
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3vbf_VP0        SHENSNSATEGSTINYTTINYYKDSYAATAGKQSLKQDPDKFANPVKDIFTEMAAPLK--
4qpg_VP0        ------------------------------------------------------------
3nap_VP0        ----------------------------KQMNVNSSQDTTFEQRSQEKVQAGEINESIEF
1b35_VP0        -------------------------------------ENSHIENEDKRLTSEQK------

4rhv_VP0        SDRVQQITLGNSTITTQEAANAVVCYAEWPEYLP--DVDASDVNKTSKPDTSVCRFYTLD
3vbf_VP0        SDRVAQLTIGNSTITTQEAANIIVGYGEWPSYCS--DSDATAVDKPTRPDVSVNRFYTLD
4qpg_VP0        ---------GASYFTSVDQS--SVHTAEVGSHQI--EPLKTSVDKPGSKKTQGEKFFLIH
3nap_VP0        RNQITTFVHDNPIITEQLIGDSPQPSGDVRSVSD--ARTHSIIDFLERPQFIGS--FLWN
1b35_VP0        --EIVHFVSEGVTPSTTALPDIVNLSTNYLDKNTREDRIHSIKDFLSRPIIIATNLWSVS
                              :            :  .         :  :            :

4rhv_VP0        SKTWTTGSKGWCWKLPDALKDMGVFGQN------MFFHSLGRSGYTVHVQCNATKFHSGC
3vbf_VP0        TKLWEKSSKGWYWKFPDVLTETGVFGQN------AQFHYLYRSGFCIHVQCNASKFHQGA
4qpg_VP0        SARWLT-THALFHEVAKLDVVKLLYNEQFAVQGLLRYHTYARFGIEIQVQINPTPFQQGG
3nap_VP0        TSDIEN-KEIFSLKLPDALMSPMIREKLS------GFTSFS-ASTVFHIQVNAHPFQCGR
1b35_VP0        DP---VEKQLYTANFPEVLISNAMYQDKLK-----GFVGLR-ATLVVKVQVNSQPFQQGR
                       ..    :...      :  .         :         .::* *.  *: *

4rhv_VP0        LLVVVIPEHQLASHEGGN----VSVKYTFTHPGERGIDLSSANEVGGPVKDVLYNMNGTL
3vbf_VP0        LLVAVLPEYVIGTVAGGTGTEDTHPPYKQTQPGADGFELQHP-----YVLD-----AGIP
4qpg_VP0        LICAMVPGDQSYGS----------------------------------------------
3nap_VP0        LVLAAVPVPDILPLHRLN-------------------------------------MLSFD
1b35_VP0        LMLQYIPYAQYMPNRVTL--------------------------------------INET
                *:   :*

4rhv_VP0        LGNLLIRPHQFINLRTNNTATIVIPYINSVPIDSMTR--HNNVSLMVIPIAPLTVPTG--
3vbf_VP0        ISQLTVCPHQWINLRTNNCATIIVPYINALPFDSALN--HCNFGLLVVPISPLDYDQG--
4qpg_VP0        IASLTVYPHGLLNCNINNVVRIKVPFIYTRGAYHFKDPQYPVWELTIRVWSELNIGTG--
3nap_VP0        VSNVITLPHVQLDISKETEVLLKIPYVSPFVQYDLVTKFTPWAAFLAHVYAPLNTPSA--
1b35_VP0        LQGRSGCPRTDLELSVGTEVEMRIPYVSPHLYYNLITGQGSFGSIYVVVYSQLHDQVSGT
                :      *:  ::    . . : :*:: .               :     : *    .

4rhv_VP0        ATPSLPITVTIAPMCTEFSGIRSKSIVPQ------------------
3vbf_VP0        ATPVIPITITLAPMCSEFAGLR--QAVTQ------------------
4qpg_VP0        TSAYTSLNVLARFTDLELHGLTPLST---------------------
3nap_VP0        ASLQVNVFAHFEDIKLGFPTSAIVAQ---------------------
1b35_VP0        GSIEYTVWAHLEDVDVQYPTGANIFTGNEAYIKGTSRYDAAQKAHAA
                 .    .
```

🟪 Examples of residues conserved among all picornavirus

🟥 Examples of residues conserved among enteroviruses

🟩 Examples of residues conserved among insect picorna-like virus

🟦 Sequence highly conserved among picornavirus

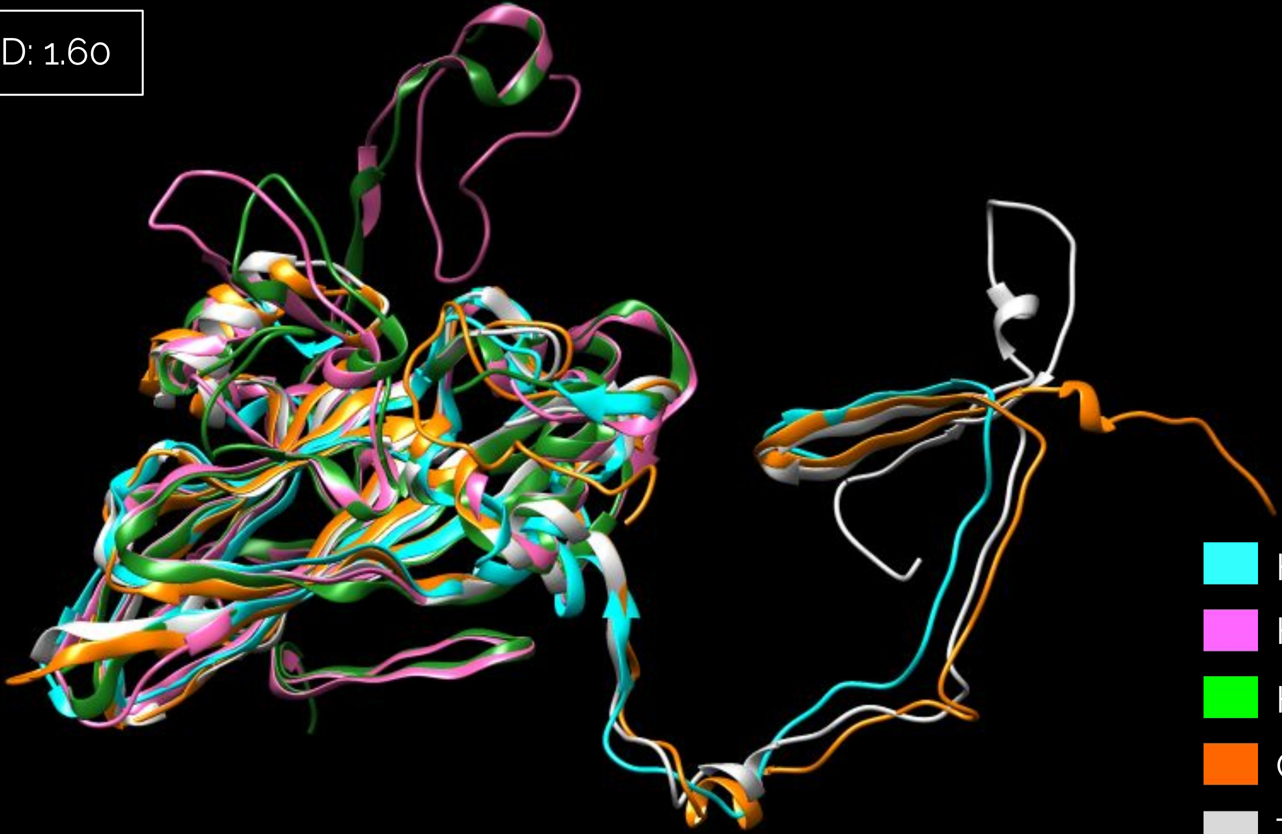
3VBF: Human Enterovirus A71
4RHV: Human Rhinovirus B14
4QPG: Human Hepatitis A Virus
3NAP: Triatoma Virus
1B35: Cricket Paralysis Virus

VP0 Sequence identity

	3VBF (Enterovirus A71)	**4RHV (Rhinovirus B14)**	**4QPG (Hepatitis A virus)**	**3NAP (Triatoma Virus)**	**1B35 (Cricket paralysis virus)**
3VBF (Enterovirus A71)	100%				
4RHV (Rhinovirus B14)	**52,54%**	100%			
4QPG (Hepatitis A virus)	**22,55%**	**20,59%**	100%		
3NAP (Triatoma virus)	15,38%	15,38%	**14,71%**	100%	
1B35 (Cricket paralysis virus)	13,33%	12,94%	**12,25%**	**25,10%**	100%

Phylogenetic Analysis: VP0 (VP4 + VP2)

RMSD: 1.60



🟦 Human Hepatitis A Virus

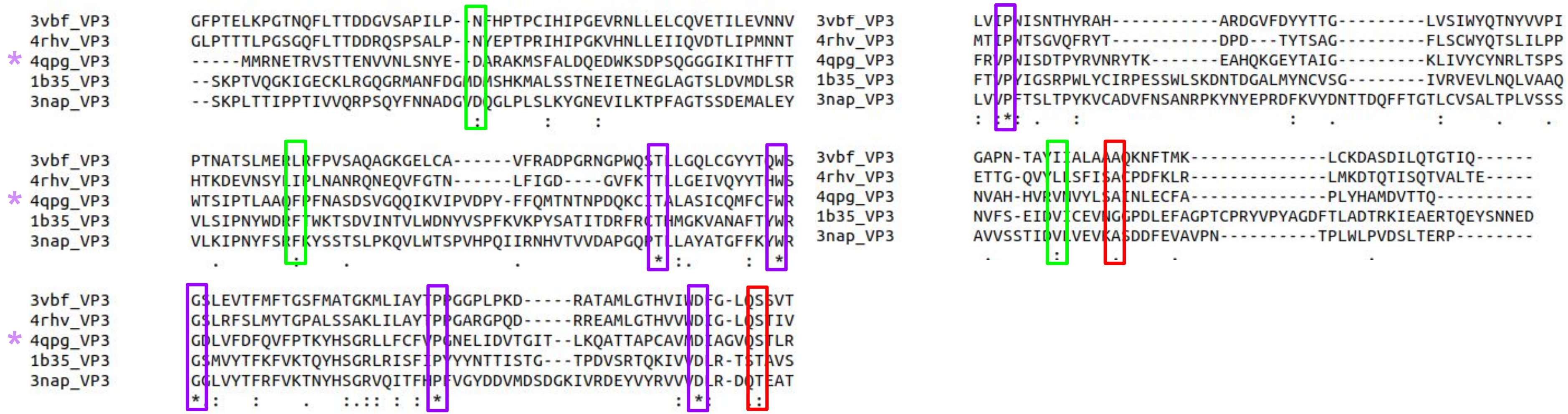
🟪 Human Enterovirus A71

🟩 Human Rhinovirus B14

🟧 Cricket Paralysis Virus

⬜ Triatoma Virus

Conservation study, MSA: VP3



```
  3vbf_VP3        GFPTELKPGTNQFLTTDDGVSAPILP--NFHPTPCIHIPGEVRNLLELCQVETILEVNNV
  4rhv_VP3        GLPTTTLPGSGQFLTTDDRQSPSALP--NYEPTPRIHIPGKVHNLLEIIQVDTLIPMNNT
* 4qpg_VP3        -----MMRNETRVSTTENVVNLSNYE--DARAKMSFALDQEDWKSDPSQGGGIKITHFTT
  1b35_VP3        --SKPTVQGKIGECKLRGQGRMANFDGMDMSHKMALSSTNEIETNEGLAGTSLDVMDLSR
  3nap_VP3        --SKPLTTIPPTIVVQRPSQYFNNADGVDQGLPLSLKYGNEVILKTPFAGTSSDEMALEY
                                              :      :    :

  3vbf_VP3        PTNATSLMERLRFPVSAQAGKGELCA------VFRADPGRNGPWQSTLLGQLCGYYTQWS
  4rhv_VP3        HTKDEVNSYLIPLNANRQNEQVFGTN------LFIGD----GVFKTTLLGEIVQYYTHWS
* 4qpg_VP3        WTSIPTLAAQFPFNASDSVGQQIKVIPVDPY-FFQMTNTNPDQKCITALASICQMFCFWR
  1b35_VP3        VLSIPNYWDRFTWKTSDVINTVLWDNYVSPFKVKPYSATITDRFRCTHMGKVANAFTYWR
  3nap_VP3        VLKIPNYFSRFKYSSTSLPKQVLWTSPVHPQIIRNHVTVVDAPGQPTLLAYATGFFKYWR
                    .       :    .                .             * :.     :  *

  3vbf_VP3        GSLEVTFMFTGSFMATGKMLIAYTPPGGPLPKD-----RATAMLGTHVIWDFG-LQSSVT
  4rhv_VP3        GSLRFSLMYTGPALSSAKLILAYTPPGARGPQD-----RREAMLGTHVVWDIG-LQSTIV
* 4qpg_VP3        GDLVFDFQVFPTKYHSGRLLFCFVPGNELIDVTGIT--LKQATTAPCAVMDIAGVQSTLR
  1b35_VP3        GSMVYTFKFVKTQYHSGRLRISFIPYYYNTTISTG---TPDVSRTQKIVVDLR-TSTAVS
  3nap_VP3        GGLVYTFRFVKTNYHSGRVQITFHPFVGYDDVMSDGKIVRDEYVYRVVVVDLR-DQTEAT
                  * :   :    .   :.:: : : *                       : *:   .:

  3vbf_VP3        LVIPWISNTHYRAH-----------ARDGVFDYYTTG---------LVSIWYQTNYVVPI
  4rhv_VP3        MTIPWTSGVQFRYT-----------DPD---TYTSAG---------FLSCWYQTSLILPP
  4qpg_VP3        FRVPWISDTPYRVNRYTK-------EAHQKGEYTAIG---------KLIVYCYNRLTSPS
  1b35_VP3        FTVPYIGSRPWLYCIRPESSWLSKDNTDGALMYNCVSG--------IVRVEVLNQLVAAQ
  3nap_VP3        LVVPFTSLTPYKVCADVFNSANRPKYNYEPRDFKVYDNTTDQFFTGTLCVSALTPLVSSS
                  : :*: .   :                     :   .          :     .    .

  3vbf_VP3        GAPN-TAYIIALAAAQKNFTMK--------------LCKDASDILQTGTIQ------
  4rhv_VP3        ETTG-QVYLLSFISACPDFKLR--------------LMKDTQTISQTVALTE-----
  4qpg_VP3        NVAH-HVRVNVYLSAINLECFA--------------PLYHAMDVTTQ----------
  1b35_VP3        NVFS-EIDVICEVNGGPDLEFAGPTCPRYVPYAGDFTLADTRKIEAERTQEYSNNED
  3nap_VP3        AVVSSTIDVLVEVKASDDFEVAVPN----------TPLWLPVDSLTERP--------
                   .      :     .     .                   .
```

🟪 Examples of residues conserved among all picornavirus

🟥 Examples of residues conserved among enteroviruses

🟩 Examples of residues conserved among insect picorna-like virus

3VBF: Human Enterovirus A71
4RHV: Human Rhinovirus B14
4QPG: Human Hepatitis A Virus
3NAP: Triatoma Virus
1B35: Cricket Paralysis Virus

VP3 Sequence identity

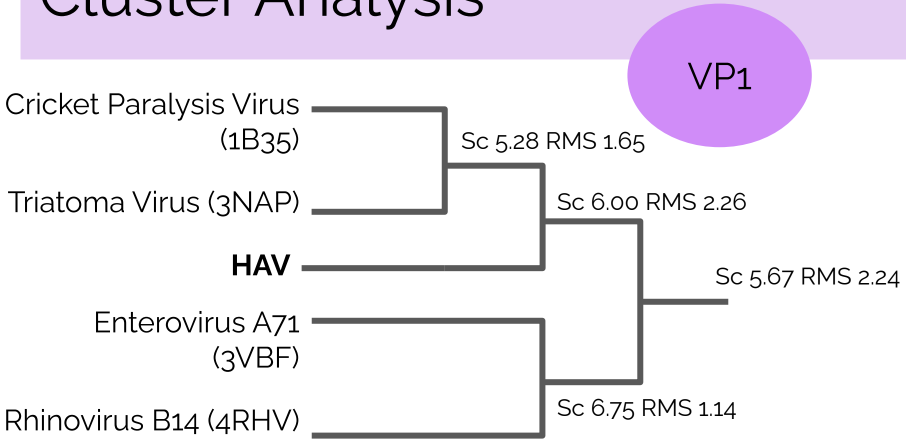
	3VBF (Enterovirus A71)	**4RHV (Rhinovirus B14)**	**4QPG (Hepatitis A virus)**	**3NAP (Triatoma Virus)**	**1B35 (Cricket paralysis virus)**
3VBF (Enterovirus A71)	100%				
4RHV (Rhinovirus B14)	**42,37%**	100%			
4QPG (Hepatitis A virus)	**15,29%**	**17,80%**	100%		
3NAP (Triatoma virus)	15,70%	11,86%	**23,17%**	100%	
1B35 (Cricket paralysis virus)	12,81%	11,44%	**19,92%**	**29,71%**	100%

Phylogenetic Analysis: VP3

RMSD: 1.97

🟦 Human Hepatitis A Virus
🟪 Human Enterovirus A71
🟩 Human Rhinovirus B14
🟧 Cricket Paralysis Virus
⬜ Triatoma Virus

Cluster Analysis



VP1

Cricket Paralysis Virus (1B35)

Triatoma Virus (3NAP)

HAV

Enterovirus A71 (3VBF)

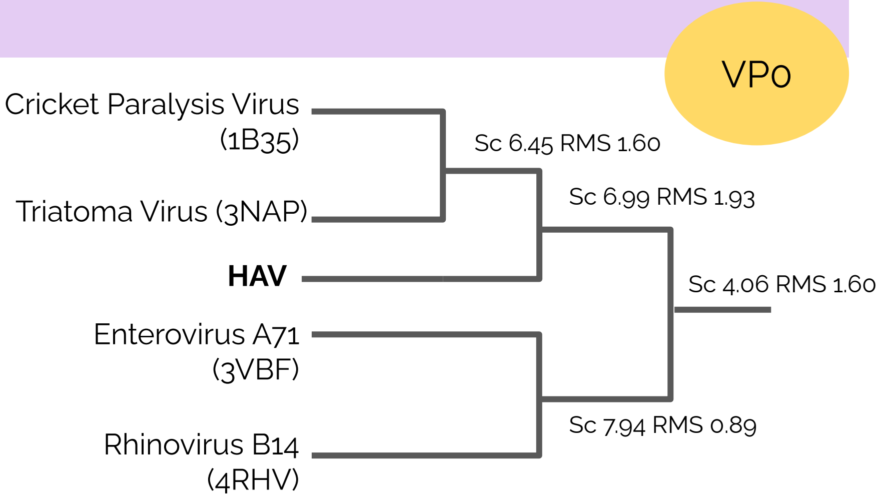
Rhinovirus B14 (4RHV)

Sc 5.28 RMS 1.65

Sc 6.00 RMS 2.26

Sc 5.67 RMS 2.24

Sc 6.75 RMS 1.14



VP0

Cricket Paralysis Virus (1B35)

Triatoma Virus (3NAP)

HAV

Enterovirus A71 (3VBF)

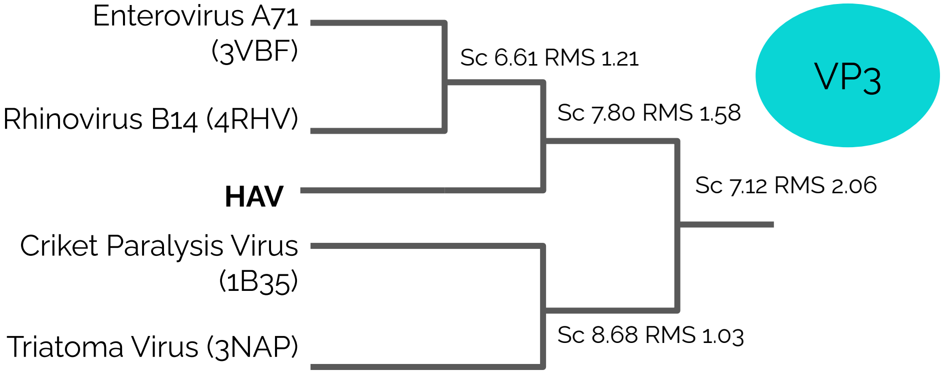
Rhinovirus B14 (4RHV)

Sc 6.45 RMS 1.60

Sc 6.99 RMS 1.93

Sc 4.06 RMS 1.60

Sc 7.94 RMS 0.89



VP3

Enterovirus A71 (3VBF)

Rhinovirus B14 (4RHV)

HAV

Criket Paralysis Virus (1B35)

Triatoma Virus (3NAP)

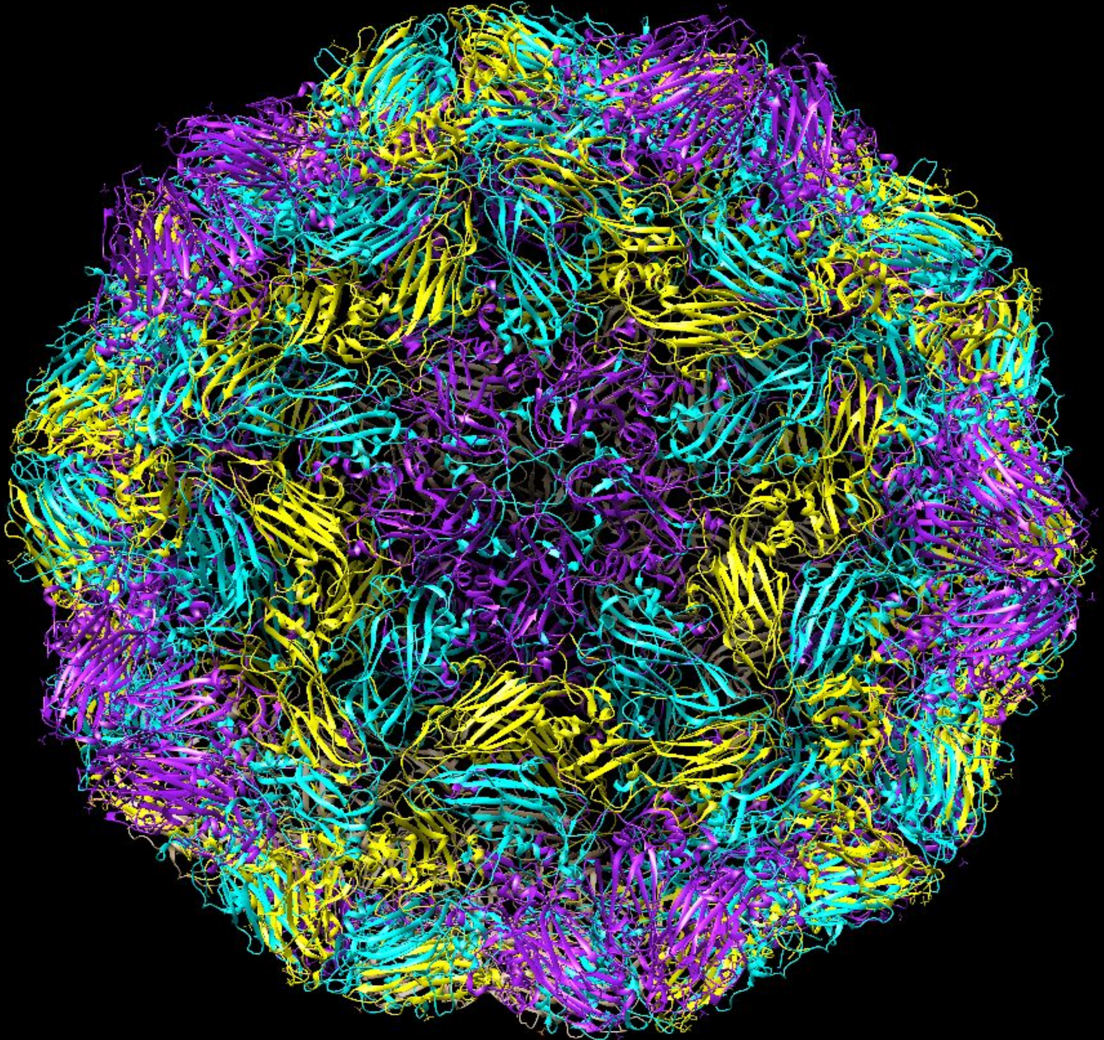
Sc 6.61 RMS 1.21

Sc 7.80 RMS 1.58

Sc 7.12 RMS 2.06

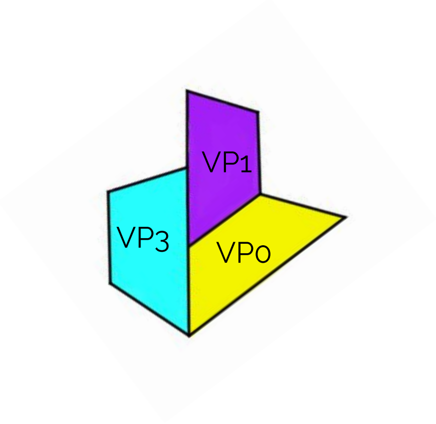
Sc 8.68 RMS 1.03

CAPSID INTERACTIONS



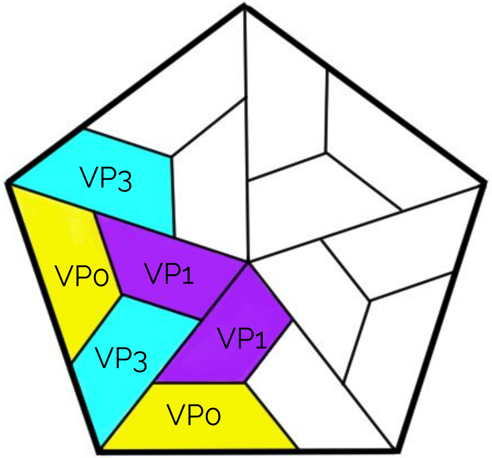
Types of capsid interactions

INTRAPROTOMERIC



VP0-VP1
VP0-VP3
VP3-VP1

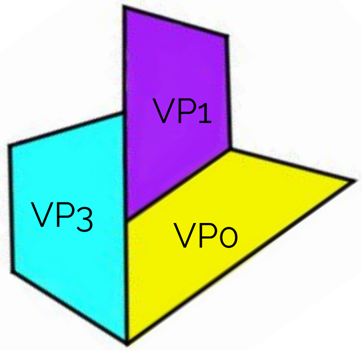
INTERPROTOMERIC



VP1-VP1
VP0-VP3
VP1-VP3

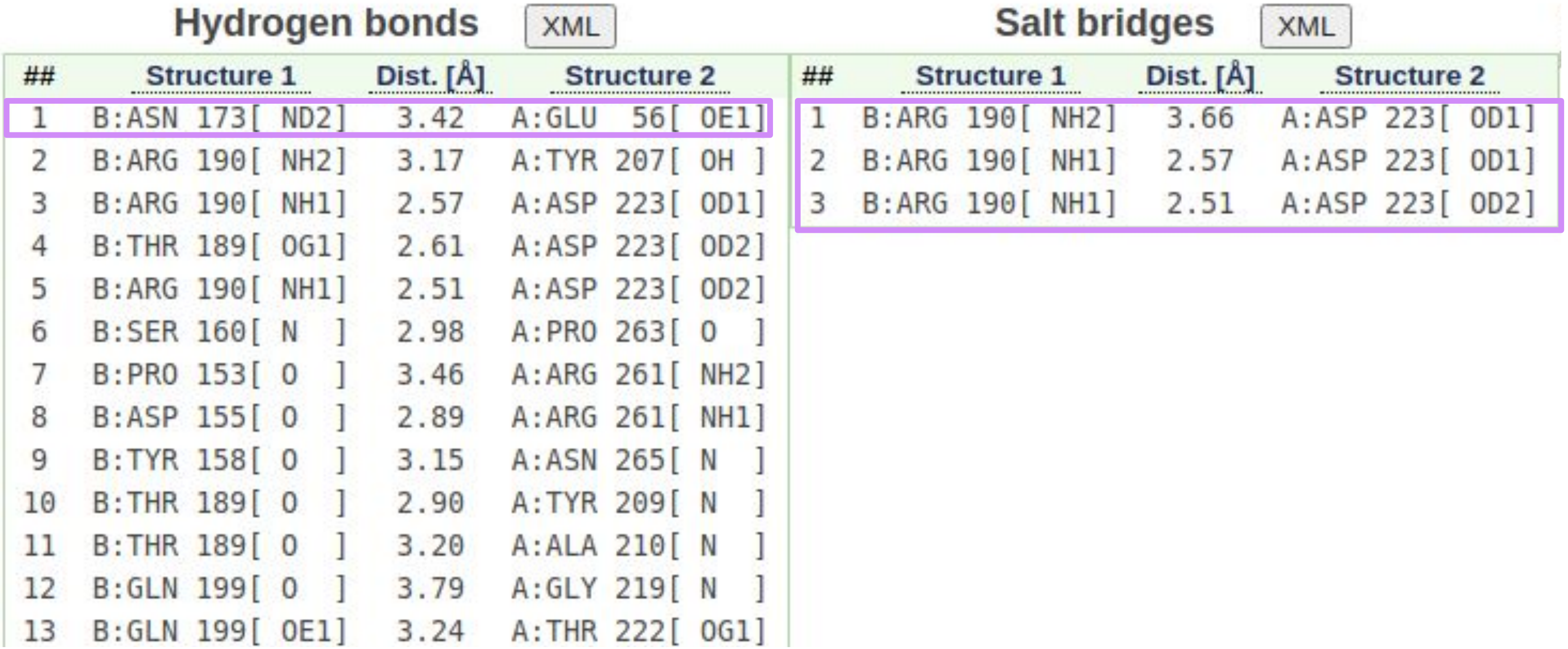
Types of capsid interactions

INTRAPROTOMERIC



VP0-VP1
VP0-VP3
VP3-VP1

Interactions between VP0-VP1



Hydrogen bonds

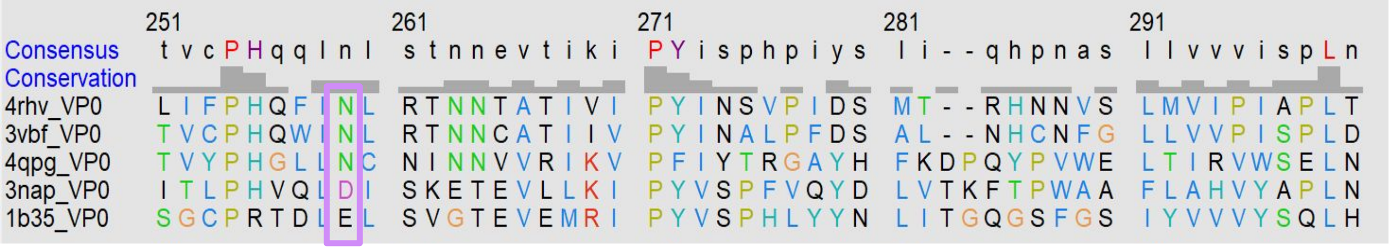
##	Structure 1	Dist. [Å]	Structure 2
1	B:ASN 173[ND2]	3.42	A:GLU 56[OE1]
2	B:ARG 190[NH2]	3.17	A:TYR 207[OH]
3	B:ARG 190[NH1]	2.57	A:ASP 223[OD1]
4	B:THR 189[OG1]	2.61	A:ASP 223[OD2]
5	B:ARG 190[NH1]	2.51	A:ASP 223[OD2]
6	B:SER 160[N]	2.98	A:PRO 263[O]
7	B:PRO 153[O]	3.46	A:ARG 261[NH2]
8	B:ASP 155[O]	2.89	A:ARG 261[NH1]
9	B:TYR 158[O]	3.15	A:ASN 265[N]
10	B:THR 189[O]	2.90	A:TYR 209[N]
11	B:THR 189[O]	3.20	A:ALA 210[N]
12	B:GLN 199[O]	3.79	A:GLY 219[N]
13	B:GLN 199[OE1]	3.24	A:THR 222[OG1]

Salt bridges

##	Structure 1	Dist. [Å]	Structure 2
1	B:ARG 190[NH2]	3.66	A:ASP 223[OD1]
2	B:ARG 190[NH1]	2.57	A:ASP 223[OD1]
3	B:ARG 190[NH1]	2.51	A:ASP 223[OD2]

Data from PDBePISA

Interactions between VP0-VP1

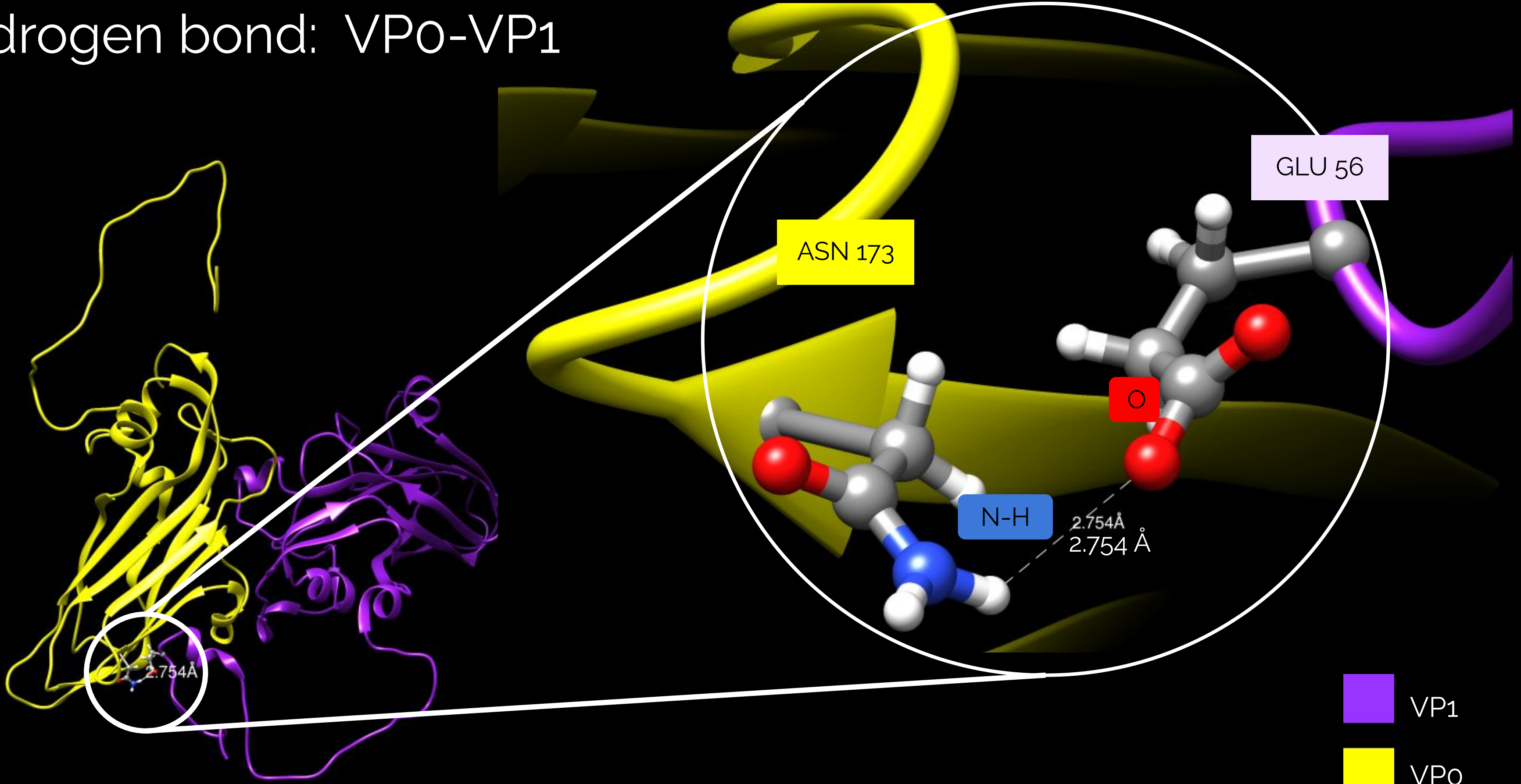


	251	261	271	281	291
Consensus	tvcPHqqlnl	stnnevtiki	PYisphpiys	li--qhpnas	llvvvispLn
Conservation					
4rhv_VP0	LIFPHQFINL	RTNNTATIVI	PYINSVPIDS	MT--RHNNVS	LMVIPIAPLT
3vbf_VP0	TVCPHQWINL	RTNNCATIIV	PYINALPFDS	AL--NHCNFG	LLVVPISPLD
4qpg_VP0	TVYPHGLLNC	NINNVVRIKV	PFIYTRGAYH	FKDPQYPVWE	LTIRVWSELN
3nap_VP0	ITLPHVQLDI	SKETEVLLKI	PYVSPFVQYD	LVTKFTPWAA	FLAHVYAPLN
1b35_VP0	SGCPRTDLEL	SVGTEVEMRI	PYVSPHLYYN	LITGQGSFGS	IYVVVYSQLH

Asparagine (N) is conserved among Human Hepatitis A Virus, Human Enterovirus A71 and Human Rhinovirus B14

3VBF: Human Enterovirus A71
4RHV: Human Rhinovirus B14
4QPG: Human Hepatitis A Virus
3NAP: Triatoma Virus
1B35: Cricket Paralysis Virus

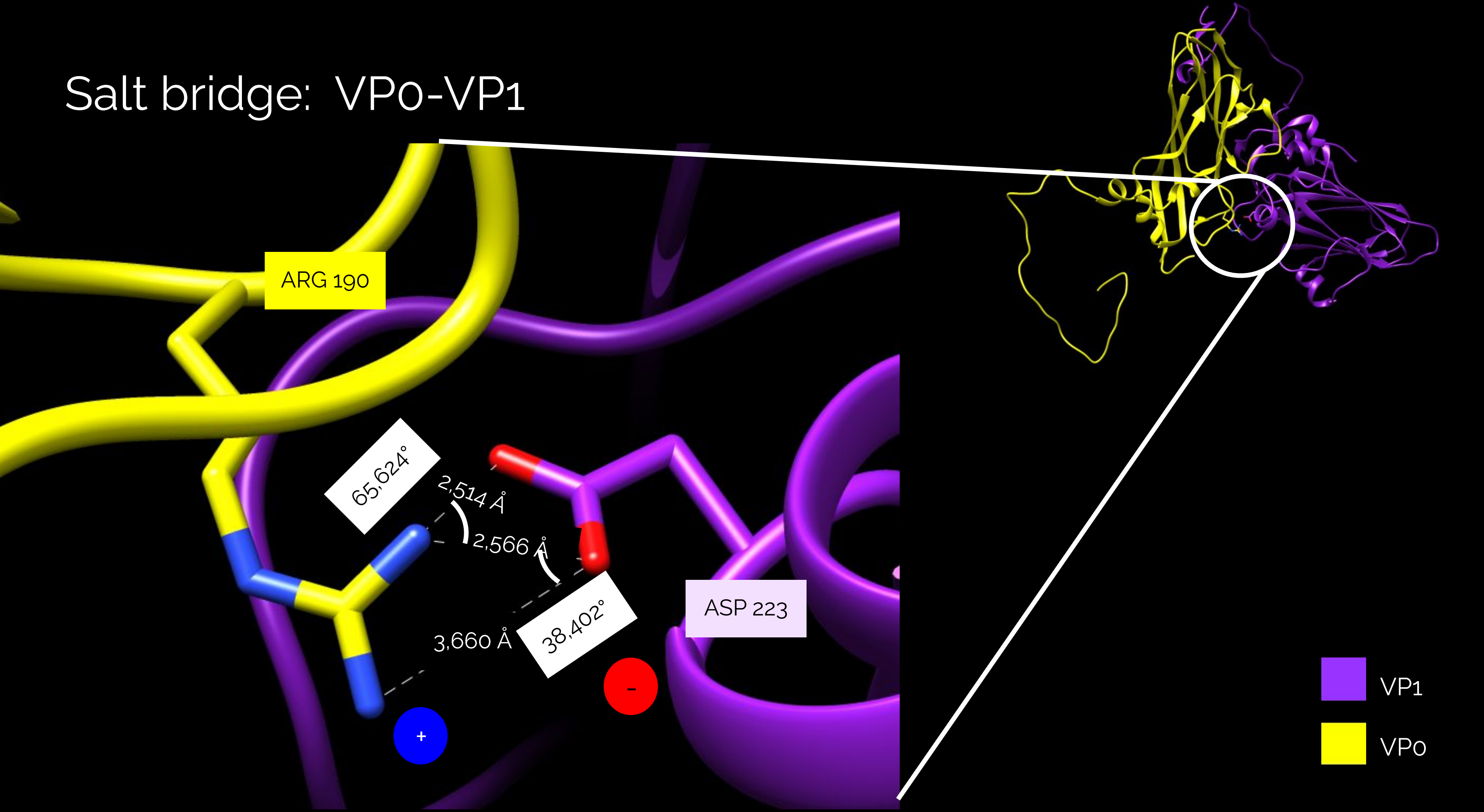
Hydrogen bond: VP0-VP1



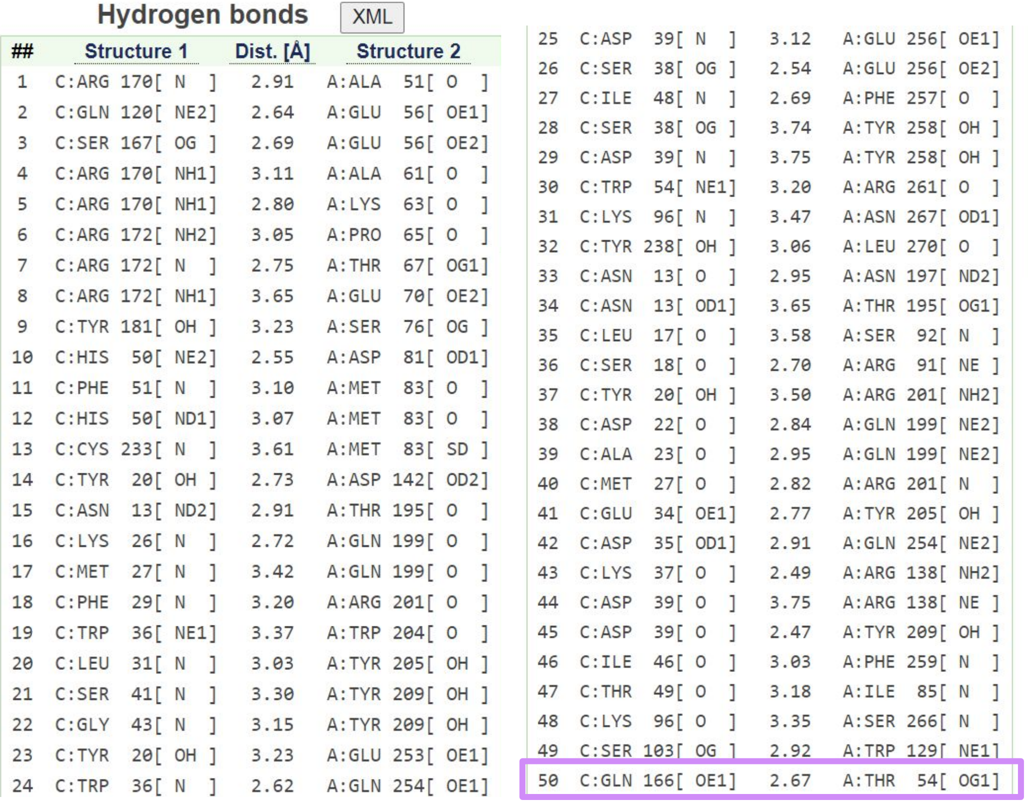
🟪 VP1

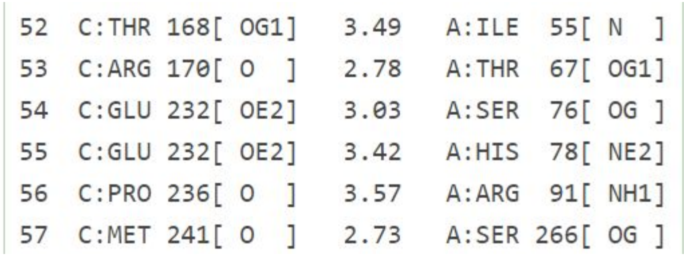
🟨 VP0

Salt bridge: VP0-VP1



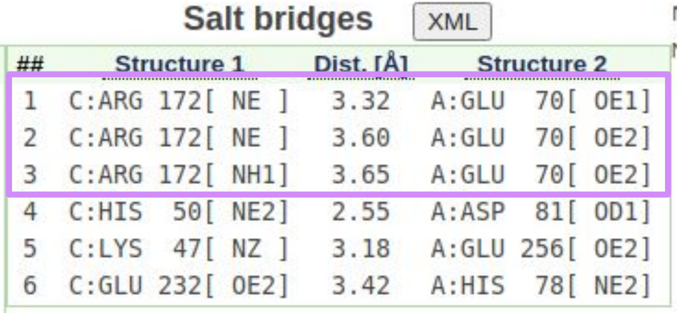
Interactions between VP3 and VP1





Hydrogen bonds XML

##	Structure 1	Dist. [Å]	Structure 2
1	C:ARG 170[N]	2.91	A:ALA 51[O]
2	C:GLN 120[NE2]	2.64	A:GLU 56[OE1]
3	C:SER 167[OG]	2.69	A:GLU 56[OE2]
4	C:ARG 170[NH1]	3.11	A:ALA 61[O]
5	C:ARG 170[NH1]	2.80	A:LYS 63[O]
6	C:ARG 172[NH2]	3.05	A:PRO 65[O]
7	C:ARG 172[N]	2.75	A:THR 67[OG1]
8	C:ARG 172[NH1]	3.65	A:GLU 70[OE2]
9	C:TYR 181[OH]	3.23	A:SER 76[OG]
10	C:HIS 50[NE2]	2.55	A:ASP 81[OD1]
11	C:PHE 51[N]	3.10	A:MET 83[O]
12	C:HIS 50[ND1]	3.07	A:MET 83[O]
13	C:CYS 233[N]	3.61	A:MET 83[SD]
14	C:TYR 20[OH]	2.73	A:ASP 142[OD2]
15	C:ASN 13[ND2]	2.91	A:THR 195[O]
16	C:LYS 26[N]	2.72	A:GLN 199[O]
17	C:MET 27[N]	3.42	A:GLN 199[O]
18	C:PHE 29[N]	3.20	A:ARG 201[O]
19	C:TRP 36[NE1]	3.37	A:TRP 204[O]
20	C:LEU 31[N]	3.03	A:TYR 205[OH]
21	C:SER 41[N]	3.30	A:TYR 209[OH]
22	C:GLY 43[N]	3.15	A:TYR 209[OH]
23	C:TYR 20[OH]	3.23	A:GLU 253[OE1]
24	C:TRP 36[N]	2.62	A:GLN 254[OE1]
25	C:ASP 39[N]	3.12	A:GLU 256[OE1]
26	C:SER 38[OG]	2.54	A:GLU 256[OE2]
27	C:ILE 48[N]	2.69	A:PHE 257[O]
28	C:SER 38[OG]	3.74	A:TYR 258[OH]
29	C:ASP 39[N]	3.75	A:TYR 258[OH]
30	C:TRP 54[NE1]	3.20	A:ARG 261[O]
31	C:LYS 96[N]	3.47	A:ASN 267[OD1]
32	C:TYR 238[OH]	3.06	A:LEU 270[O]
33	C:ASN 13[O]	2.95	A:ASN 197[ND2]
34	C:ASN 13[OD1]	3.65	A:THR 195[OG1]
35	C:LEU 17[O]	3.58	A:SER 92[N]
36	C:SER 18[O]	2.70	A:ARG 91[NE]
37	C:TYR 20[OH]	3.50	A:ARG 201[NH2]
38	C:ASP 22[O]	2.84	A:GLN 199[NE2]
39	C:ALA 23[O]	2.95	A:GLN 199[NE2]
40	C:MET 27[O]	2.82	A:ARG 201[N]
41	C:GLU 34[OE1]	2.77	A:TYR 205[OH]
42	C:ASP 35[OD1]	2.91	A:GLN 254[NE2]
43	C:LYS 37[O]	2.49	A:ARG 138[NH2]
44	C:ASP 39[O]	3.75	A:ARG 138[NE]
45	C:ASP 39[O]	2.47	A:TYR 209[OH]
46	C:ILE 46[O]	3.03	A:PHE 259[N]
47	C:THR 49[O]	3.18	A:ILE 85[N]
48	C:LYS 96[O]	3.35	A:SER 266[N]
49	C:SER 103[OG]	2.92	A:TRP 129[NE1]
50	C:GLN 166[OE1]	2.67	A:THR 54[OG1]
52	C:THR 168[OG1]	3.49	A:ILE 55[N]
53	C:ARG 170[O]	2.78	A:THR 67[OG1]
54	C:GLU 232[OE2]	3.03	A:SER 76[OG]
55	C:GLU 232[OE2]	3.42	A:HIS 78[NE2]
56	C:PRO 236[O]	3.57	A:ARG 91[NH1]
57	C:MET 241[O]	2.73	A:SER 266[OG]

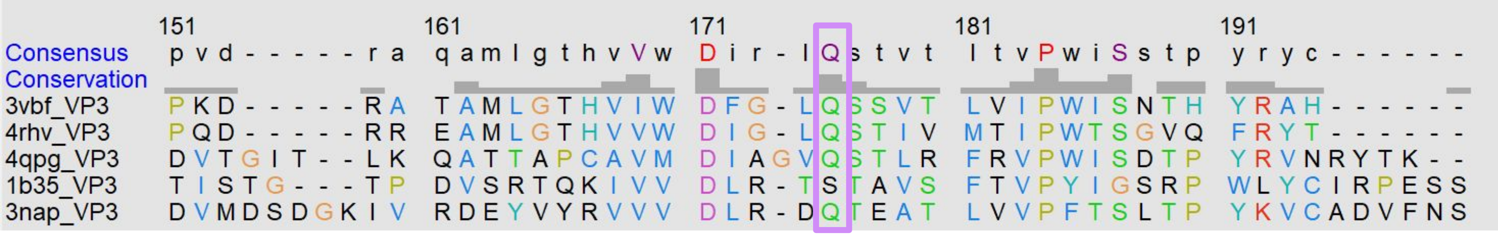


Salt bridges XML

##	Structure 1	Dist. [Å]	Structure 2
1	C:ARG 172[NE]	3.32	A:GLU 70[OE1]
2	C:ARG 172[NE]	3.60	A:GLU 70[OE2]
3	C:ARG 172[NH1]	3.65	A:GLU 70[OE2]
4	C:HIS 50[NE2]	2.55	A:ASP 81[OD1]
5	C:LYS 47[NZ]	3.18	A:GLU 256[OE2]
6	C:GLU 232[OE2]	3.42	A:HIS 78[NE2]

Data from PDBePISA

Interactions between VP3-VP1

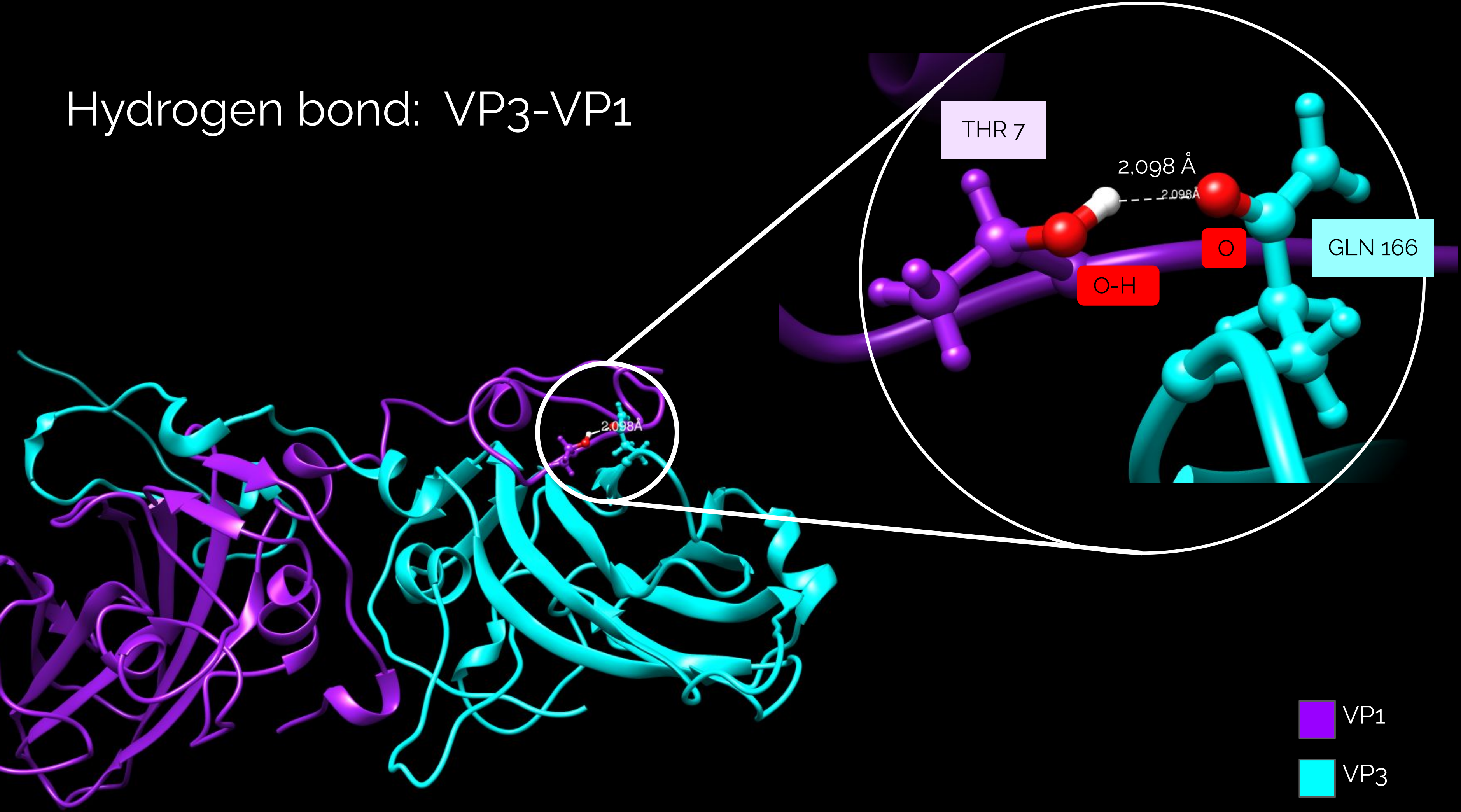


```
             151        161        171        181        191
Consensus    pvd-----ra qamlgthvVw Dir-lQstvt ltvPwiSstp yryc------
Conservation
3vbf_VP3     PKD-----RA TAMLGTHVIW DFG-LQSSVT LVIPWISNTH YRAH------
4rhv_VP3     PQD-----RR EAMLGTHVVW DIG-LQSTIV MTIPWTSGVQ FRYT------
4qpg_VP3     DVTGIT--LK QATTAPCAVM DIAGVQSTLR FRVPWISDTP YRVNRYTK--
1b35_VP3     TISTG---TP DVSRTQKIVV DLR-TSTAVS FTVPYIGSRP WLYCIRPESS
3nap_VP3     DVMDSDGKIV RDEYVYRVVV DLR-DQTEAT LVVPFTSLTP YKVCADVFNS
```

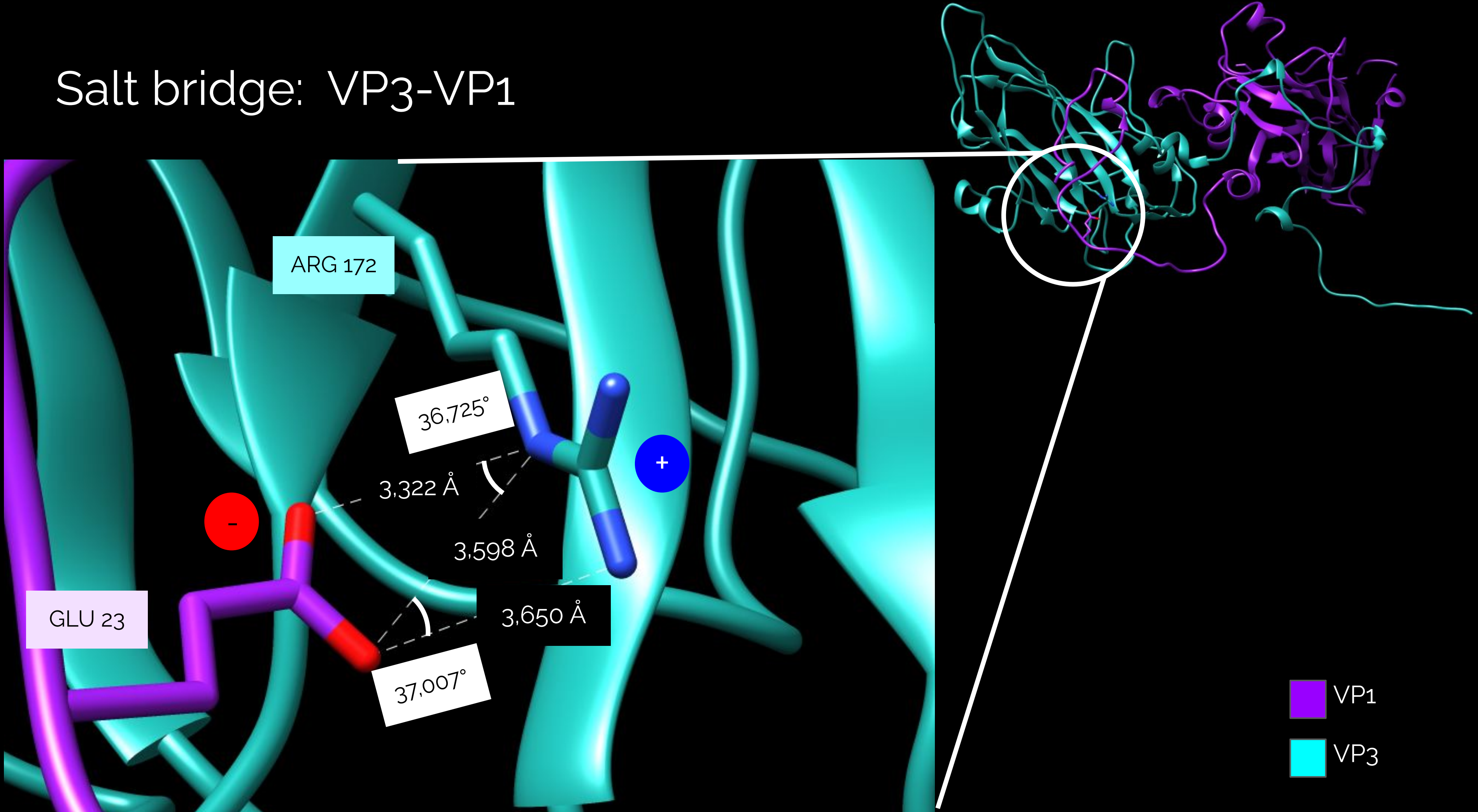
Glutamine (Q) is conserved among Human Hepatitis A Virus, Human Enterovirus A71, Human Rhinovirus B14 and Cricket Paralysis virus

3VBF: Human Enterovirus A71
4RHV: Human Rhinovirus B14
4QPG: Human Hepatitis A Virus
3NAP: Triatoma Virus
1B35: Cricket Paralysis Virus

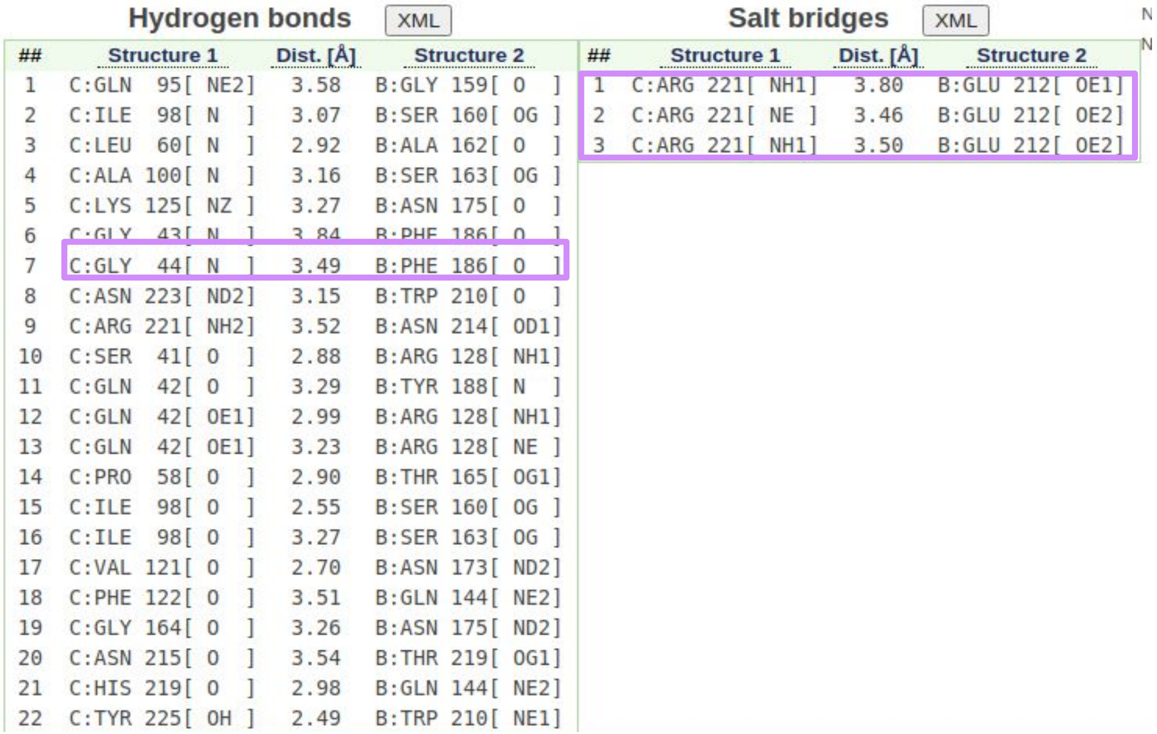
Hydrogen bond: VP3-VP1



Salt bridge: VP3-VP1



Interactions between VP3 and VP0



Hydrogen bonds

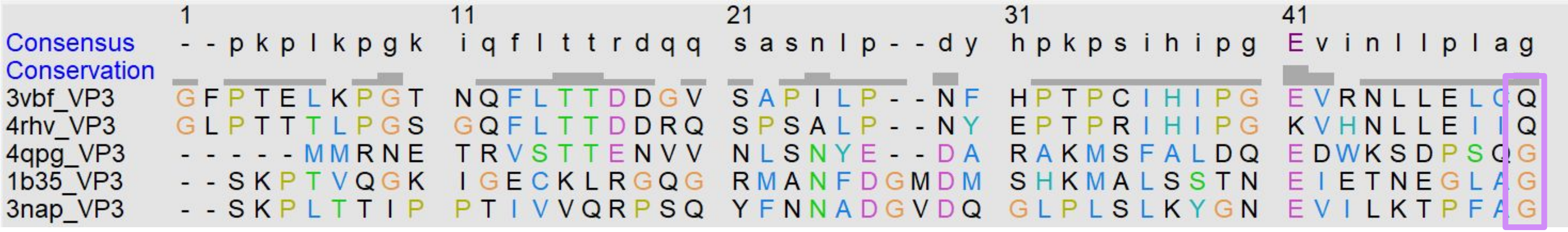
##	Structure 1	Dist. [Å]	Structure 2
1	C:GLN 95[NE2]	3.58	B:GLY 159[O]
2	C:ILE 98[N]	3.07	B:SER 160[OG]
3	C:LEU 60[N]	2.92	B:ALA 162[O]
4	C:ALA 100[N]	3.16	B:SER 163[OG]
5	C:LYS 125[NZ]	3.27	B:ASN 175[O]
6	C:GLY 43[N]	3.84	B:PHE 186[O]
7	C:GLY 44[N]	3.49	B:PHE 186[O]
8	C:ASN 223[ND2]	3.15	B:TRP 210[O]
9	C:ARG 221[NH2]	3.52	B:ASN 214[OD1]
10	C:SER 41[O]	2.88	B:ARG 128[NH1]
11	C:GLN 42[O]	3.29	B:TYR 188[N]
12	C:GLN 42[OE1]	2.99	B:ARG 128[NH1]
13	C:GLN 42[OE1]	3.23	B:ARG 128[NE]
14	C:PRO 58[O]	2.90	B:THR 165[OG1]
15	C:ILE 98[O]	2.55	B:SER 160[OG]
16	C:ILE 98[O]	3.27	B:SER 163[OG]
17	C:VAL 121[O]	2.70	B:ASN 173[ND2]
18	C:PHE 122[O]	3.51	B:GLN 144[NE2]
19	C:GLY 164[O]	3.26	B:ASN 175[ND2]
20	C:ASN 215[O]	3.54	B:THR 219[OG1]
21	C:HIS 219[O]	2.98	B:GLN 144[NE2]
22	C:TYR 225[OH]	2.49	B:TRP 210[NE1]

Salt bridges

##	Structure 1	Dist. [Å]	Structure 2
1	C:ARG 221[NH1]	3.80	B:GLU 212[OE1]
2	C:ARG 221[NE]	3.46	B:GLU 212[OE2]
3	C:ARG 221[NH1]	3.50	B:GLU 212[OE2]

Data from PDBePISA

Interactions between VP3 and VP0

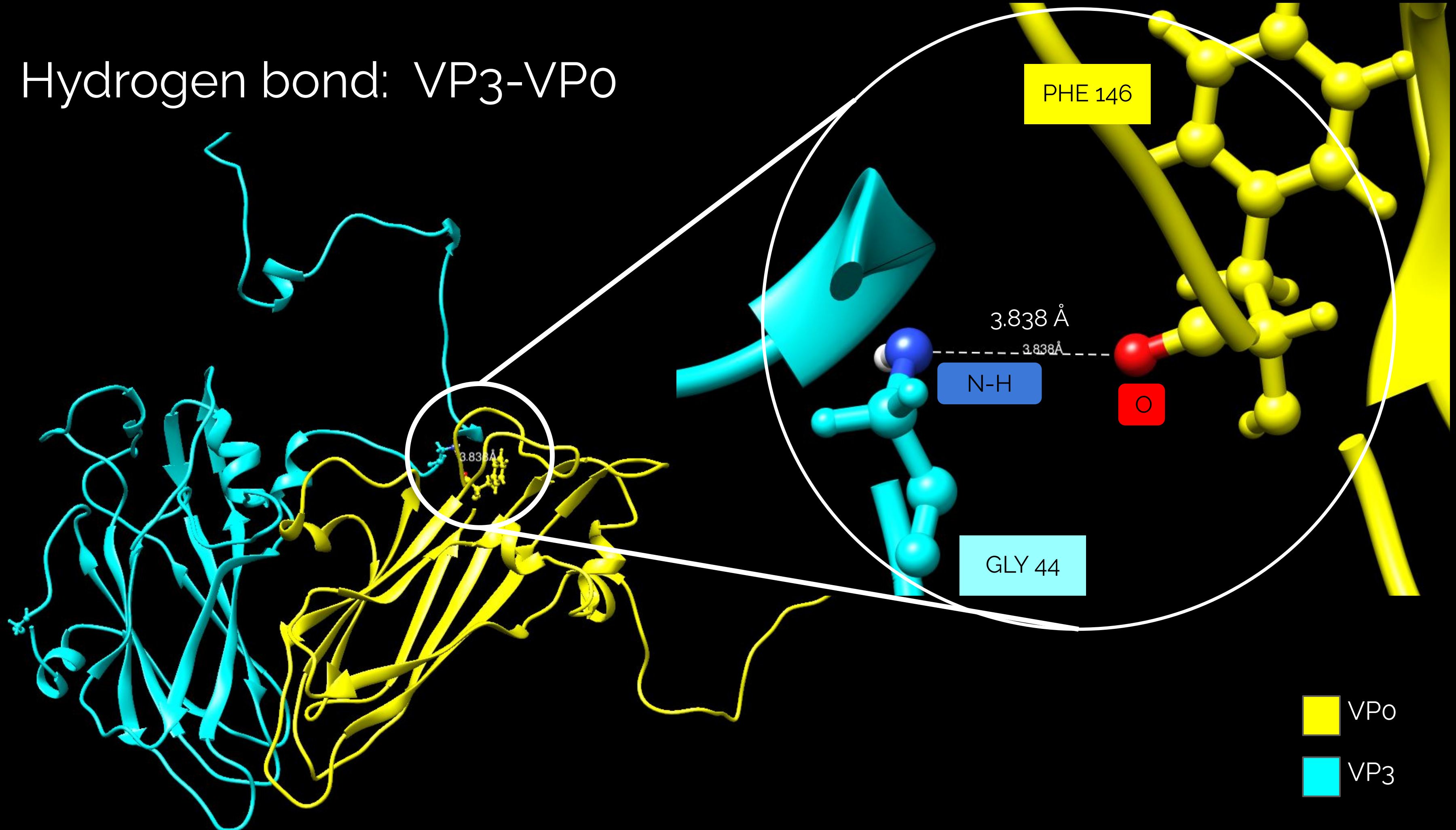


```
              1                    11                   21                   31                   41
Consensus     - - p k p l k p g k  i q f l t t r d q q  s a s n l p - - d y  h p k p s i h i p g  E v i n l l p l a g
Conservation
3vbf_VP3      G F P T E L K P G T  N Q F L T T D D G V  S A P I L P - - N F  H P T P C I H I P G  E V R N L L E L C Q
4rhv_VP3      G L P T T T L P G S  G Q F L T T D D R Q  S P S A L P - - N Y  E P T P R I H I P G  K V H N L L E I I Q
4qpg_VP3      - - - - - M M R N E  T R V S T T E N V V  N L S N Y E - - D A  R A K M S F A L D Q  E D W K S D P S Q G
1b35_VP3      - - S K P T V Q G K  I G E C K L R G Q G  R M A N F D G M D M  S H K M A L S S T N  E I E T N E G L A G
3nap_VP3      - - S K P L T T I P  P T I V V Q R P S Q  Y F N N A D G V D Q  G L P L S L K Y G N  E V I L K T P F A G
```

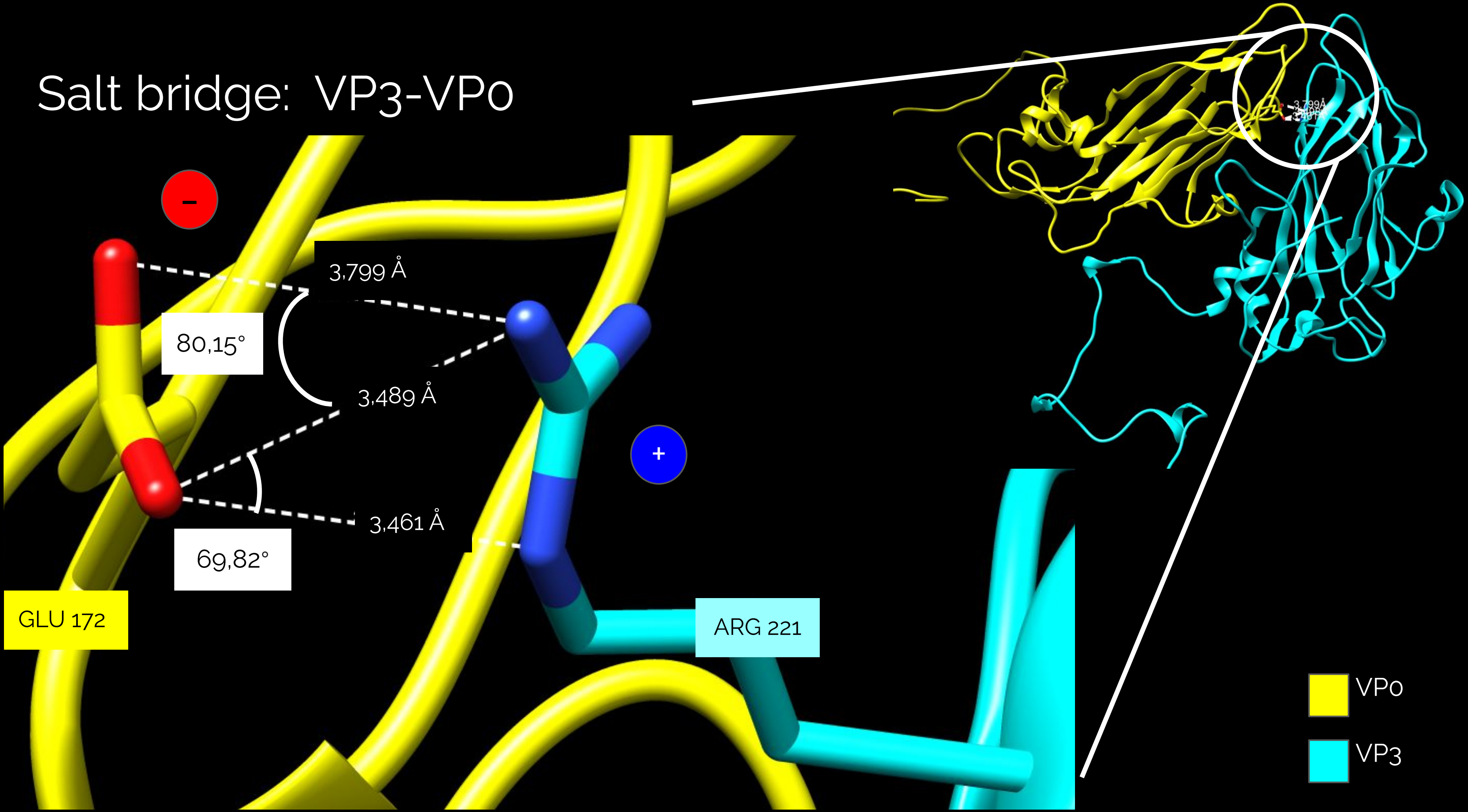
Glycine (G) is conserved among Human Hepatitis A Virus, Triatoma Virus and Cricket Paralysis virus

3VBF: Human Enterovirus A71
4RHV: Human Rhinovirus B14
4QPG: Human Hepatitis A Virus
3NAP: Triatoma Virus
1B35: Cricket Paralysis Virus

Hydrogen bond: VP3-VP0

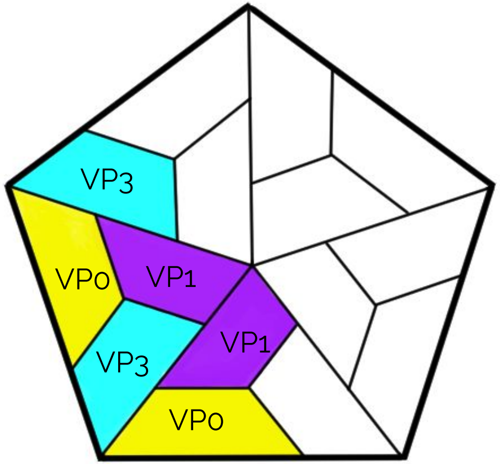


Salt bridge: VP3-VP0



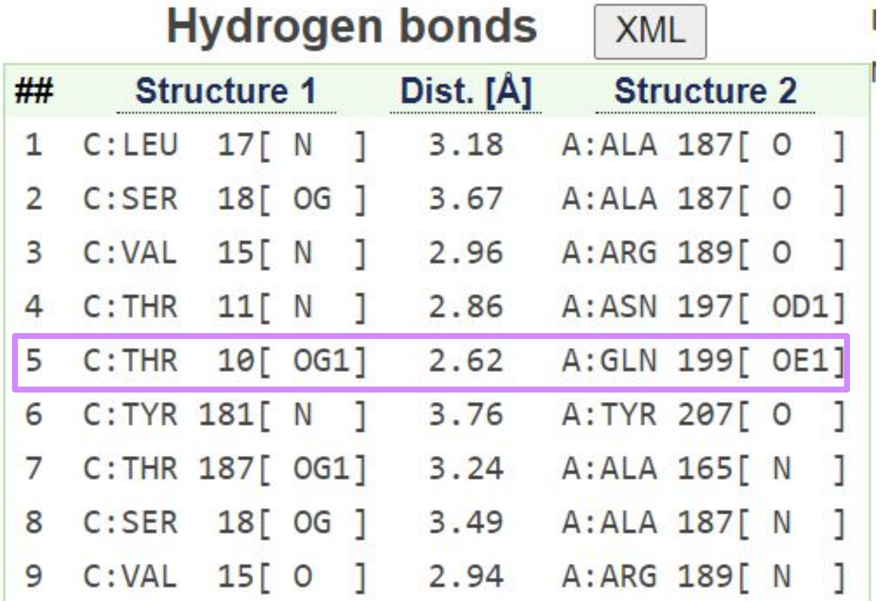
Types of capsid interactions

INTERPROTOMERIC



VP1-VP3
VP0-VP3
VP1-VP1

Interactions between VP1 and VP3

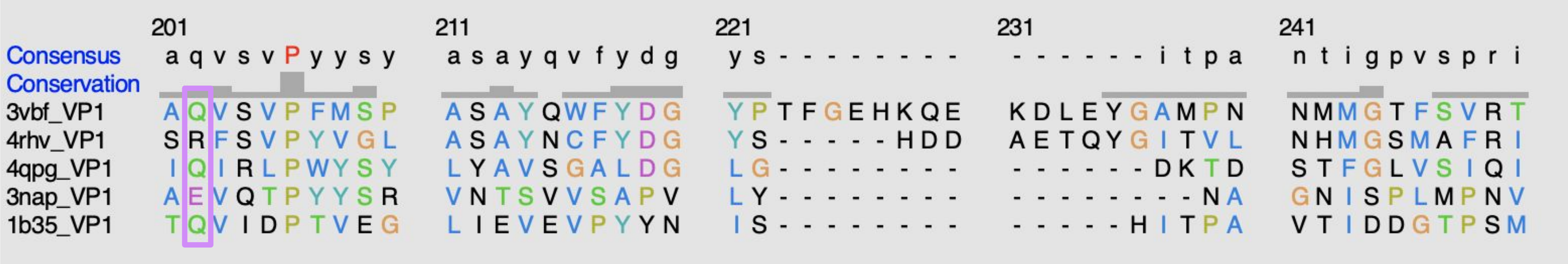


Hydrogen bonds

##	Structure 1	Dist. [Å]	Structure 2
1	C:LEU 17[N]	3.18	A:ALA 187[O]
2	C:SER 18[OG]	3.67	A:ALA 187[O]
3	C:VAL 15[N]	2.96	A:ARG 189[O]
4	C:THR 11[N]	2.86	A:ASN 197[OD1]
5	C:THR 10[OG1]	2.62	A:GLN 199[OE1]
6	C:TYR 181[N]	3.76	A:TYR 207[O]
7	C:THR 187[OG1]	3.24	A:ALA 165[N]
8	C:SER 18[OG]	3.49	A:ALA 187[N]
9	C:VAL 15[O]	2.94	A:ARG 189[N]

Data from PDBePISA

Interactions between VP1 and VP3

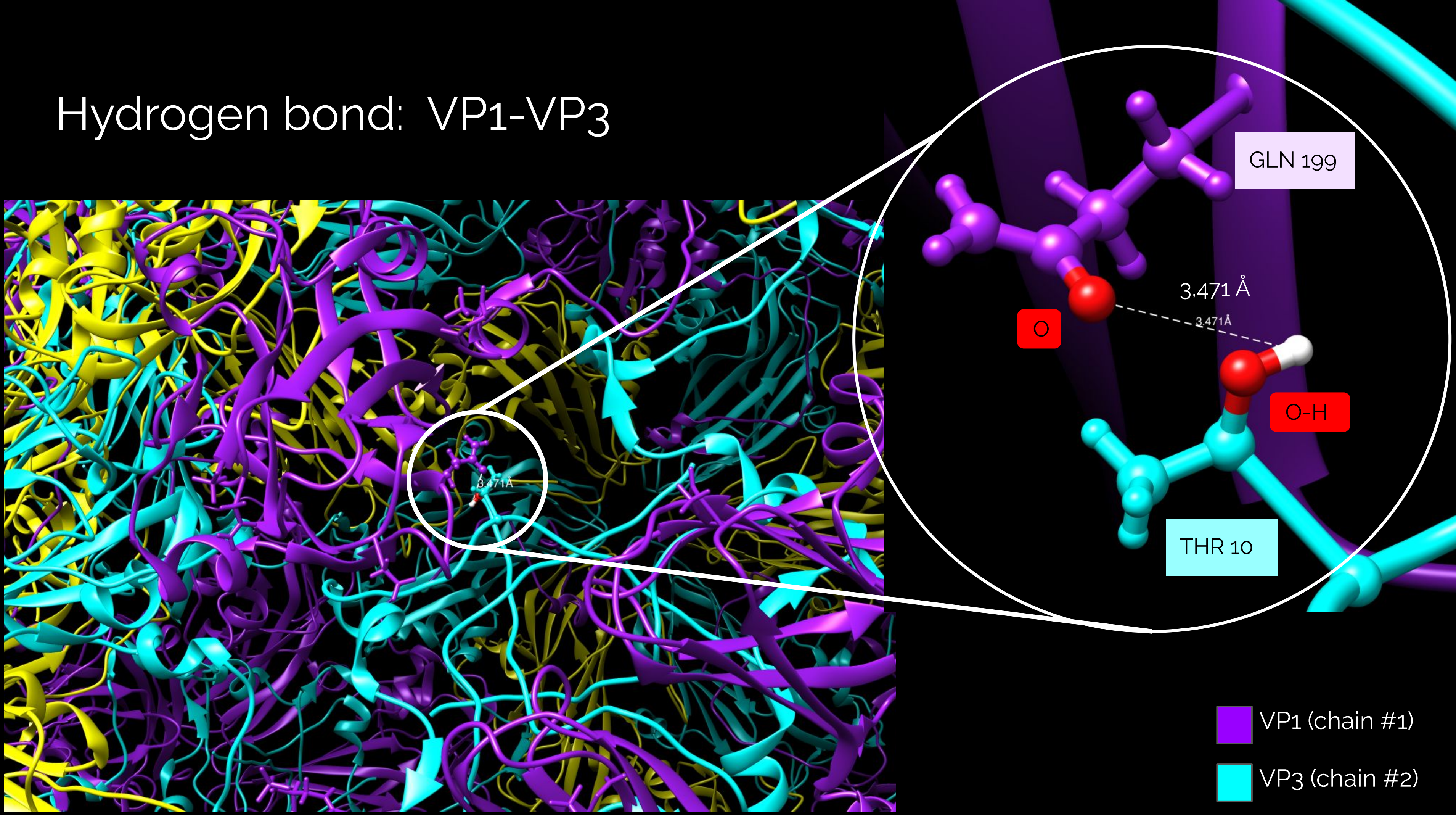


	201	211	221	231	241
Consensus	a q v s v P y y s y	a s a y q v f y d g	y s - - - - - - - -	- - - - - - i t p a	n t i g p v s p r i
Conservation					
3vbf_VP1	A Q V S V P F M S P	A S A Y Q W F Y D G	Y P T F G E H K Q E	K D L E Y G A M P N	N M M G T F S V R T
4rhv_VP1	S R F S V P Y V G L	A S A Y N C F Y D G	Y S - - - - - H D D	A E T Q Y G I T V L	N H M G S M A F R I
4qpg_VP1	I Q I R L P W Y S Y	L Y A V S G A L D G	L G - - - - - - - -	- - - - - - D K T D	S T F G L V S I Q I
3nap_VP1	A E V Q T P Y Y S R	V N T S V V S A P V	L Y - - - - - - - -	- - - - - - - - N A	G N I S P L M P N V
1b35_VP1	T Q V I D P T V E G	L I E V E V P Y Y N	I S - - - - - - - -	- - - - - H I T P A	V T I D D G T P S M

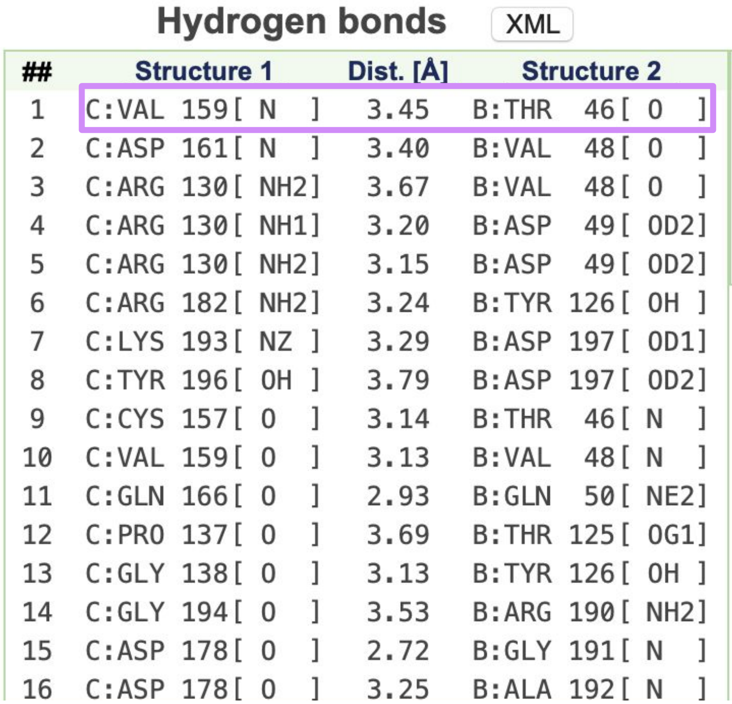
Glutamine (Q) is conserved among Human Hepatitis A Virus, Human Enterovirus A71 and Cricket Paralysis virus

3VBF: Human Enterovirus A71
4RHV: Human Rhinovirus B14
4QPG: Human Hepatitis A Virus
3NAP: Triatoma Virus
1B35: Cricket Paralysis Virus

Hydrogen bond: VP1-VP3

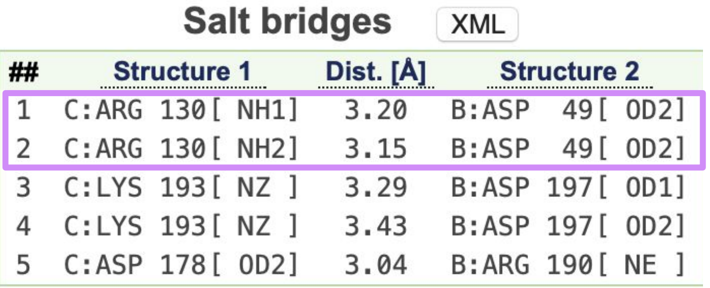


Interactions between VP3 and VP0



Hydrogen bonds XML

##	Structure 1	Dist. [Å]	Structure 2
1	C:VAL 159[N]	3.45	B:THR 46[O]
2	C:ASP 161[N]	3.40	B:VAL 48[O]
3	C:ARG 130[NH2]	3.67	B:VAL 48[O]
4	C:ARG 130[NH1]	3.20	B:ASP 49[OD2]
5	C:ARG 130[NH2]	3.15	B:ASP 49[OD2]
6	C:ARG 182[NH2]	3.24	B:TYR 126[OH]
7	C:LYS 193[NZ]	3.29	B:ASP 197[OD1]
8	C:TYR 196[OH]	3.79	B:ASP 197[OD2]
9	C:CYS 157[O]	3.14	B:THR 46[N]
10	C:VAL 159[O]	3.13	B:VAL 48[N]
11	C:GLN 166[O]	2.93	B:GLN 50[NE2]
12	C:PRO 137[O]	3.69	B:THR 125[OG1]
13	C:GLY 138[O]	3.13	B:TYR 126[OH]
14	C:GLY 194[O]	3.53	B:ARG 190[NH2]
15	C:ASP 178[O]	2.72	B:GLY 191[N]
16	C:ASP 178[O]	3.25	B:ALA 192[N]

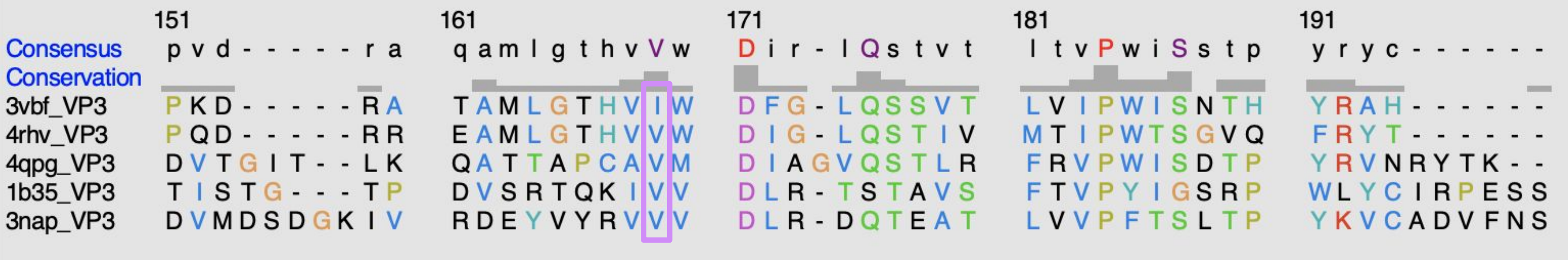


Salt bridges XML

##	Structure 1	Dist. [Å]	Structure 2
1	C:ARG 130[NH1]	3.20	B:ASP 49[OD2]
2	C:ARG 130[NH2]	3.15	B:ASP 49[OD2]
3	C:LYS 193[NZ]	3.29	B:ASP 197[OD1]
4	C:LYS 193[NZ]	3.43	B:ASP 197[OD2]
5	C:ASP 178[OD2]	3.04	B:ARG 190[NE]

Data from PDBePISA

Interactions between VP3 and VP0

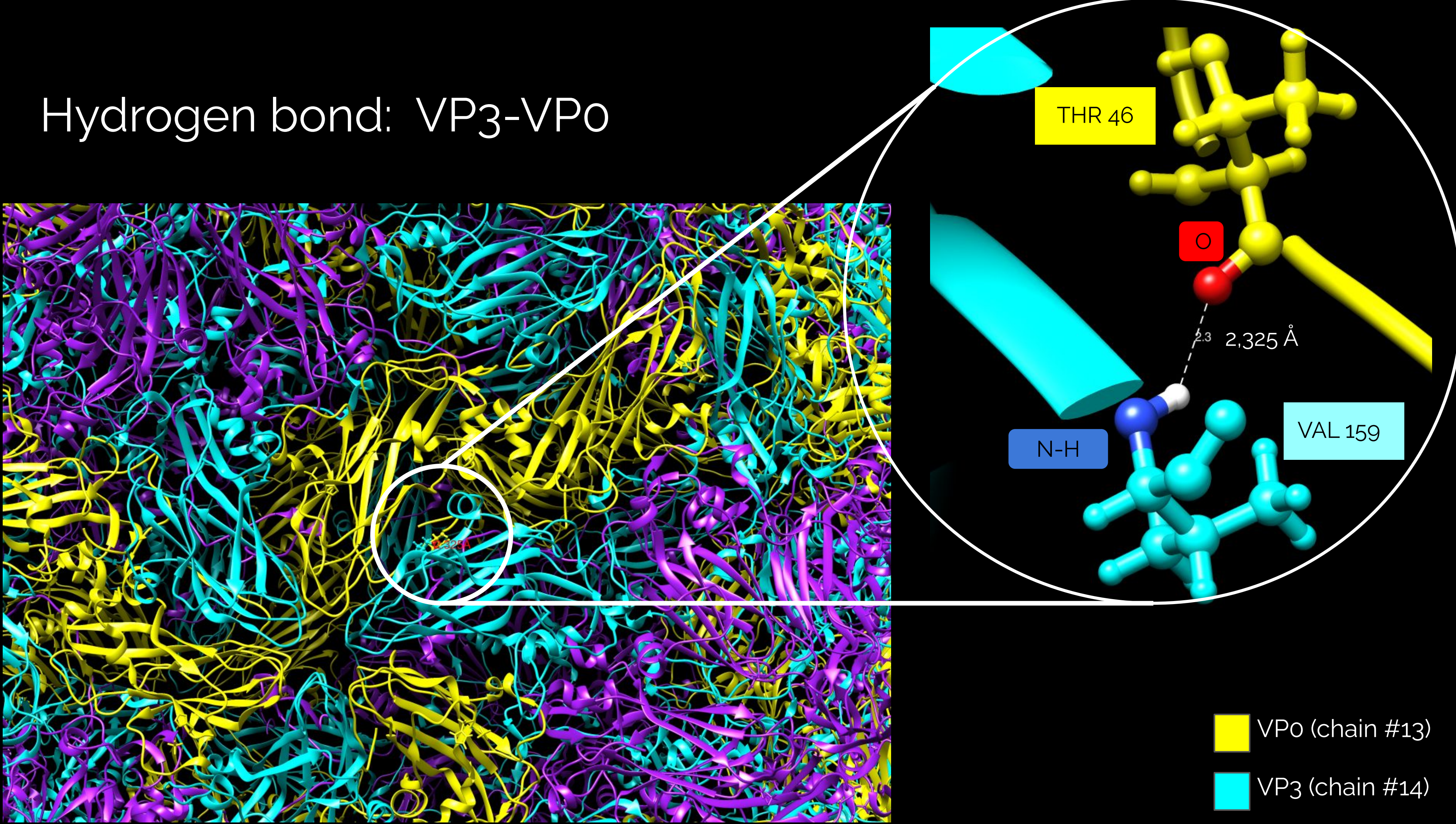


```
              151                   161                   171                   181                   191
Consensus     p v d - - - - - r a   q a m l g t h v V w   D i r - l Q s t v t   l t v P w i S s t p   y r y c - - - - - -
Conservation
3vbf_VP3      P K D - - - - - R A   T A M L G T H V I W   D F G - L Q S S V T   L V I P W I S N T H   Y R A H - - - - - -
4rhv_VP3      P Q D - - - - - R R   E A M L G T H V V W   D I G - L Q S T I V   M T I P W T S G V Q   F R Y T - - - - - -
4qpg_VP3      D V T G I T - - L K   Q A T T A P C A V M   D I A G V Q S T L R   F R V P W I S D T P   Y R V N R Y T K - -
1b35_VP3      T I S T G - - - T P   D V S R T Q K I V V   D L R - T S T A V S   F T V P Y I G S R P   W L Y C I R P E S S
3nap_VP3      D V M D S D G K I V   R D E Y V Y R V V V   D L R - D Q T E A T   L V V P F T S L T P   Y K V C A D V F N S
```

Valine (V) is conserved among Human Hepatitis A Virus, Human Rhinovirus B14, Triatoma Virus and Cricket Paralysis virus

3VBF: Human Enterovirus A71
4RHV: Human Rhinovirus B14
4QPG: Human Hepatitis A Virus
3NAP: Triatoma Virus
1B35: Cricket Paralysis Virus

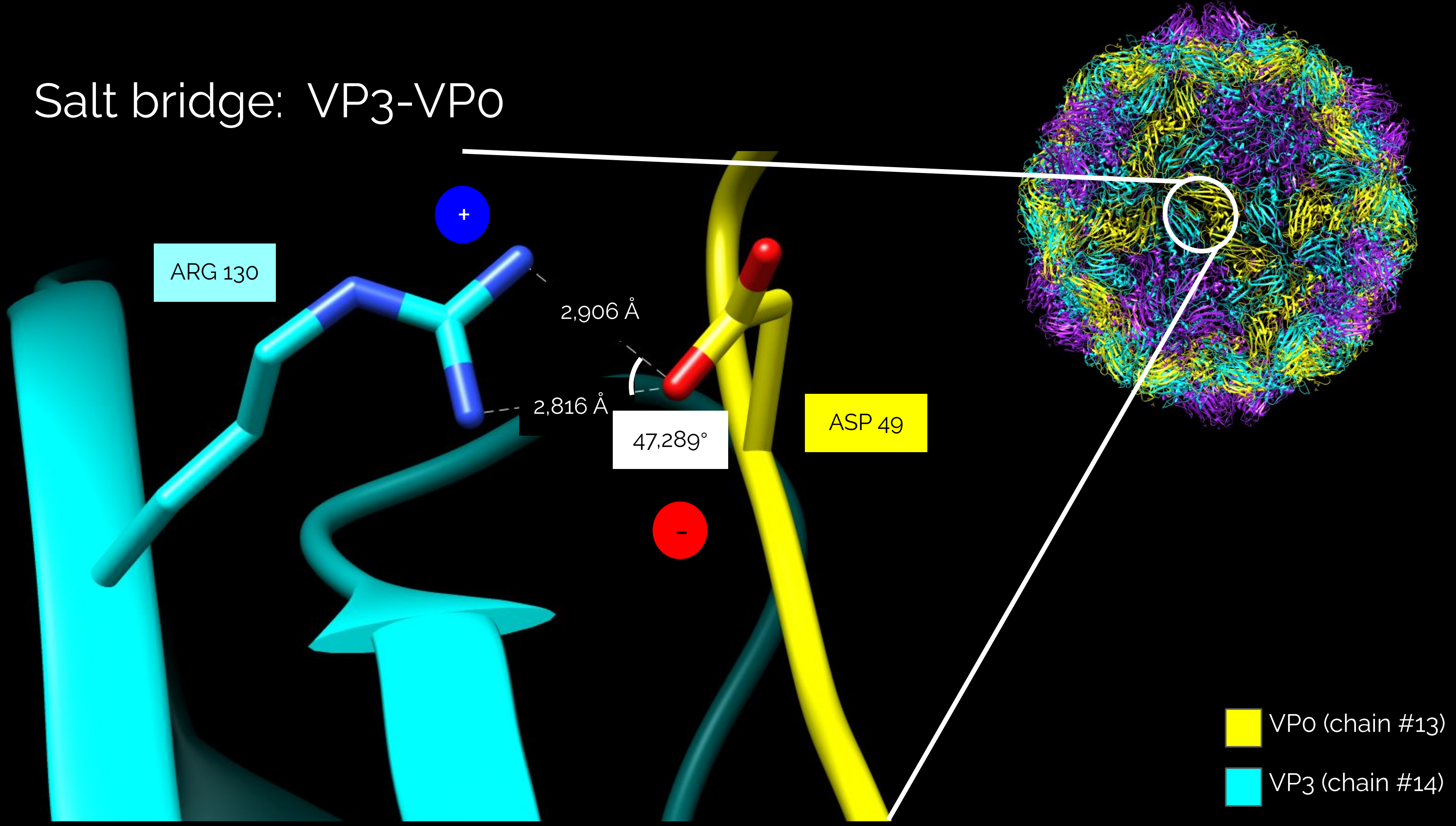
Hydrogen bond: VP3-VP0



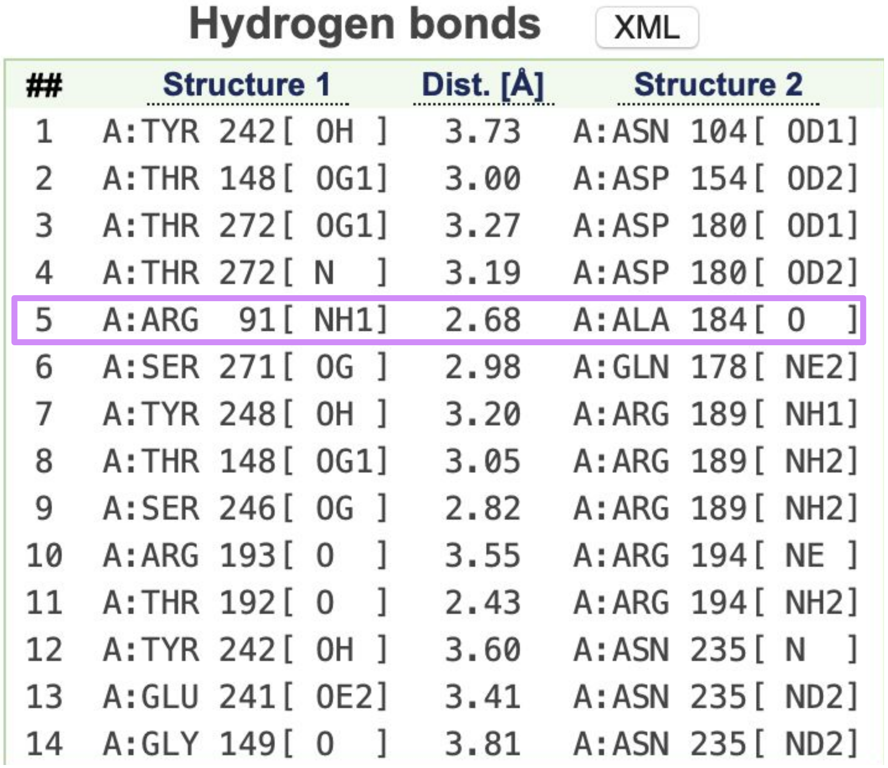
🟨 VP0 (chain #13)

🟦 VP3 (chain #14)

Salt bridge: VP3-VP0



Interactions between VP1 and VP1

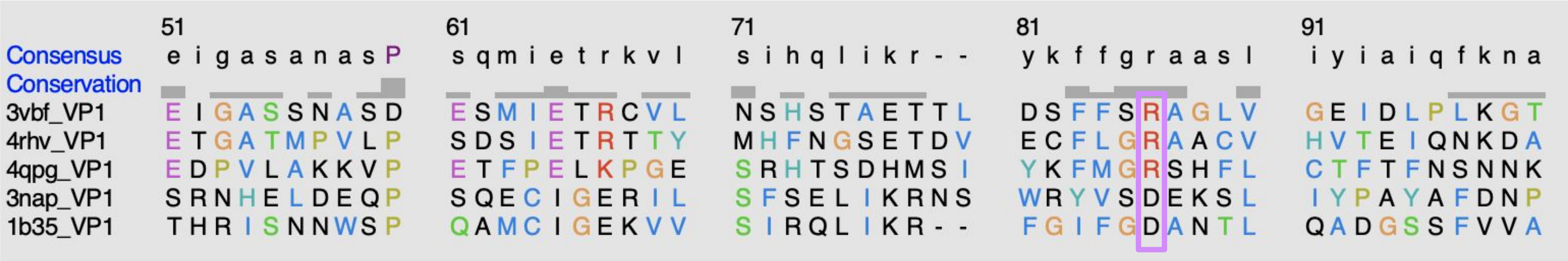


Hydrogen bonds

##	Structure 1	Dist. [Å]	Structure 2
1	A:TYR 242[OH]	3.73	A:ASN 104[OD1]
2	A:THR 148[OG1]	3.00	A:ASP 154[OD2]
3	A:THR 272[OG1]	3.27	A:ASP 180[OD1]
4	A:THR 272[N]	3.19	A:ASP 180[OD2]
5	A:ARG 91[NH1]	2.68	A:ALA 184[O]
6	A:SER 271[OG]	2.98	A:GLN 178[NE2]
7	A:TYR 248[OH]	3.20	A:ARG 189[NH1]
8	A:THR 148[OG1]	3.05	A:ARG 189[NH2]
9	A:SER 246[OG]	2.82	A:ARG 189[NH2]
10	A:ARG 193[O]	3.55	A:ARG 194[NE]
11	A:THR 192[O]	2.43	A:ARG 194[NH2]
12	A:TYR 242[OH]	3.60	A:ASN 235[N]
13	A:GLU 241[OE2]	3.41	A:ASN 235[ND2]
14	A:GLY 149[O]	3.81	A:ASN 235[ND2]

Data from PDBePISA

Interactions between VP1 and VP1

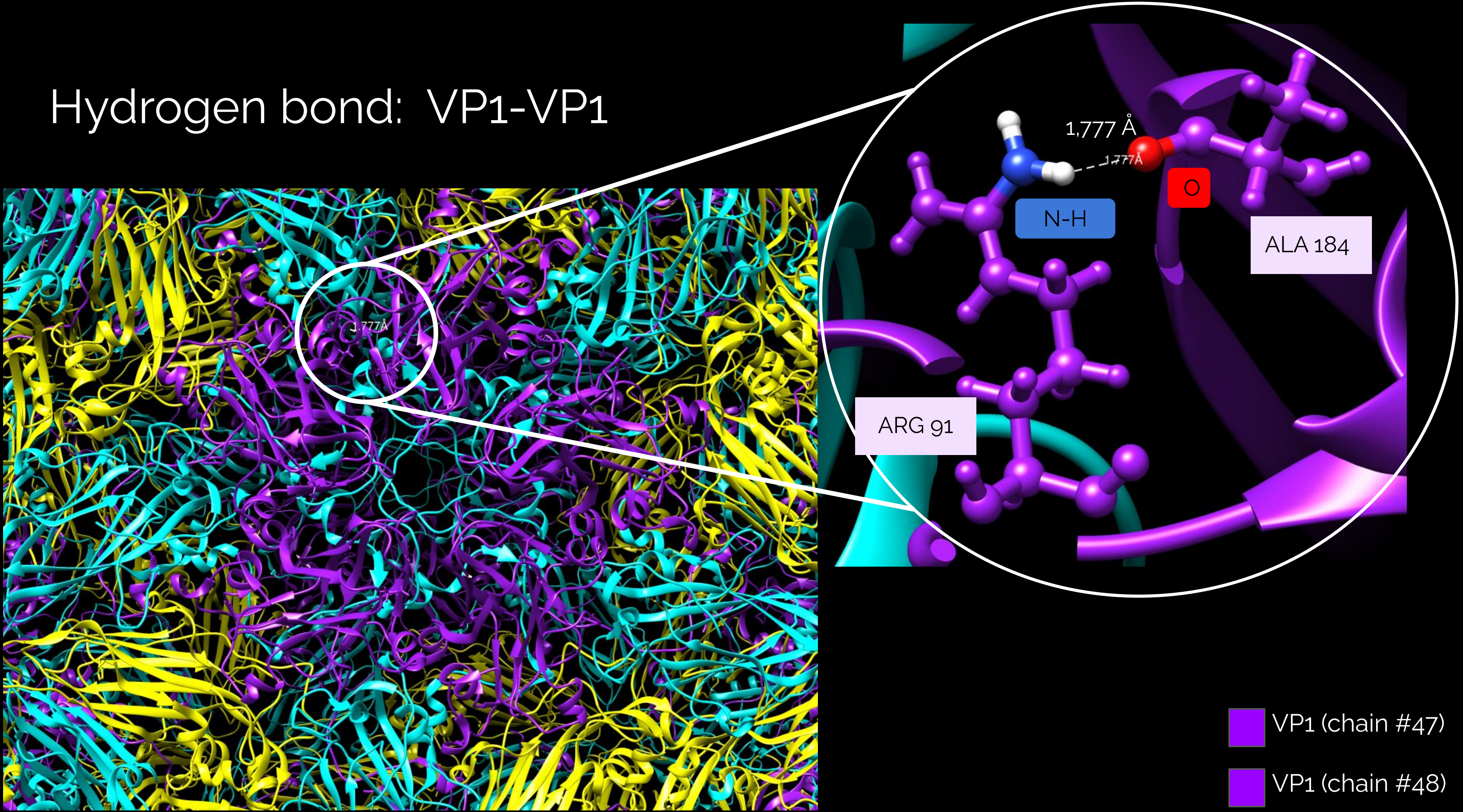


	51	61	71	81	91
Consensus	e i g a s a n a s P	s q m i e t r k v l	s i h q l i k r - -	y k f f g r a a s l	i y i a i q f k n a
Conservation					
3vbf_VP1	E I G A S S N A S D	E S M I E T R C V L	N S H S T A E T T L	D S F F S R A G L V	G E I D L P L K G T
4rhv_VP1	E T G A T M P V L P	S D S I E T R T T Y	M H F N G S E T D V	E C F L G R A A C V	H V T E I Q N K D A
4qpg_VP1	E D P V L A K K V P	E T F P E L K P G E	S R H T S D H M S I	Y K F M G R S H F L	C T F T F N S N N K
3nap_VP1	S R N H E L D E Q P	S Q E C I G E R I L	S F S E L I K R N S	W R Y V S D E K S L	I Y P A Y A F D N P
1b35_VP1	T H R I S N N W S P	Q A M C I G E K V V	S I R Q L I K R - -	F G I F G D A N T L	Q A D G S S F V V A

Arginine (R) is conserved among Human Hepatitis A Virus, Human Enterovirus A71 and Human Rhinovirus B14

3VBF: Human Enterovirus A71
4RHV: Human Rhinovirus B14
4QPG: Human Hepatitis A Virus
3NAP: Triatoma Virus
1B35: Cricket Paralysis Virus

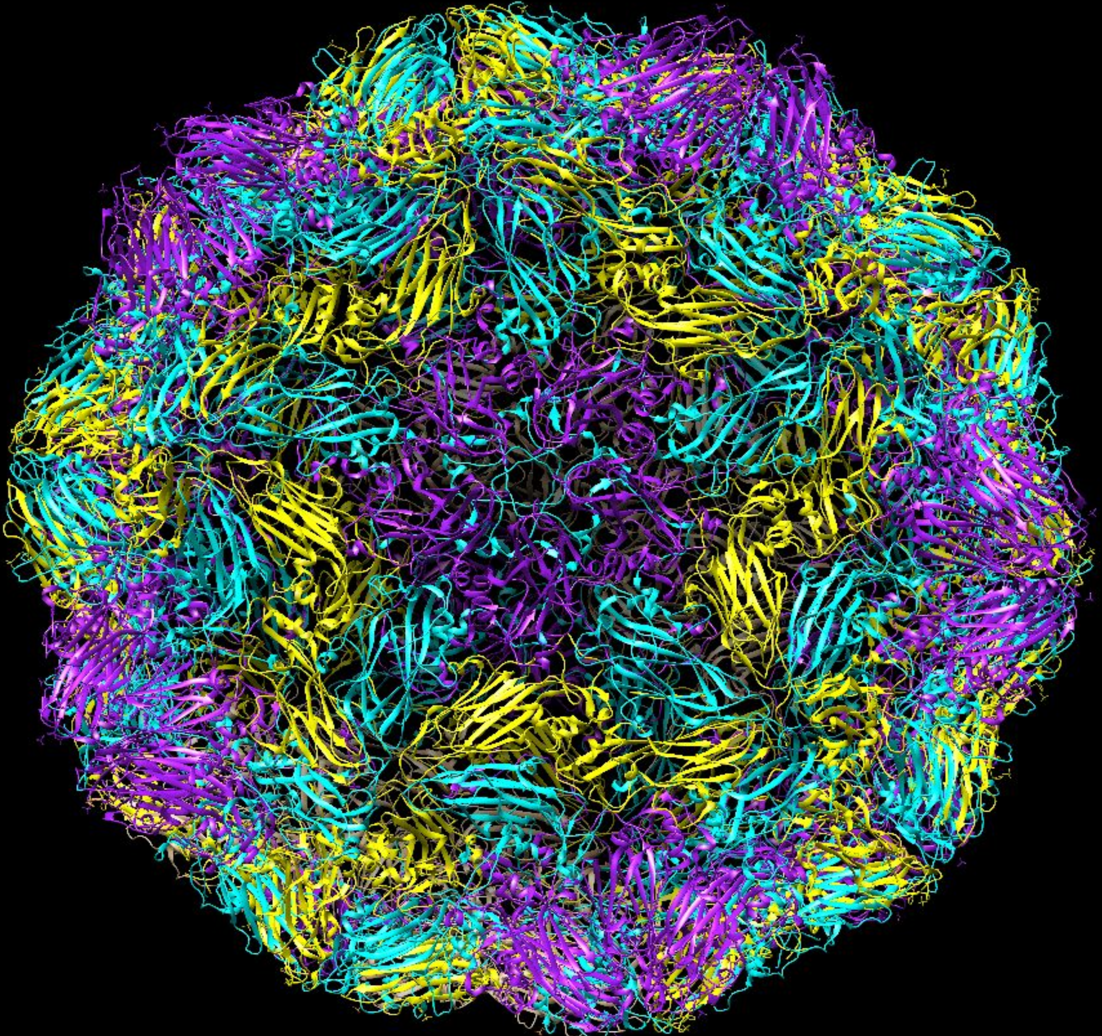
Hydrogen bond: VP1-VP1



🟪 VP1 (chain #47)

🟪 VP1 (chain #48)

STUDY CASE: R10 ANTIBODY AND HAV



Hepatitis A issue

HAV infects 1,4 million people annually

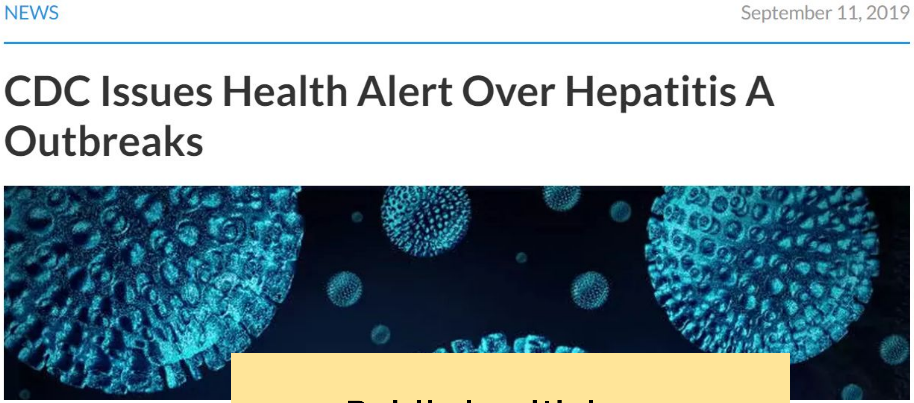
There is a vaccine ✓

But there are **no** licensed therapeutic drugs ✗

What problems does HAV imply?

It is unusually **stable**, making disinfection difficult.

Lack of **information**

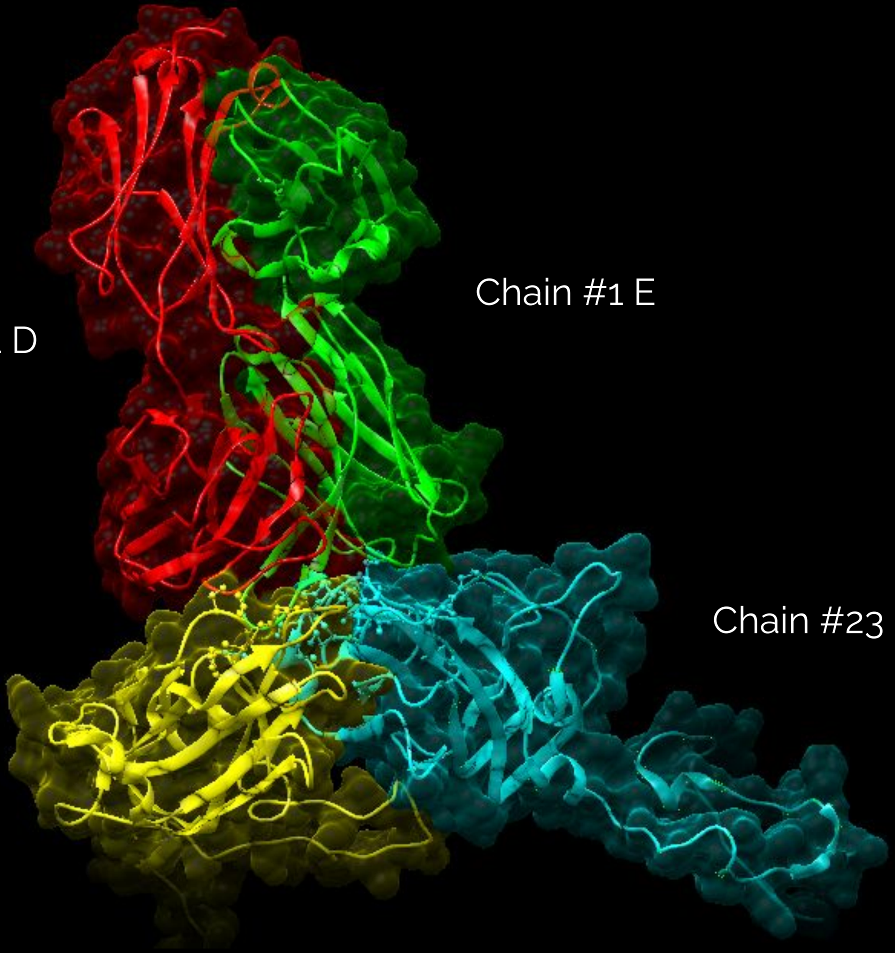


NEWS September 11, 2019

CDC Issues Health Alert Over Hepatitis A Outbreaks

Public health issue

R10 NAb - HAV interaction

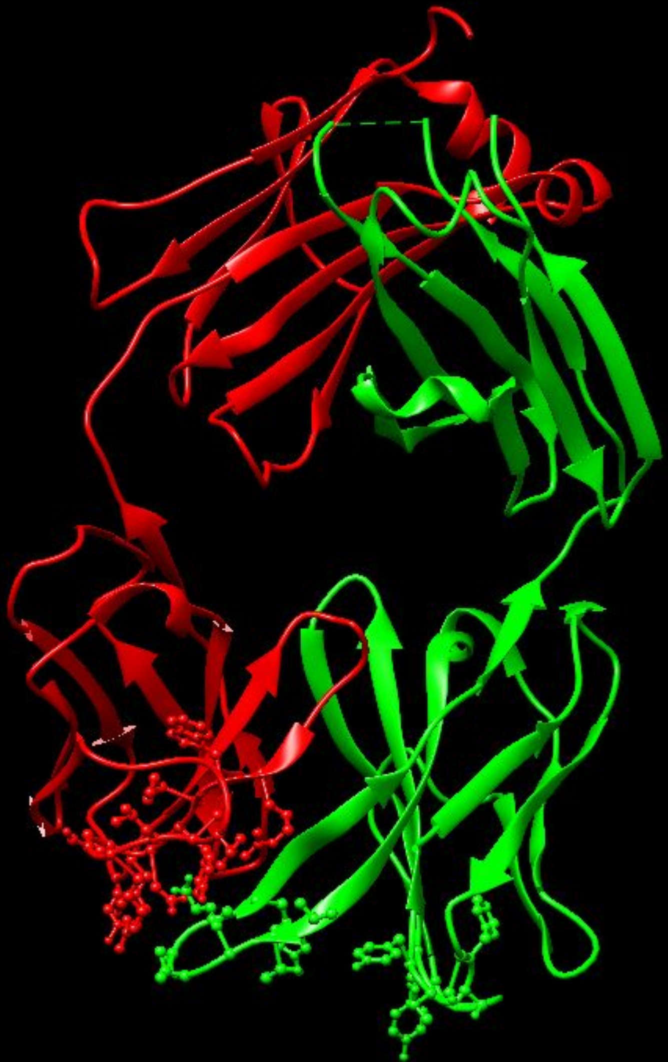


🟨 HAV VP2 (chain B)
🟦 HAV VP3 (chain C)
🟩 R10 heavy chain (chain E)
🟥 R10 light chain (chain D)

R10 CDRs

Interaction surface comprises four of the six complementary determining regions (CDRs):

- H1 (residues 28–32)
- H2 (residues 52–57)
- H3 (residues 100–106)
- L1 (residues 30–31)



🟩 R10 heavy chain (chain E)

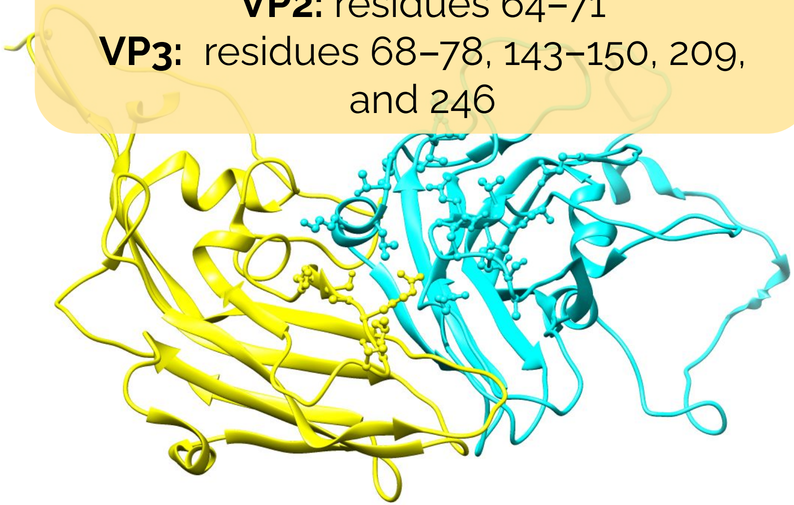
🟥 R10 light chain (chain D)

HAV Epitope: Strain Analysis

Conservation analysis of the R10 epitope on HAV capsids of 6 human strains.

HAV R10 Epitope

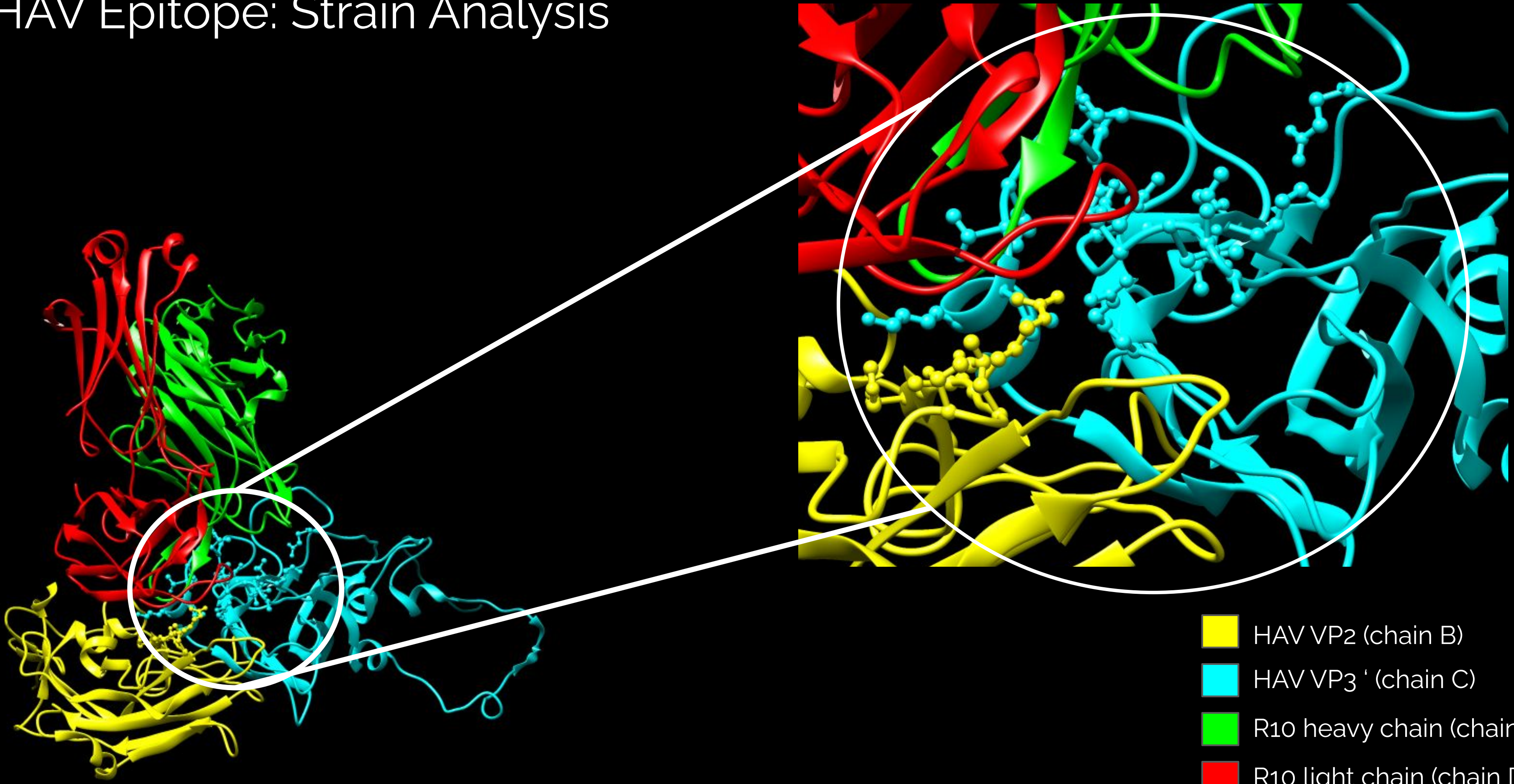
VP2: residues 64–71
VP3: residues 68–78, 143–150, 209, and 246



HAV strains analysed

IA → Germany (Q67825)
IB → Australia (P08617)
IIA → France (Q5Y944)
IIB → Sierra Leone (Q8V0N6)
IIIA → Norway (Q9DWR1)
IIIB → Japan (A5LGW7)

HAV Epitope: Strain Analysis



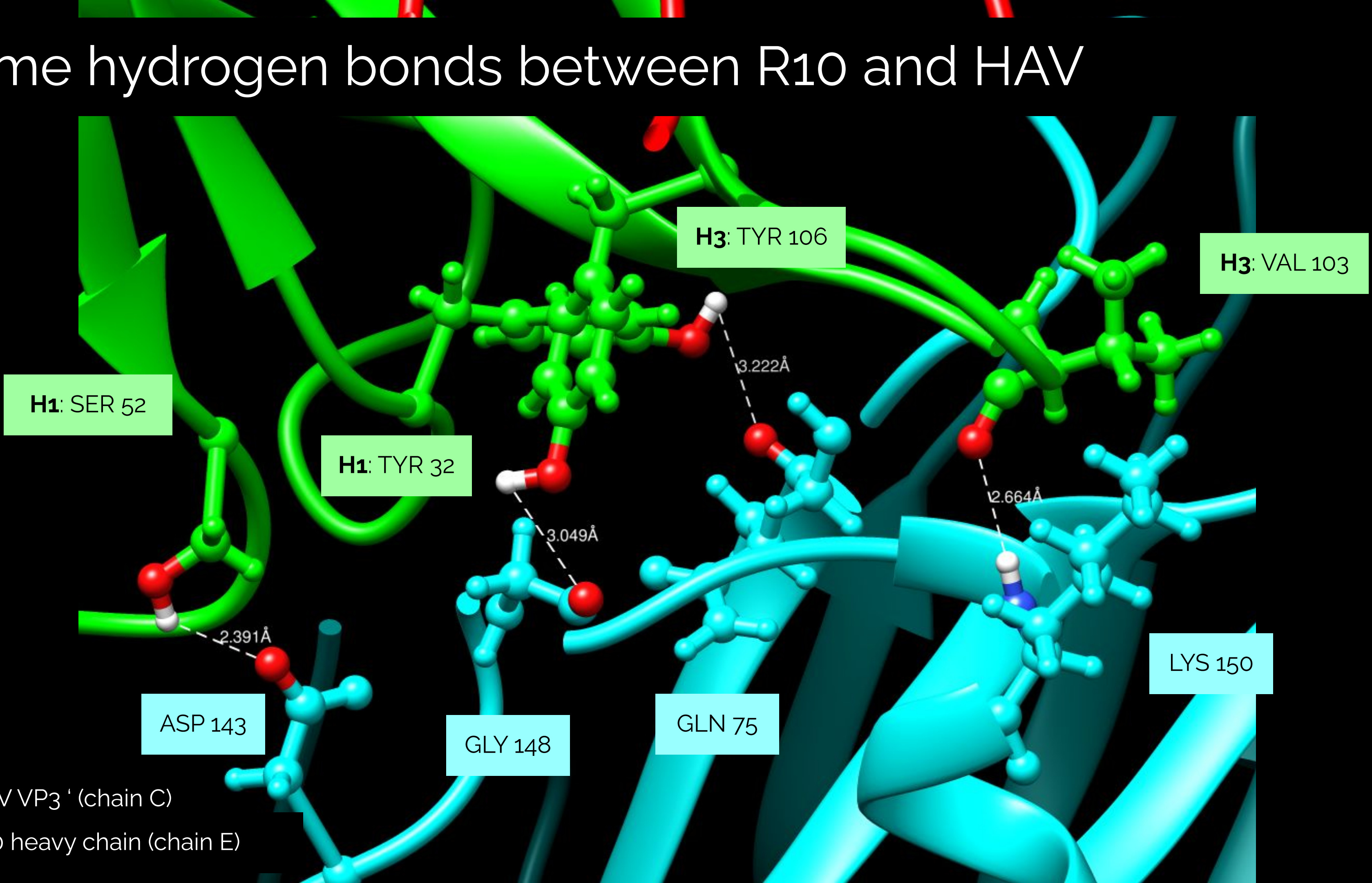
🟨 HAV VP2 (chain B)

🟦 HAV VP3 ‘ (chain C)

🟩 R10 heavy chain (chain E)

🟥 R10 light chain (chain D)

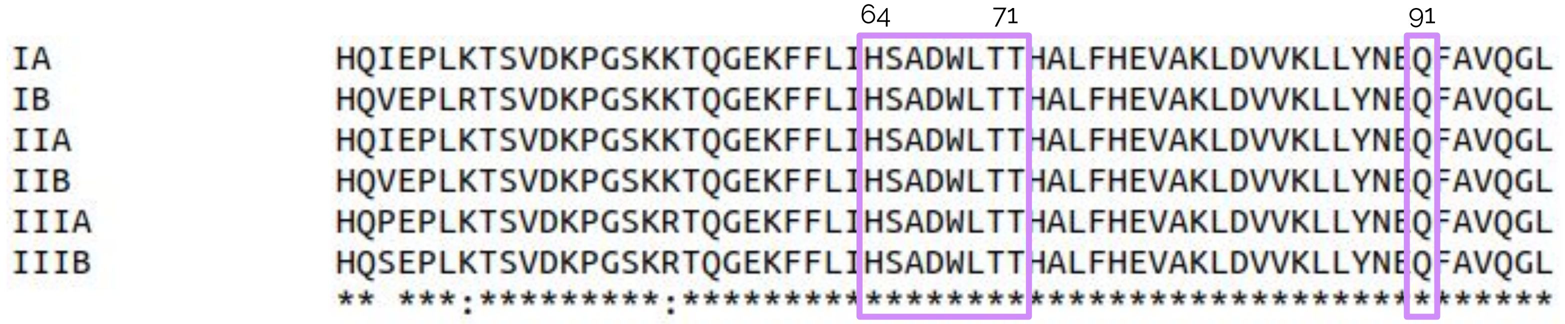
Some hydrogen bonds between R10 and HAV



- 🟦 HAV VP3 ' (chain C)
- 🟩 R10 heavy chain (chain E)

HAV Epitope: Strain Analysis (MSA)

VP2



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IA      HQIEPLKTSVDKPGSKKTQGEKFFLIHSADWLTTHALFHEVAKLDVVKLLYNEQFAVQGL
IB      HQVEPLRTSVDKPGSKKTQGEKFFLIHSADWLTTHALFHEVAKLDVVKLLYNEQFAVQGL
IIA     HQIEPLKTSVDKPGSKKTQGEKFFLIHSADWLTTHALFHEVAKLDVVKLLYNEQFAVQGL
IIB     HQVEPLKTSVDKPGSKKTQGEKFFLIHSADWLTTHALFHEVAKLDVVKLLYNEQFAVQGL
IIIA    HQPEPLKTSVDKPGSKRTQGEKFFLIHSADWLTTHALFHEVAKLDVVKLLYNEQFAVQGL
IIIB    HQSEPLKTSVDKPGSKRTQGEKFFLIHSADWLTTHALFHEVAKLDVVKLLYNEQFAVQGL
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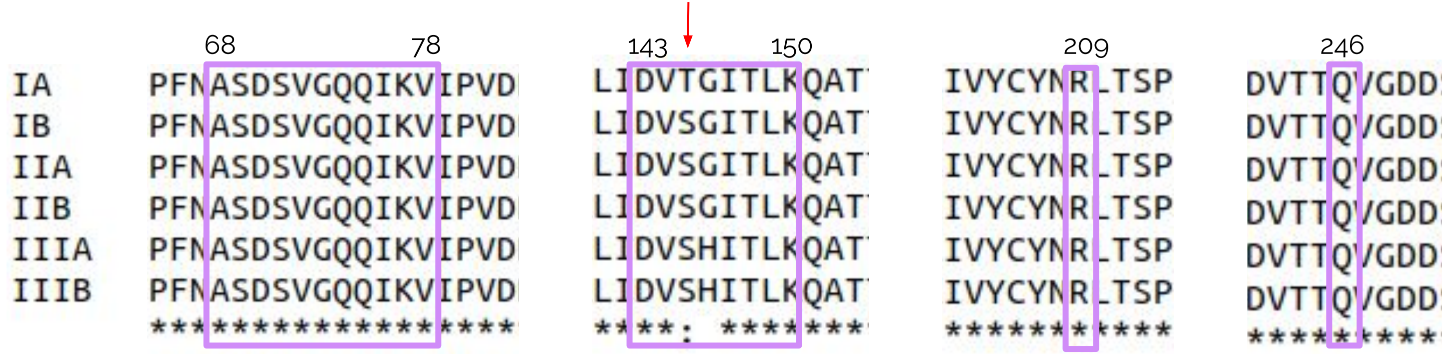
VP3



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IA      PFNASDSVGQQIKVIPVD    LIDVTGITLKQAT    IVYCYNRLTSP    DVTTQVGDD
IB      PFNASDSVGQQIKVIPVD    LIDVSGITLKQAT    IVYCYNRLTSP    DVTTQVGDD
IIA     PFNASDSVGQQIKVIPVD    LIDVSGITLKQAT    IVYCYNRLTSP    DVTTQVGDD
IIB     PFNASDSVGQQIKVIPVD    LIDVSGITLKQAT    IVYCYNRLTSP    DVTTQVGDD
IIIA    PFNASDSVGQQIKVIPVD    LIDVSHITLKQAT    IVYCYNRLTSP    DVTTQVGDD
IIIB    PFNASDSVGQQIKVIPVD    LIDVSHITLKQAT    IVYCYNRLTSP    DVTTQVGDD
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IA: Germany (Q67825) **IB:** Australia (P08617) **IIA:** France (Q5Y944) **IIB:** Sierra Leone (Q8V0N6) **IIIA:** Norway (Q9DWR1) **IIIB:** Japan (A5LGW7)

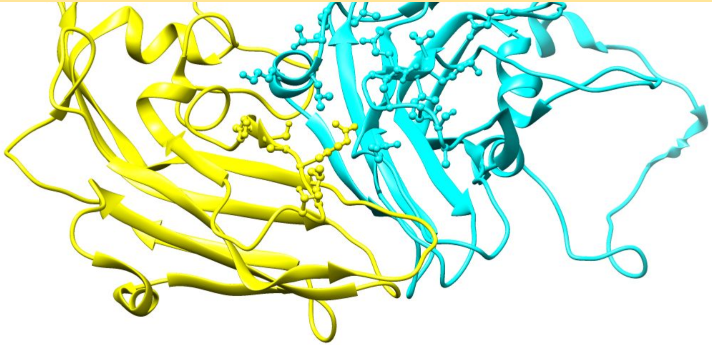
☐ Epitope residues location

HAV Epitope: Strain Analysis

The R10 epitope is **highly conserved** among the six strains

↓

R10 antibody is likely to strongly bind to most human HAVs strains, so it is able to destabilize the capsid and neutralize virus infection.



Final remarks

HAV shares characteristics from both “classical” mammalian picornaviruses and insect picorna-like viruses.

HAV may represent a **link** between them

Further research is needed to to explain more of its unique biology:

- Structural analyses of the capsid
- Capture of assembly states

Thank you for your attention!

Do you have any questions?

Bibliography

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Questions ?

1. HAV belongs to the family of:

a) Coronaviridae
b) Onaviridae
c) Circoviridae
d) Picornaviridae
e) Retroviridae

2. HAV capsid has:

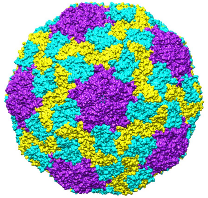
a) 6-fold axis of symmetry
b) 5-fold axis of symmetry
c) 3-fold axis of symmetry
d) 2-fold axis of symmetry
e) B, C and D are correct

3. Choose the false statement. HAV has...

a) An icosahedral capsid
b) A jelly roll supersecondary structure
c) A canyon
d) An angle switch at VP2
e) No hydrophobic pocket

4. How many pentamers form the HAV capsid?

a) 160
b) 10
c) 5
d) 12
e) 26



Questions ?

5. VP2 angle switch makes HAV more similar to:

a) Classical mammalian picornavirus
b) Insect picornavirus
c) Enterovirus
d) All are correct
e) None are correct

6. SCOP classifies HAV viral proteins as:

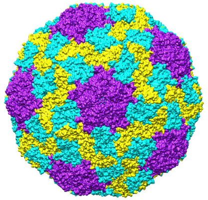
a) Alpha and Beta proteins (a/b)
b) Small proteins
c) All-alpha proteins
d) Alpha and Beta proteins (a+b)
e) All-beta proteins

7. VP0 cleaves into:

a) VP1 and VP3
b) VP1 and VP2
c) VP2 and VP3
d) VP3 and VP4
e) VP2 and VP4

8. Which interactions can be found in the HAV capsid?

a) Hydrogen bonds
b) Salt bridges
c) a and b are correct
d) Disulfide bonds
e) No hydrophobic pocket



Questions ?

9. Choose the true statement about the study case:

a) R10 Antibody interacts with VP1
b) R10 Antibody neutralizes the HAV
c) Six CDRs of R10 Antibody are involved in the interaction with the epitope
d) The R10 epitope is not highly conserved
e) R10 Antibody is not able to destabilize the HAV capsid.

10. Choose the true statement:

a) HAV is a single-stranded RNA-positive virus
b) HAV is chronic and highly fatal
c) HAV infects the gastrointestinal-tract
d) HAV is transmitted mainly by air
e) All the above are incorrect