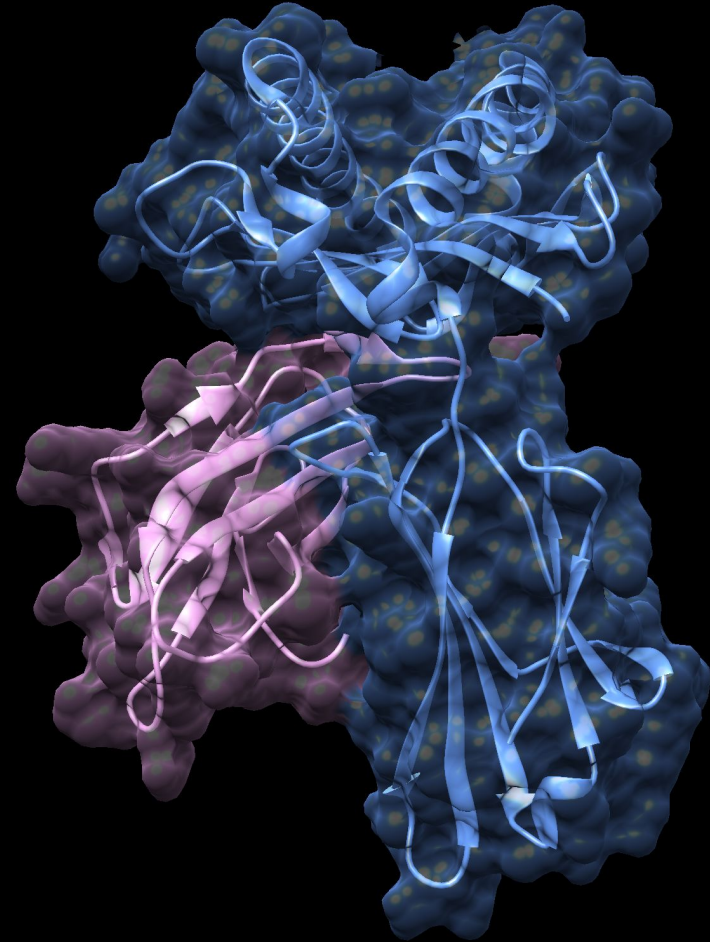


HLA | HUMAN LEUKOCYTE ANTIGEN

An structural analysis

Marina Carreras, Mireia Roig, Mònica Sancho
Structural Biology | Human Biology | 23-24



HLA | **Table of contents**

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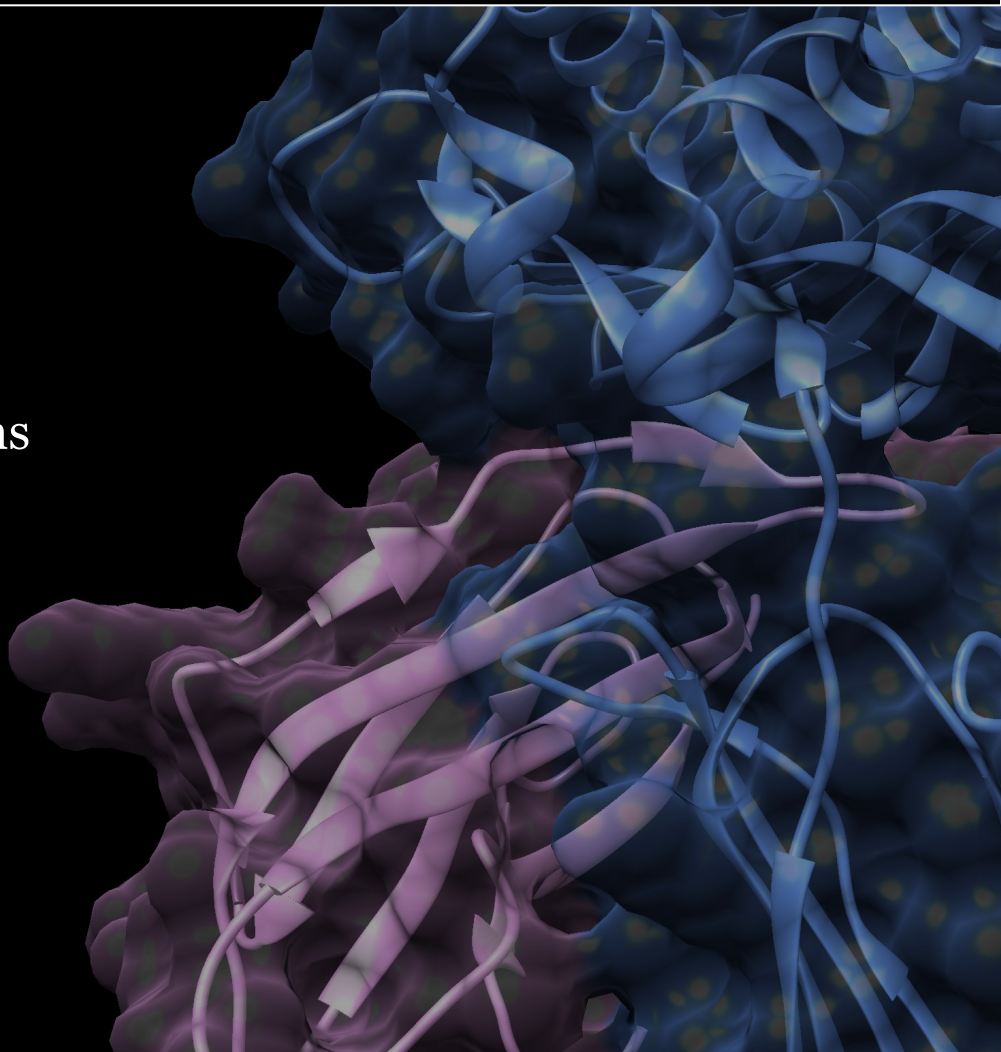
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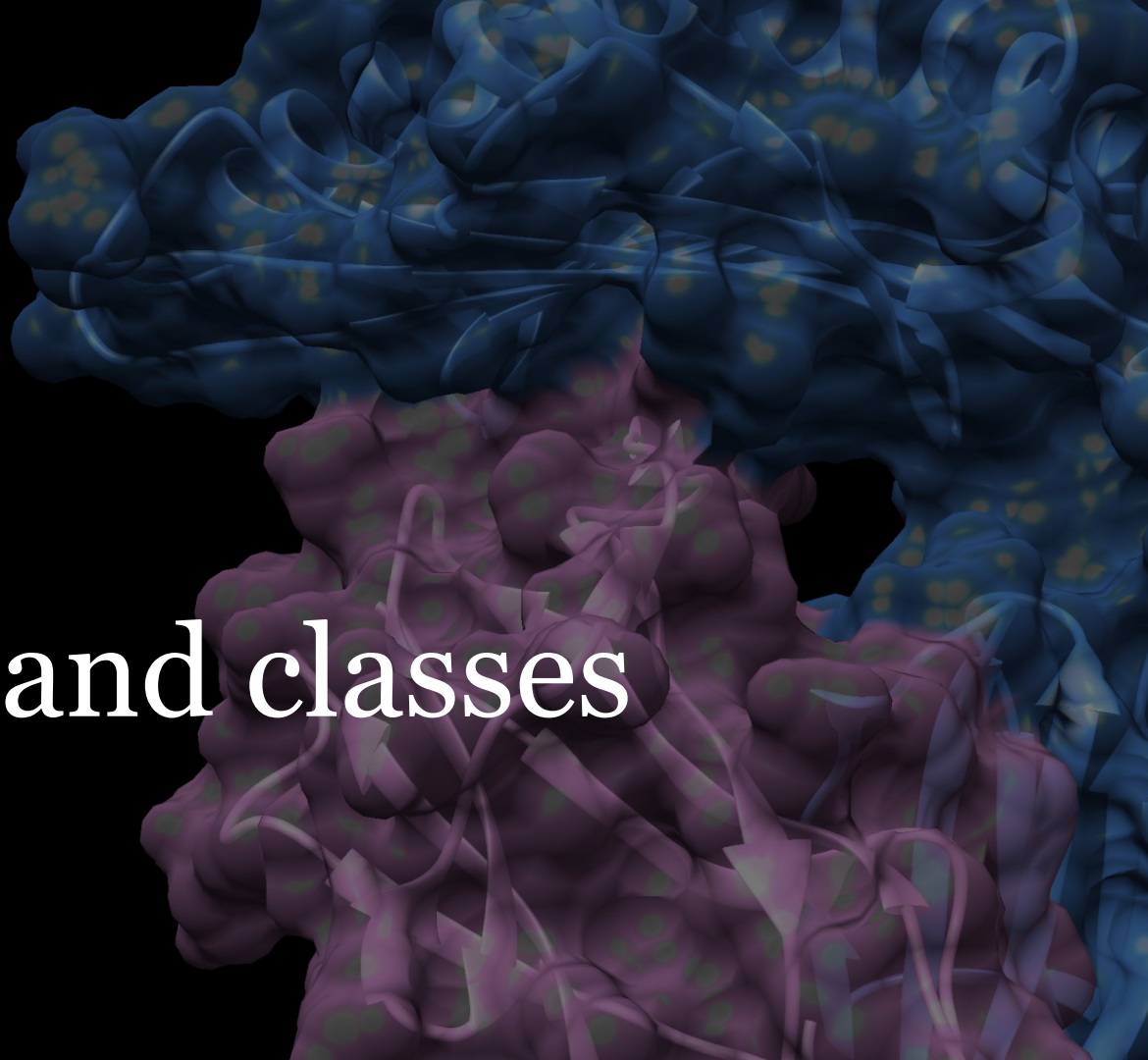
Evolution:
structure and sequence



01

HLA:

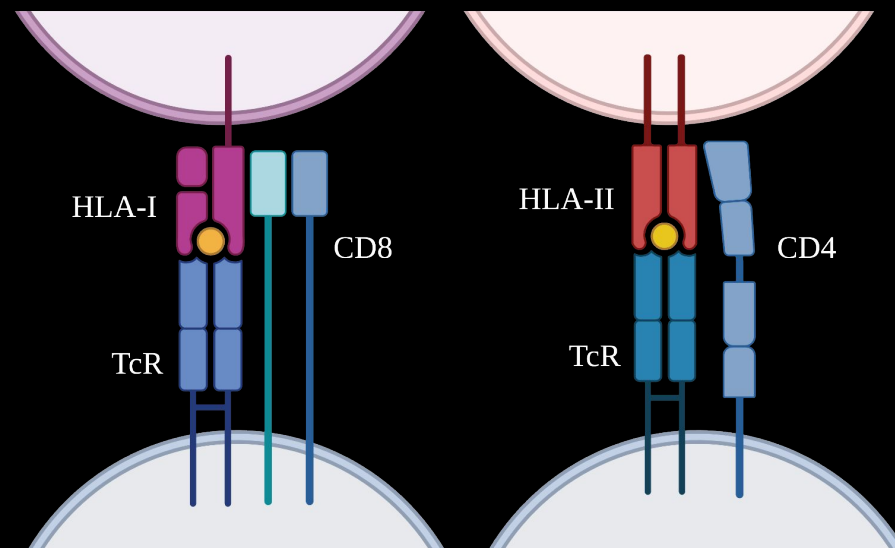
function and classes



HLA molecules | HLA-I and HLA-II

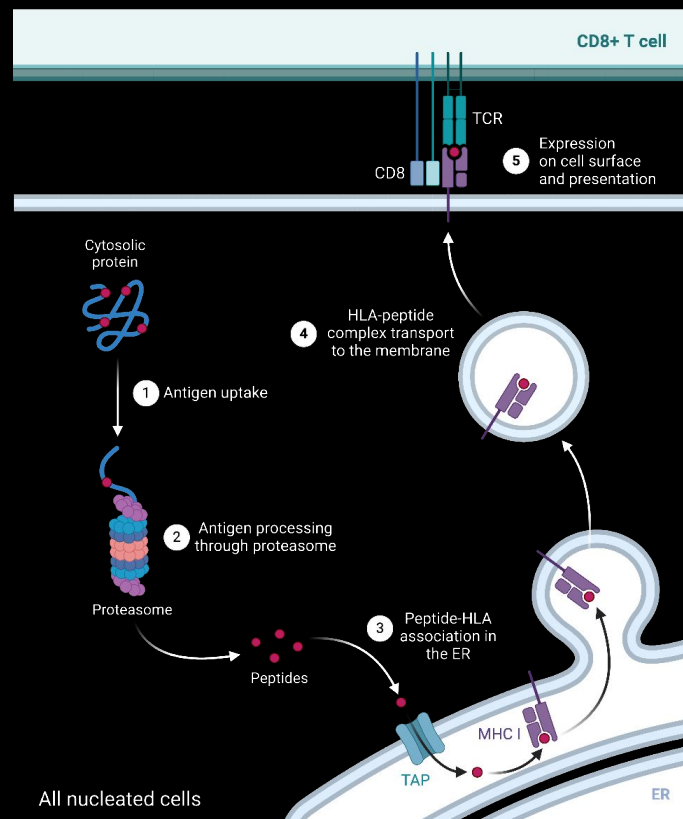
There are two classes of HLA molecules:

	HLA-I	HLA-II
Localization	All nucleated cells	Antigen presenting cells
T cell	CD8+	CD4+
Peptides' localization	Intracellular	Extracellular
Peptides' length	8-10 amino acids	15-25 amino acids

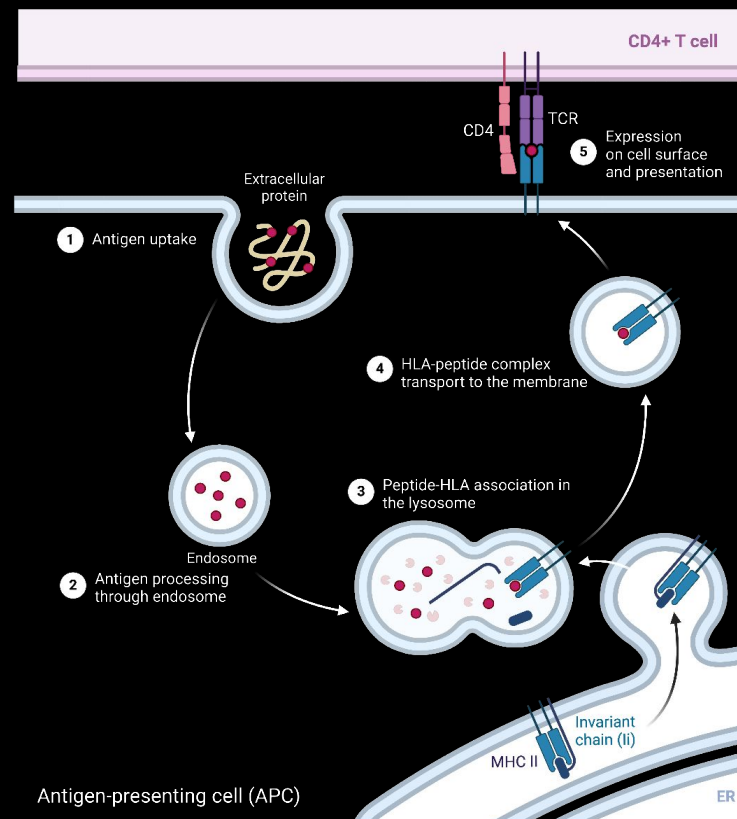


Function of HLA molecules | Antigen presentation

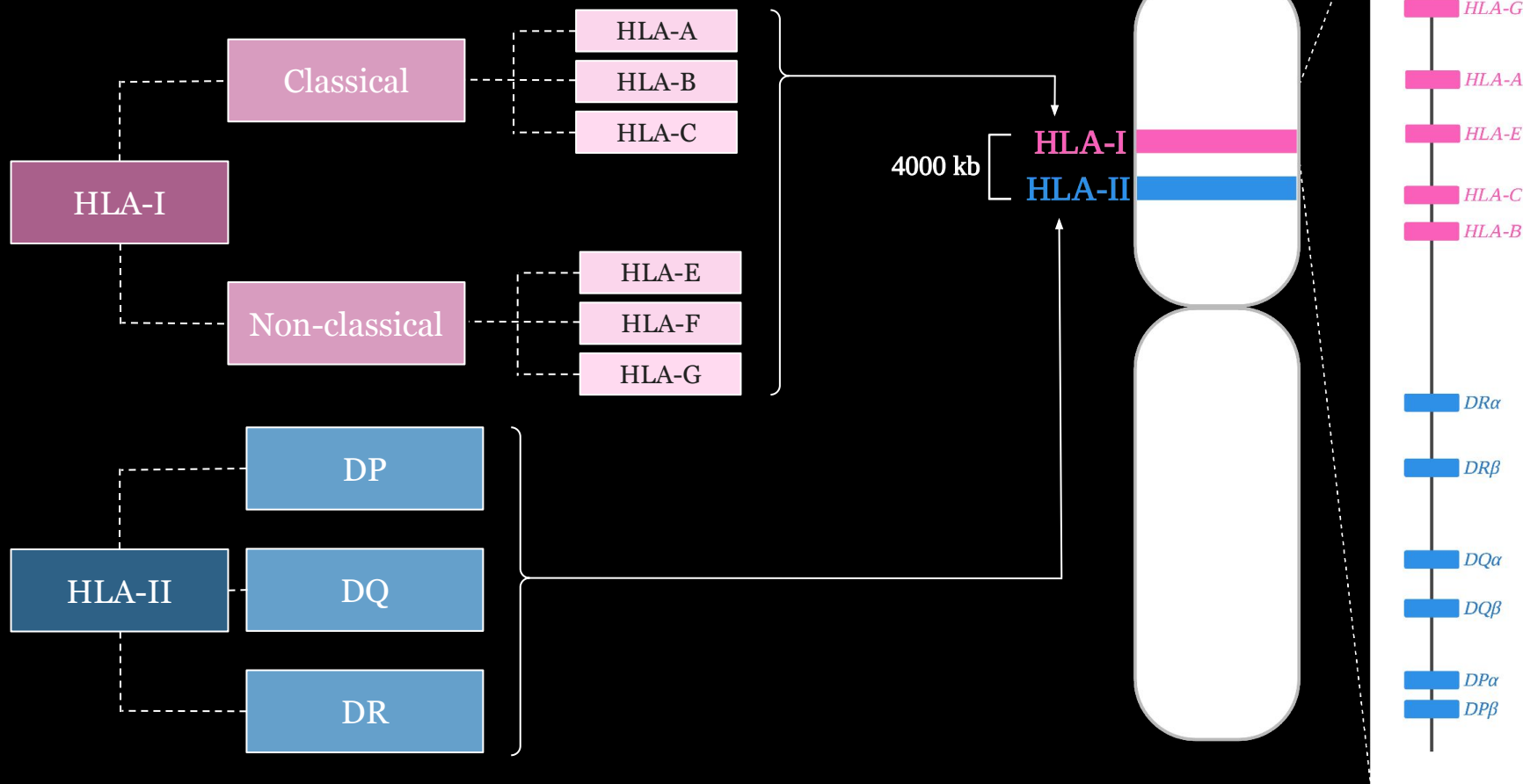
HLA-I pathway



HLA-II pathway



HLA molecules | Subclasses and genetics





02

Structure:
folds, domains and bonds

HLA structure | Chains

HLA-I

α -chain

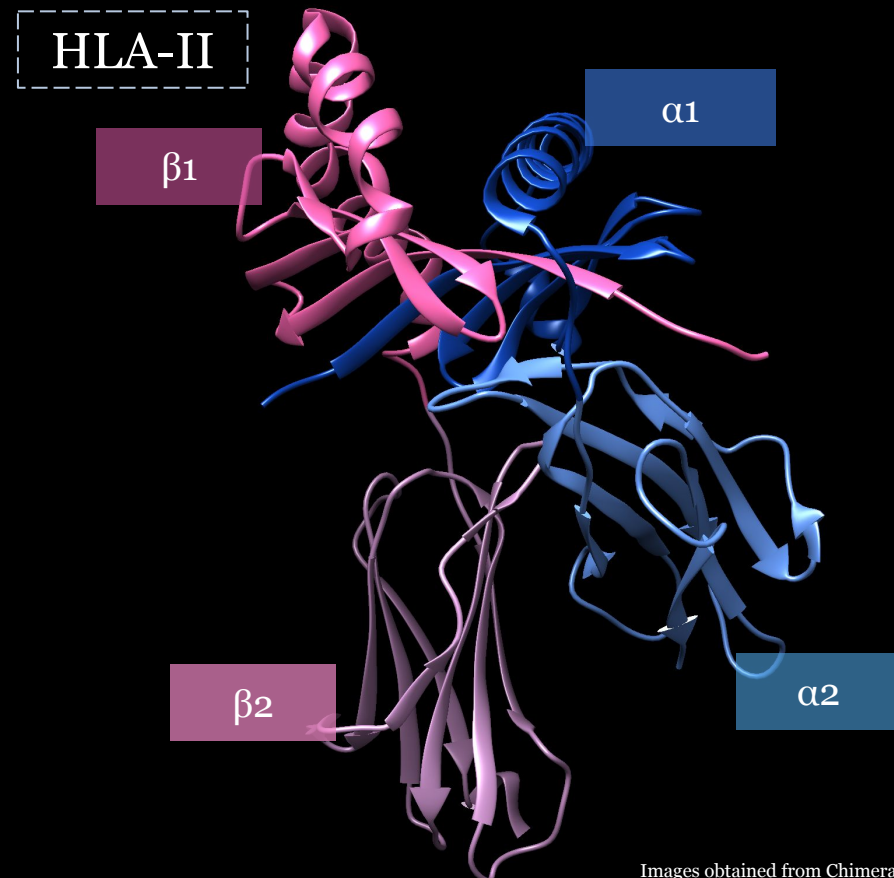
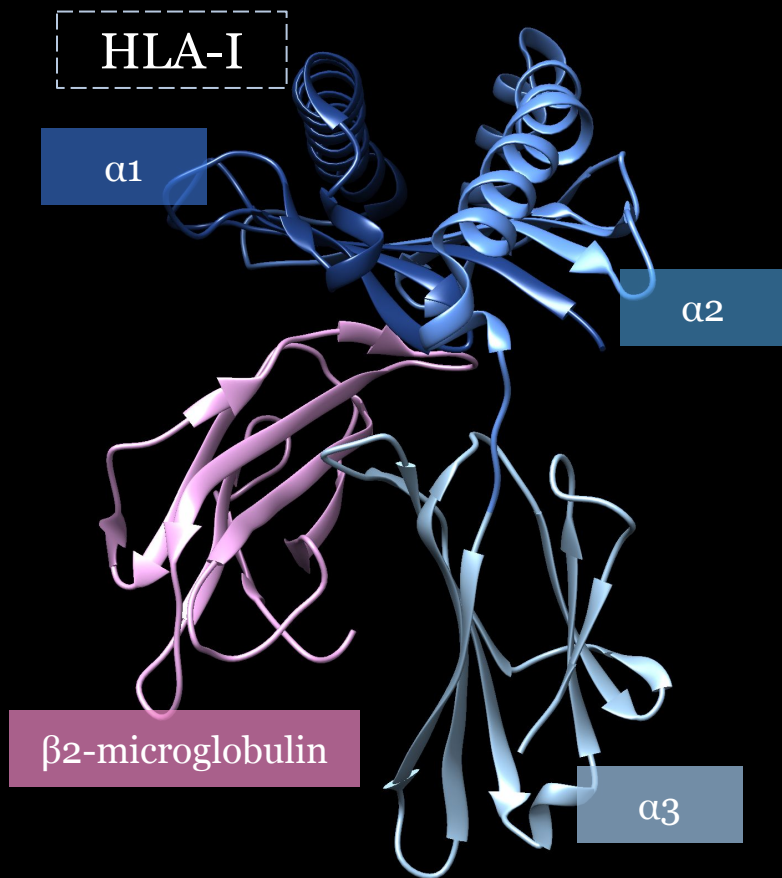
β 2-microglobulin

HLA-II

α -chain

β -chain

HLA structure | Domains



HLA structure | SCOP classification

HLA-I

$\alpha 3$ domain and
 $\beta 2$ -microglobulin



HLA-II

$\alpha 2$ and $\beta 2$ domains



■ β -sheet
■ Helix

Class

All beta proteins



Fold

Immunoglobulin-like
beta-sandwich



Domain

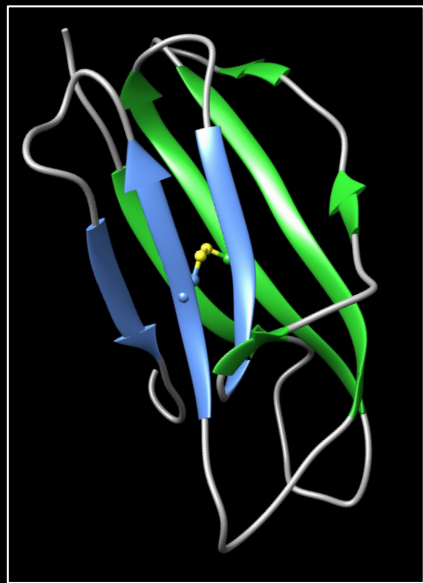
Immunoglobulin (Ig)
domain-like



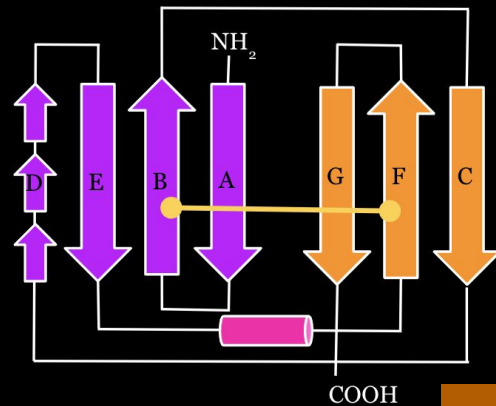
Family

C1 set domains-like

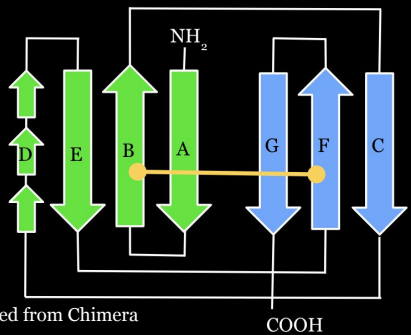
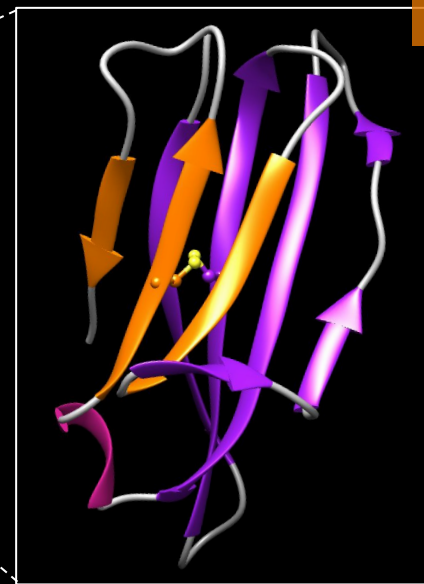
HLA-I structure | Ig-like beta-sandwich



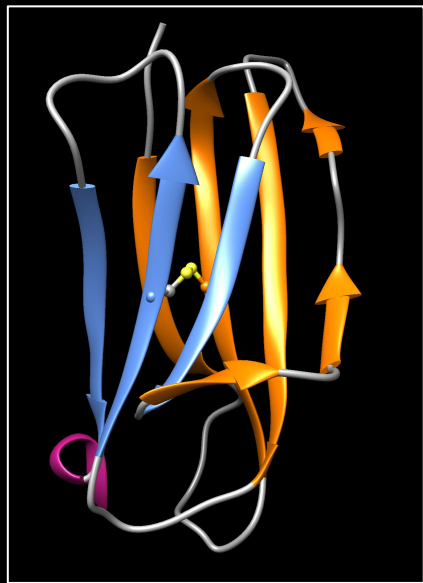
β 2-microglobulin



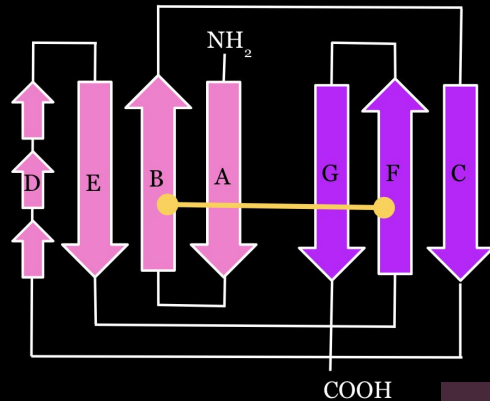
α 3



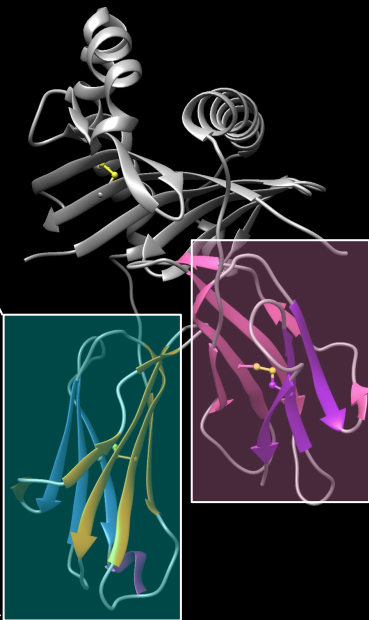
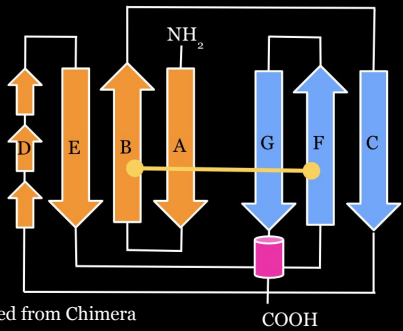
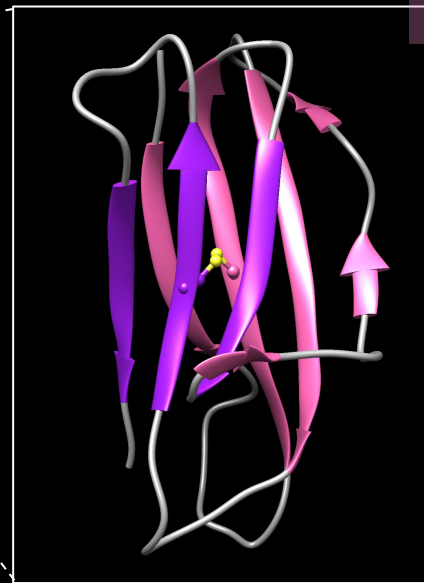
HLA-II structure | Ig-like beta-sandwich



$\beta 2$



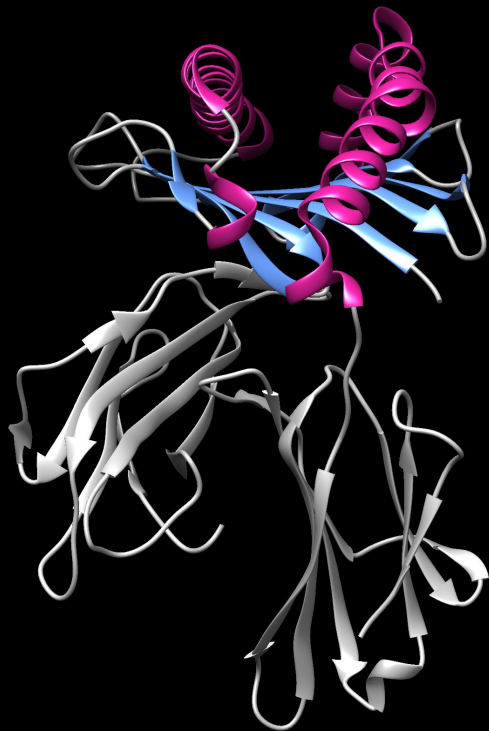
$\alpha 2$



HLA structure | SCOP classification

HLA-I



$\alpha 1$ and $\alpha 2$ domains

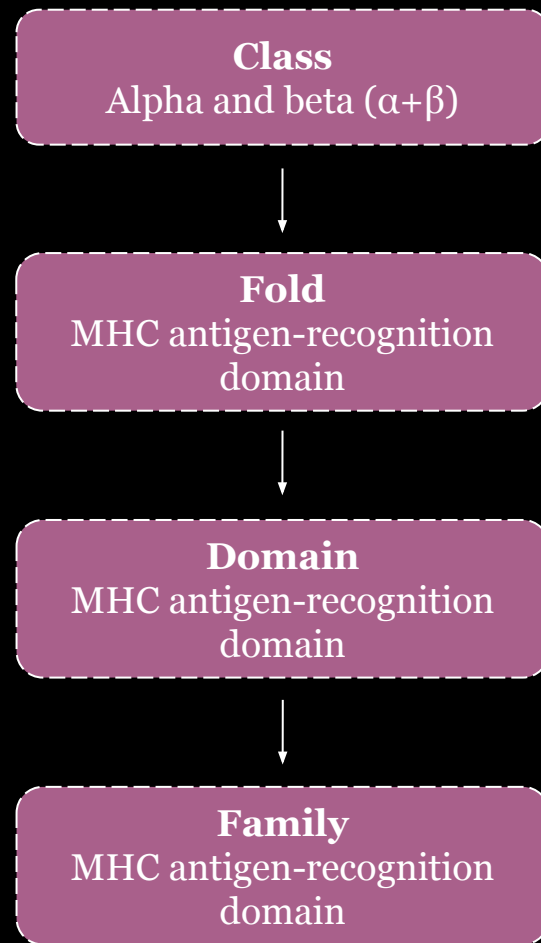


HLA-II

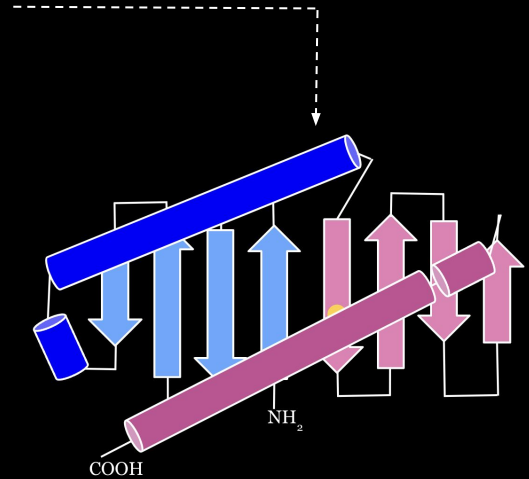
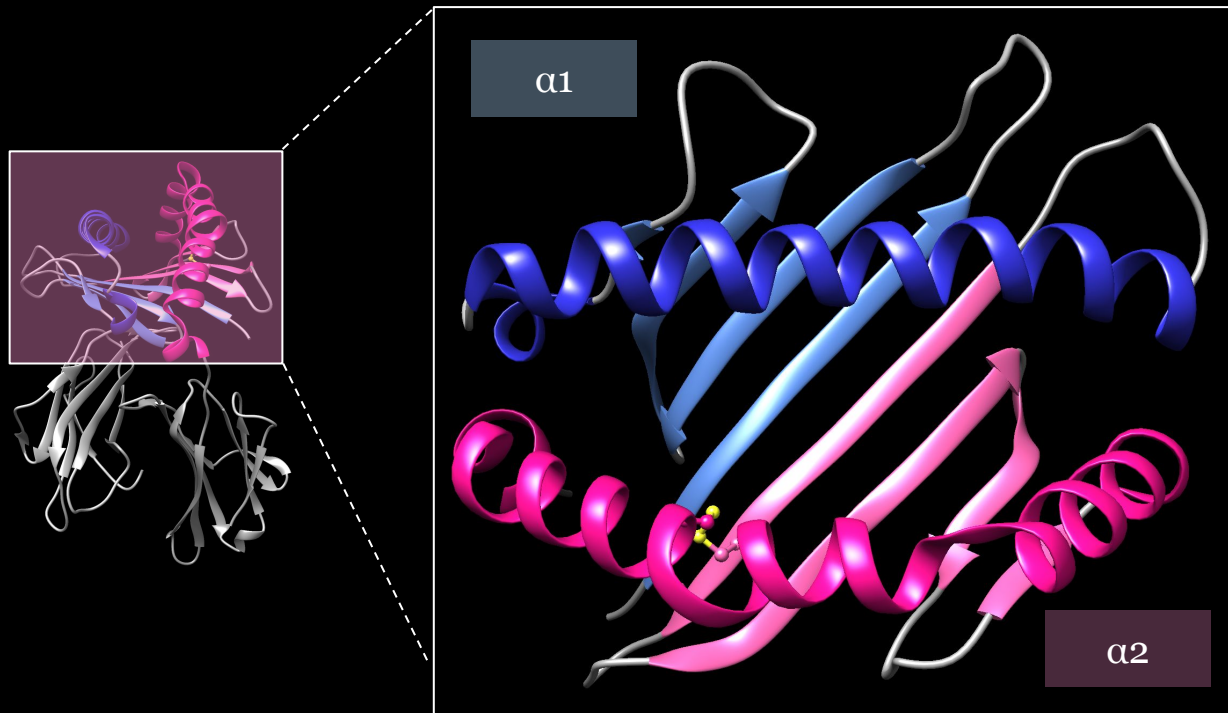
$\alpha 1$ and $\beta 1$ domains



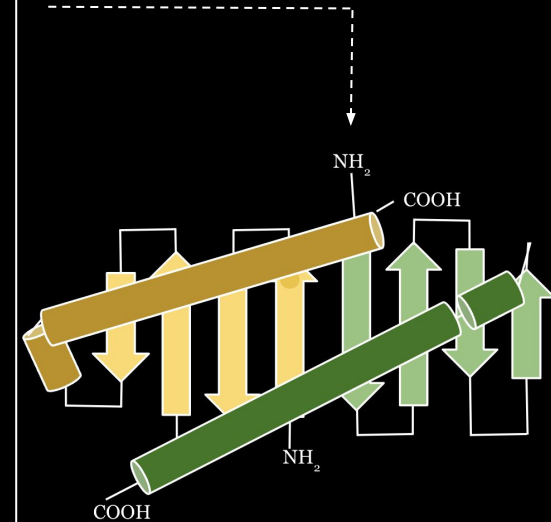
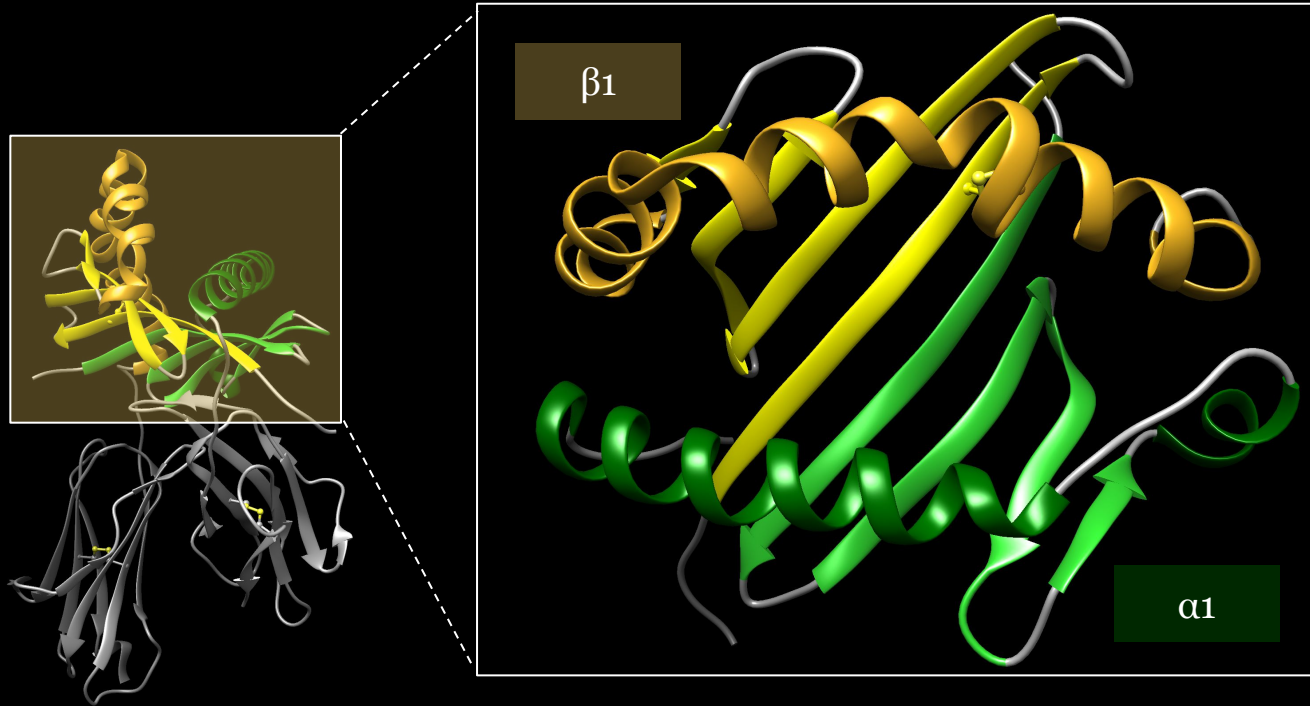
 β -sheet
 Helix



HLA-I structure | MHC antigen-recognition domain

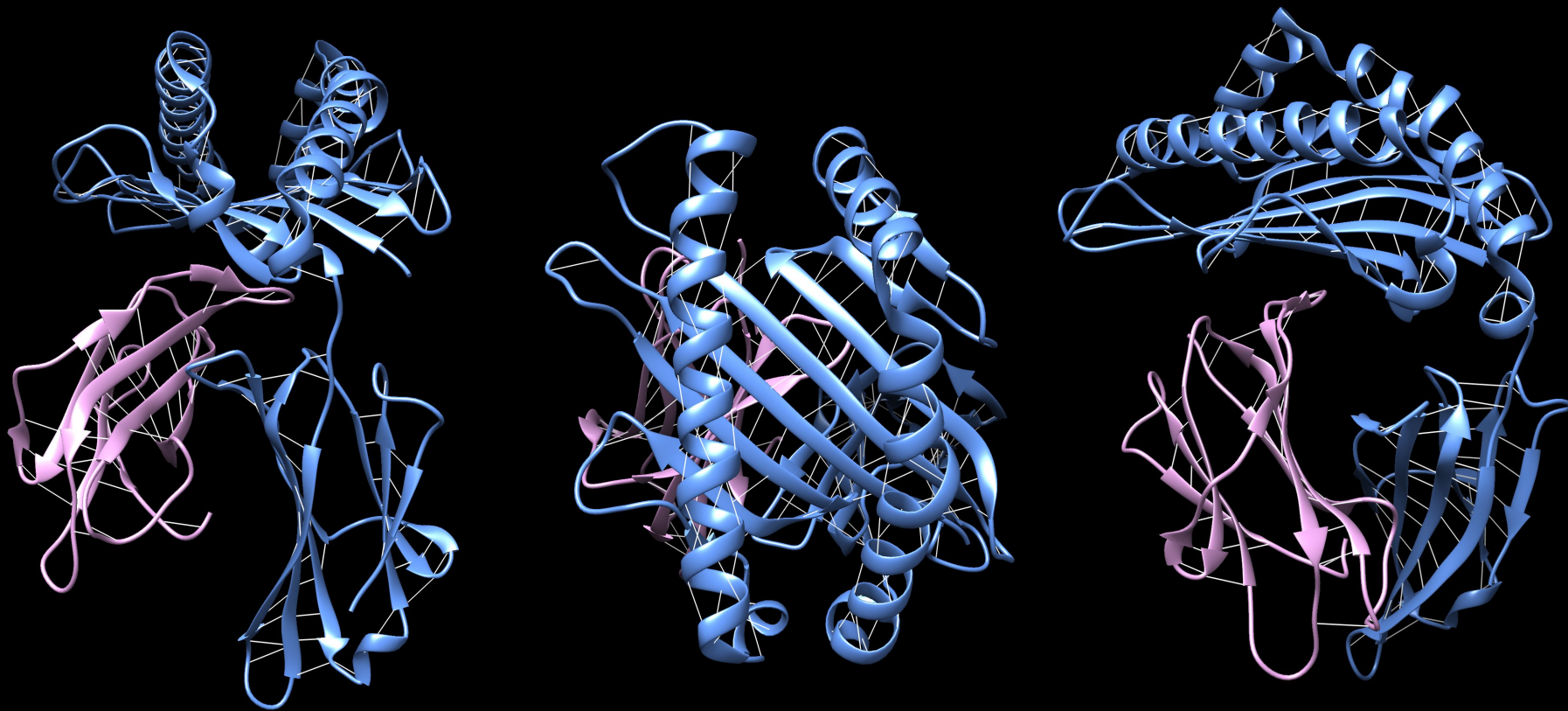


HLA-II structure | MHC antigen-recognition domain



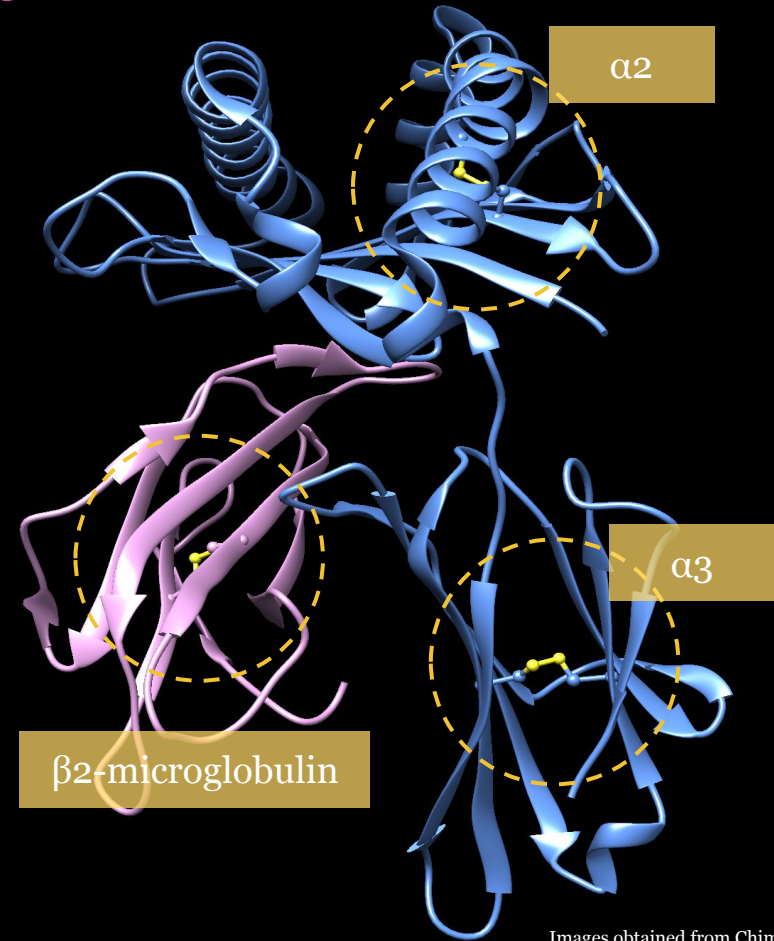
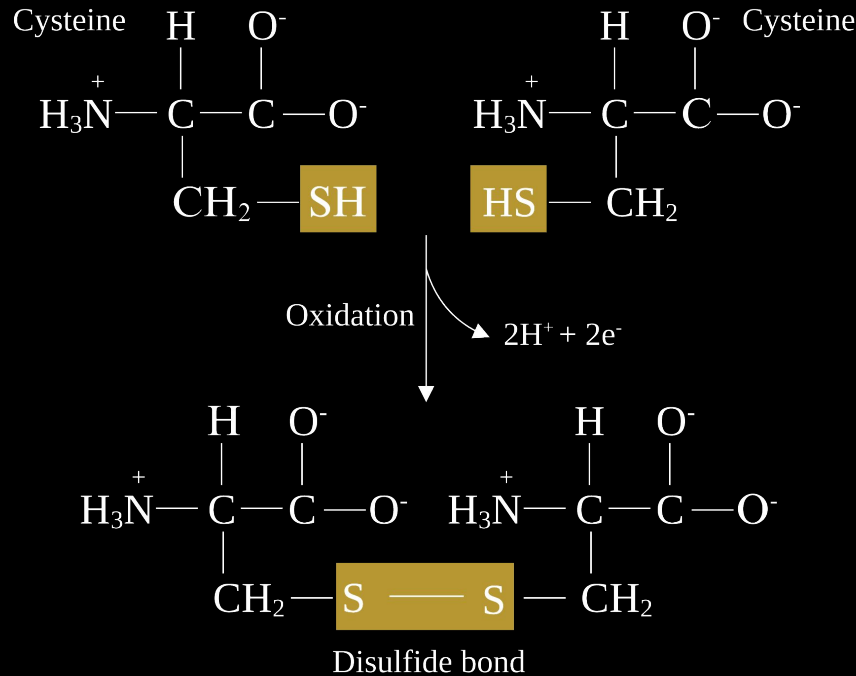
Structure stabilization| Intrachain hydrogen bonds

Intrachain hydrogen bonds are important to **stabilize** protein structures.



Structure stabilization| Disulfide bonds

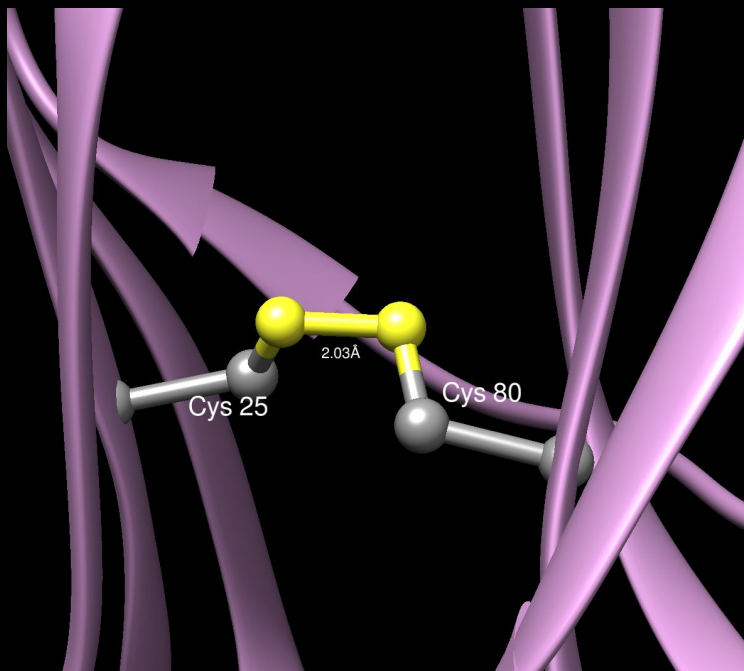
Disulfide bonds are **covalent** bonds that form after the oxidation of two sulfhydryl groups. They are highly **strong** and so, they can **stabilize** tertiary and quaternary structures of proteins.



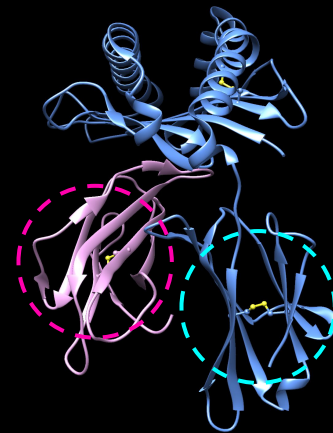
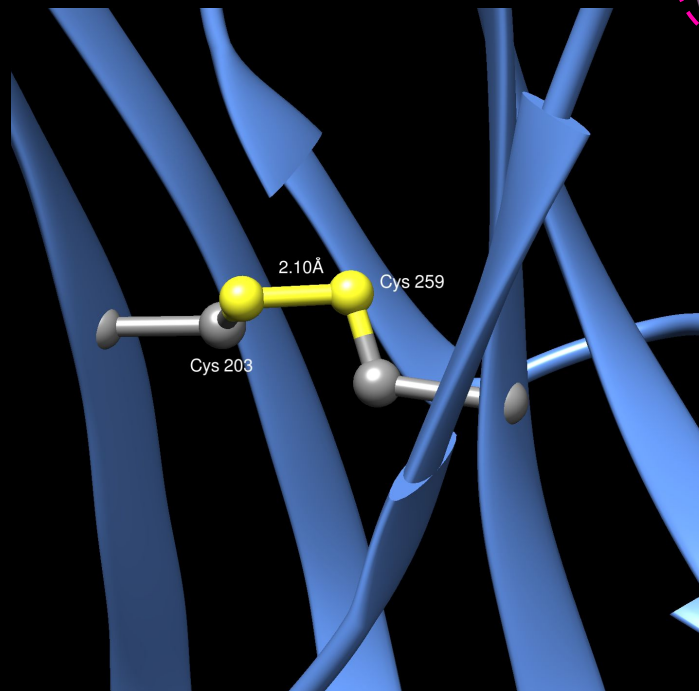
Structure stabilization| Disulfide bonds

The disulfide bonds link the two sheets of the β -sandwich structure in β 2-microglobulin and the α 3 domain.

β 2-microglobulin



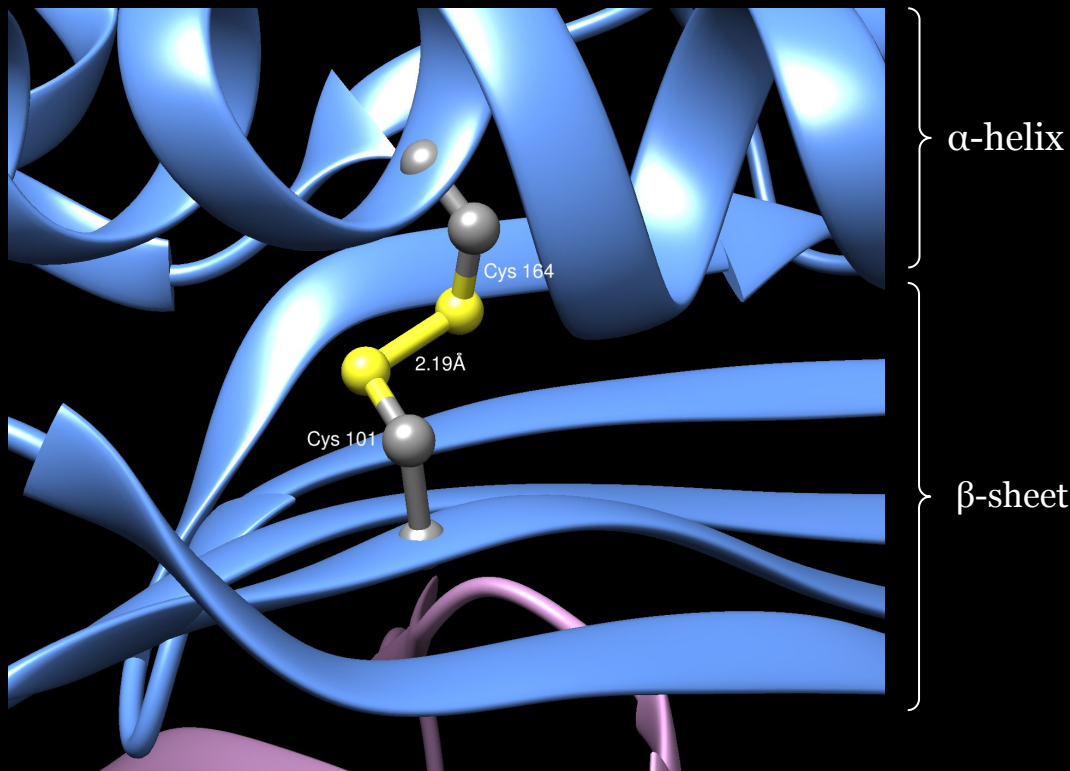
α 3



Structure stabilization| Disulfide bonds

The disulfide bond links the α -helix with the β -sheet in the $\alpha 2$ domain.

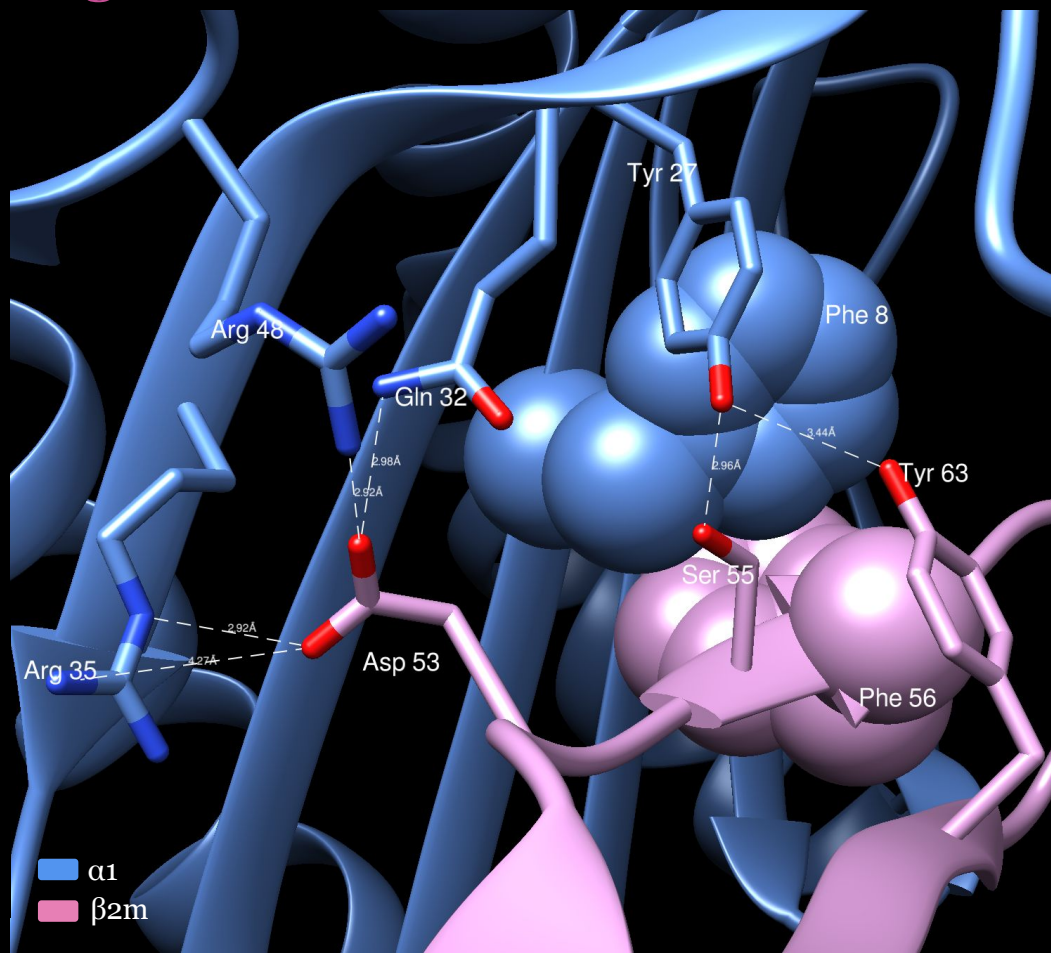
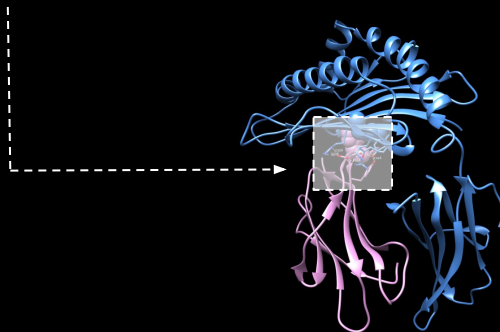
$\alpha 2$



Structure stabilization | β 2-microglobulin and α 1 interactions

The main interactions between β 2-microglobulin (β 2m) and the α 1 domain are the following ones:

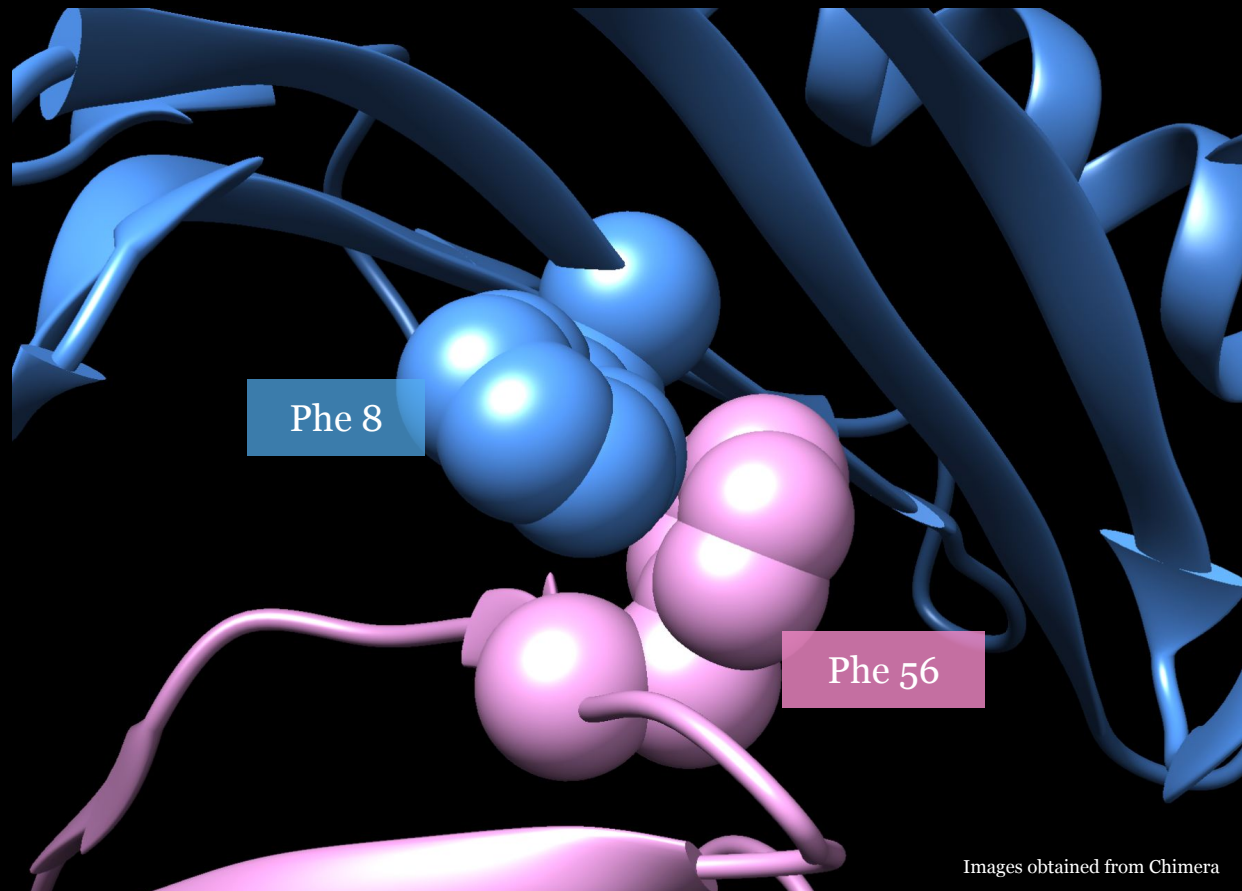
β 2m	α 1	Type of bond	Distance (Å)
Asp 53	Gln 32	H-Bond	2.98
	Arg 35	Ionic bond	4.27
	Arg 48	Ionic bond	2.92
Ser 55	Tyr 27	H-Bond	2.96
Phe 56	Phe 8	Hydrophobic	
Tyr 63	Tyr 27	H-Bond	3.44



Structure stabilization | β 2-microglobulin and α 1 interactions

Hydrophobic interaction

The **hydrophobic interaction** is described as the tendency of **nonpolar** groups or residues to aggregate in water solution.



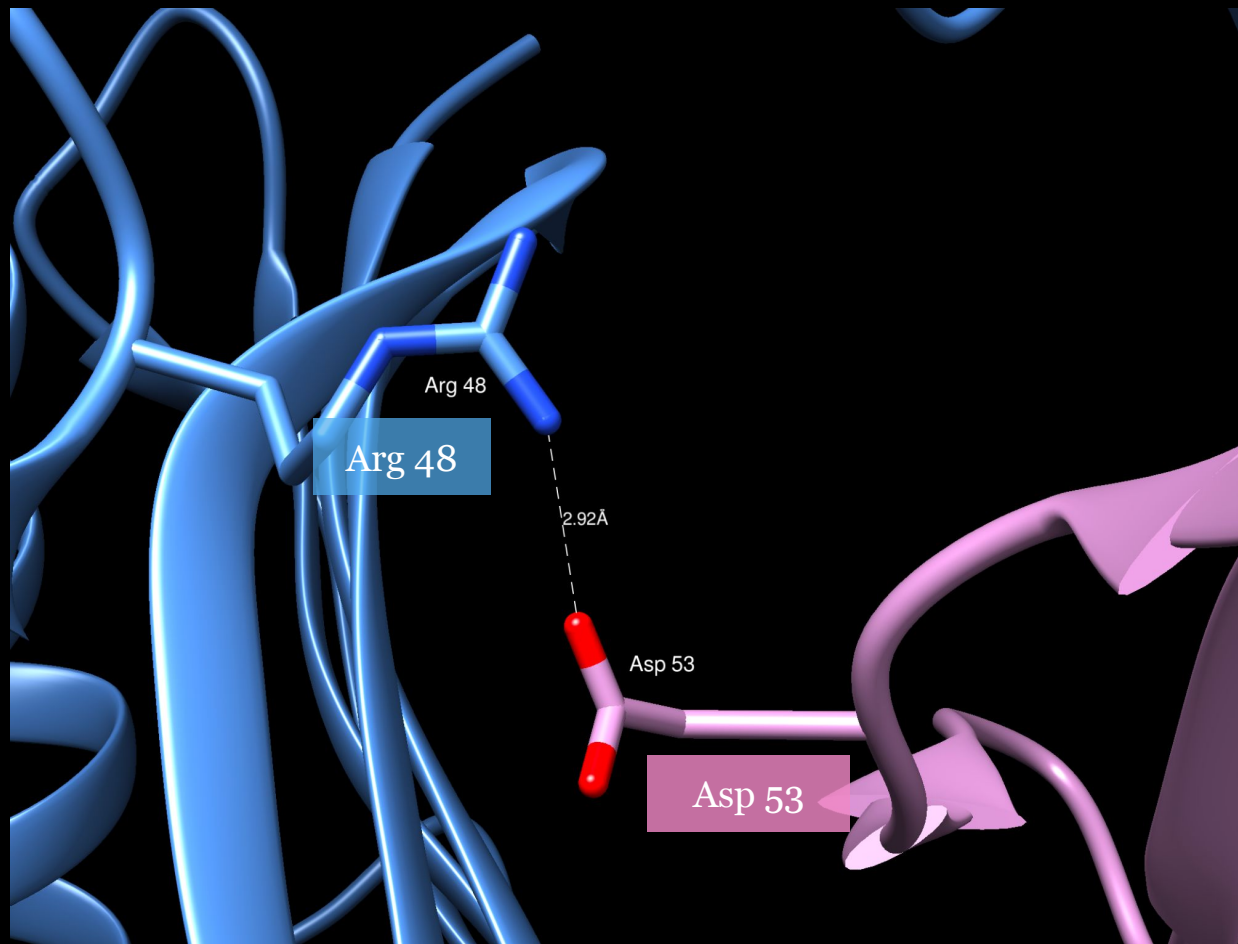
Structure stabilization | $\beta 2$ -microglobulin and $\alpha 1$ interactions

Ionic bond

An **ionic bond** is an **electrostatic interaction** between two oppositely charged groups.



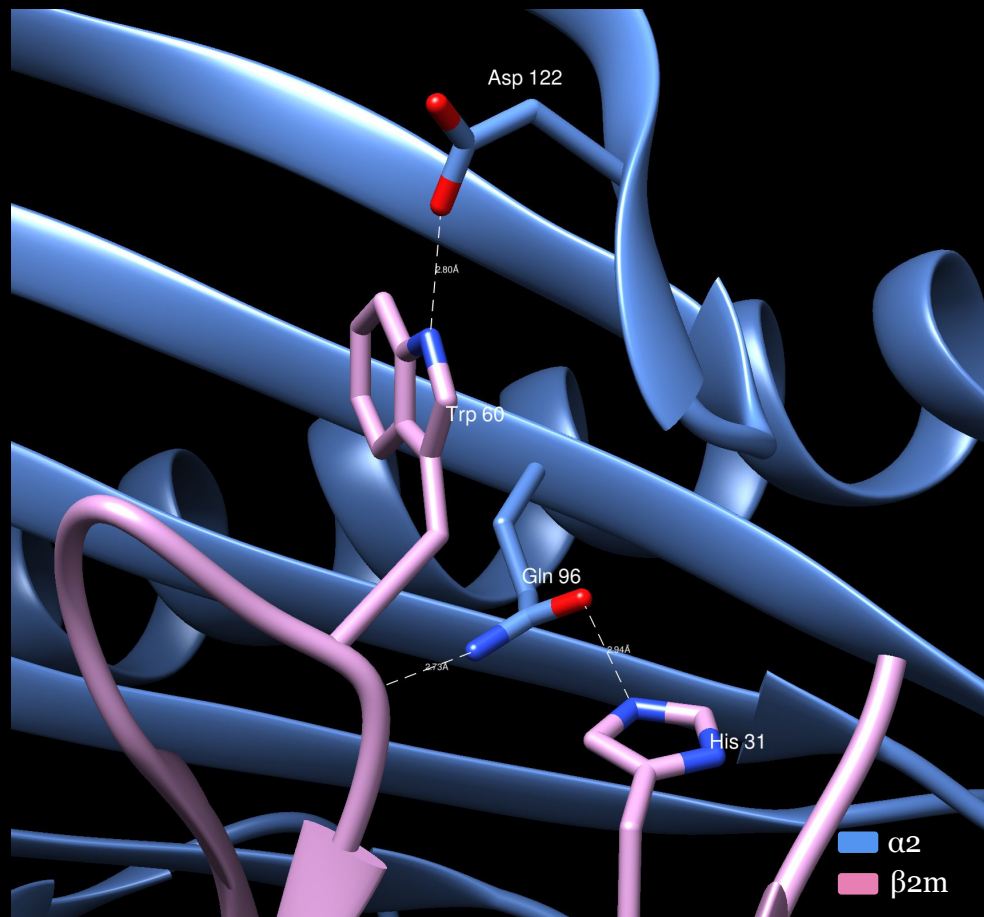
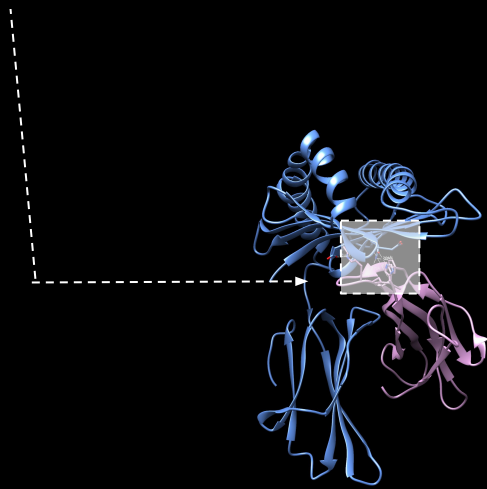
■ $\alpha 1$
■ $\beta 2m$



Structure stabilization | β 2-microglobulin and α 2 interactions

The main interactions between β 2-microglobulin (β 2m) and the α 2 domain are the following ones:

β 2m	α 2	Type of bond	Distance (Å)
His 31	Gln 96	H-Bond	2.94
Trp 60		H-Bond	2.73
	Asp 122	H-Bond	2.80



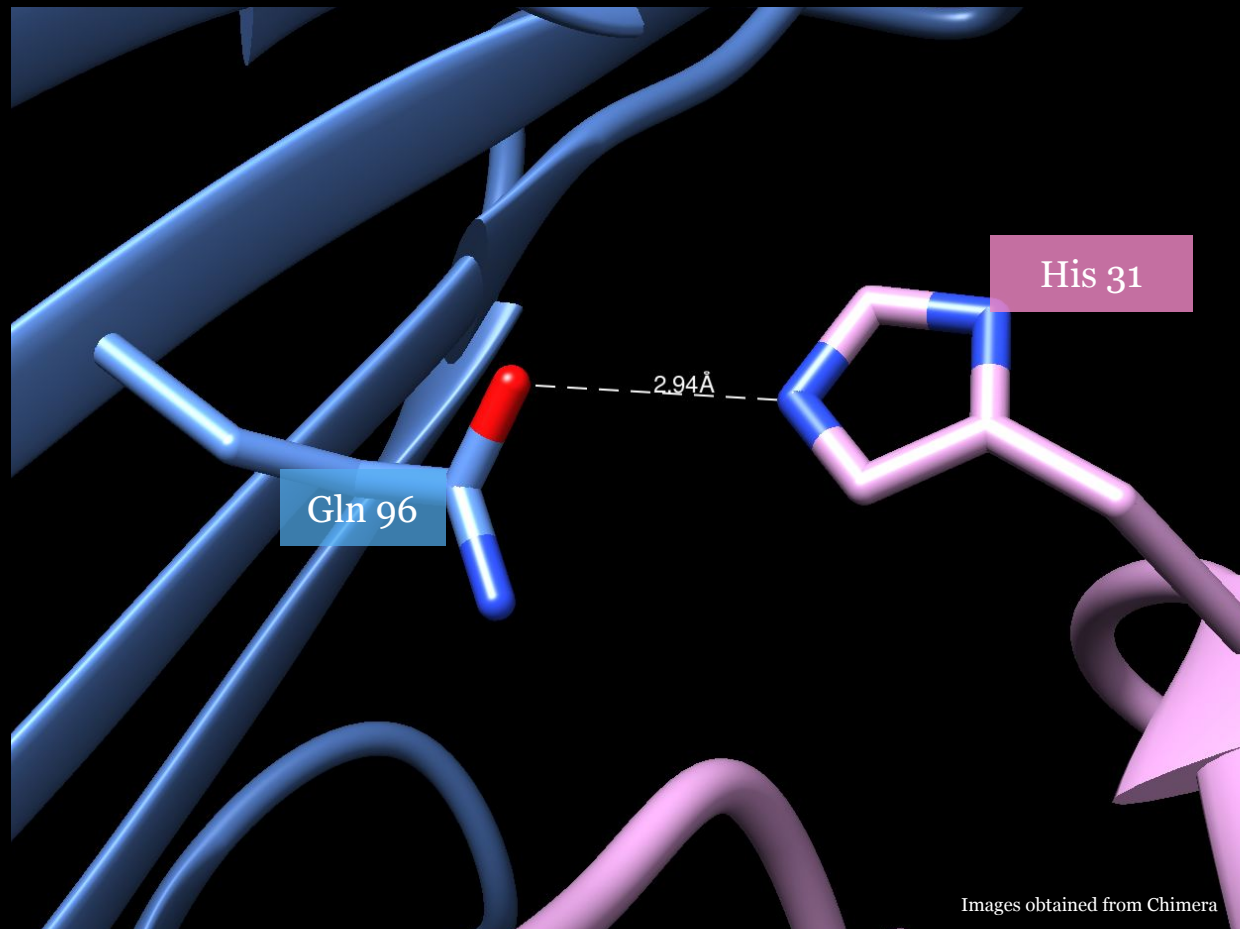
Structure stabilization | β 2-microglobulin and α 2 interactions

Hydrogen bond

Hydrogen bonds are **dipole-dipole attractions** between an electronegative atom bonded to a hydrogen (bonded to a second electronegative atom).



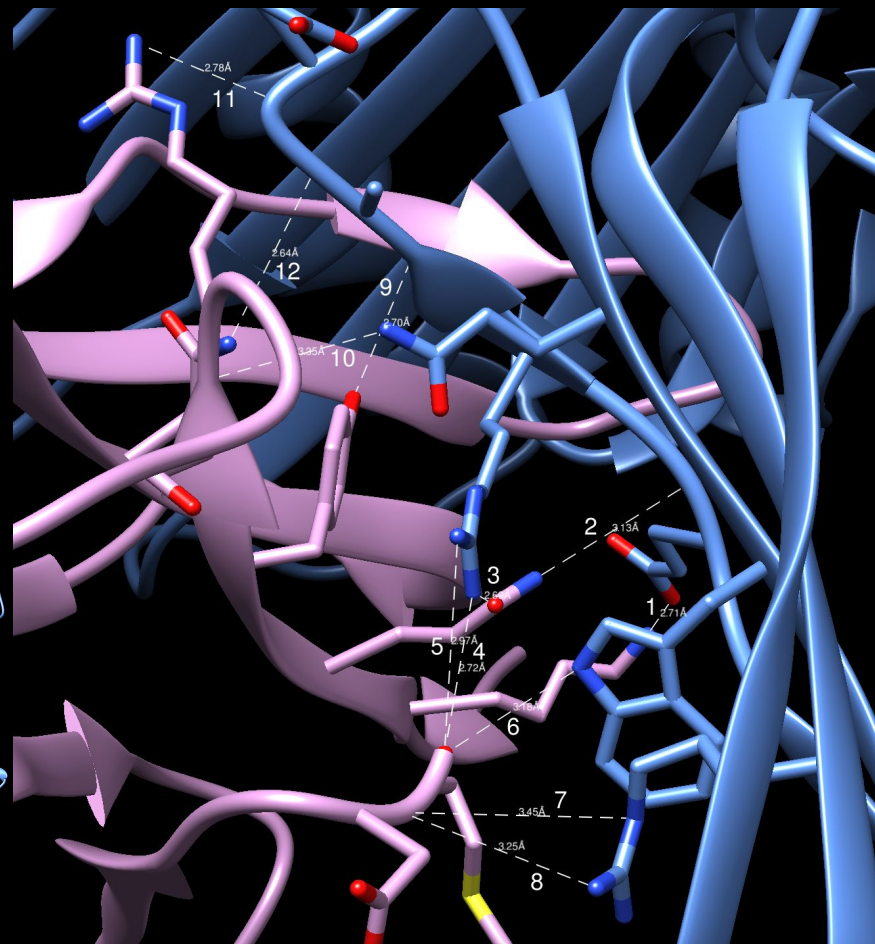
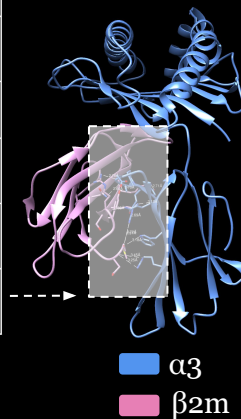
■ α 2
■ β 2m



Structure stabilization | β 2-microglobulin and α 3 interactions

The main interactions between β 2-microglobulin (β 2m) and the α 3 domain are the following ones:

β 2m	α 2	Type of bond	Distance (Å)
Lys 6	Glu 232	Salt bridge	2.71
Gln 8		H-Bond	3.13
	Arg 234	H-Bond	2.69
Tyr 10	Pro 235	H-Bond	2.70
Ser 11	Gln 242	H-Bond	3.35
Arg 12	Gly 237	H-Bond	2.78
Asn 24	Ala 236	H-Bond	2.54
Asp 98	Arg 202	2 H-Bond	3.25/3.45
Met 99	Arg 234	2 H-Bond	2.72/2.97
	Trp 244	H-Bond	3.18



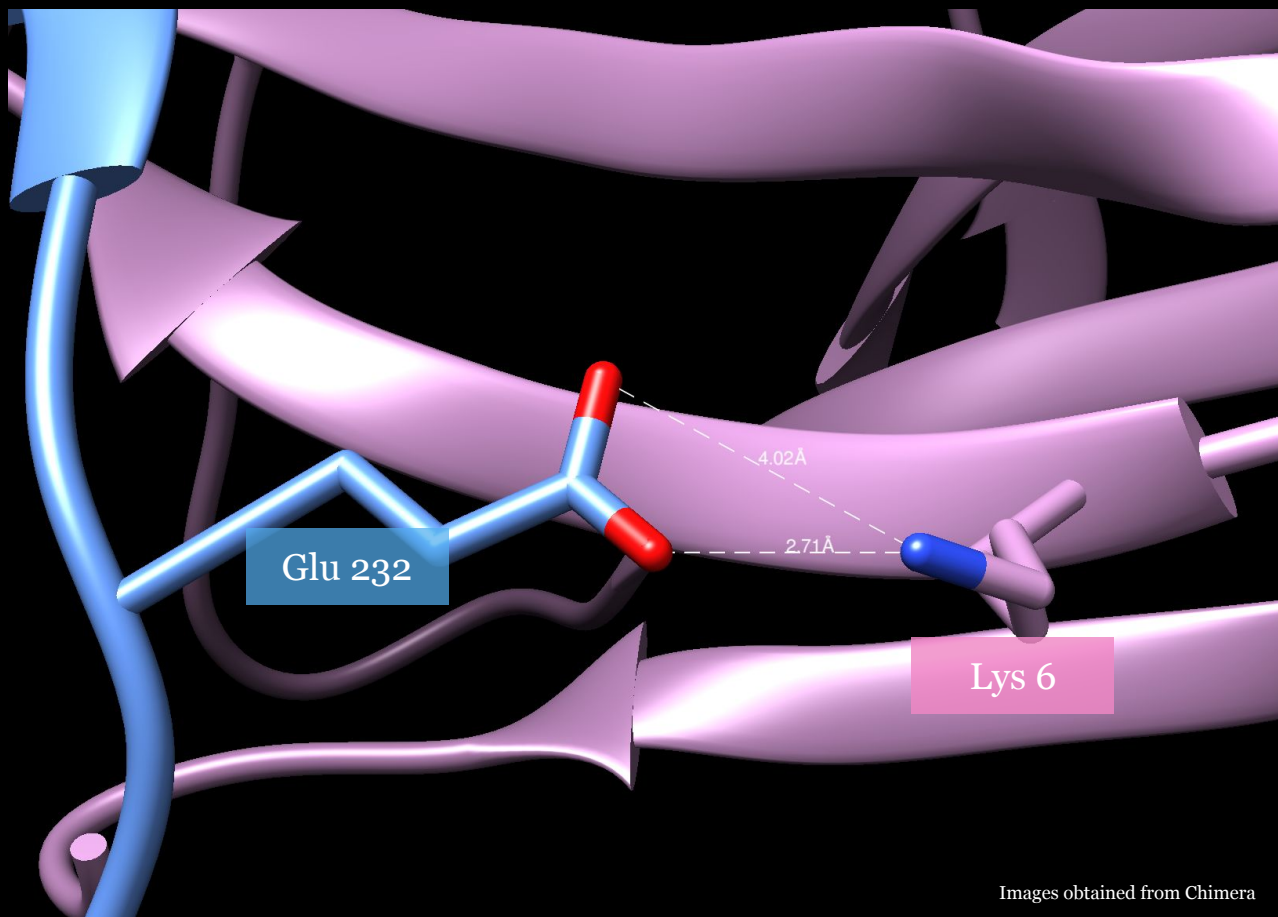
Structure stabilization | β 2-microglobulin and α 3 interactions

Salt bridge

A **salt bridge** combines electrostatic interactions and hydrogen bonds.



■ α 3
■ β 2m



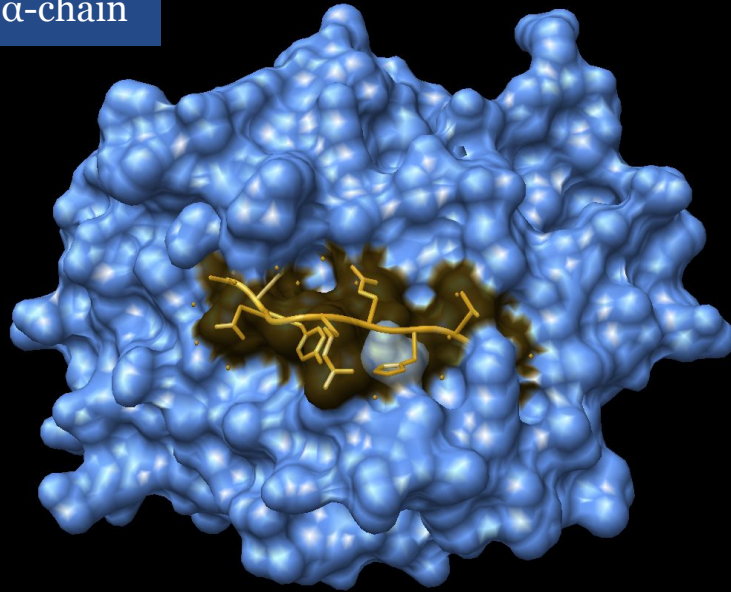


03

Binding groove:
pockets and interactions

HLA I and HLA II | Binding groove

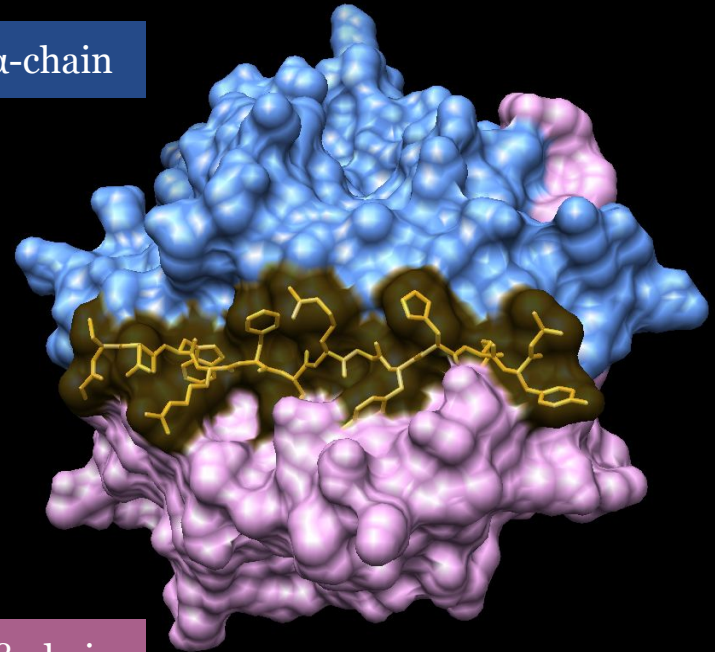
α -chain



α -chain

HLA-I
6 pockets (A-F)
Closed binding cleft

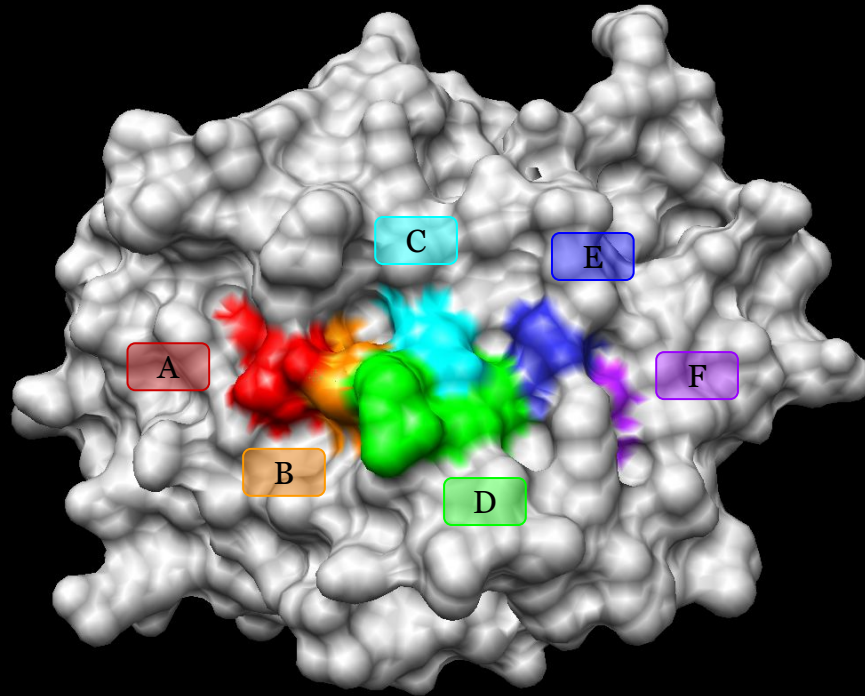
α -chain



β -chain

HLA-II
9 pockets (A-I)
Open binding cleft

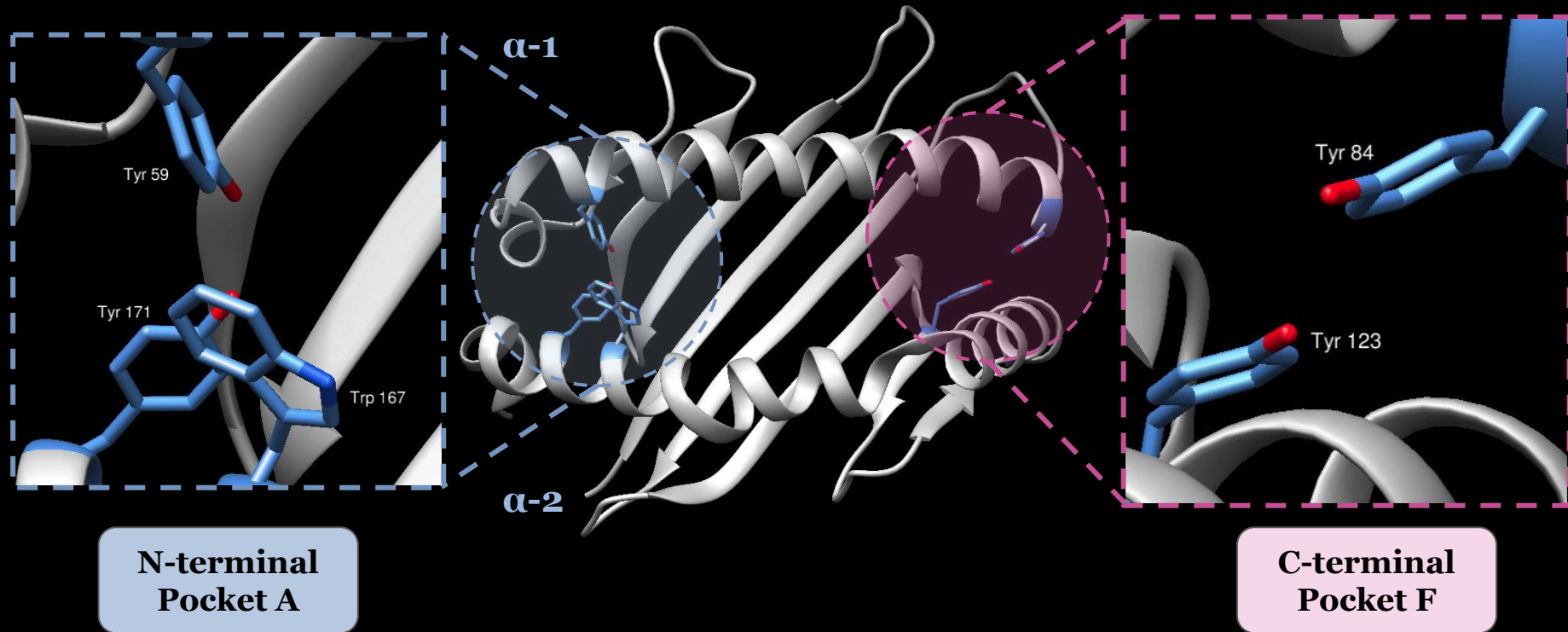
HLA I | Binding groove



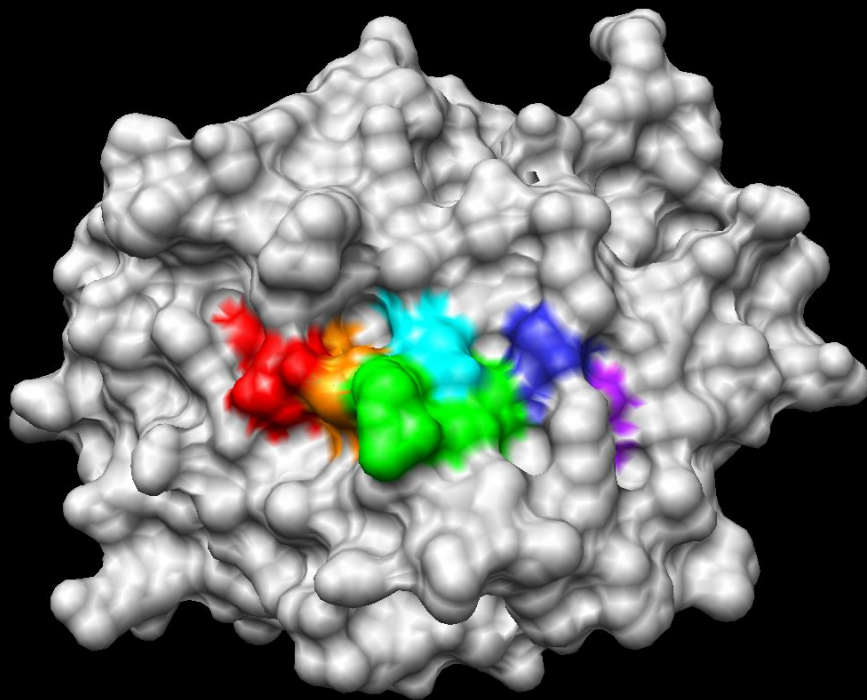
Pocket	Role of the pocket
A	Wall of the N-terminal part of the binding cleft
B	Bind primary anchor residue P2
C	Bind secondary anchor residue at P3 and P5/P6 when presents, face pocket D
D	Bind secondary anchor residue at P3 and P5/P6 when presents, face pocket C
E	Overlap with C/D pockets and secondary anchor residue at P5/P6 when presents and the C-terminal part of the peptide
F	Bind primary anchor residue P Ω , wall of the C-terminal part of the binding cleft

Adapted from Nguyen et al.

HLA I | N and C termini

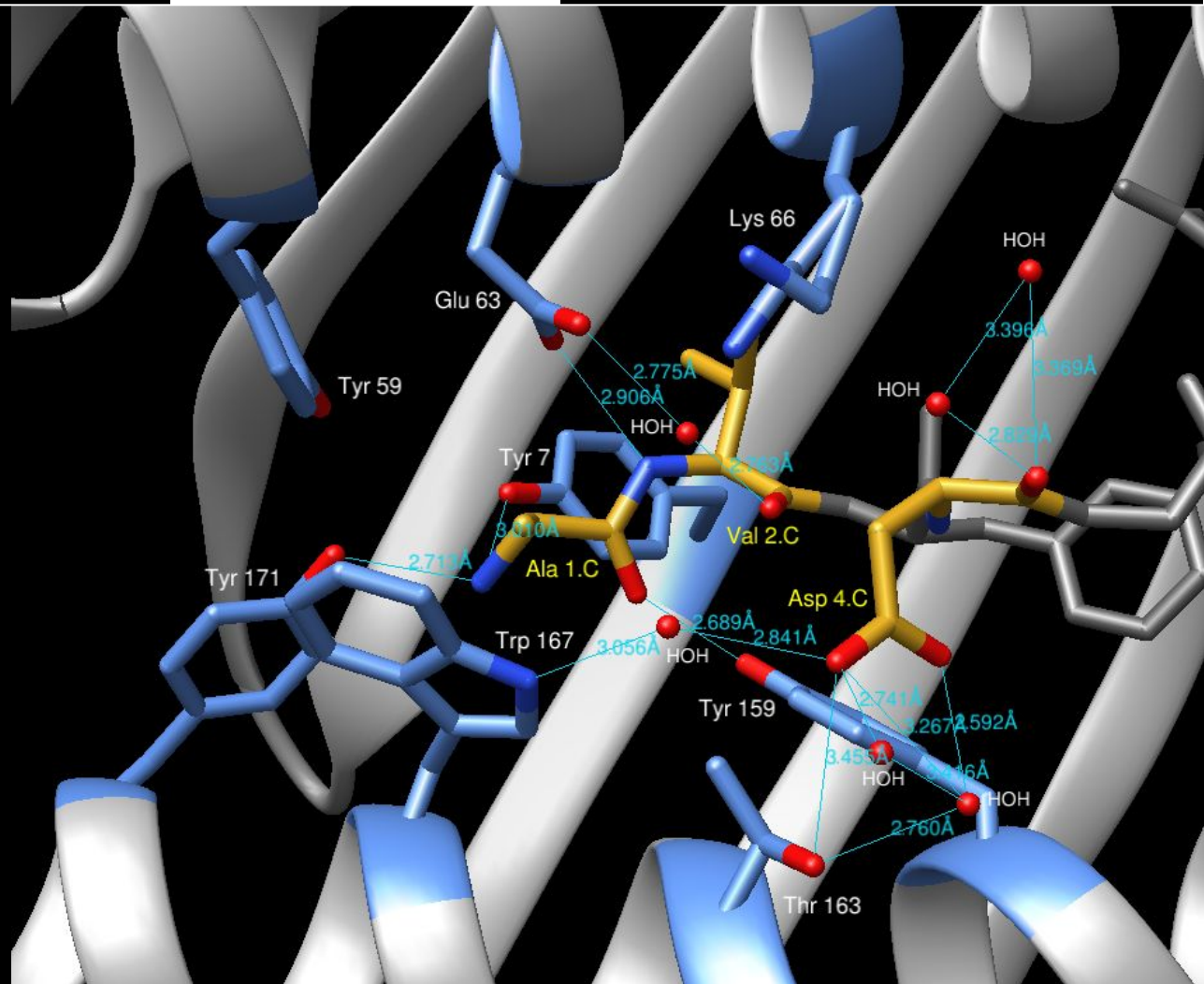
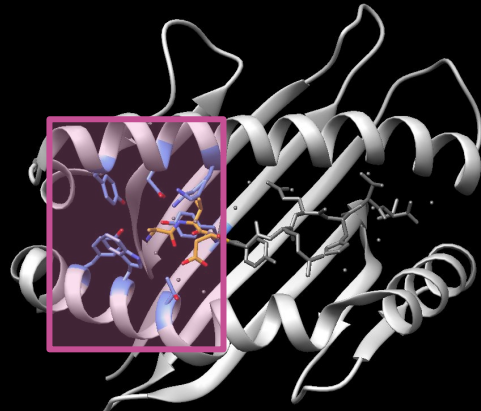
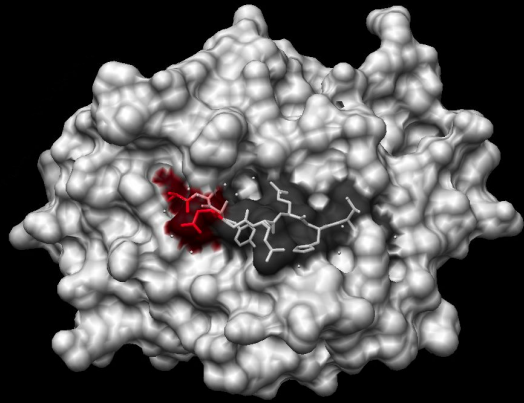


HLA I | Binding groove



MAGE-A4 AVYDGREHTV	
Pocket	Peptide residue
A	Ala 1, Asp 4
B	Val 2
C	Glu 7
D	Tyr 3, Gly 5, Arg 6, His 8
E	Thr 9
F	Val 10

Pocket A

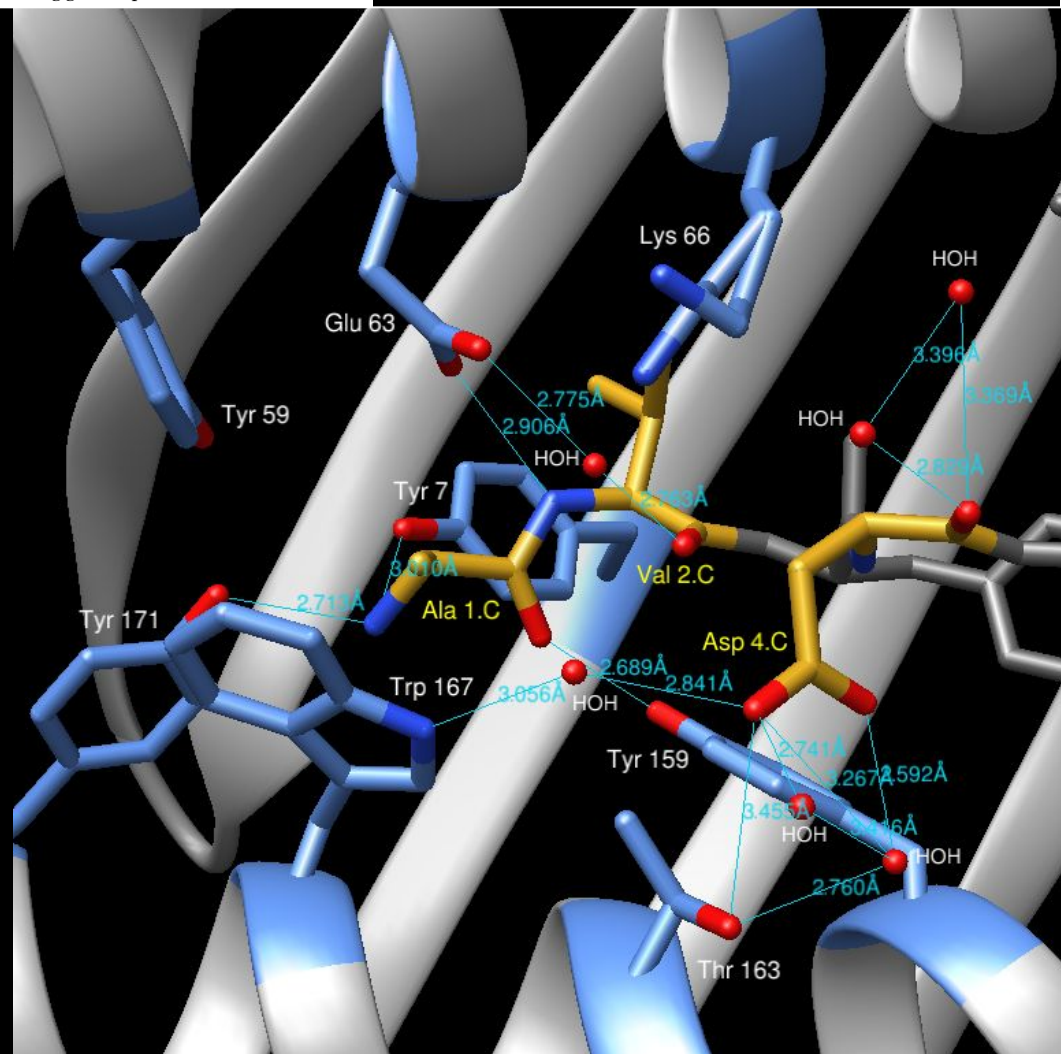


Pocket A

Hydrogen bonds

Peptide	Atom	HLA-I	Atom	Length (Å)
Ala 1	N	Tyr 7	OH	3.01
	O2	Trp 159	OH	2.68
	N	Tyr 171	OH	2.71
	N	Met 5	SD	3.05

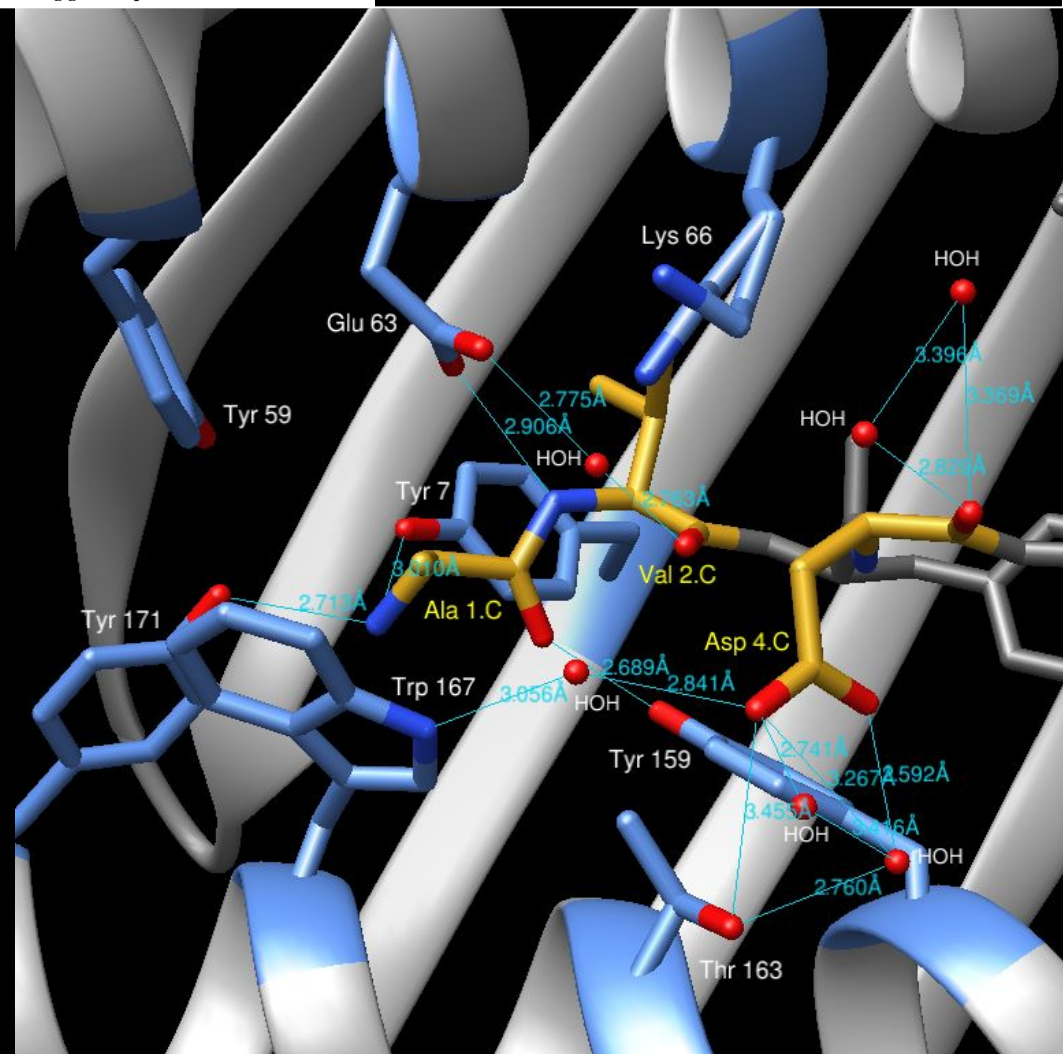
■ Peptide-molecule bond



Pocket A

Hydrogen bonds

Peptide	Atom	HLA-I	Atom	Length (Å)
Val 2	N	Glu 63	OE2	2.90
	O2	HOH 106	HOH	2.76
Asp 4	OD1	HOH 102	O	2.59
	OD2	HOH 102	O	3.26
	OD2	HOH 103	O	2.74
	O2	HOH 107	O	2.82
	OD2	HOH 108	O	2.84
	O2	HOH 114	O	3.36
	OD2	Thr 163	OG1	3.46

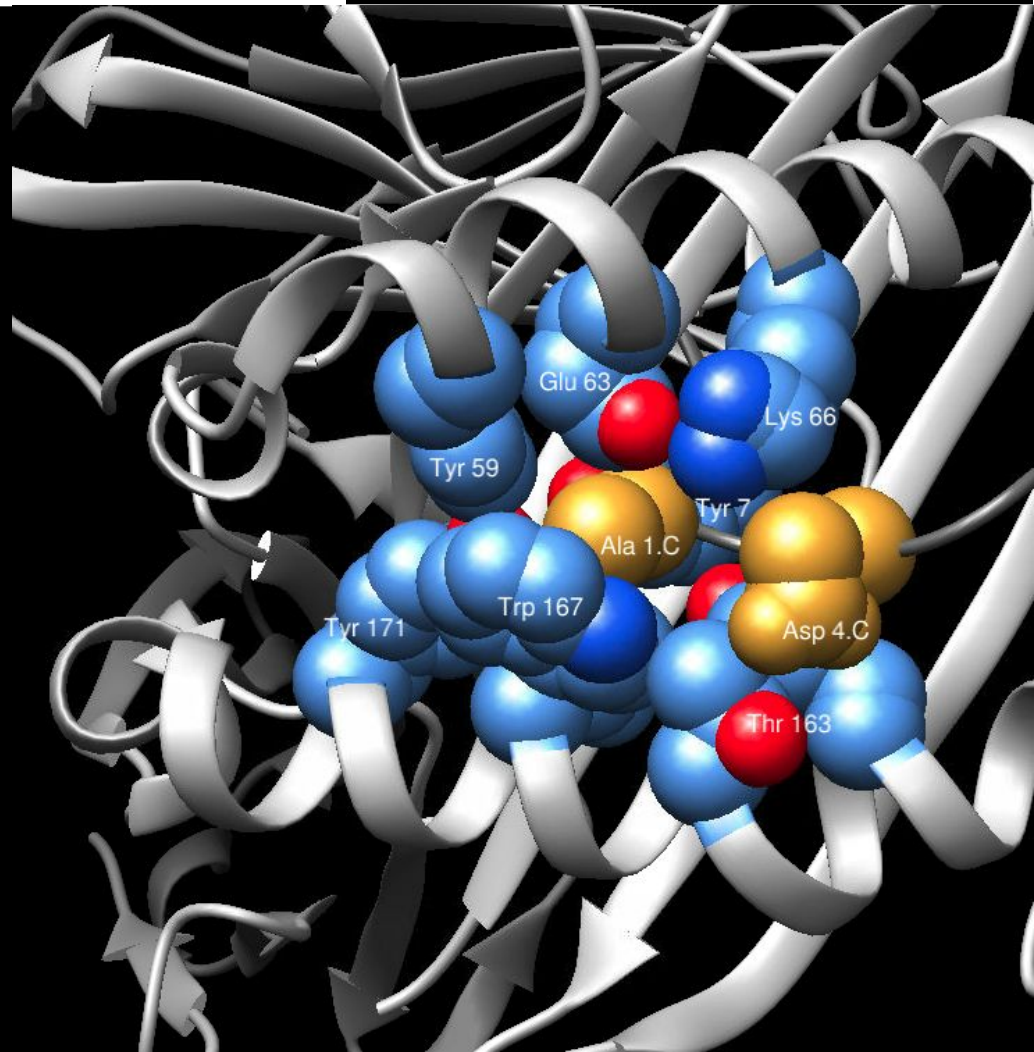


Pocket A

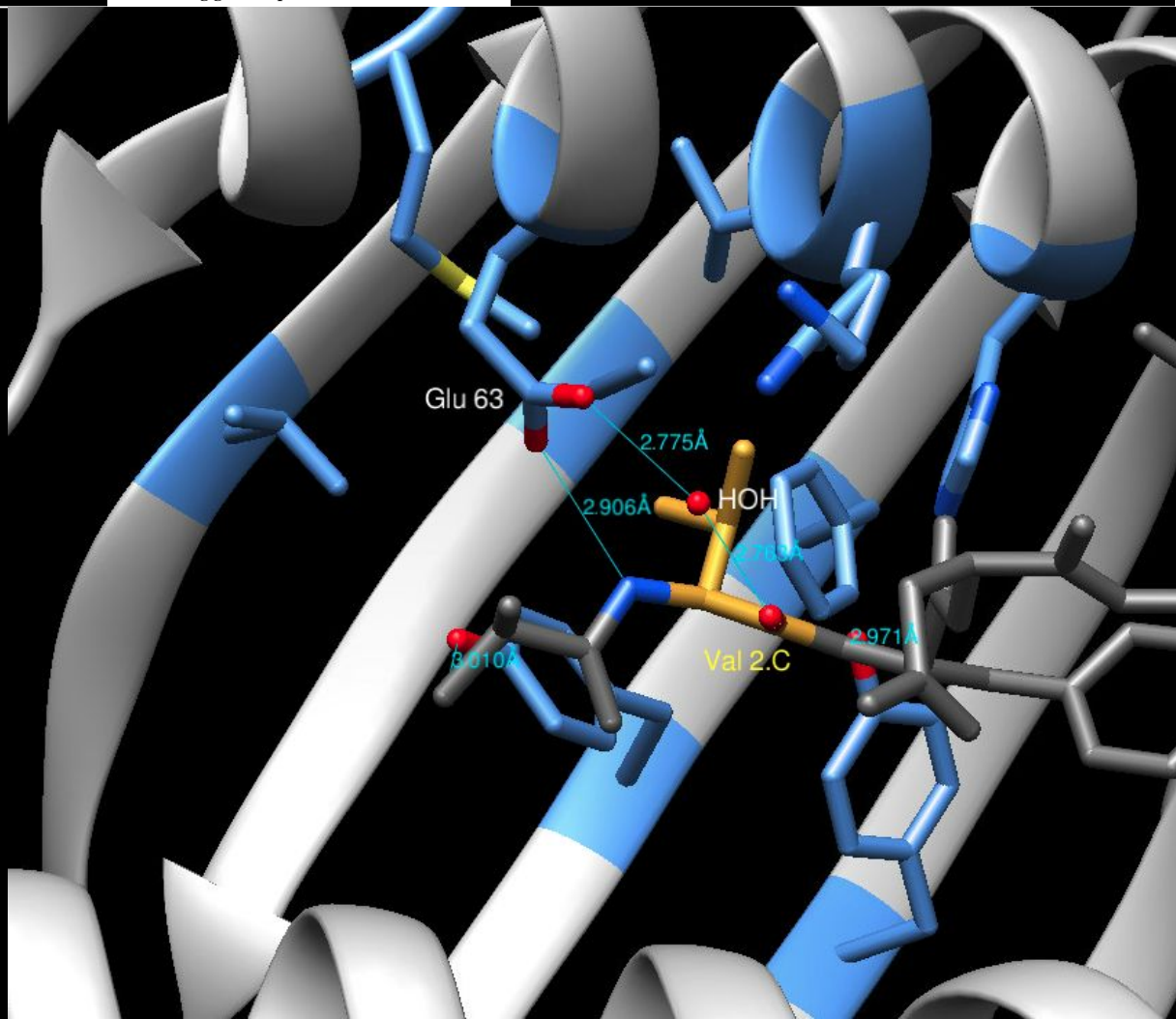
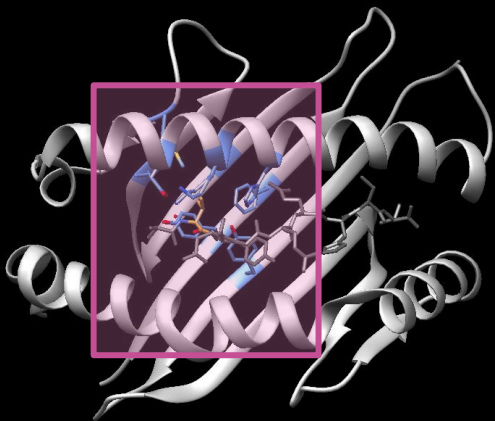
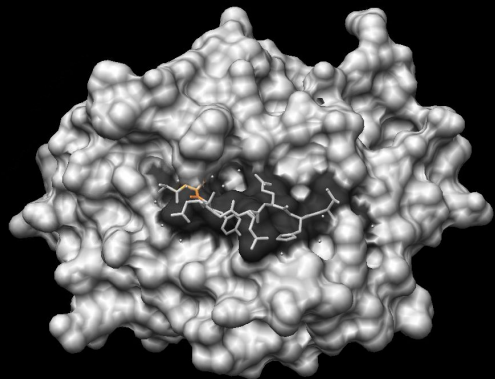
Van der Waals interactions

Peptide	HLA-I
Ala 1	Tyr 7
	Glu 63
	Tyr 59
	Lys 66
	Thr 163
	Trp 167
	Trp 171

■ Non polar residue



Pocket B

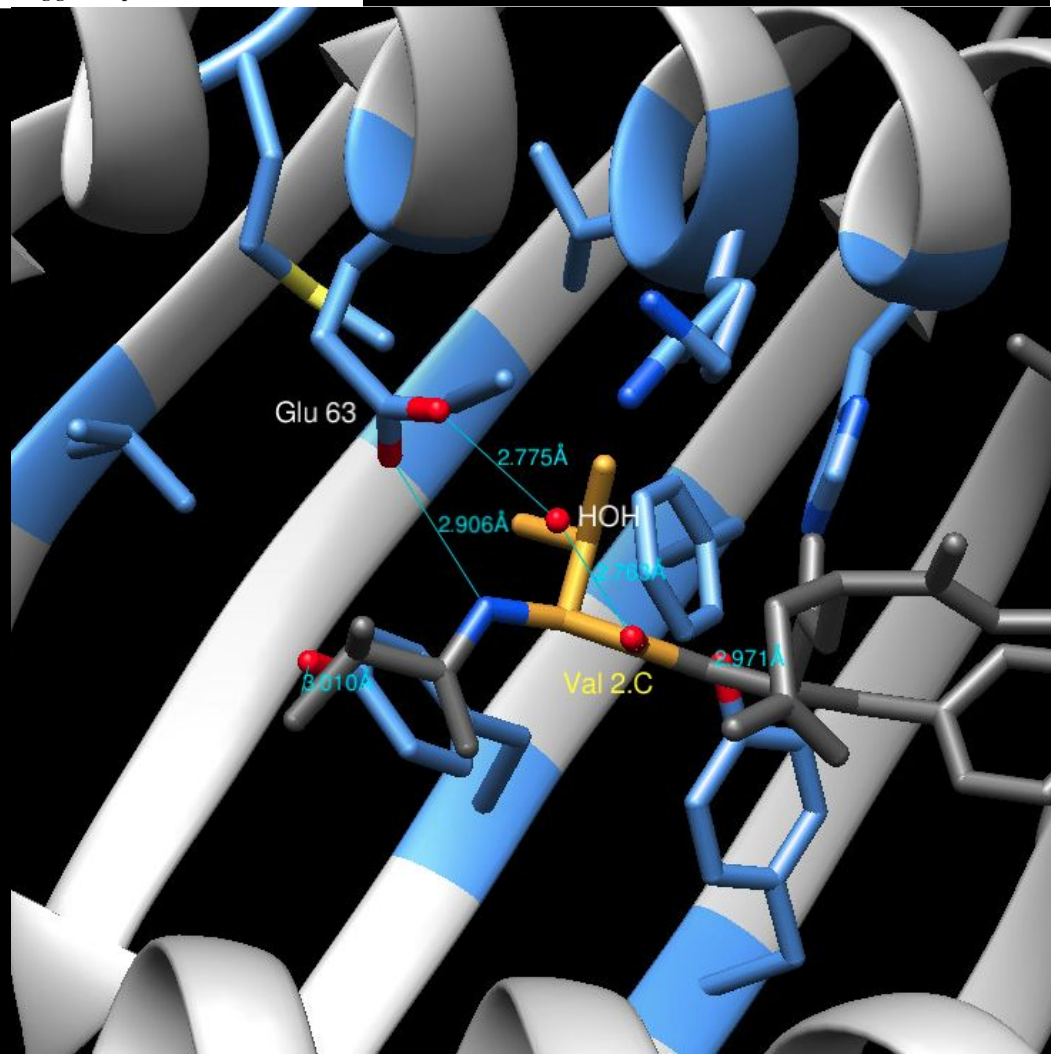


Pocket B

Hydrogen bonds

Peptide	Atom	HLA-I	Atom	Length (Å)
Val 2	N	Glu 63	OE2	2.90
	O2	Glu 63	O2	2.77
	O2	HOH 106	HOH	2.76

■ Peptide-molecule bond

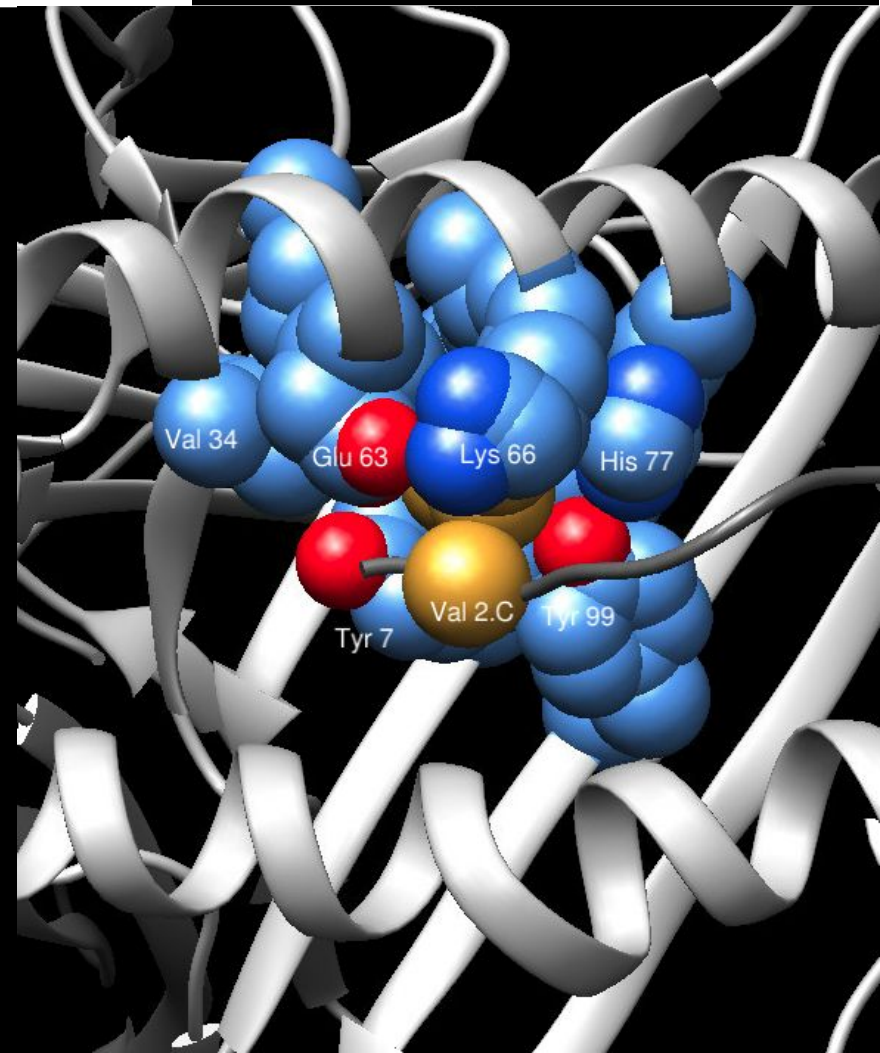


Pocket B

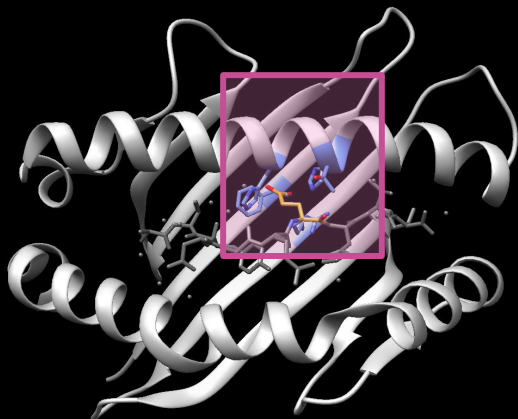
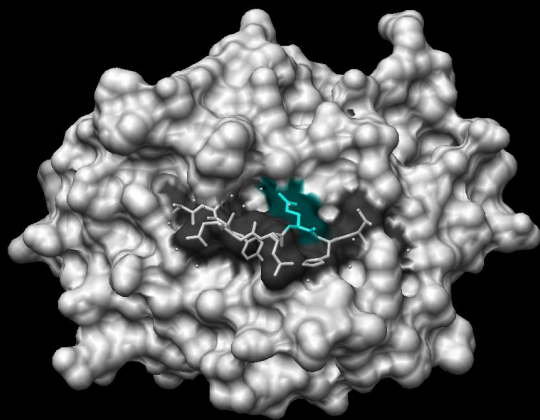
Van der Waals interactions

Peptide	HLA-I
Val 2	Tyr 7
	Glu 63
	Lys 66
	His 77
	Tyr 99

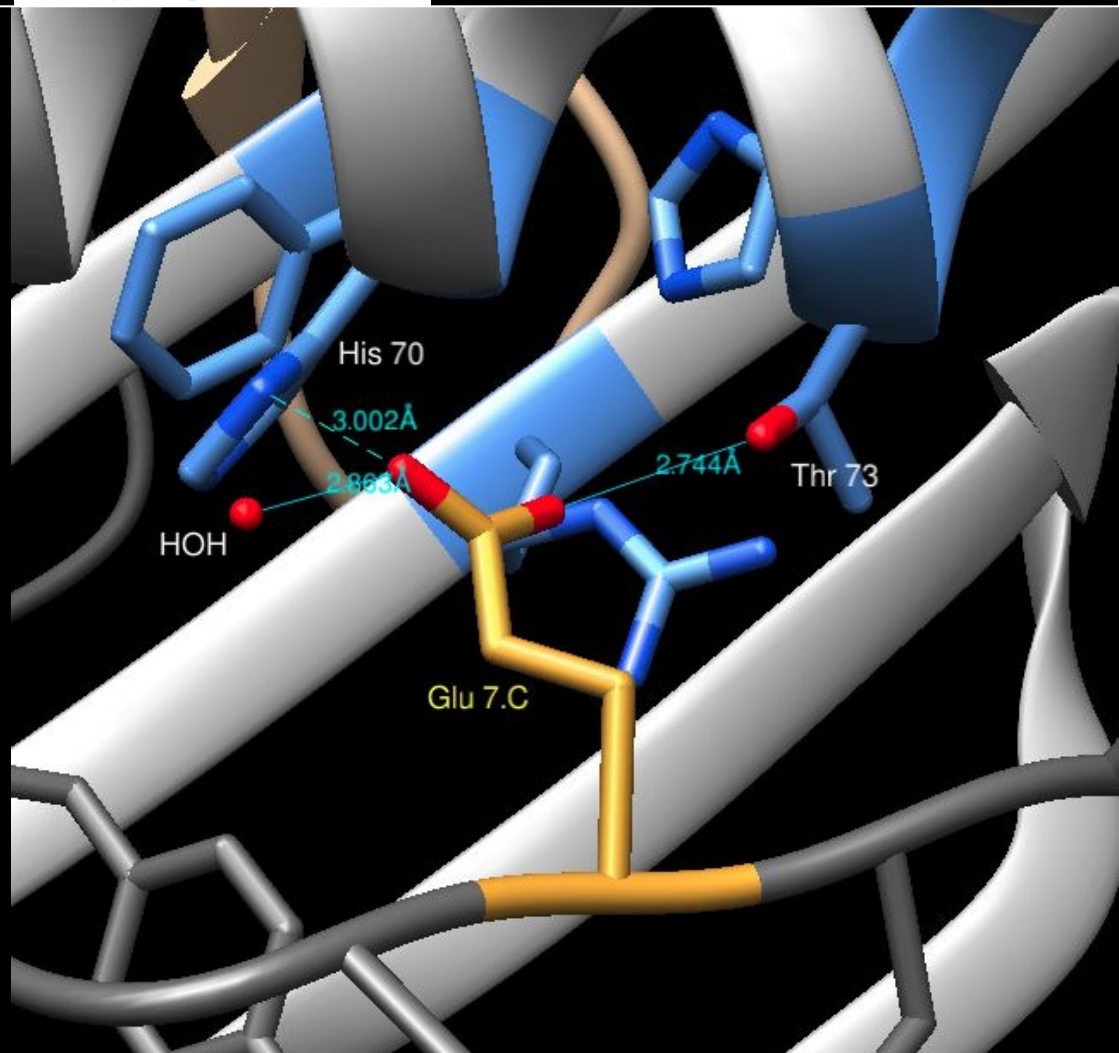
■ Non polar residue



Pocket C



Binding groove: pockets and interactions

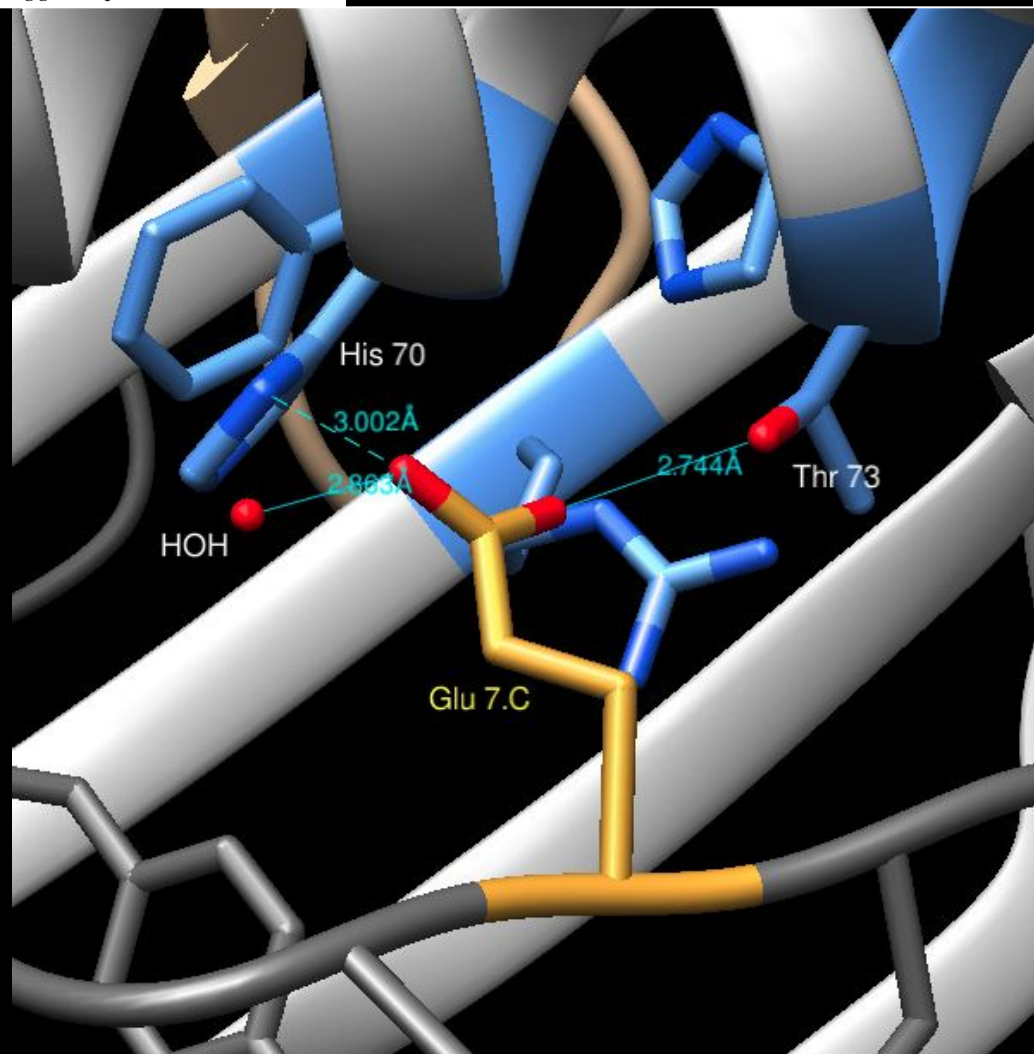


Pocket C

Hydrogen bonds

Peptide	Atom	HLA-I	Atom	Length (Å)
Glu 7	OE1	Thr 73	O	2.74
	OE2	His 70	N	3.00
	OE2	HOH 109	O	2.86

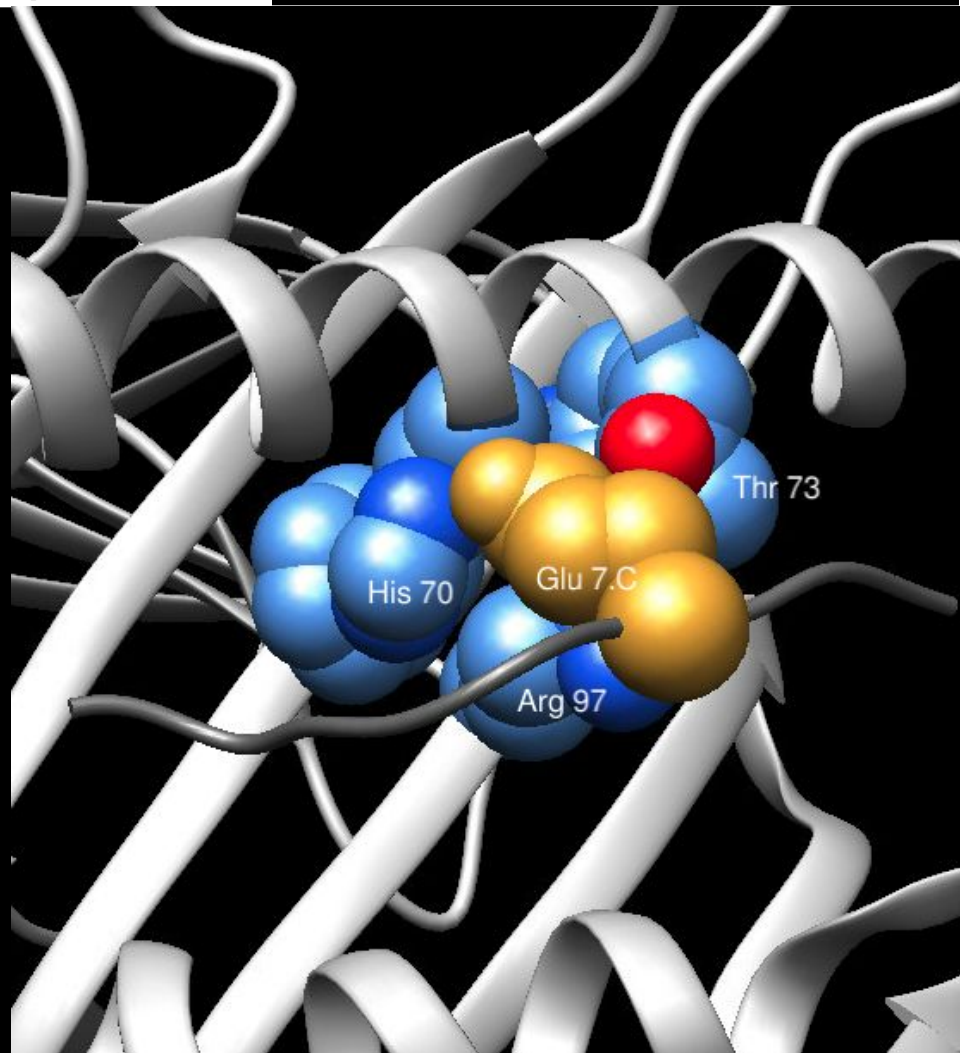
■ Peptide-molecule bond



Pocket C

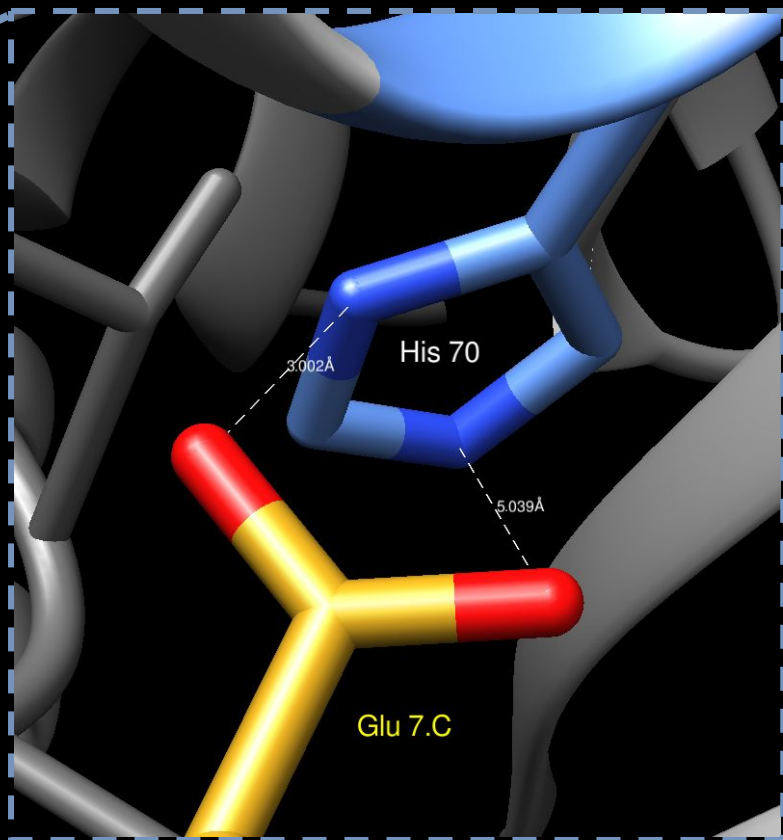
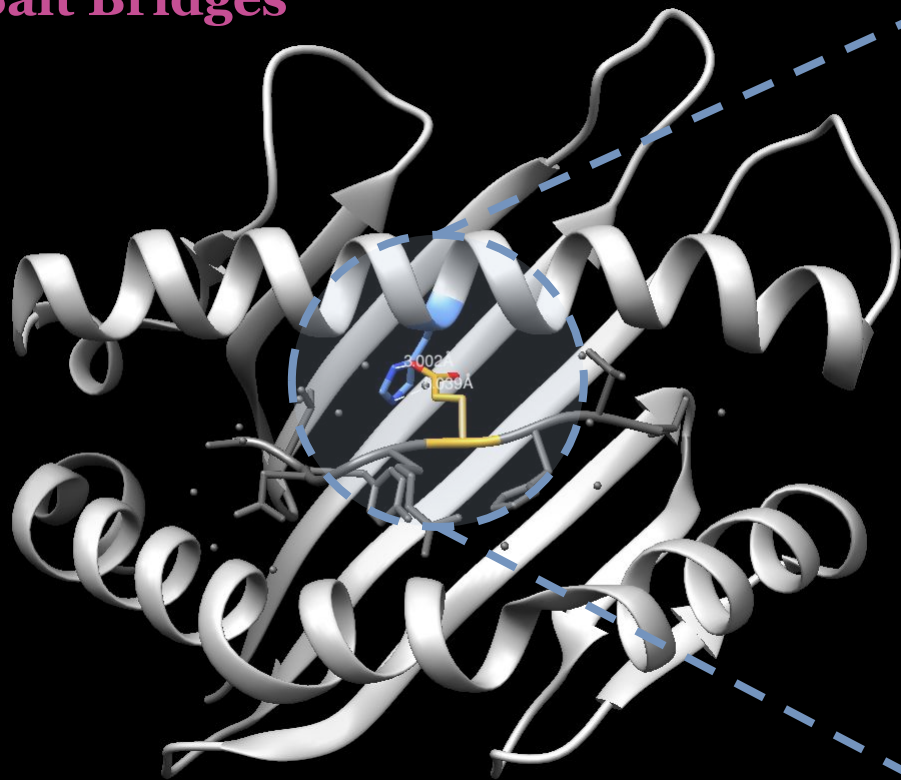
Van der Waals interactions

Peptide	HLA-I
Glu 7	His 70
	Thr 73
	Arg 97

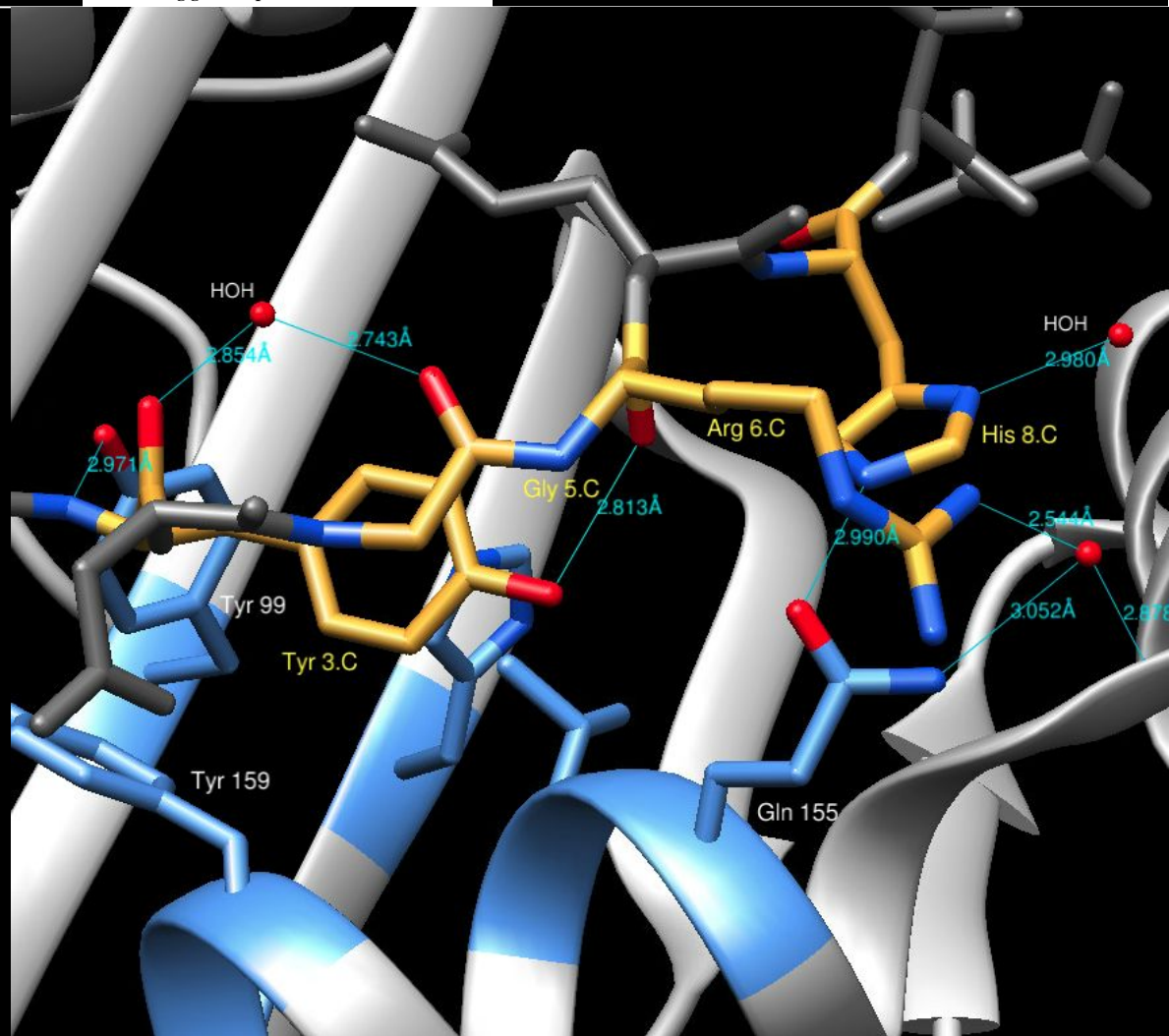
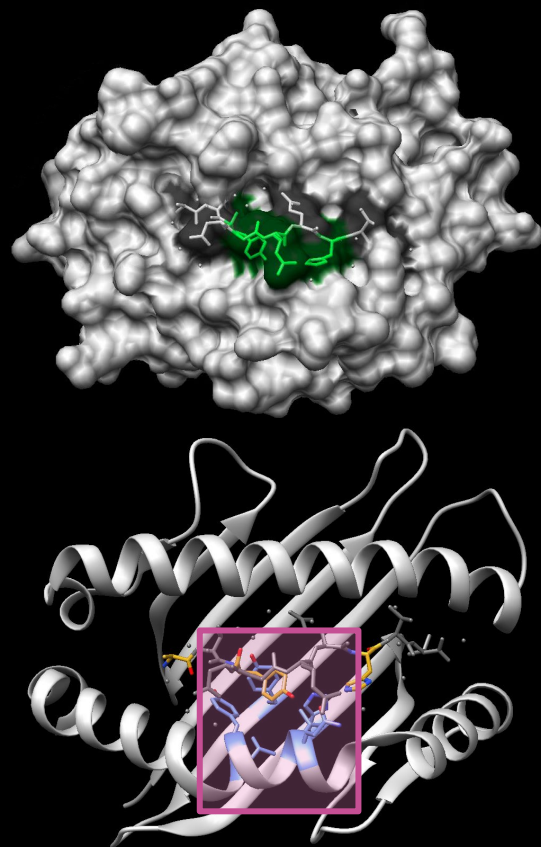


Pocket C

Salt Bridges



Pocket D

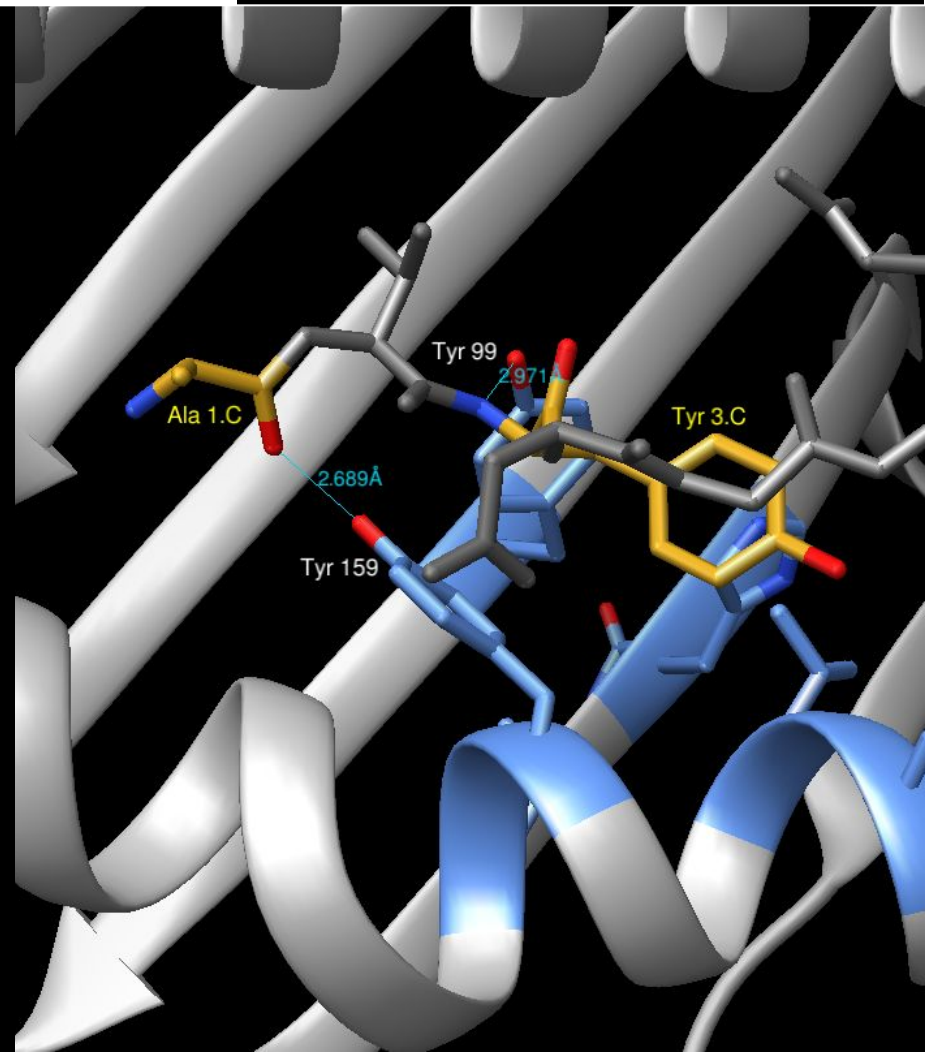


Pocket D

Hydrogen bonds

Peptide	Atom	HLA-I	Atom	Length (Å)
Ala 1	O2	Trp 159	OH	2.68


■ Peptide-molecule bond




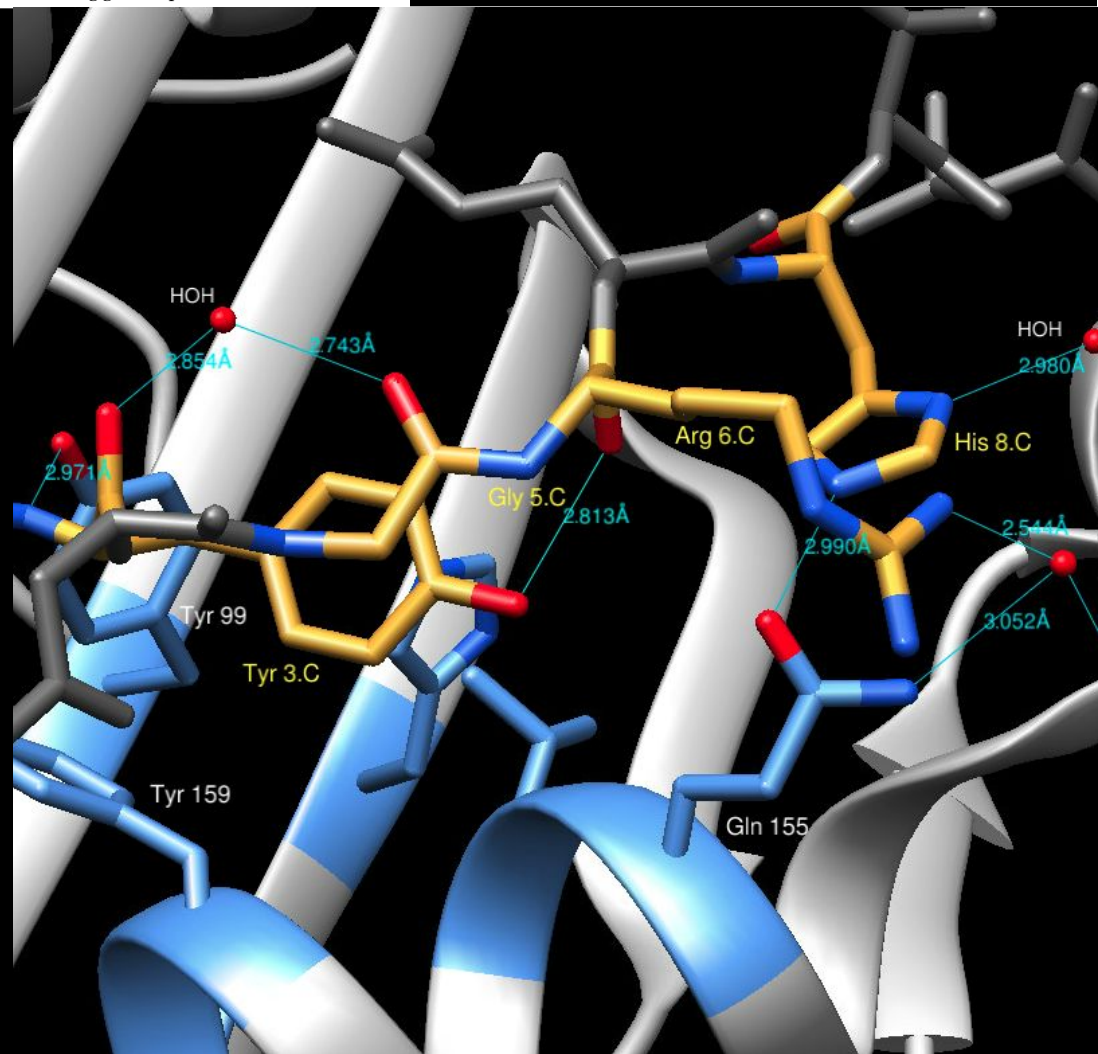
Pocket D

Hydrogen bonds

Peptide	Atom	HLA-I	Atom	Length (Å)
Tyr 3	N	Tyr 99	OH	2.97
	O	HOH 104	O	2.85
	O	Gly 5 (P)	O2	2.74
	OH	Arg 6 (P)	O	2.81
His 8	ND1	HOH 112	O	2.95
	NE2	Gln 155	OE1	2.99

 Peptide-molecule bond

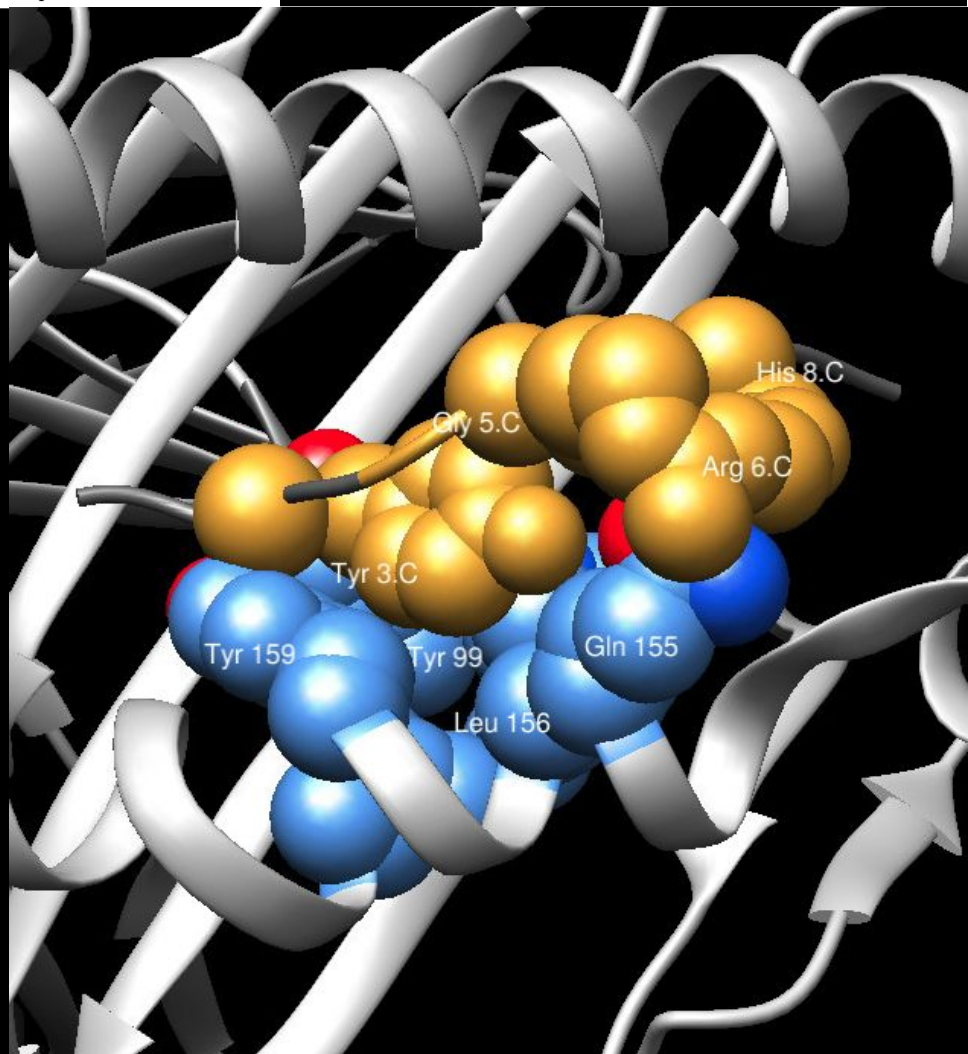
 Peptide-peptide bond



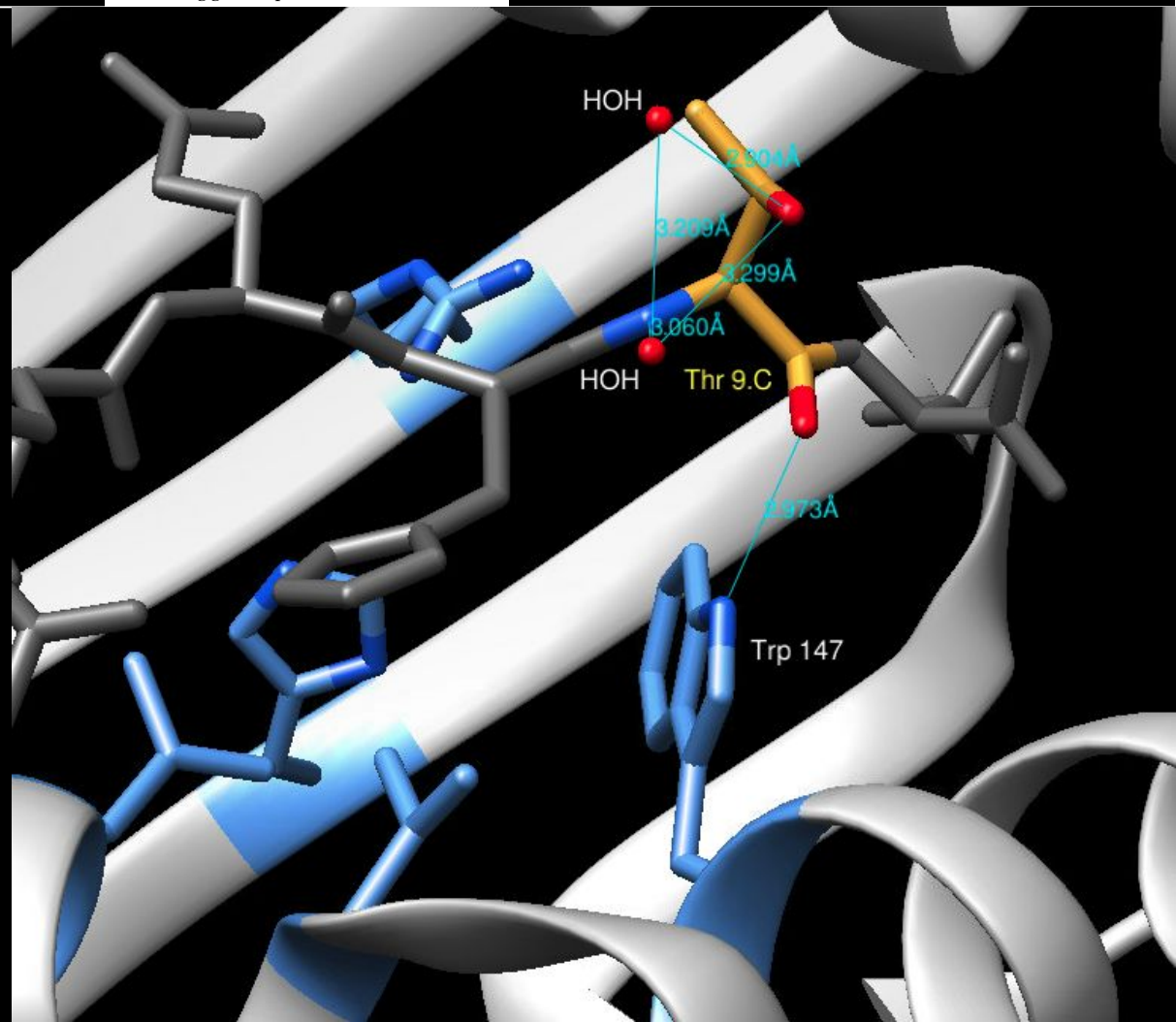
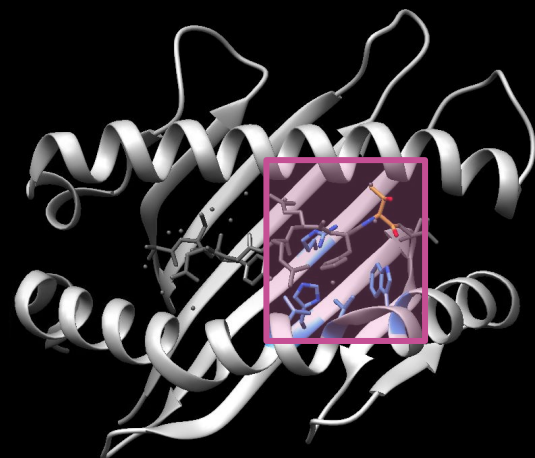
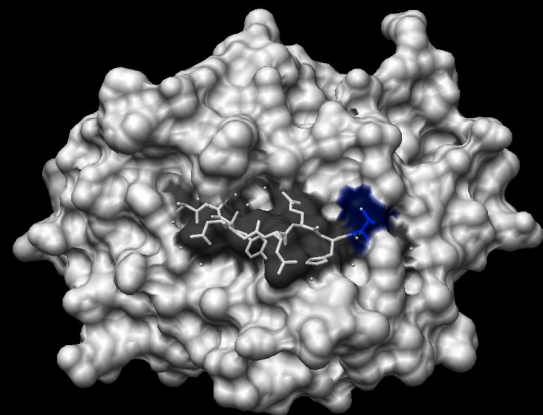
Pocket D

Van der Waals interactions

Peptide	HLA-I
Tyr 3	Tyr 99
	Leu 156
	Tyr 159
	Gly 5 (P)
	Arg 6 (P)
His 8	Gln 155



Pocket E

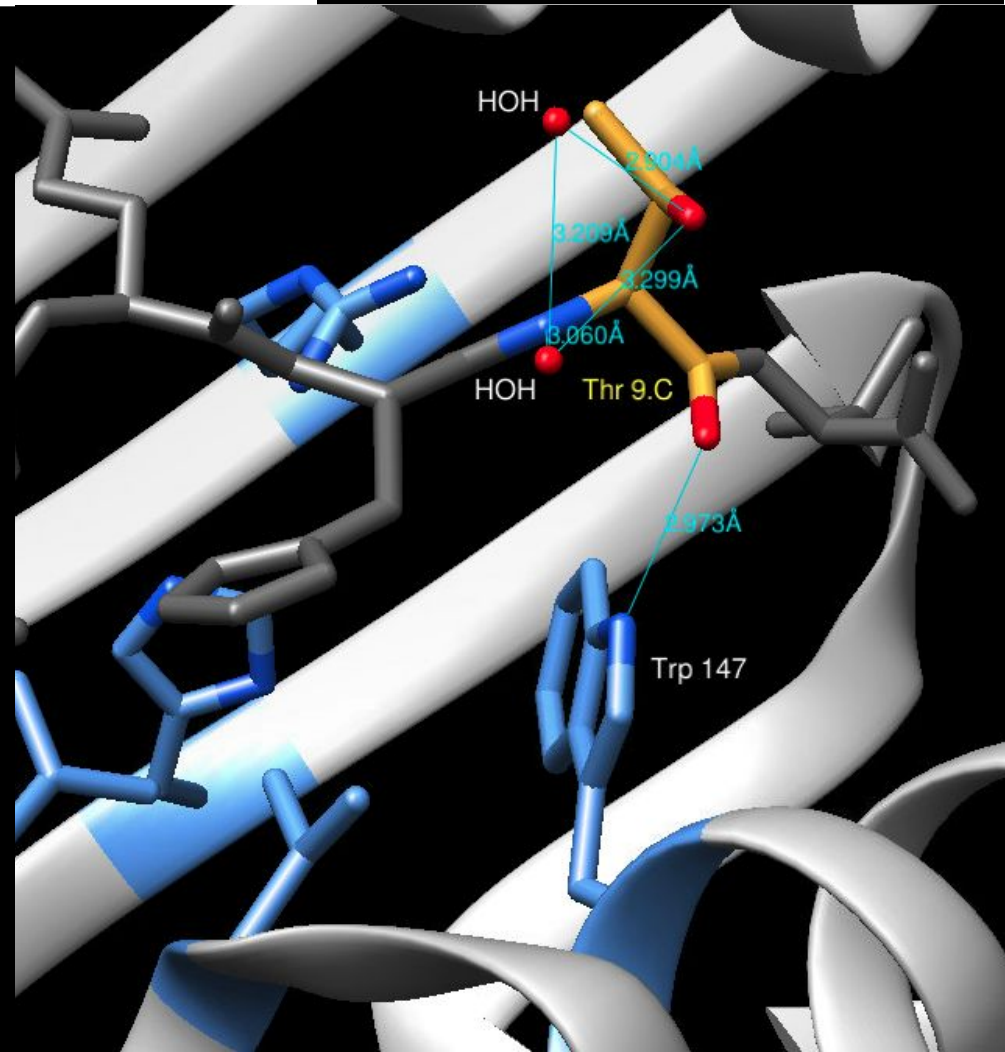


Pocket E

Hydrogen bonds

Peptide	Atom	HLA-I	Atom	Length (Å)
Thr 9	OG1	HOH 110	O	2.90
	OG1	HOH 113	O	3.29
	O	Trp 147	NE1	2.97

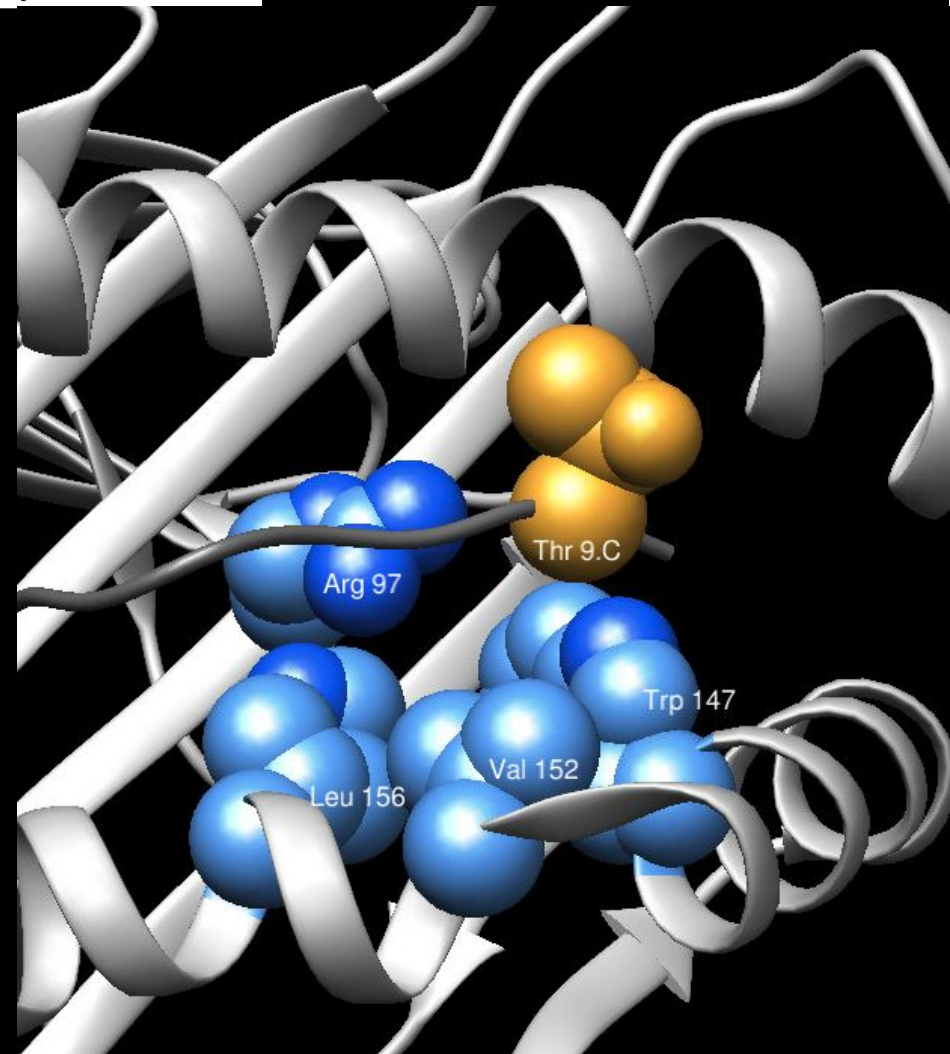
■ Peptide-molecule bond



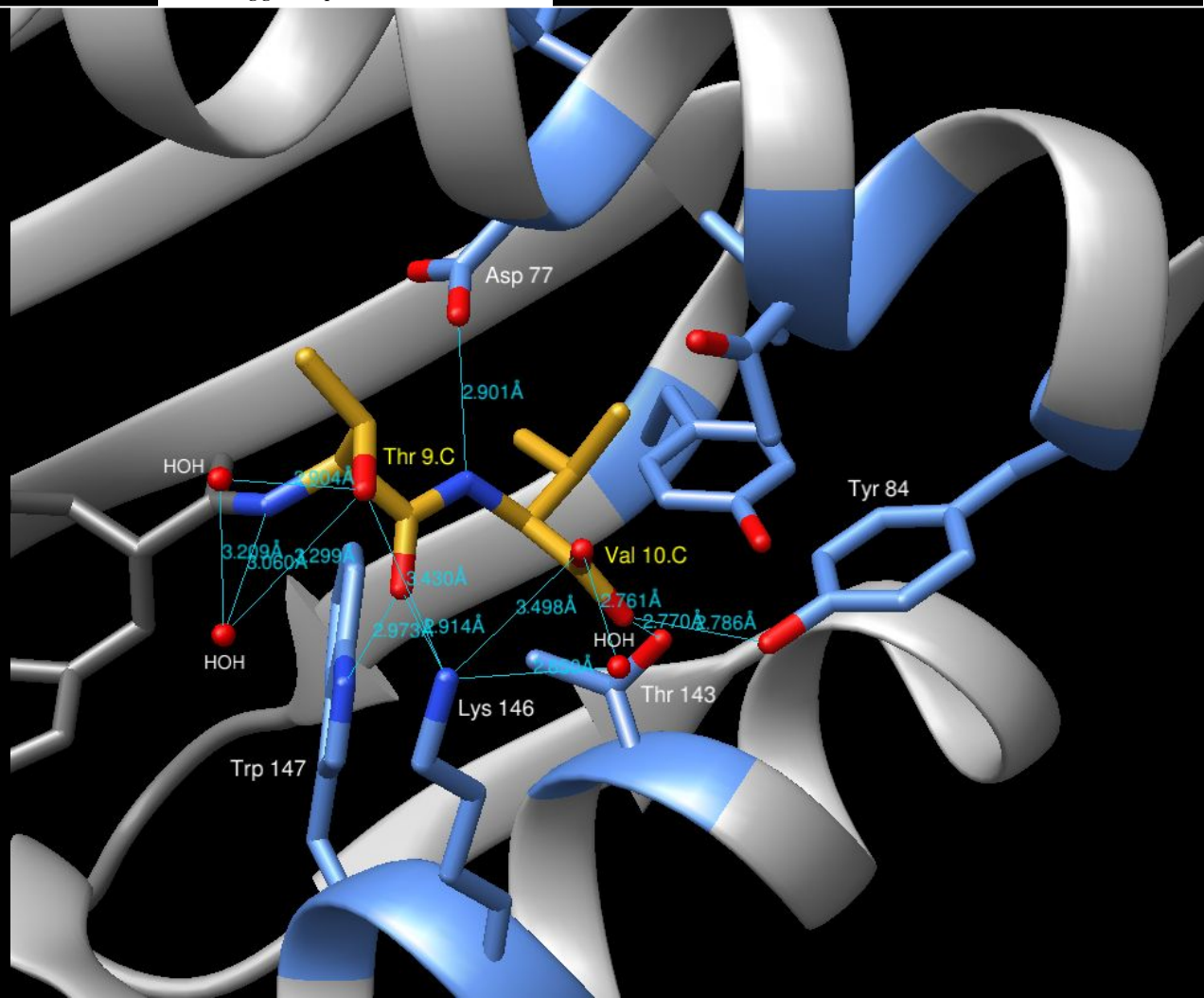
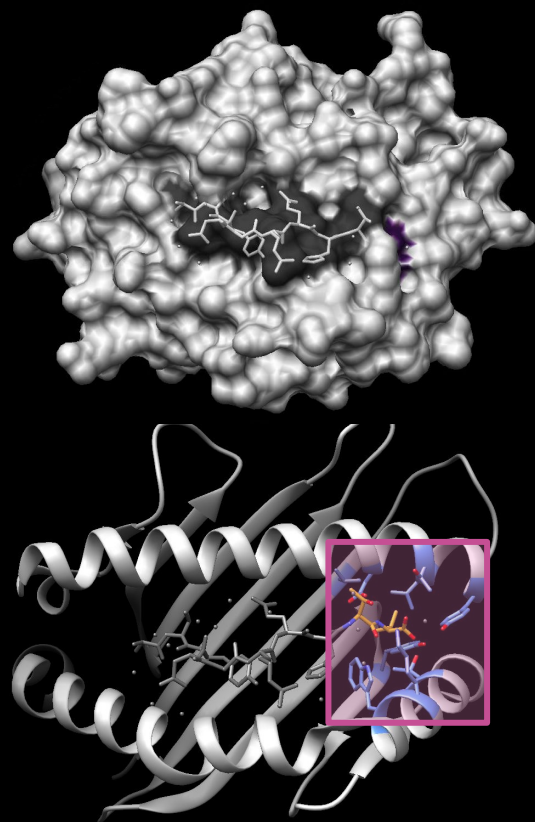
Pocket E

Van der Waals interactions

Peptide	HLA-I
Thr 9	Arg 97
	Trp 147
	Val 152
	Leu 156



Pocket F

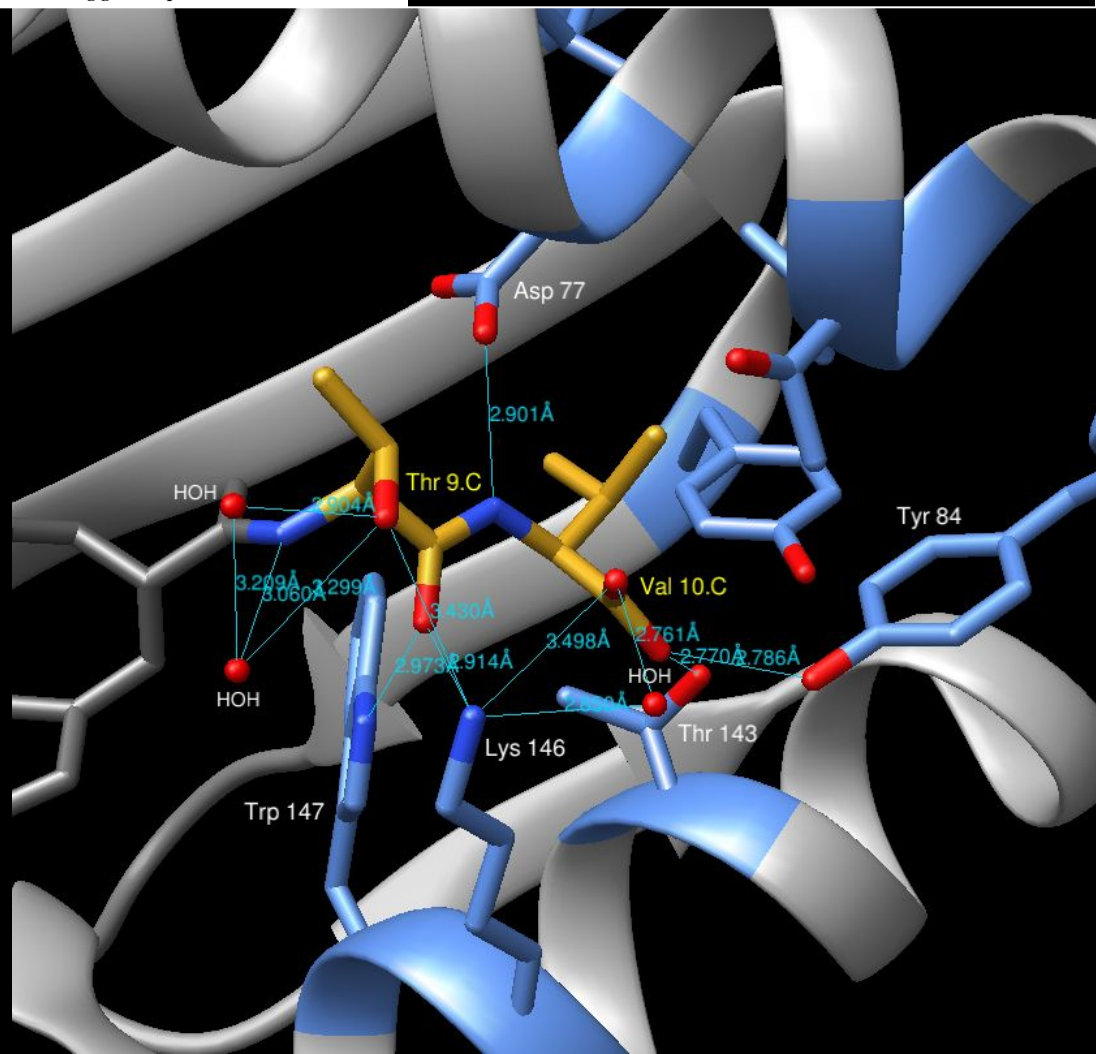


Pocket F

Hydrogen bonds

Peptide	Atom	HLA-I	Atom	Length (Å)
Thr 9	O	Trp 147	NE1	2.97
	OG1	Lys 146	Nz	2.91
	O	Lys 146	Nz	3.43
Val 10	OXT	Asp 77	O2	2.90
	OXT	HOH 105	O	2.76
	OXT	Lys 146	Nz	3.49
	OXT	Lys 146	Nz	2.85

■ Peptide-molecule bond

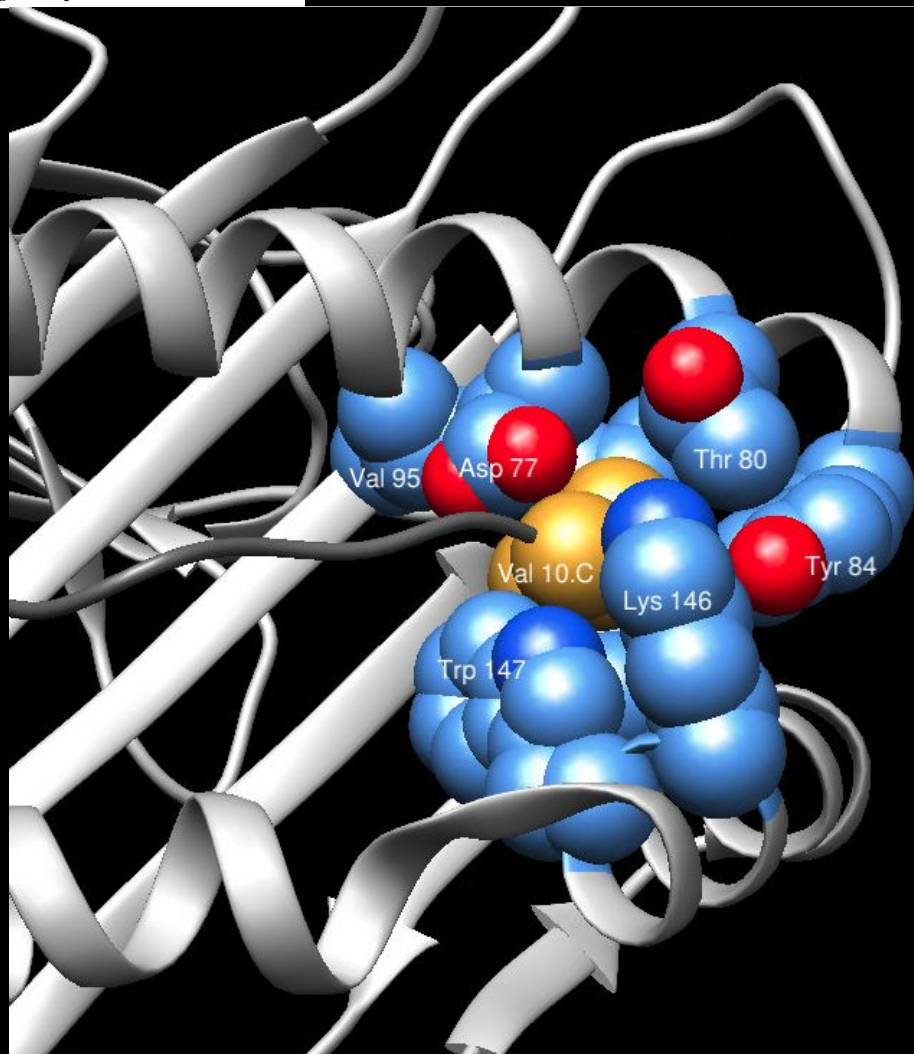


Pocket F

Van der Waals interactions

Peptide	HLA-I
Val 10	Asp 77
	Thr 80
	Val 81
	Tyr 84
	Val 95
	Tyr 123
	Lys 146
	Trp 147

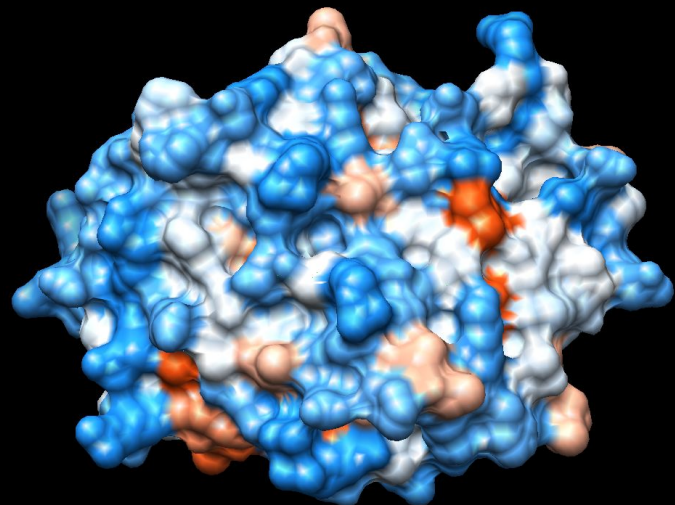
Non polar residue



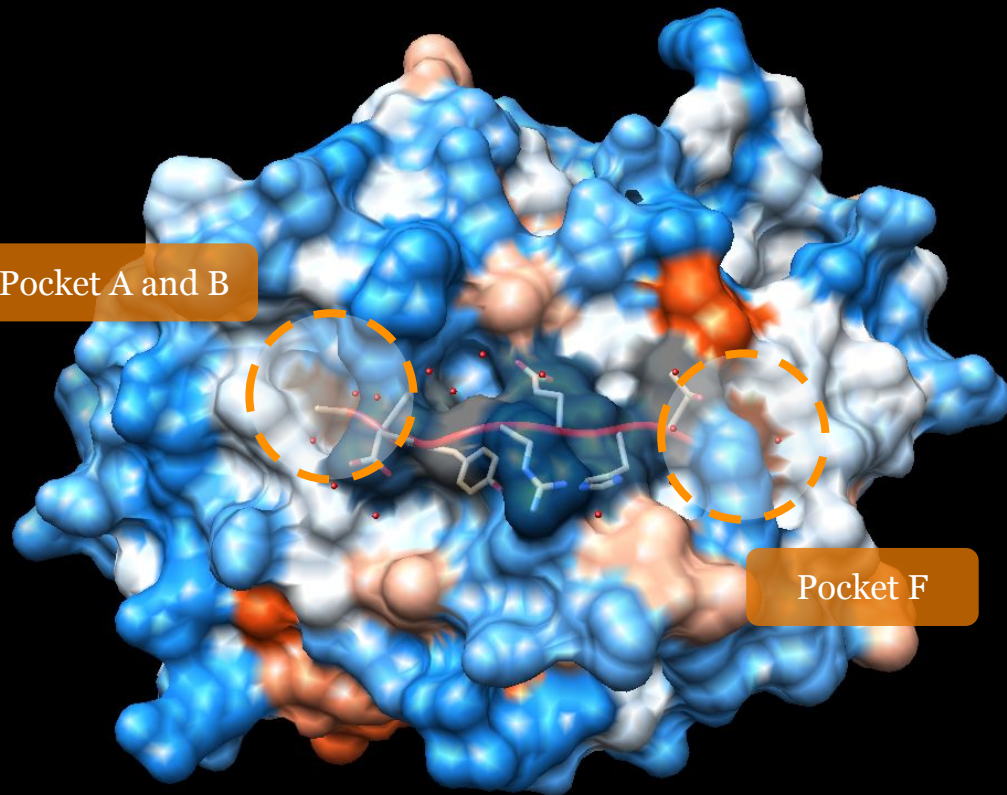
Hydrophobicity pockets

Hydrophobic pockets

Pocket A
Pocket B
Pocket F



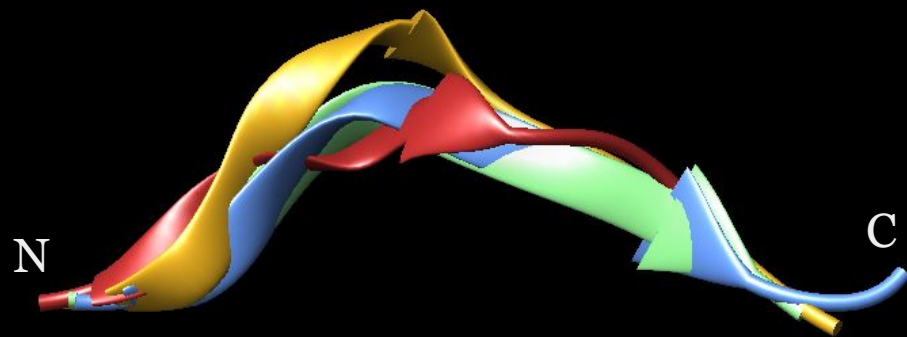
Pocket A and B



A 3D surface representation of a protein binding site, similar to the one on the left, but with a ligand molecule bound inside. The ligand is shown as a stick model with a blue carbon backbone and red oxygen atoms. Two orange dashed circles highlight specific regions: one labeled "Pocket A and B" and another labeled "Pocket F". The surface is colored blue (hydrophobic) and white (polar), with orange-colored regions representing hydrophobic pockets.

Pocket F

Peptides diversity | Alignment



- Chain A. HBV
- Chain B. MAGE-A4
- Chain C. MAGE-A3
- Chain D. Calreticulin

Alignment with Chimera

	1										11
Consensus	f	l	-	-	g	p	p	a	l	v	-
Conservation											
Hepatitis	F	L	-	-	-	P	S	D	F	F	P
MAGE-A3	F	L	W	-	G	P	R	A	L	V	-
CALRETICULIN	M	L	L	-	S	V	P	L	L	L	G
MAGE-A4	A	V	Y	D	G	R	E	H	T	V	-

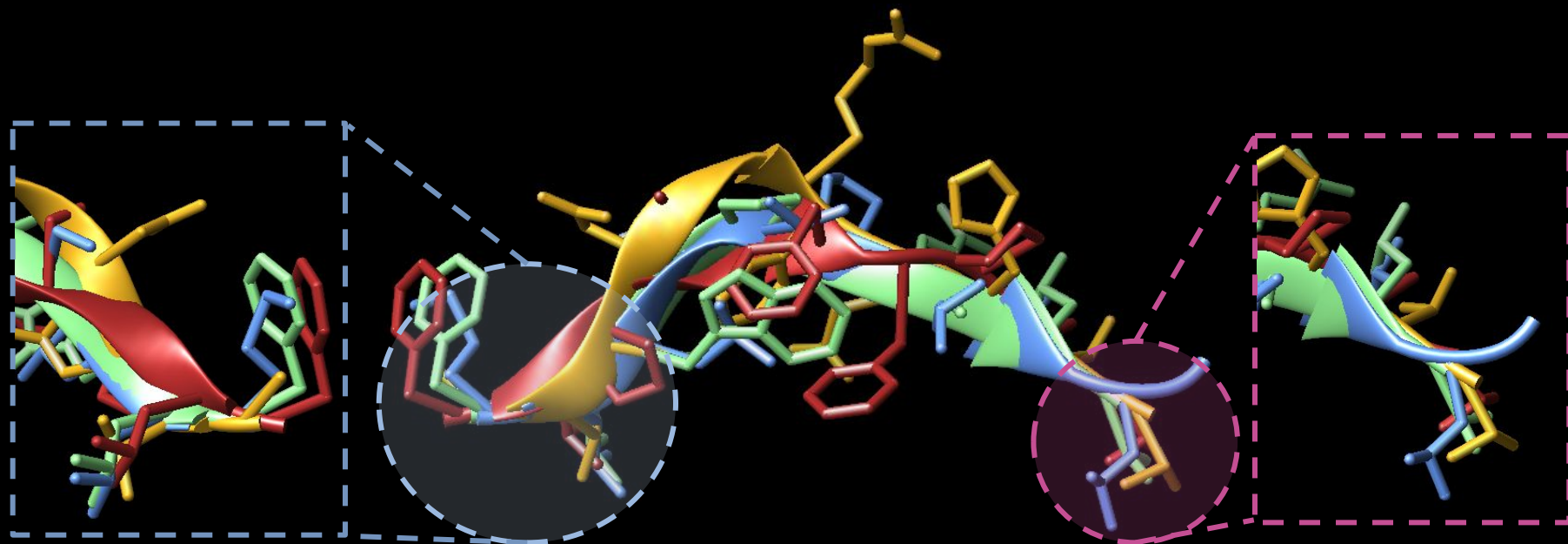
Pocket A

Pocket B

Pocket F

Hydrophobic amino acids

Peptides diversity | STAMP



Residue P1 and P2

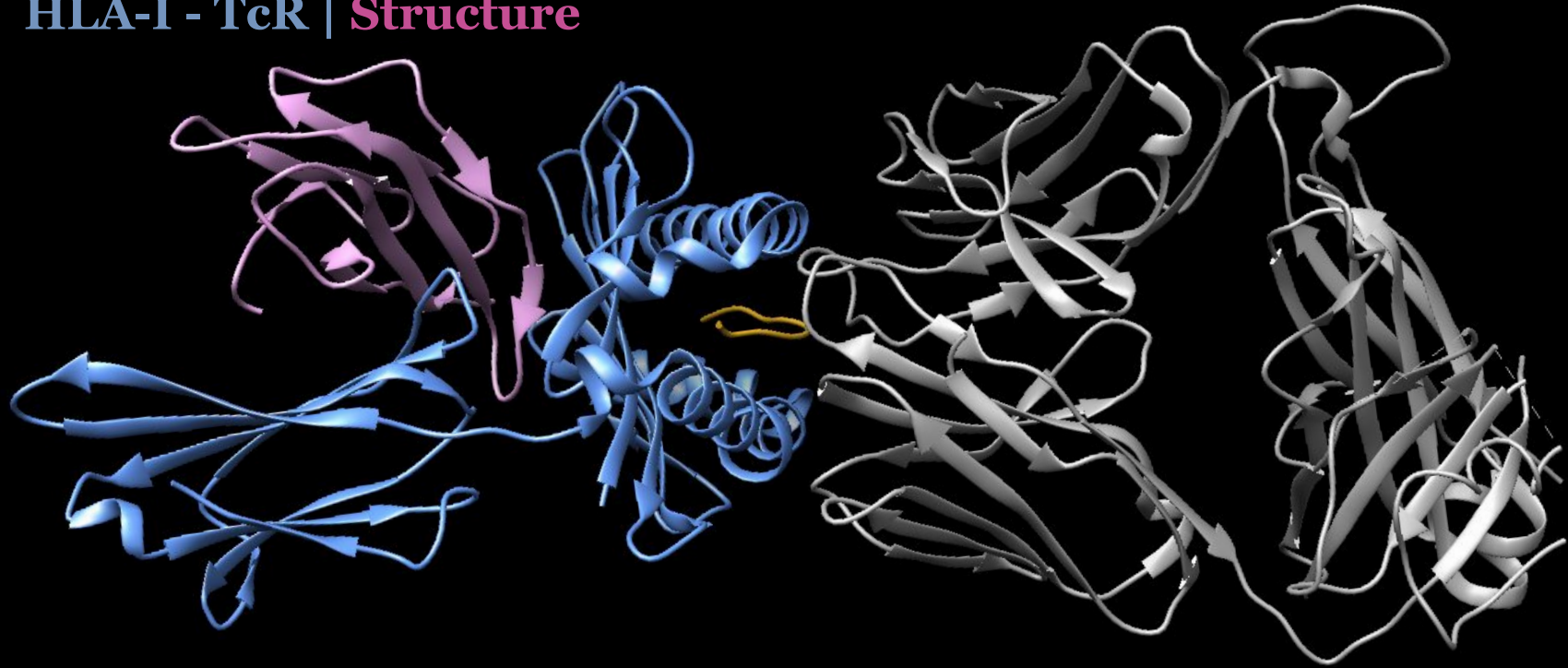
Residue P Ω

A 3D ribbon diagram of a protein complex, likely a T cell receptor and CD8 co-receptor, rendered in blue and purple colors. The structure is complex, with many loops and helices, and is set against a black background.

04

**T cell receptor and CD8:
residues and interactions**

HLA-I - TcR | Structure



HLA-I

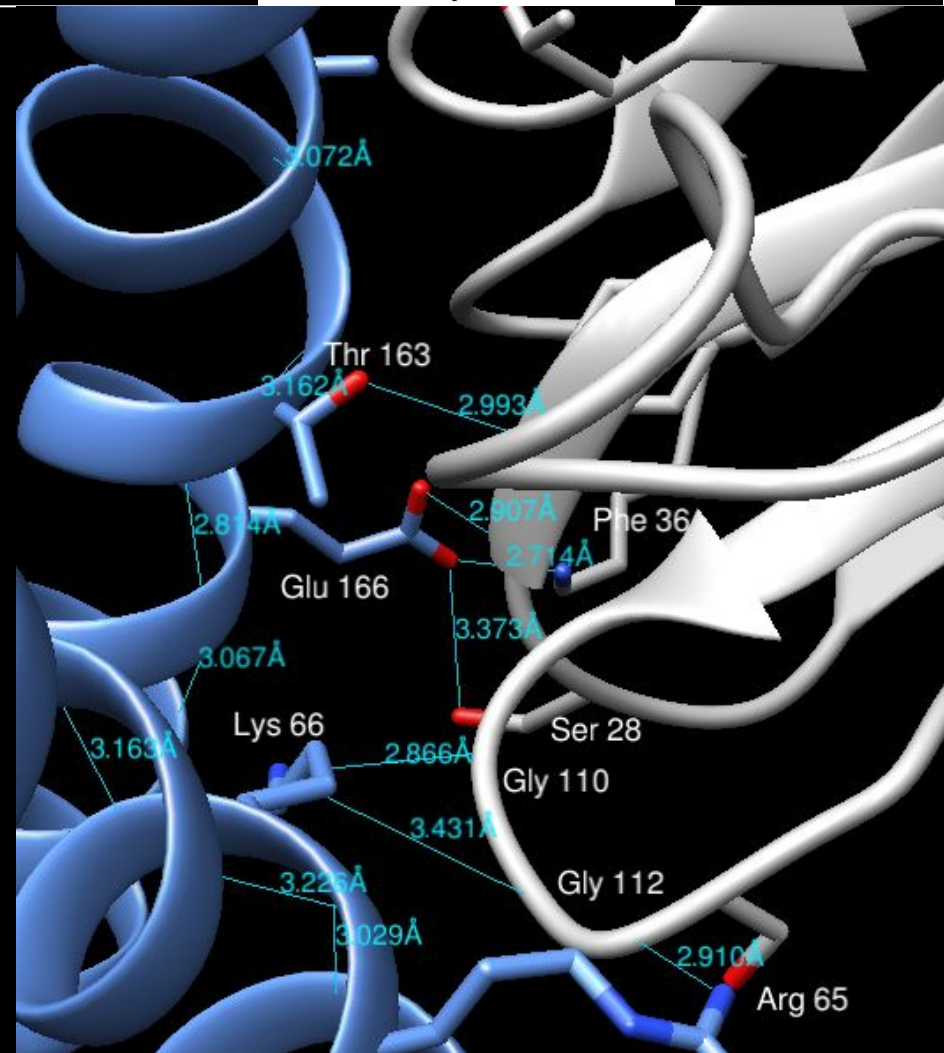
Peptide

β 2-microglobulin

TCR

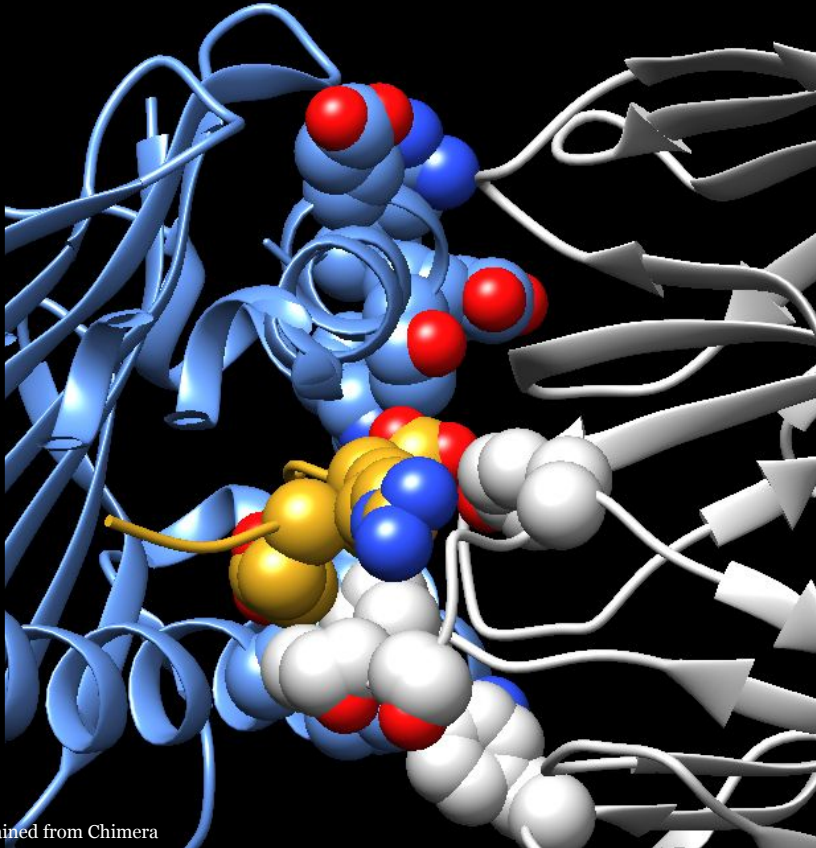
HLA-I - TcR | Hydrogen bonds

TCR	HLA-I	Length (Å)
Ser 28	Glu 166	3.37
Phe 36	Thr 163	2.71
Phe 36	Glu 166	2.90
Ser 109	Lys 66	2.86
Gly 110	Lys 66	3.43
Gly 112	Arg 65	2.91
Ser 113	Arg 65	2.90
Tyr 51	Asp 227	3.01
Ser 34	Gln 226	3.85
Leu 94	Ile 101	3.05
Ile 101	Gln 226	3.01



HLA-I - TcR - Peptide

Van der Waals interactions



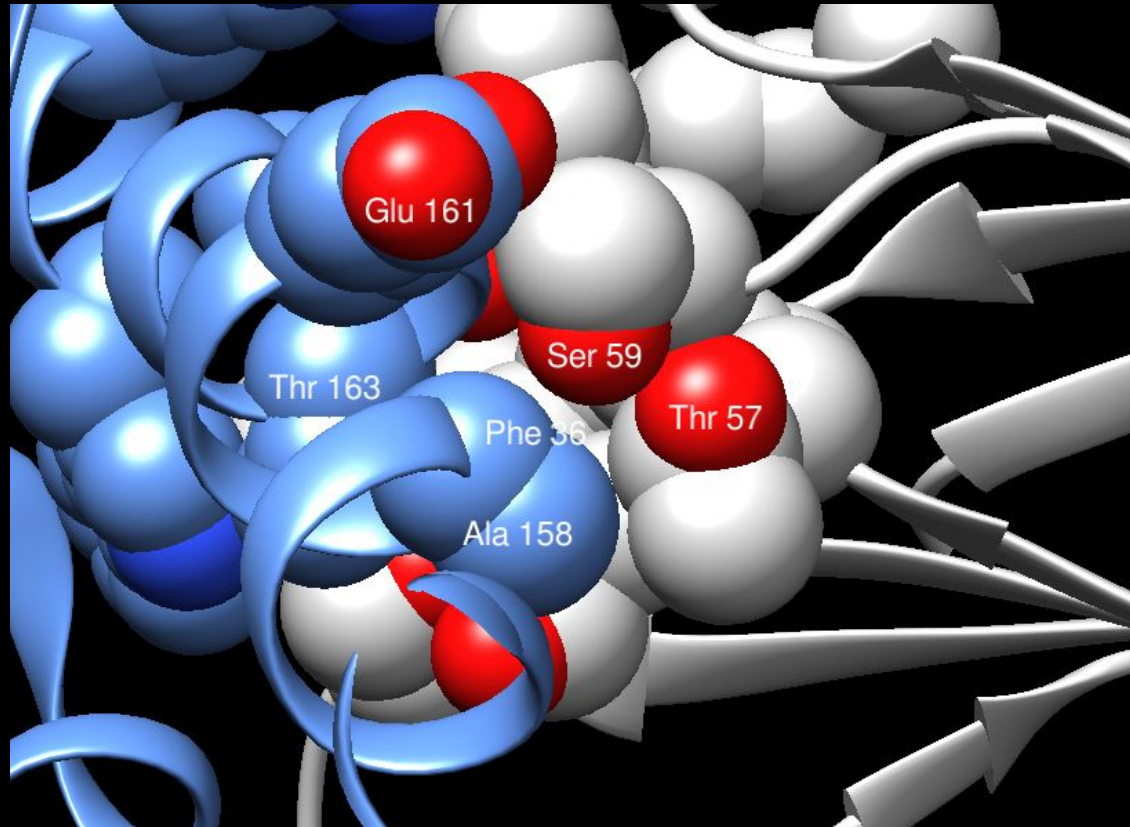
Images obtained from Chimera

TCR	HLA-I
Ser 28	Glu 166
Pro 29	Glu 166
Pro 29	Trp 167
Phe 36	Thr 163
Phe 36	Glu 166
Ser 37	Thr 163
Thr 57	Ala 158
Phe 58	Glu 161
Phe 58	Gly 162
Ser 59	Ala 158
Ser 59	Glu 161
Asp 83	Arg 169

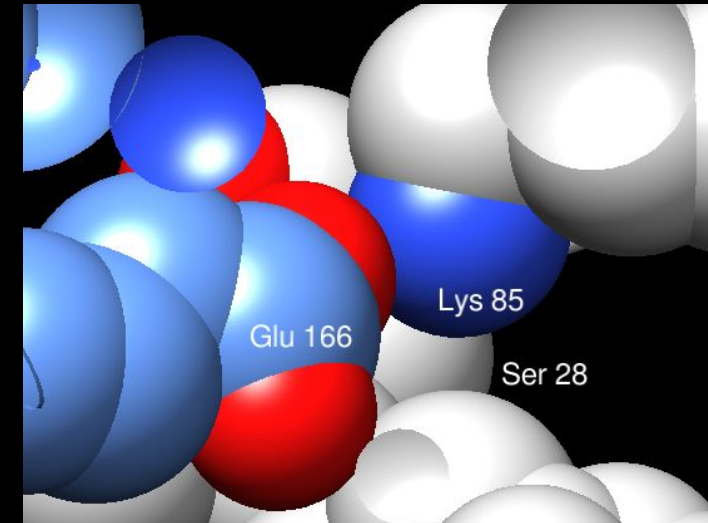
TCR	HLA-I
Lys 85	Glu 166
Ser 109	Thr 163
Ser 109	Trp 167
Gly 110	Gly 62
Gly 110	Lys 66
TCR	Peptide
Ser 37	Asp 4
Ser 109	Asp 4
Tyr 114	Asp 4
Met 110	Gly 5
Met 110	Glu 7
Asp 112	Arg 6

HLA-I - TcR

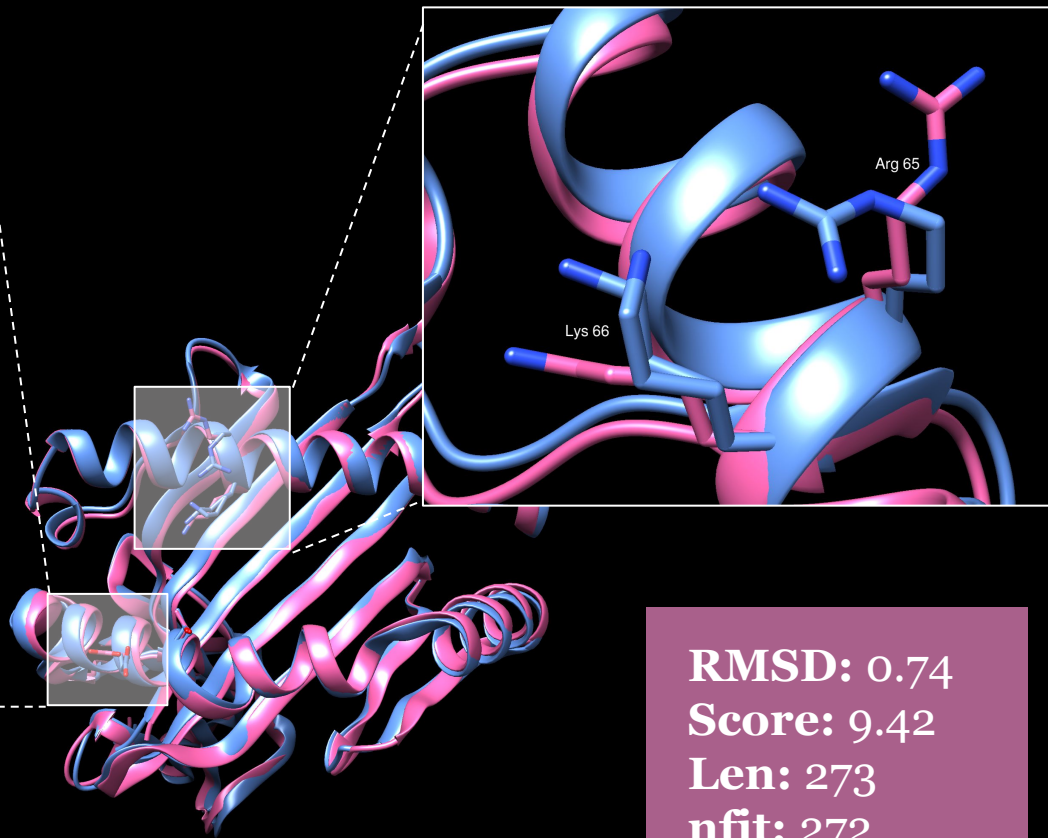
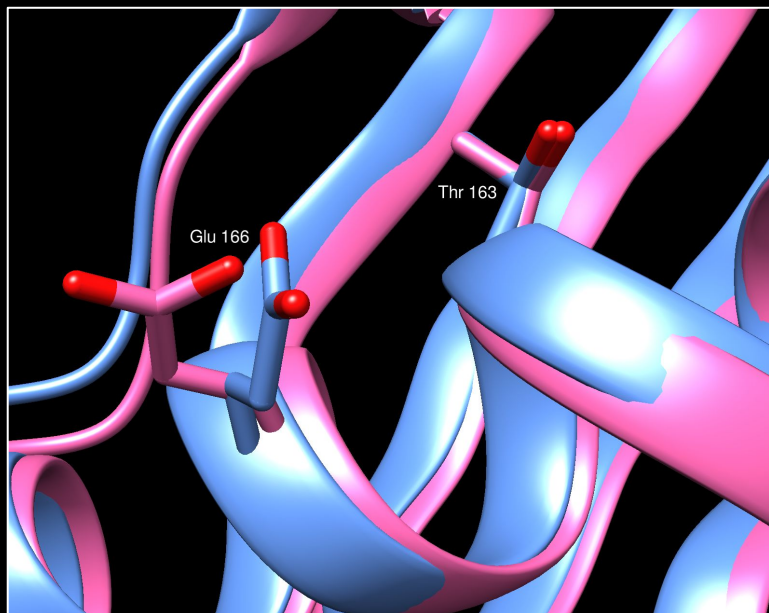
Van der Waals interactions



TCR	HLA-I
Ser 59	Glu 161
Phe 36	Thr 163
Thr 57	Ala 158
Lys 85	Glu 166
Ser 28	Glu 166



HLA-I and TcR | STAMP



HLA-I not binded to TcR
HLA-I binded to TcR

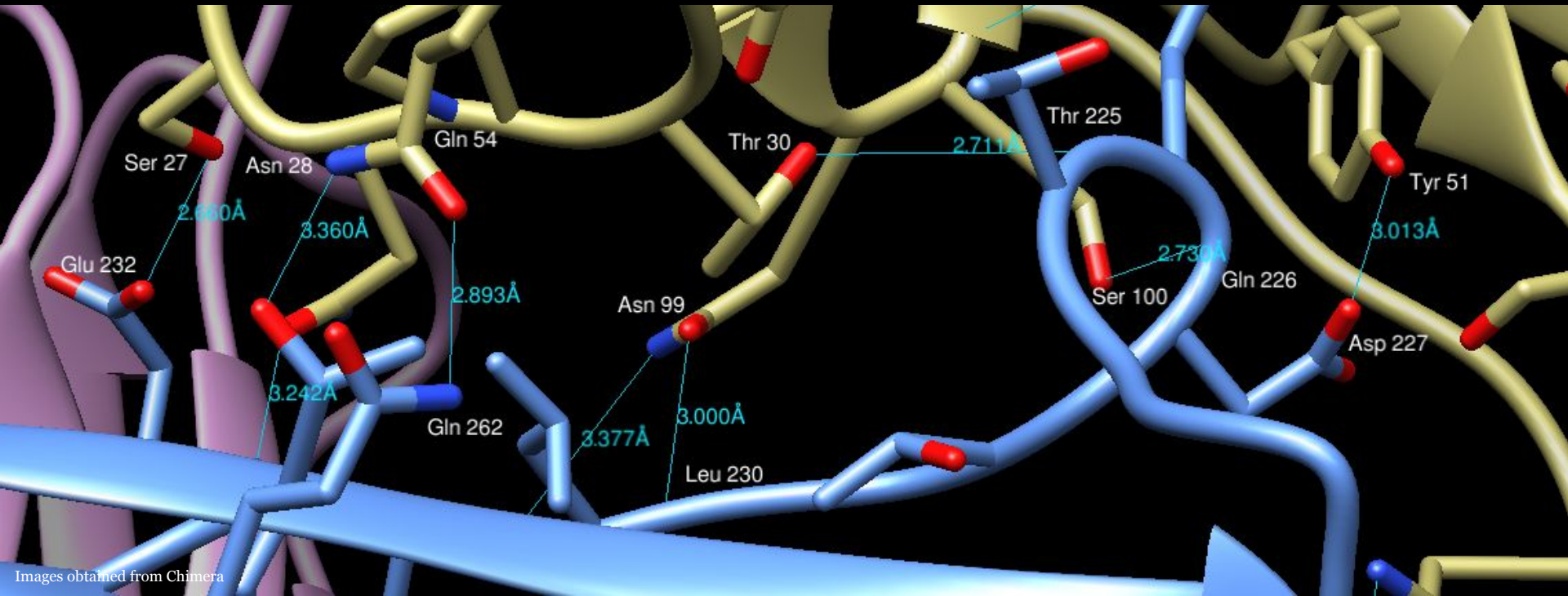
RMSD: 0.74
Score: 9.42
Len: 273
nfit: 272

CD8 - HLA-I

Hydrogen bonds

CD8	HLA-I	Length (Å)
Gln 54	Gln 262	2.89
Ser 27	Glu 232	2.68
Asn 99	Leu 230	3.00

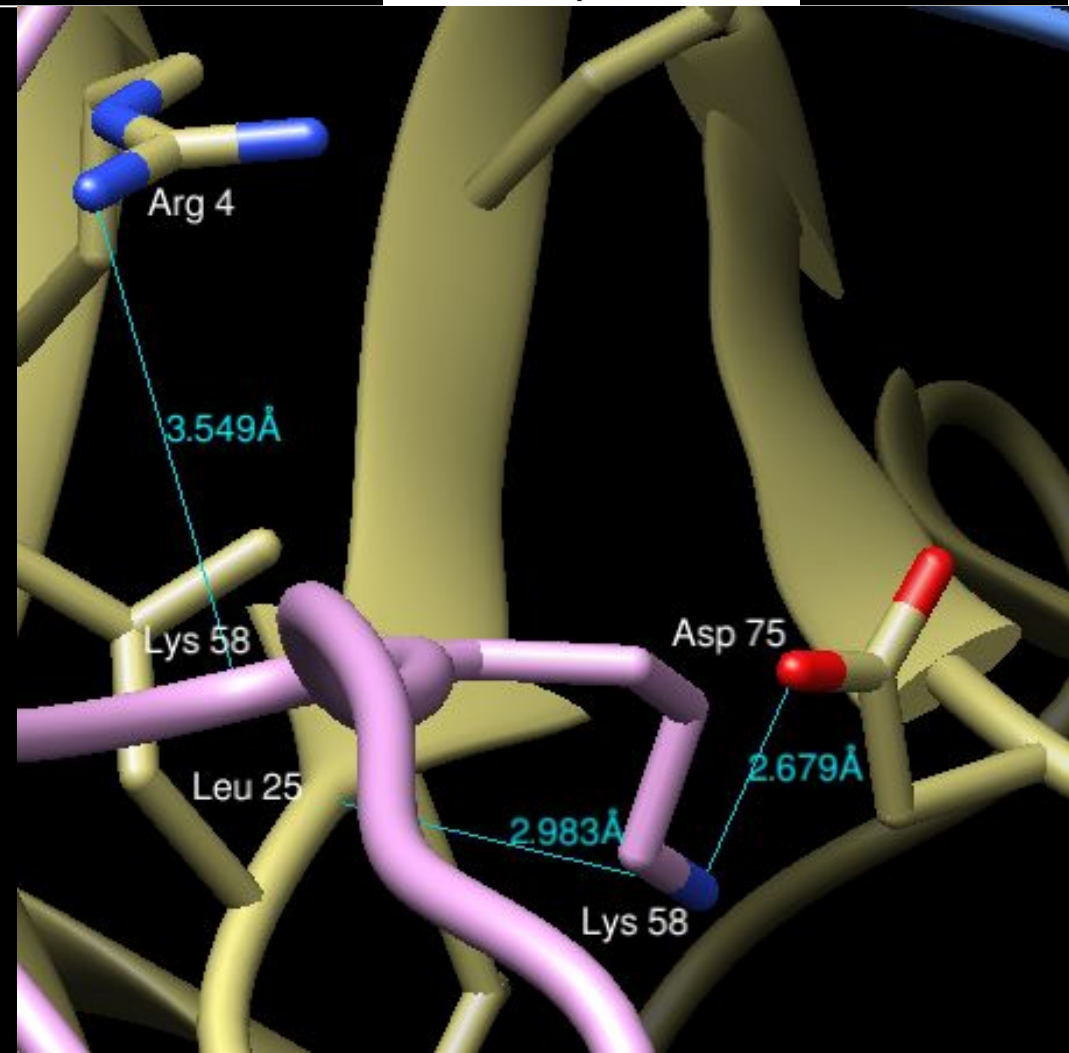
CD8	HLA-I	Length (Å)
Thr 30	Thr 225	2.71
Ser 100	Gln 226	2.73
Tyr 51	Asp 227	3.01



CD8 - β 2-microglobulin

Hydrogen bonds

CD8	β 2-microglobulin	Length (Å)
Arg 4	Lys 58	3.54
Leu 25	Lys 58	2.98
Asp 75	Lys 58	2.67



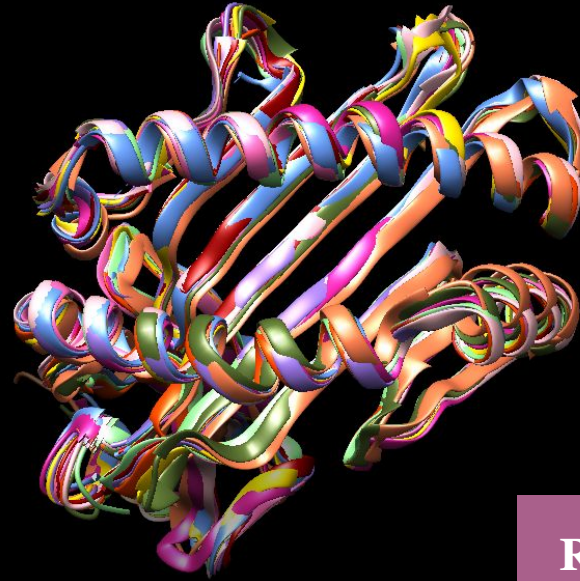


05

Evolution:
structure and sequence

HLA-I paralogues | STAMP

α -chain



RMSD: 1.44
Score: 9.48
Len: 278
nfit: 261

HLA-Ia paralogues | Inner interactions in HLA-Ia

α -chain

- H-Bond-involved
- Salt bridge-involved
- Disulfur bond-involved
- Hydrophobic bond-involved

Consensus Conservation	1	11	21	31	41	51	61	71	81
HLA-C1	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-C2	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-B6	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-B4	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-B3	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-B5	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-B2	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-B1	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-A3	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-A1	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
HLA-A2	GSHSMRYFYT	SVSRPGRGEP	RFIAVGIVDD	TQFVRFDSDA	ASPREERAP	WIEQEGPEYW	DRETQICKAQ	AQTDREDLRT	LRGYYNQSEA
Consensus Conservation	91	101	111	121	131	141	151	161	171
HLA-C1	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-C2	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-B6	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-B4	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-B3	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-B5	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-B2	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-B1	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-A3	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-A1	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
HLA-A2	GSHTIQRMYG	CDVGPDRILL	RGYNQYAYDG	KDYIALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGTCVWEWLR	YLENGKETLQ
Consensus Conservation	181	191	201	211	221	231	241	251	261
HLA-C1	RADPPKTHVT	HHPVSDHEAT	LRWCWALGFYP	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-C2	RADPPKTHVT	HHPVSDHEAT	LRWCWALGFYP	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B6	RADPPKTHVT	HHPVSDHEAT	LRWCWALGFYP	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B4	RADPPKTHVT	HHPVSDHEAT	LRWCWALGFYP	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B3	RADPPKTHVT	HHPVSDHEAT	LRWCWALGFYP	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B5	RADPPKTHVT	HHPVSDHEAT	LRWCWALGFYP	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B2	RADPPKTHVT	HHPVSDHEAT	LRWCWALGFYP	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B1	RADPPKTHVT	HHPVSDHEAT	LRWCWALGFYP	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-A3	RTDAPKTHMT	HHAVSDHEAT	LRWCWALSFPY	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-A1	RTDAPKTHMT	HHAVSDHEAT	LRWCWALSFPY	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-A2	RTDAPKTHMT	HHAVSDHEAT	LRWCWALSFPY	AEITLTWQWD	GEDQTQDTEL	VEITRPAAGDT	FQKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL

HLA-Ia paralogues| Inner interactions in HLA-I

β 2-microglobulin

	1	11	21	31	41
Consensus	- I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
Conservation					
B5101_HLA	- I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
CW3_HLA	M I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
B27_HLA	- I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
AW68_HLA	- I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
CW4_HLA	M I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
B8_HLA	- I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
2709_HLA	M I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
A1101_HLA	M I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
B3508_HLA	- I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
A201_HLA	- - Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
B1402_HLA	- I Q R T P K I Q V	Y S R H P A E N G K	S N F L N C Y V S G	F H P S D I E V D L	L K N G E R I E K V
	51	61	71	81	91
Consensus	E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
Conservation					
B5101_HLA	E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
CW3_HLA	I E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
B27_HLA	E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
AW68_HLA	E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
CW4_HLA	I E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
B8_HLA	E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
2709_HLA	I E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
A1101_HLA	I E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
B3508_HLA	E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
A201_HLA	E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M
B1402_HLA	E H S D L S F S K D	W S F Y L L Y Y T E	F T P T E K D E Y A	C R V N H V T L S Q	P K I V K W D R D M

- H-Bond-involved
- Salt bridge-involved
- Disulfur bond-involved
- Hydrophobic bond-involved



RMSD: 0.40
Score: 9.72
Len: 100
nfit: 98

HLA-Ia paralogues | Binding groove

α -chain


- Cleft wall
- Pocket B
- Pocket F

Conserved	Variable
Conserved	Variable

Consensus	1	11	21	31	41	51	61	71	81
Conservation									
HLA-C1	GSHSMRYFYT	AVSRPGRGEP	RFIAVG YVDD	TQVVRFDSDA	ASPRGEPRAP	WIEQEGPEYW	DRETQICKAK	AQTDREDLRT	LRGYNQSEA
HLA-C2	GSHSMRYFYT	SVSWPGRGEP	RFIAVG YVDD	TQVVRFDSDA	ASPRGEPRAP	WVEQEGPEYW	DRETQICKAK	AQADRVNLRK	LRGYNQSEAD
HLA-B6	GSHSMRYFYT	AMSRPGRGEP	RFIAVG YVDD	TQVVRFDSDA	ASPRGEPRAP	WIEQEGPEYW	DRNTQIFKTN	TQTYRENLRI	ALRYNQSEAD
HLA-B4	GSHSMRYFYT	AMSRPGRGEP	RFIAVG YVDD	TQVVRFDSDA	ASPRGEPRAP	WIEQEGPEYW	DRNTQIFKTN	TQTYRENLRI	ALRYNQSEAD
HLA-B3	GSHSMRYFYD	AMSRPGRGEP	RFISVG YVDD	TQVVRFDSDA	A-- -- --P	WIEQEGPEYW	DRNTQIFKTN	TQTDRESLRN	LRGYNQSEAD
HLA-B5	GSHSMRYFYT	AVSRPGRGEP	RFISVG YVDD	TQVVRFDSDA	ASPREPRAP	WIEQEGPEYW	DRNTQICKTN	TQTDRESLRN	LRGYNQSEAD
HLA-B2	GSHSMRYFYH	SVSRPGRGEP	RFITVG YVDD	TLFVRFDSDA	ASPREPRAP	WIEQEGPEYW	DRETQICKAK	AQTDREDLRT	LRYYNQSEAD
HLA-B1	GSHSMRYFYH	SVSRPGRGEP	RFITVG YVDD	TLFVRFDSDA	ASPREPRAP	WIEQEGPEYW	DRETQICKAK	AQTDREDLRT	LRYYNQSEAD
HLA-A3	GSHSMRYFYT	SVSRPGRGEP	RFIAVG YVDD	TQVVRFDSDA	ASQRM	WIEQEGPEYW	DRNTRNVKAQ	SQTDRVDLGT	LRGYNQSEAD
HLA-A1	GSHSMRYFFT	SVSRPGRGEP	RFIAVG YVDD	TQVVRFDSDA	ASQRM	WIEQEGPEYW	DGETRNVKAH	SQTHRVDLGT	LRGYNQSEAD
HLA-A2	GSHSMRYFYT	SVSRPGRGEP	RFIAVG YVDD	TQVVRFDSDA	ASQRM	WIEQEGPEYW	DGETRNVKAQ	SQTHRVDLGT	LRGYNQSEAD
Consensus	91	101	111	121	131	141	151	161	171
Conservation									
HLA-C1	GSHTIQRMYG	CDVGPDGRLL	RGYNQYAYDG	KDYALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGLCVELLRR	YLNKGKETLQ
HLA-C2	GSHTIQRMFG	CDLGPDPGRLL	RGYNQFAYDG	KDYALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGLCVELLRR	YLNKGKETLQ
HLA-B6	GSHTWQTMYG	CDVGPDGRLL	RGHNQYAYDG	KDYALNEDL	RSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGLCVELLRR	YLNKGKETLQ
HLA-B4	GSHTIQRMYG	CDLGPDPGRLL	RGHDQYAYDG	KDYALNEDL	RSWTAADTAA	QITQRKWEAA	RVAEQRAYL	EGLCVELLRR	YLNKGKETLQ
HLA-B3	GSHTIQSMYG	CDVGPDGRLL	RGHNQYAYDG	KDYALNEDL	RSWTAADTAA	QITQRKWEAA	RVAEQRAYL	EGLCVELLRR	YLNKGKETLQ
HLA-B5	GSHTLQWMYG	CDVGPDGRLL	RGYNQFAYDG	KDYALNEDL	SSWTAADTAA	QITQRKWEAA	REAEQLRAYL	EGLCVELLRR	YLNKGKETLQ
HLA-B2	GSHTLQNMYG	CDVGPDGRLL	RGYHQDAYDG	KDYALNEDL	SSWTAADTAA	QITQRKWEAA	RVAEQRAYL	EGECVELLRR	YLNKGKETLQ
HLA-B1	GSHTLQNMYG	CDVGPDGRLL	RGYHQDAYDG	KDYALNEDL	SSWTAADTAA	QITQRKWEAA	RVAEQRAYL	EGECVELLRR	YLNKGKETLQ
HLA-A3	GSHTIQMYG	CDVGSDFRFL	RGYRQDAYDG	KDYALKEDL	RSWTAADMAA	QTKHKWEAA	HVAEQRAYL	EGLCVELLRR	YLNKGKETLQ
HLA-A1	GSHTVQRMYG	CDVGSDFRFL	RGYHQDAYDG	KDYALKEDL	RSWTAADMAA	QTKHKWEAA	HVAEQRAYL	EGLCVELLRR	YLNKGKETLQ
HLA-A2	GSHTIQIMYG	CDVGSDFRFL	RGYRQDAYDG	KDYALKEDL	RSWTAADMAA	QITKRKWEAA	HAAEQRAYL	EGLCVELLRR	YLNKGKETLQ
Consensus	181	191	201	211	221	231	241	251	261
Conservation									
HLA-C1	RAEHPKTHVT	HHPVSDHEAT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDGT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-C2	RAEHPKTHVT	HHPVSDHEAT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDGT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B6	RADPPKTHVT	HHPVSDHEAT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDRT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B4	RADPPKTHVT	HHPVSDHEAT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDRT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B3	RADPPKTHVT	HHPISDHEAT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDRT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B5	RADPPKTHVT	HHPISDHEAT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDRT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B2	RADPPKTHVT	HHPISDHEAT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDRT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-B1	RADPPKTHVT	HHPISDHEAT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDRT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-A3	RTDAPKTHMT	HHAVSDHEAT	LRCWALSFPY	AEITLTWQRD	GEDQTQDTEL	VETRPAGDGT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-A1	RTDAPKTHMT	HHAVSDHEAT	LRCWALSFPY	AEITLTWQRD	GEDQTQDTEL	VETRPAGDGT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL
HLA-A2	RTDPPKTHMT	HHPISDHEAT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDGT	FQKWAADVVP	SGEEQRYTCH	VQHEGLPKPL

HLA-Ia paralogues | HLA-I - TcR interactions

α -chain

 H-Bond-involved

 Van der Waals interactions

Consensus Conservation	1	11	21	31	41	51	61	71	81
HLA-C1	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-C2	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-B6	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-B4	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-B3	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-B5	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-B2	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-B1	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-A3	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-A1	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
HLA-A2	GS S HS M RYFY T	A V SR P GRGEP	R F Ia V GYVDD	TQFVRFDS S DA	AS P reEPRAP	WI E QEGPEYW	D R E T Q I C K a q	AQTDRVSLRN	L R GY N QSE A
Consensus Conservation	91	101	111	121	131	141	151	161	171
HLA-C1	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-C2	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-B6	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-B4	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-B3	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-B5	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-B2	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-B1	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-A3	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-A1	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
HLA-A2	GS S HT I Q r MYG	CD V GP D GR I L	R G Yn Q y A YD G	K D YI A L N ED L	r S WT A AD t AA	Q I T q R K WEAA	r v AE Q I R AY L	E G T C VE W L R R	Y L ENG K ET L Q
Consensus Conservation	181	191	201	211	221	231	241	251	261
HLA-C1	R A EH P K T H V T	H H P V S D HEAT	L R CW A L G F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-C2	R A EH P K T H V T	H H P V S D HEAT	L R CW A L G F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-B6	R A EH P K T H V T	H H P V S D HEAT	L R CW A L G F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-B4	R A EH P K T H V T	H H P V S D HEAT	L R CW A L G F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-B3	R A EH P K T H V T	H H P V S D HEAT	L R CW A L G F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-B5	R A EH P K T H V T	H H P V S D HEAT	L R CW A L G F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-B2	R A EH P K T H V T	H H P V S D HEAT	L R CW A L G F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-B1	R A EH P K T H V T	H H P V S D HEAT	L R CW A L G F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-A3	R T D A P K T H M T	H H A V S D HEAT	L R CW A L S F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-A1	R T D A P K T H M T	H H A V S D HEAT	L R CW A L S F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L
HLA-A2	R T D A P K T H M T	H H P I S D HEAT	L R CW A L G F Y P	A E I T L T W Q R D	G E D Q T Q D T E L	V E T R P A G D G T	F Q KW A A V V V P	S G E E Q R Y T C H	V Q HE G L P K P L

HLA-Ia paralogues | HLA-I - CD8 interactions

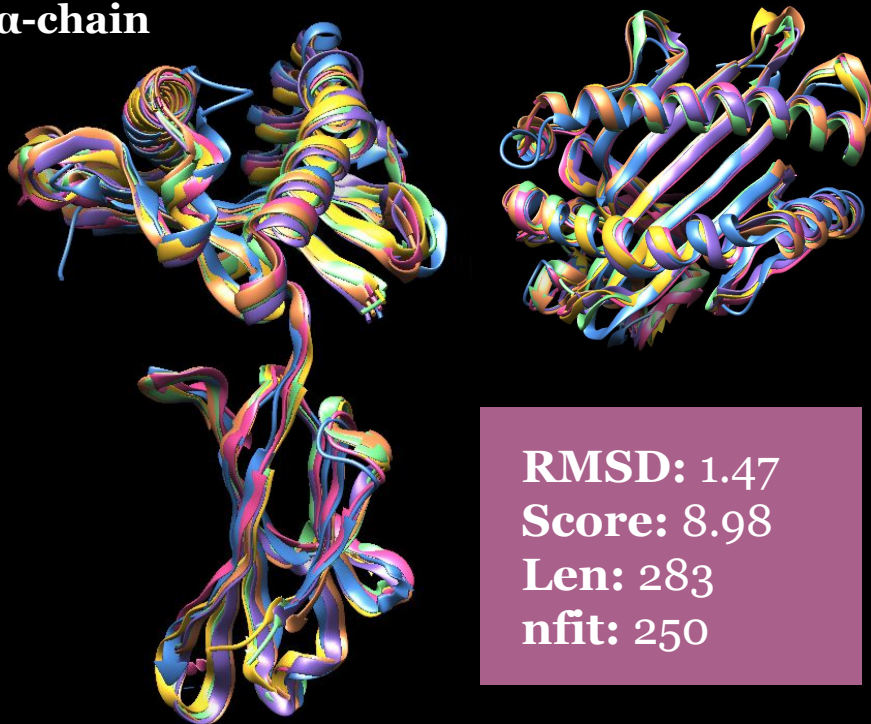
α-chain

H-Bond-involved

Consensus Conservation	1	11	21	31	41	51	61	71	81
HLA-C1	GS ^H SMRY ^F y ^T	s ^v SRPGRGEP	RF ^I a ^V GYVDD	TQFVRFDS ^D A	AS ^p Re ^E PRAP	WI ^E QEGPEY ^W	DRe ^T q ⁱ c ^k a ^q	a ^Q T ^d Re ^d L ^r t	L ^r g ^Y YNQSE ^A
HLA-C2	GS ^H SMRY ^F Y ^T	AV ^S RPGRGEP	HF ^I AVGYVDD	TQFVRFDS ^D A	AS ^p RGEP ^R EP	WV ^E QEGPEY ^W	DRE ^T QKY ^K RQ	AQ ^T DRVSL ^R N	LR ^G YYNQSE ^A
HLA-B6	GS ^H SMRY ^F Y ^T	AM ^S RPGRGEP	RF ^I AVGYVDD	TQFVRFDS ^D A	AS ^p RT ^E PRAP	WI ^E QEGPEY ^W	DR ^N TQIF ^K TN	TQ ^T YRSL ^R N	AL ^R YYNQSE ^A
HLA-B4	GS ^H SMRY ^F Y ^T	AM ^S RPGRGEP	RF ^I AVGYVDD	TQFVRFDS ^D A	AS ^p RT ^E PRAP	WI ^E QEGPEY ^W	DR ^N TQIF ^K TN	TQ ^T YRSL ^R N	LR ^G YYNQSE ^A
HLA-B3	GS ^H SMRY ^F Y ^T	AM ^S RPGRGEP	RF ^I SVGYVDD	TQFVRFDS ^D A	A- - - - - P	WI ^E QEGPEY ^W	DR ^N TQIF ^K TN	TQ ^T DRSL ^R N	LR ^G YYNQSE ^A
HLA-B5	GS ^H SMRY ^F Y ^T	AV ^S RPGRGEP	RF ^I SVGYVDD	TQFVRFDS ^D A	AS ^p RE ^E PRAP	WI ^E QEGPEY ^W	DR ^N TQICK ^T N	TQ ^T DRSL ^R N	LR ^G YYNQSE ^A
HLA-B2	GS ^H SMRY ^F HT	S ^V SRPGRGEP	RF ^I TVGYVDD	TLFVRFDS ^D A	AS ^p RE ^E PRAP	WI ^E QEGPEY ^W	DR ^E TQICK ^A K	AQ ^T DR ^E DL ^R T	LL ^R YYNQSE ^A
HLA-B1	GS ^H SMRY ^F HT	S ^V SRPGRGEP	RF ^I TVGYVDD	TLFVRFDS ^D A	AS ^p RE ^E PRAP	WI ^E QEGPEY ^W	DR ^E TQICK ^A K	AQ ^T DR ^E DL ^R T	LL ^R YYNQSE ^A
HLA-A3	GS ^H SMRY ^F Y ^T	S ^V SRPGRGEP	RF ^I AVGYVDD	TQFVRFDS ^D A	AS ^Q RME ^P RAP	WI ^E QEGPEY ^W	DR ^N TRNV ^K AQ	SQ ^T DRVDL ^G T	LR ^G YYNQSE ^A
HLA-A1	GS ^H SMRY ^F Y ^T	S ^V SRPGRGEP	RF ^I AVGYVDD	TQFVRFDS ^D A	AS ^Q RME ^P RAP	WI ^E QEGPEY ^W	DG ^E TRKV ^K AH	SQ ^T HRVDL ^G T	LR ^G YYNQSE ^A
HLA-A2	GS ^H SMRY ^F Y ^T	S ^V SRPGRGEP	RF ^I AVGYVDD	TQFVRFDS ^D A	AS ^Q RME ^P RAP	WI ^E QEGPEY ^W	DQ ^E TRNV ^K AQ	SQ ^T DRVDL ^G T	LR ^G YYNQSE ^A
Consensus Conservation	91	101	111	121	131	141	151	161	171
HLA-C1	GS ^H T ^I Q ^r MY ^G	CD ^V GP ^D GR ^I L	RG ^y n ^Q y ^A YD ^G	KD ^Y I ^A LNED ^L	r ^S WTAA ^D t ^A A	Q ^I T ^q RKWE ^A A	r ^v AEQ ^I RAY ^L	EG ^t CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
HLA-C2	GS ^H T ^I Q ^r MY ^G	CD ^V GP ^D GR ^L L	RG ^Y D ^Q y ^A YD ^G	KD ^Y I ^A LNED ^L	RS ^W TAA ^D TAA	Q ^I T ^Q RKWE ^A A	RE ^A EQLRAY ^L	EG ^L CV ^E WL ^R R	Y ^L KNGK ^E T ^L Q
HLA-B6	GS ^H T ^L Q ^r MY ^G	CD ^L GP ^D GR ^L L	RG ^Y N ^Q y ^A YD ^G	KD ^Y I ^A LNED ^L	RS ^W TAA ^D TAA	Q ^I T ^Q RKWE ^A A	RE ^A EQLRAY ^L	EG ^L CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
HLA-B4	GS ^H T ^L Q ^r MY ^G	CD ^L GP ^D GR ^L L	RG ^H N ^Q y ^A YD ^G	KD ^Y I ^A LNED ^L	RS ^W TAA ^D TAA	Q ^I T ^Q RKWE ^A A	RE ^A EQLRAY ^L	EG ^L CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
HLA-B3	GS ^H T ^L Q ^r MY ^G	CD ^L GP ^D GR ^L L	RG ^H N ^Q y ^A YD ^G	KD ^Y I ^A LNED ^L	RS ^W TAA ^D TAA	Q ^I T ^Q RKWE ^A A	RE ^A EQLRAY ^L	EG ^L CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
HLA-B5	GS ^H T ^L Q ^r MY ^G	CD ^V GP ^D GR ^L L	RG ^Y N ^Q y ^A YD ^G	KD ^Y I ^A LNED ^L	RS ^W TAA ^D TAA	Q ^I T ^Q RKWE ^A A	RE ^A EQLRAY ^L	EG ^L CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
HLA-B2	GS ^H T ^L Q ^r MY ^G	CD ^V GP ^D GR ^L L	RG ^Y H ^Q y ^A YD ^G	KD ^Y I ^A LNED ^L	RS ^W TAA ^D TAA	Q ^I T ^Q RKWE ^A A	RE ^A EQLRAY ^L	EG ^L CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
HLA-B1	GS ^H T ^L Q ^r MY ^G	CD ^V GP ^D GR ^L L	RG ^Y H ^Q y ^A YD ^G	KD ^Y I ^A LNED ^L	RS ^W TAA ^D TAA	Q ^I T ^Q RKWE ^A A	RE ^A EQLRAY ^L	EG ^L CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
HLA-A3	GS ^H T ^I Q ^r MY ^G	CD ^V GS ^D GR ^F L	RG ^Y R ^Q y ^A YD ^G	KD ^Y I ^A LKED ^L	RS ^W TAA ^D MAA	Q ^T T ^K HKWE ^A A	HV ^A EQLRAY ^L	EG ^T CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
HLA-A1	GS ^H T ^V Q ^r MY ^G	CD ^V GS ^D WR ^F L	RG ^Y H ^Q y ^A YD ^G	KD ^Y I ^A LKED ^L	RS ^W TAA ^D MAA	Q ^T T ^K HKWE ^A A	HV ^A EQLRAY ^L	EG ^T CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
HLA-A2	GS ^H T ^I Q ^r MY ^G	CD ^V GP ^D GR ^F L	RG ^Y R ^Q y ^A YD ^G	KD ^Y I ^A LNED ^L	RS ^W TAA ^D MAA	Q ^I T ^K RKWE ^A A	HV ^A EQRAY ^L	EG ^R CV ^E WL ^R R	Y ^L ENGK ^E T ^L Q
Consensus Conservation	181	191	201	211	221	231	241	251	261
HLA-C1	RA ^E HP ^K THV ^T	HH ^P V ^S DE ^H EAT	LRC ^W AL ^G FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^G r ^T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-C2	RA ^E HP ^K THV ^T	HH ^P V ^S DE ^H EAT	LRC ^W AL ^G FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^G T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-B6	RA ^D PP ^K THV ^T	HH ^P V ^S DE ^H EAT	LRC ^W AL ^G FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^R T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-B4	RA ^D PP ^K THV ^T	HH ^P V ^S DE ^H EAT	LRC ^W AL ^G FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^R T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-B3	RA ^D PP ^K THV ^T	HH ^P I ^S DE ^H EAT	LRC ^W AL ^G FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^R T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-B5	RA ^D PP ^K THV ^T	HH ^P I ^S DE ^H EAT	LRC ^W AL ^G FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^R T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-B2	RA ^D PP ^K THV ^T	HH ^P I ^S DE ^H EAT	LRC ^W AL ^G FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^R T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-B1	RA ^D PP ^K THV ^T	HH ^P I ^S DE ^H EAT	LRC ^W AL ^G FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^R T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-A3	RT ^D AP ^K THMT	HH ^A V ^S DE ^H EAT	LRC ^W AL ^S FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^G T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-A1	RT ^D AP ^K THMT	HH ^A V ^S DE ^H EAT	LRC ^W AL ^S FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^G T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L
HLA-A2	RT ^D PP ^K THMT	HH ^P I ^S DE ^H EAT	LRC ^W AL ^G FYP	AE ^I T ^L TW ^Q RD	GED ^Q TQ ^D TEL	VE ^T RPAGD ^G T	FQ ^K WAAV ^V VP	SG ^E EQRY ^T CH	VQ ^H EGL ^P K ^P L

HLA-A orthologs | STAMP and dendrogram

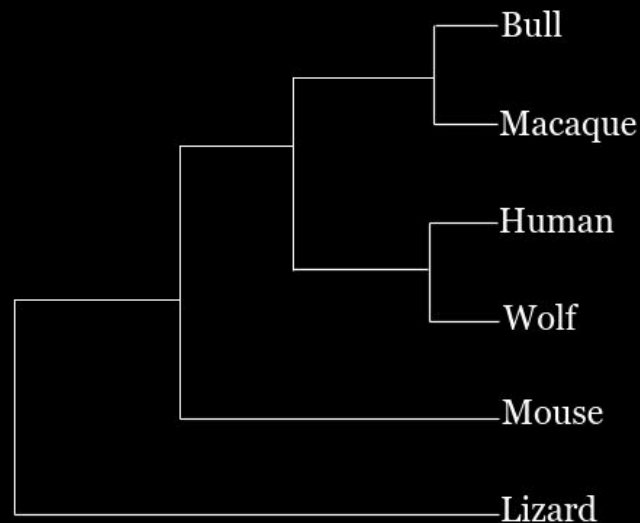
α -chain



RMSD: 1.47
Score: 8.98
Len: 283
nfit: 250



Structural dendrogram



HLA-A orthologs | STAMP and dendrogram

α -chain

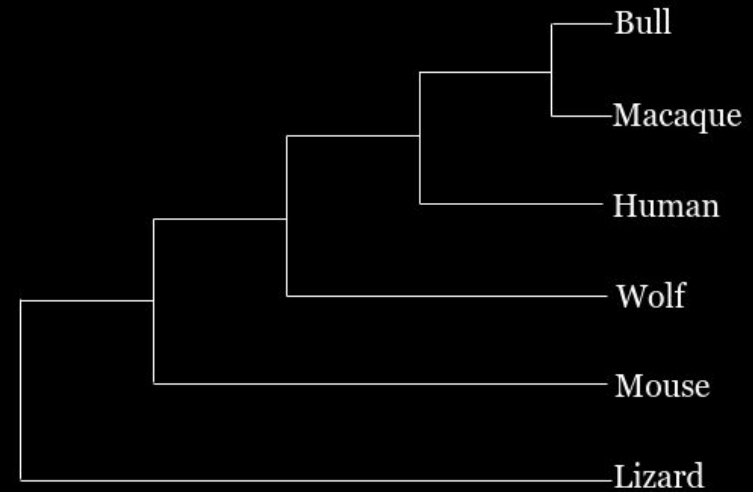
β 2-microglobulin



RMSD: 1.44
Score: 9.19
Len: 384
nfit: 342



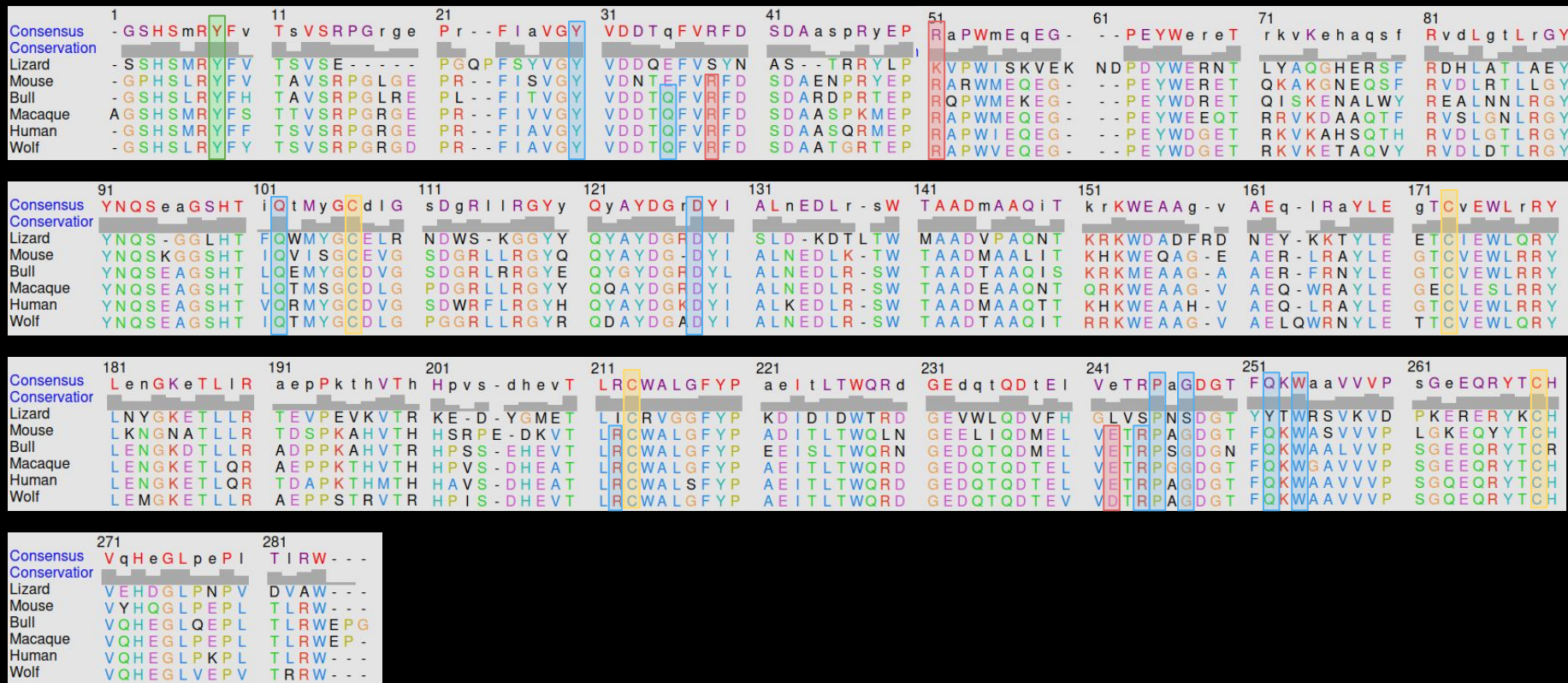
Structural dendrogram



HLA-A orthologs | Inner interactions in HLA-I

α -chain

- H-Bond-involved
- Salt bridge-involved
- Disulfur bond-involved
- Hydrophobic bond-involved



HLA-A orthologs | Inner interactions in HLA-I

β 2-microglobulin

- H-Bond-involved
- Salt bridge-involved
- Disulfur bond-involved
- Hydrophobic bond-involved

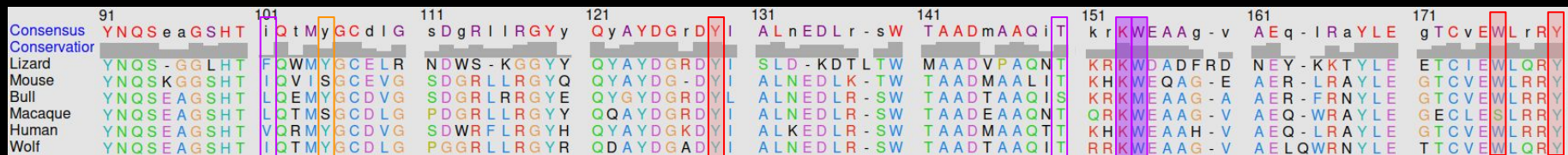
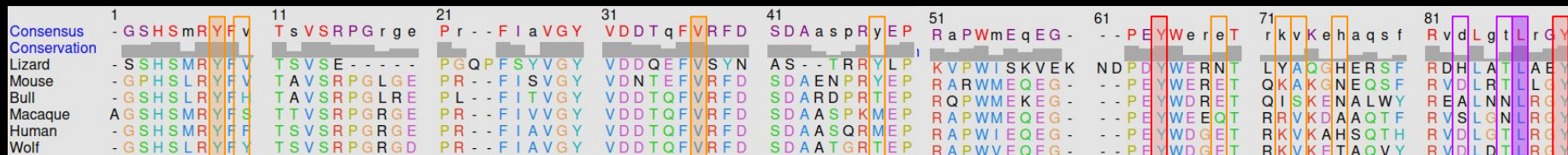


HLA-A orthologs | Binding groove

α -chain

- Cleft wall
- Pocket B
- Pocket F

Conserved	Variable
Conserved	Variable



HLA-A orthologs | HLA-I - TcR interactions

α -chain

 H-Bond-involved

 Van der Waals interactions

	1	11	21	31	41	51	61	71	81
Consensus	- GSHSmRYFv	TsVSRPG rge	Pr - - F l a VGY	VDDTqFVRFD	SDAaspRYEP	RaPWmEqEG -	- - PEYWer eT	rkvKehaqs f	RvdLgtLrGY
Conservation	- SSSHmRYFV	TSVSE - - - -	PGQPFSYVGY	VDDQEFVSYN	AS - - TRRYLP	KVPWISKVEK	NDPDYWERNT	LYAQGHERSF	RDHLATLAEY
Lizard	- SSSHmRYFV	TSVSE - - - -	PGQPFSYVGY	VDDQEFVSYN	AS - - TRRYLP	KVPWISKVEK	NDPDYWERNT	LYAQGHERSF	RDHLATLAEY
Mouse	- GPHSLRYFV	TAVSRPGLGE	PR - - FISVGY	VDNTEFVRFD	SDAENPRYEP	RARWMEQEG -	- - PEYWERET	QKAKGNEQSF	RVDLRTLLEGY
Bull	- GSHSLRYFV	TAVSRPGLRE	PL - - FITVGY	VDDTQFVRFD	SDARDPRTEP	RQPWMEKEG -	- - PEYWDR ET	QISKENALWY	REALNNLRGY
Macaque	AGSHSMRYFS	TTVSRPGRGE	PR - - FIVVGY	VDDTQFVRFD	SDAASPMEP	RAPWMEQEG -	- - PEYWEQET	RRVKDAAQTF	RVSLSNLRGY
Human	- GSHSLRYFF	TSVSRPGRGE	PR - - FIAVGY	VDDTQFVRFD	SDAASQRMPE	RAPWIEQEG -	- - PEYWDGET	RKVKAHSQTH	RVDLGLTLRGY
Wolf	- GSHSLRYFY	TSVSRPGRGD	PR - - FIAVGY	VDDTQFVRFD	SDAATGRTEP	RAPWVEQEG -	- - PEYWDGET	RKVKEETAQVY	RVDLDTLRGY

	91	101	111	121	131	141	151	161	171
Consensus	YNQSe aGSHT	iQtMyGCd lG	sDgRl lRGYy	QyAYDGrDYI	ALnEDLr - sW	TAAADmAAQIT	krKWEAAg - v	AEq - lR aYLE	gTc vEWLrRY
Conservation	YNQS - GGLHT	FQWMYGCELR	NDWS - KGGYY	QYAYDGRDYI	S LD - KDTL TW	MAADVP AQNT	KRKWDADFRD	NEY - KKTYLE	ETCIEWLQRY
Lizard	YNQS - GGLHT	FQWMYGCELR	NDWS - KGGYY	QYAYDGRDYI	S LD - KDTL TW	MAADVP AQNT	KRKWDADFRD	NEY - KKTYLE	ETCIEWLQRY
Mouse	YNQSKGGSH	LQVISGCEVG	SDGRLLRGYQ	QYAYDG - DYI	ALNEDL - TW	TAAADMAALIT	KHKWEQAG - E	AER - LRAYLE	GTCVEWLRRY
Bull	YNQSEAGSHT	LQEMSGCDVG	SDGRLLRGYE	QYGYDGRDYL	ALNEDL - SW	TAAATAAQIS	KRKMEAAg - A	AER - FRNYLE	GTCVEWLRRY
Macaque	YNQSEAGSHT	LQTMSCDVLG	PDGRLLRGYH	QYAYDGRDYI	ALNEDL - SW	TAADEAAQNT	QRKWEAAg - V	AEQ - WRAYLE	GTCVEWLRRY
Human	YNQSEAGSHT	VQRMYGCDVG	SDWRFLRGYH	QYAYDGKDYI	ALNEDL - SW	TAAADMAAQIT	KHKWEAAH - V	AEQ - LRAYLE	GTCVEWLRRY
Wolf	YNQSEAGSHT	IQTMYGCDLG	PGGRLLRGYR	QDAYDGADYI	ALNEDL - SW	TAAATAAQIT	RRKWEAAg - V	ALQWRNYLE	TTTCVEWLQRY

	181	191	201	211	221	231	241	251	261
Consensus	LenGKeTLIR	aepPkthVTh	Hpv s - dhevT	LRCWALGFYP	ae i tLTWQRd	GEDqtQDT e l	VeTRPaGDGT	FQKWaaVVVP	sGeEQRYTCH
Conservation	LNyGKETLLR	TEVPEVKVTR	KE - D - YGMET	LICRVGGFYF	KDIDIDWTRD	GEVWLQDVFH	GLVSPNSDGT	YYTWRSVKVD	PKERERYKCH
Lizard	LNyGKETLLR	TEVPEVKVTR	KE - D - YGMET	LICRVGGFYF	KDIDIDWTRD	GEVWLQDVFH	GLVSPNSDGT	YYTWRSVKVD	PKERERYKCH
Mouse	LKNGNATLLR	TDSPKAHVTH	HSRPE - DKVT	LRCWALGFYP	ADITLTWQLN	GEELIQDMEL	VETRPAGDGT	FQKWAASVVP	LKQEQQYTCH
Bull	LENGKDTLLR	ADPPKAHVTH	HPSS - DHEVT	LRCWALGFYP	EEISLTWQRN	GEDQTQDMEL	VETRPAGDGT	FQKWAALVVP	SGEQRYTCH
Macaque	LENGKETLQR	AEPKTHVTH	HPVS - DHEAT	LRCWALGFYP	AEITLTWQRN	GEDQTQDTL	VETRPAGDGT	FQKWAALVVP	SGEQRYTCH
Human	LENGKETLQR	TDAPKTHMTH	HAVS - DHEAT	LRCWALSFPY	AEITLTWQRD	GEDQTQDTL	VETRPAGDGT	FQKWAALVVP	SGEQRYTCH
Wolf	LEMKGKETLLR	AEPSTRTVTR	HPIS - DHEVT	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEV	VDTRPAGDGT	FQKWAALVVP	SGEQRYTCH

	271	281
Consensus	VqHeGLpePl	TIRW - - -
Conservation	VEHDGLPNPV	DVAW - - -
Lizard	VEHDGLPNPV	DVAW - - -
Mouse	VYHQGLPEPL	TLRW - - -
Bull	VQHEGLQEPPL	TLRWEPG
Macaque	VQHEGLPEPL	TLRWEP -
Human	VQHEGLPKPL	TLRW - - -
Wolf	VQHEGLVEPV	TLRW - - -

HLA-A orthologs | HLA-I - CD8 interactions

α -chain

H-Bond-involved

	1	11	21	31	41	51	61	71	81
Consensus	- GSHSmRYFv	TsVSRPG rge	Pr - - F l a VGy	VDDTqFVRFD	SDAaspRyEP	RaPWmEqEG -	- - PEYWereT	rkvKehaqs f	RvdLgtLRgy
Conservation									
Lizard	- SSHSmRYFv	TSVSE - - - -	PGQPFSYVGy	VDDQEFVSYN	AS - - TRRYLP	KVPWISKVEK	NDPDYWERNT	LYAQGHERSF	RDHLATLAEY
Mouse	- GPHSLRYFv	TAVSRPGLGE	PR - - FISVGy	VDNTEFVRFD	SDAENPRYEP	RARWMEQEG -	- - PEYWERET	QKAKGNEQSF	RVDLRTLGLY
Bull	- GSHSLRYFh	TAVSRPGLRE	PL - - FITVGy	VDDTQFVRFD	SDARDPRTEP	RQPWMEKEG -	- - PEYWDRET	QISKENALWY	REALNNLRGY
Macaque	AGSHSMRYFS	TTVSRPGRGE	PR - - FITVGy	VDDTQFVRFD	SDAASPMEP	RAPWMEQEG -	- - PEYWEQET	RRVKDAAQTf	RVSGLNLRGY
Human	- GSHSLRYFF	TSVSRPGRGE	PR - - F l a VGy	VDDTQFVRFD	SDAASQRMPE	RAPWIEQEG -	- - PEYWDGET	RKVKAHSQTH	RVDLGLTLRGY
Wolf	- GSHSLRYFY	TSVSRPGRGD	PR - - F l a VGy	VDDTQFVRFD	SDAATGRTEP	RAPWVEQEG -	- - PEYWDGET	RKVKETAQVY	RVDLDTLRGY

	91	101	111	121	131	141	151	161	171
Consensus	YNQSe a GSHT	iQtMyGCd l G	sDgRl l RGYy	QyAYDGR d Y l	ALnEDLr - sW	TAADmAAQIT	krKWEAAg - v	AEq - lRaYLE	gTCvEWLrRY
Conservation									
Lizard	YNQS - GGLHT	FQWMYGCELR	NDWS - KGGYy	QYAYDGR d Y l	S LD - KDTL TW	MAADVPAQNT	KRKWDADFRD	NEY - KKTYLE	ETCIEWLQRy
Mouse	YNQSKGGSHT	LQVISGCEVG	SDGRLLRGYQ	QYAYDG - d Y l	ALNEDLK - TW	TAADMALIT	KHKWEQAG - E	AER - LRAYLE	GTCVEWLRRY
Bull	YNQSEAGSHT	LQEMYGCDVG	SDGRLLRGYE	QYGYDGR d Y l	ALNEDLR - SW	TAADTAAQIS	KRKMEAG - A	AER - FRNYLE	GTCVEWLRRY
Macaque	YNQSEAGSHT	LQTMSCDVG	PDGRLLRGYy	QYAYDGR d Y l	ALNEDLR - SW	TAADAAAQNT	QRKWEAAG - V	AEQ - WRAYLE	GECLESLRRY
Human	YNQSEAGSHT	VQRMYGCDVG	SDWRLLRGYH	QYAYDGK d Y l	ALKEDLR - SW	TAADMAAQT	KHKWEAAH - V	AEQ - LRAYLE	GTCVEWLRRY
Wolf	YNQSEAGSHT	IQTMYGCDLG	PGGRLLRGYR	QDAYDGA d Y l	ALNEDLR - SW	TAADTAAQIT	RRKWEAAG - V	AEQLQWRNYLE	TTCVEWLQRy

	181	191	201	211	221	231	241	251	261
Consensus	LenGKeTLIR	aepPkthVTh	Hpvs - dhevT	LRCWALGFYP	ae l t LTWORd	GEDqtQD t E l	VeTRPaGDGT	FQKWaaVVP	sGeEQRYTCH
Conservation									
Lizard	LNyGKETLLR	TEVPEVKVTR	KE - D - YGMET	LICRVGGFYF	KD l D l DWTRD	GEVWLQDVVFH	GLVSPNSDGT	YYTWRSVKVD	PKERERYKCH
Mouse	LKNGNATLLR	TDSPKAHVTH	HSRPE - DKVT	LRCWALGFYP	AD l TLTWLRN	GEELIQDMEL	VE TRPAGDGT	FQKWA SVVP	LQKEQY YTCH
Bull	LENGKDTLLR	ADPPKAHVTH	HPSS - DHEVT	LRCWALGFYP	EE l SLTWQRN	GEDQTQDMEL	VE TRPAGDGT	FQKWA SVVP	SGEEQRYTCH
Macaque	LENGKETLQR	ADEPKTHVTH	HPVS - DHEAT	LRCWALGFYP	AE l TLTWQRN	GEDQTQDMEL	VE TRPAGDGT	FQKWA SVVP	SGEEQRYTCH
Human	LENGKETLQR	TDAPKTHMTH	HAVS - DHEAT	LRCWALS FYF	AE l TLTWQRD	GEDQTQDT E l	VE TRPAGDGT	FQKWA SVVP	SGEEQRYTCH
Wolf	LEMKGKETLLR	AEPpSTRVTR	HPIS - DHEVT	LRCWALGFYP	AE l TLTWQRD	GEDQTQDT E l	VD TRPAGDGT	FQKWA SVVP	SGEQRYTCH

	271	281
Consensus	VqHeGLpePl	TIRW - - -
Conservation		
Lizard	VEHDGLPNPV	DVAW - - -
Mouse	VYHQGLPEPL	TLRW - - -
Bull	VQHEGLQEP L	TLRWEPG
Macaque	VQHEGLPEPL	TLRWEP -
Human	VQHEGLPKPL	TLRW - - -
Wolf	VQHEGLVEPV	TRRW - - -



Conclusions

Conclusions

01

HLA structure

Conservation in residues involved in HLA inner interactions, especially cysteines, is important to preserve their structure and function along evolution.

02

Binding groove

The three pockets with the most important roles (A, B, F) present hydrophobicity, as well as conserved and variable residues, both between the paralogues and the orthologues.

03

TcR

TcR recognition of peptide-HLA complexes is essential for disease control and survival.

04

Evolution

The high conservation of HLA-I sequence confirms its essential role.



**Thanks for your
attention**

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Multiple choice questions

1. Which is the optimal length for a peptide bound in HLA-I?
 - a. 5-6 amino acids
 - b. 8-10 amino acids
 - c. 18-25 amino acids
 - d. +12 amino acids
 - e. 25-30 amino acids

2. Which are the pockets that form the main interactions between the peptide and the molecule?
 - a. Pocket A and B
 - b. Pocket B and D
 - c. Pocket A and F
 - d. Pocket A and D
 - e. Pocket B and F

3. Regarding the binding pockets, choose the correct answer:
 - a. HLA-I has an open binding cleft with 9 pockets but HLA-II has a closed binding cleft with 6 pockets.
 - b. The HLA-I binding groove contains both conserved and variable residues.
 - c. Pockets A and F are the wall of the cleft that close the groove.
 - d. a and c are correct.
 - e. b and c are correct.

Multiple choice questions

4. Regarding disulfide bonds in HLA-I molecules, choose the correct statement:

- a. They stabilize the Ig-like beta-sandwich structure.
- b. They are found in all the domains of HLA molecules.
- c. They connect the two β -sheets to generate the Ig-like beta-sandwich structure.
- d. a and c are correct.
- e. All of the above are correct.

5. Regarding the inner interactions of HLA molecules, choose the correct statement:

- a. The great amount of hydrogen bonds help stabilize the structure of HLA molecules.
- b. β 2-microglobulin interacts with the 3 different domains of the α -chain.
- c. Disulfide bonds are formed between the 2 different chains of HLA molecules.
- d. a and b are correct.
- e. All of the above are correct.

6. Choose the incorrect statement regarding to HLA molecules' structure:

- a. Both HLA class I and II are composed of two different chains.
- b. Class I's α 1 and α 2 domains and Class II's α 1 and β 1 domains form the antigen binding groove.
- c. SCOP classifies all the HLA domains as alpha+beta proteins.
- d. b and c are incorrect.
- e. All of the above are incorrect.

Multiple choice questions

7. Which affirmation is false?

- a. CD8 is a coreceptor for TCR.
- b. CD8 is specific for HLA-II.
- c. HLA interacts with TCR CDR1 and CDR2.
- d. Peptides interact with TCR CDR3.
- e. Between TCR and the peptide there are different Van der Waals interactions where Asp 4 is involved.

8. Which affirmation is false?

- a. In paralogs the conservation of hydrogen bonds between HLA-I and CD8 is 100%
- b. Hydrophobic interactions between HLA-I and TCR are almost fully conserved.
- c. Residues that form a salt bridge between HLA-I and TCR are conserved in all species.
- d. Wolf is the specie in which hydrogen bonds formed between HLA-I and CD8 are less conserved.
- e. All types of interactions between HLA-I and TCR in paralogs are really conserved.

9. Choose the incorrect statement about the alpha chain of HLA-A in orthologs

- a. Lizard is the specie which HLA-A structure is more different.
- b. Bull and macaques are clustered together.
- c. Humans and wolves are clustered together.
- d. Humans and macaques are clustered together.
- e. As the score is high, we can consider the dendrogram as correct.

Multiple choice questions

10. Choose the correct answer about HLA-I:

- a. The structure of HLA-I is formed with 3 α -domains and a β 2-microglobulin.
- b. HLA-I has a closed binding cleft with 6 pockets (A-F).
- c. a and b are correct.
- d. HLA-I does not have hydrophobic pockets.
- e. All of the above are correct.

HLA | HUMAN LEUKOCYTE ANTIGEN

An structural analysis

Marina Carreras, Mireia Roig, Mònica Sancho
Structural Biology | Human Biology | 23-24

