



MAJOR HISTOCOMPATIBILITY COMPLEX

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Introduction

The **major histocompatibility complex** (MHC) consists of a linked set of genetic loci encoding many of the proteins involved in antigen presentation to T cells

MAIN FUNCTION

Binding peptide fragments derived from pathogens and display them on the cell surface for recognition by the appropriate T cells.

MAIN FEATURES

Polygenic: every individual possesses a set of MHC molecules with different ranges of peptide-binding specificities.

Highly polymorphic: there are multiple variants of each gene within the population as a whole.

SCOP classification

CLASS

Alpha and beta proteins (a+b)

FOLD

MHC antigen-recognition domain

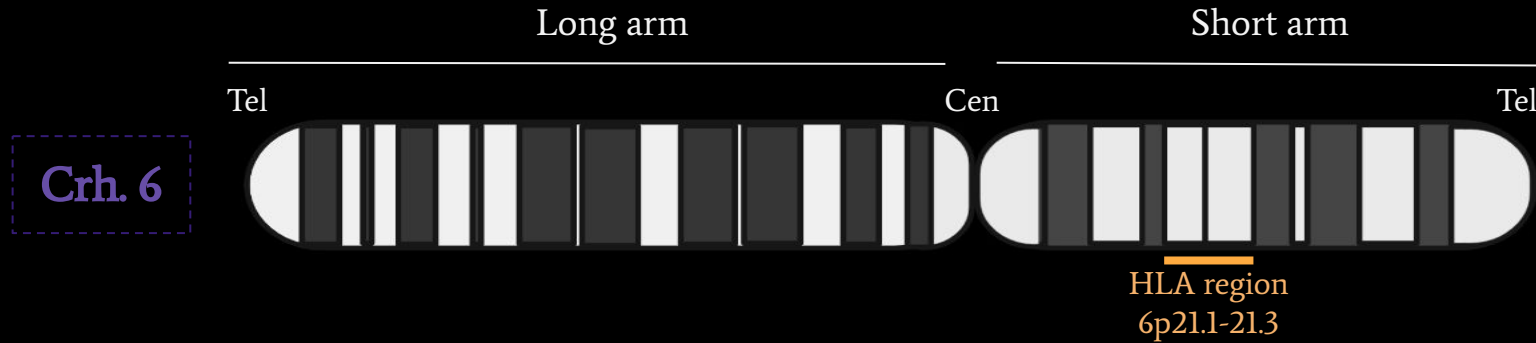
SUPERFAMILY

MHC antigen-recognition domain

FAMILY

MHC antigen-recognition domain

Introduction

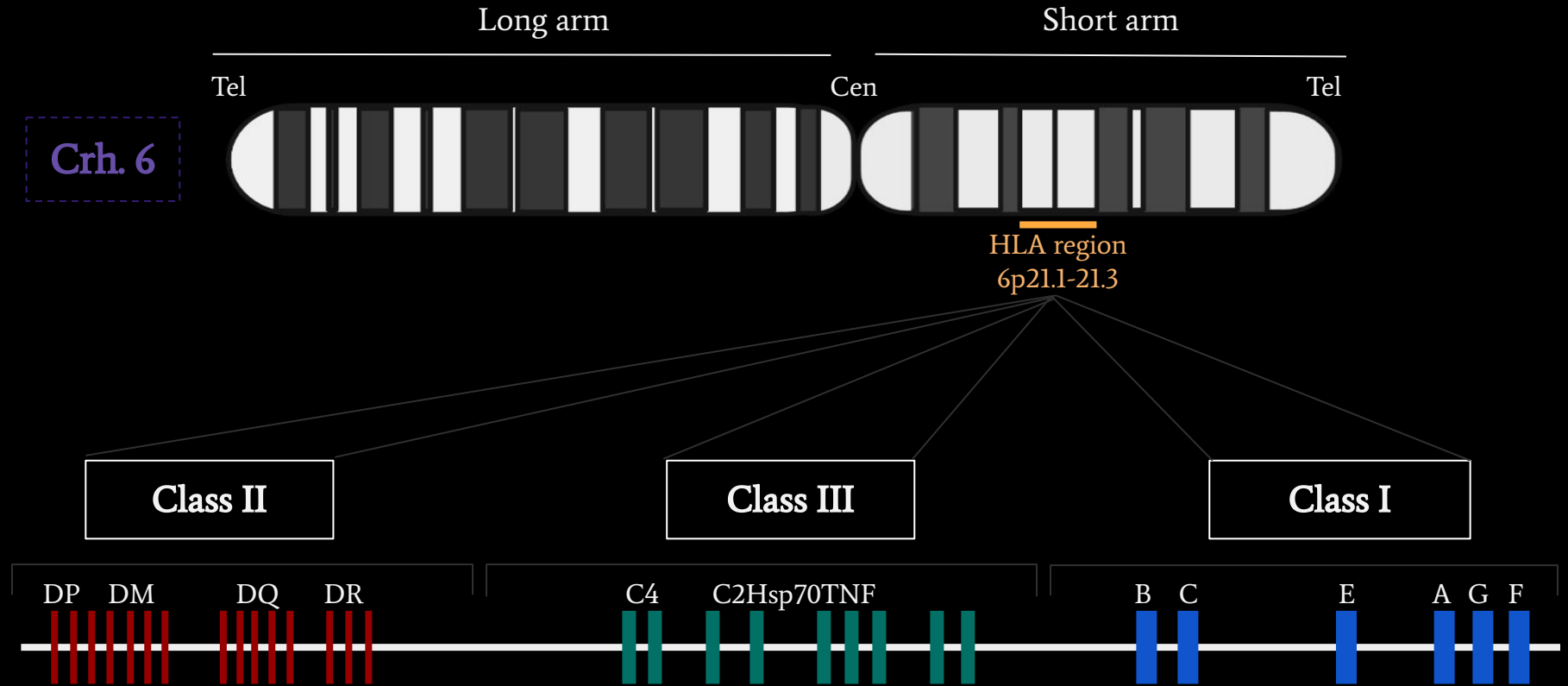


- Located in the short arm of the 6th Chr
- > 4 centimorgans of DNA: $\sim 4 \times 10^6$ bp
- Recent studies: 7×10^6 bp
- In humans contains more than 200 genes

Genes encoding the **α -chains of MHC-I** and **α , β -chains of MHC-II** are linked within the complex

Genes encoding the β 2-microglobulin are in the 15th Chr

Introduction



MHC-I vs MHC-II

	MHC class I	MHC class II
Peptide size	8-11 aa	12-25 aa
Structure	Heavy chain and β 2-microglobulin	II α and II β chains
Location	Nucleated cell types	Antigen Presenting Cells
Type of T cell	CD8+	CD4+
Subclasses	Classical: HLA-A, HLA-B and HLA-C	Classical: HLA-DP, HLA-DQ and HLA-DR
	Non-classical: HLA-E, HLA-F and HLA-G	Non-classical: HLA-DO and HLA-DM

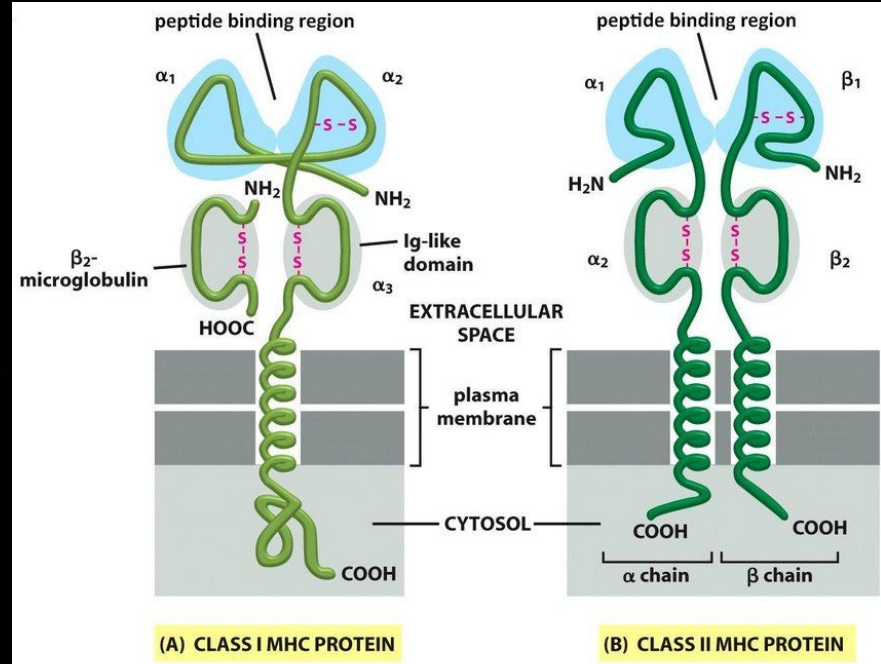
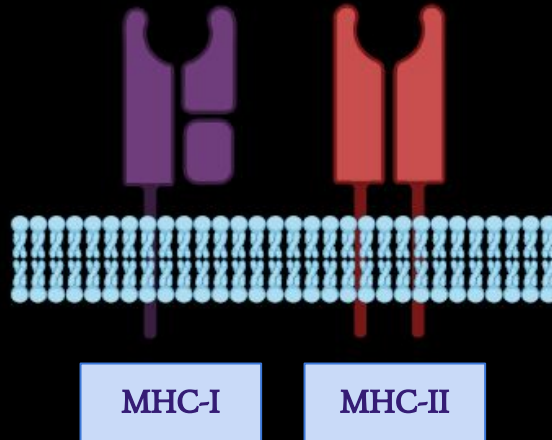
MHC-I vs MHC-II

Extracellular peptide binding site

Immunoglobulin-like domains

Transmembrane segment

Cytoplasmic segment



Manlik O. (2015) Fitness and major histocompatibility complex diversity of two bottlenose dolphin populations [Doctoral dissertation, University of New South Wales] UNSWorks. <https://www.unsw.edu.au/>

MHC-I vs MHC-II

MHC I

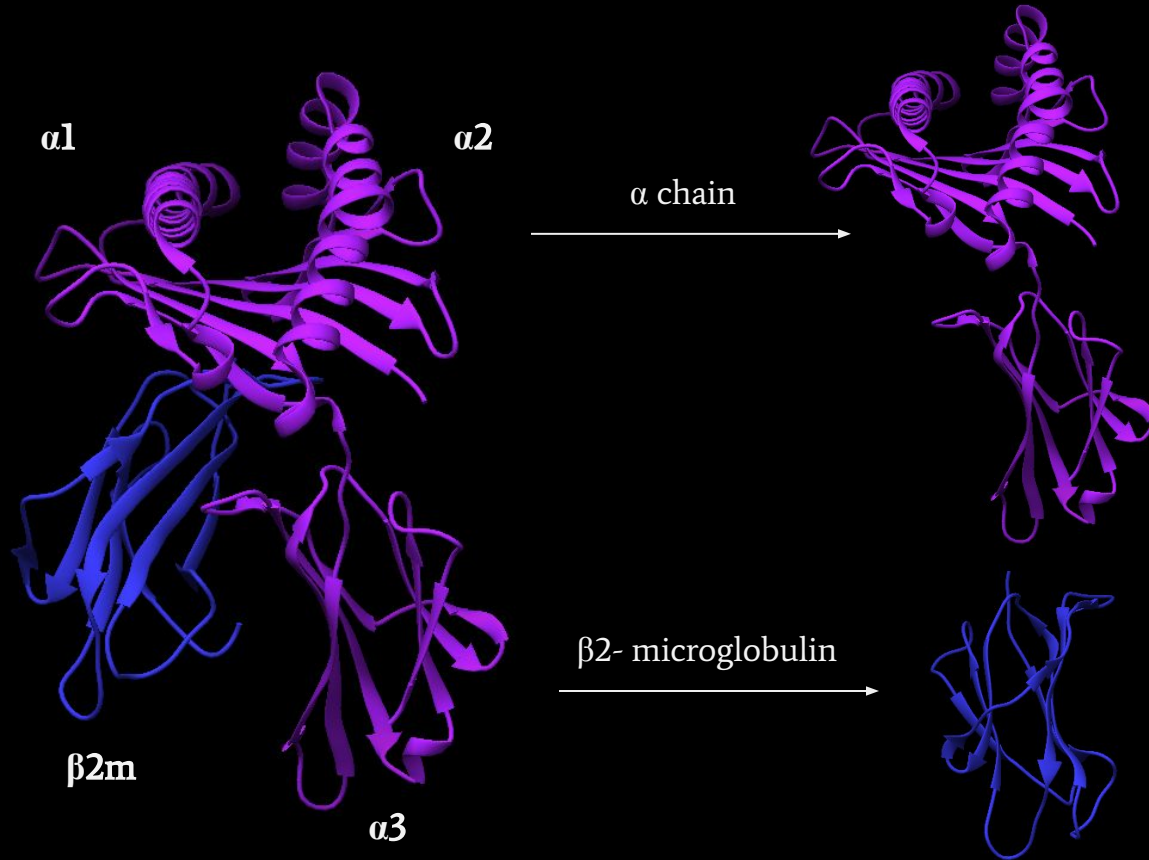


MHC II

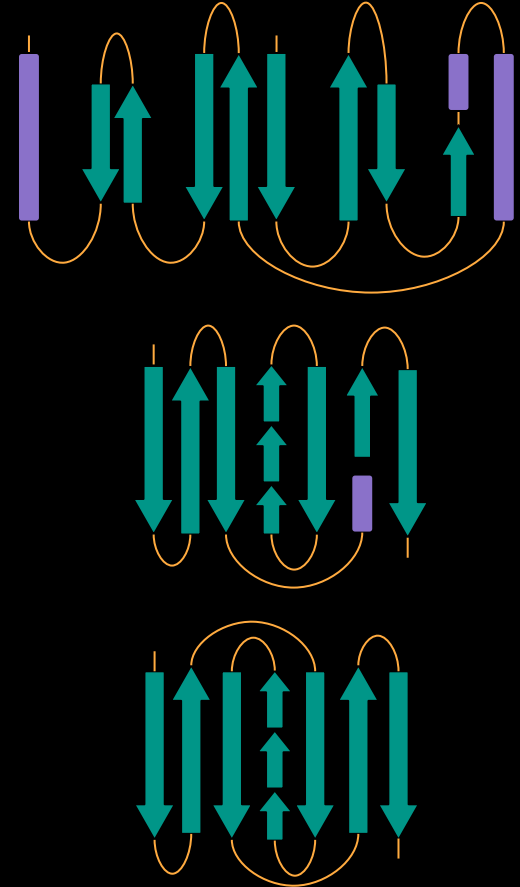
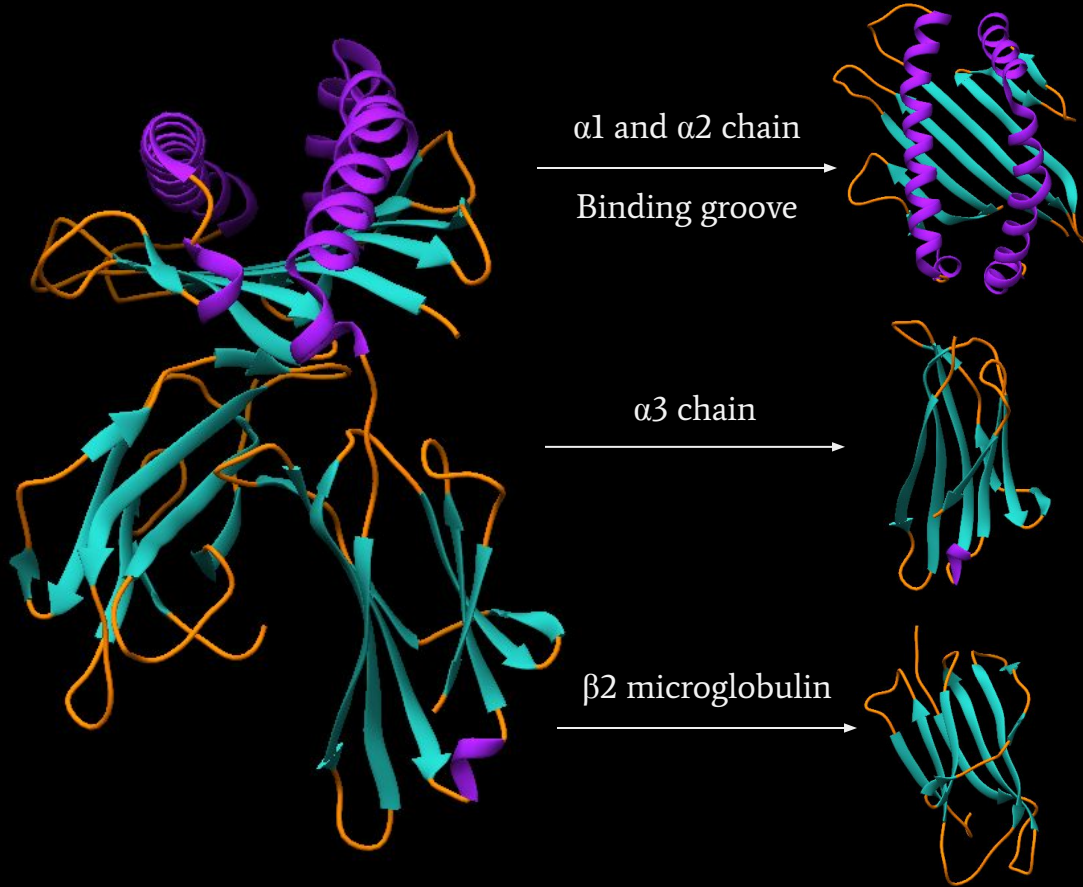


MHC-I

MHC I: DOMAINS



MHC I: DOMAINS



MHC I: SEQUENCE ALIGNMENT

	1	11	21	31	41	51
Consensus	g S H S M R Y F y T	a v S R P G R G E P	R F I a V G Y V D D	T Q F V r F D S D A	A S p r m e P R A P	W i E Q E G P E Y W
Conservation						
4NT6_1	M S H S M R Y F Y T	A V S R P G R G E P	R F I A V G Y V D D	T Q F V Q F D S D A	A S P R G E P R A P	W V E Q E G P E Y W
5VGD_1	- S H S M R Y F Y T	A V S R P G R G E P	R F I A V G Y V D D	T Q F V Q F D S D A	A S P R G E P R A P	W V E Q E G P E Y W
5XS3_1	- S H S M R Y F D T	A V S R P G R G E P	R F I S V G Y V D D	T Q F V R F D S D A	A S P R G E P R A P	W V E Q E G P E Y W
2BVO_1	G S H S M R Y F Y T	A M S R P G R G E P	R F I A V G Y V D D	T Q F V R F D S D A	A S P R M A P R A P	W I E Q E G P E Y W
2HJK_1	G S H S M R Y F Y T	A M S R P G R G E P	R F I A V G Y V D D	T Q F V R F D S D A	A S P R M A P R A P	W I E Q E G P E Y W
1K5N_1	G S H S M R Y F H T	S V S R P G R G E P	R F I T V G Y V D D	T L F V R F D S D A	A S P R E E P R A P	W I E Q E G P E Y W
3HLA_1	G S H S M R Y F F T	S V S R P G R G E P	R F I A V G Y V D D	T Q F V R F D S D A	A S Q R M E P R A P	W I E Q E G P E Y W
4HWZ_1	G S H S M R Y F Y T	S V S R P G R G E P	R F I A V G Y V D D	T Q F V R F D S D A	A S Q R M E P R A P	W I E Q E G P E Y W
2XPG_1	G S H S M R Y F F T	S V S R P G R G E P	R F I A V G Y V D D	T Q F V R F D S D A	A S Q R M E P R A P	W I E Q E G P E Y W
	61	71	81	91	101	111
Consensus	D r E T r k y K a q	a Q T d R v d L r t	l r g Y Y N Q S E A	G S H t i Q r M Y G	C D v G p D G R I L	R G y n Q y A Y D G
Conservation						
4NT6_1	D R E T Q K Y K R Q	A Q T D R V S L R N	L R G Y Y N Q S E A	G S H T L Q R M Y G	C D L G P D G R L L	R G Y N Q F A Y D G
5VGD_1	D R E T Q K Y K R Q	A Q T D R V N L R K	L R G Y Y N Q S E A	G S H T L Q R M Y G	C D L G P D G R L L	R G Y N Q F A Y D G
5XS3_1	D R E T Q K Y K R Q	A Q A D R V N L R K	L R G Y Y N Q S E D	G S H T L Q W M Y G	C D L G P D G R L L	R G Y D Q S A Y D G
2BVO_1	D G E T R N M K A S	A Q T Y R E N L R I	A L R Y Y N Q S E A	G S H I I Q V M Y G	C D V G P D G R L L	R G H N Q F A Y D G
2HJK_1	D G E T R N M K A S	A Q T Y R E N L R I	A L R Y Y N Q S E A	G S H I I Q V M Y G	C D V G P D G R L L	R G H D Q S A Y D G
1K5N_1	D R E T Q I C K A K	A Q T D R E D L R T	L L R Y Y N Q S E A	G S H T L Q N M Y G	C D V G P D G R L L	R G Y H Q H A Y D G
3HLA_1	D G E T R K V K A H	S Q T H R V D L G T	L R G Y Y N Q S E A	G S H T V Q R M Y G	C D V G S D W R F L	R G Y H Q Y A Y D G
4HWZ_1	D R N T R N V K A Q	S Q T D R V D L G T	L R G Y Y N Q S E A	G S H T I Q M M Y G	C D V G S D G R F L	R G Y R D A Y D G
2XPG_1	D Q E T R N V K A Q	S Q T D R V D L G T	L R G Y Y N Q S E A	G S H T I Q I M Y G	C D V G S D G R F L	R G Y R D A Y D G
	121	131	141	151	161	171
Consensus	K D Y I A L n E D L	r S W T A A D t A A	Q i T q r K W E A A	r v A E Q I R A Y L	E G t C V E W L R R	Y L E N G K e T L Q
Conservation						
4NT6_1	K D Y I A L N E D L	R S W T A A D T A A	Q I T Q R K W E A A	R T A E Q L R A Y L	E G T C V E W L R R	Y L E N G K K T L Q
5VGD_1	K D Y I A L N E D L	R S W T A A D K A A	Q I T Q R K W E A A	R E A E Q R R A Y L	E G T C V E W L R R	Y L E N G K K T L Q
5XS3_1	K D Y I A L N E D L	R S W T A A D T A A	Q I T Q R K W E A A	R E A E Q W R A Y L	E G T C V E W L R R	Y L E N G K E T L Q
2BVO_1	K D Y I A L N E D L	S S W T A A D T A A	Q I T Q R K W E A A	R V A E Q L R A Y L	E G L C V E W L R R	Y L E N G K E T L Q
2HJK_1	K D Y I A L N E D L	S S W T A A D T A A	Q I T Q R K W E A A	R V A E Q L R A Y L	E G L C V E W L R R	Y L E N G K E T L Q
1K5N_1	K D Y I A L N E D L	S S W T A A D T A A	Q I T Q R K W E A A	R V A E Q L R A Y L	E G E C V E W L R R	Y L E N G K E T L Q
3HLA_1	K D Y I A L K E D L	R S W T A A D M A A	Q T T K H K W E A A	H V A E Q L R A Y L	E G T C V E W L R R	Y L E N G K E T L Q
4HWZ_1	K D Y I A L K E D L	R S W T A A D M A A	Q T T K H K W E A A	H V A E Q W R A Y L	E G T C V E W L R R	Y L E N G K E T L Q
2XPG_1	K D Y I A L N E D L	R S W T A A D M A A	Q I T K R K W E A A	H E A E Q L R A Y L	D G T C V E W L R R	Y L E N G K E T L Q
	181	191	201	211	221	231
Consensus	R a d p P K T H v T	H H p v S D H E A T	L R C W 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
Conservation						
4NT6_1	R A E H P K T H V T	H H P V S D H E A T	L R C W 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
5VGD_1	R A E H P K T H V T	H H P V S D H E A T	L R C W 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
5XS3_1	R A E H P K T H V T	H H P V S D H E A T	L R C W A L G F Y P	A R 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
2BVO_1	R A D P P K T H V T	H H P I S D H E A T	L R C W 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 R T
2HJK_1	R A D P P K T H V T	H H P I S D H E A T	L R C W 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 R T
1K5N_1	R A D P P K T H V T	H H P I S D H E A T	L R C W 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 R T
3HLA_1	R T D A P K T H M T	H H A V S D H E A T	L R C W 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
4HWZ_1	R T D A P K T H M T	H H A V S D H E A T	L R C W 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
2XPG_1	R T D P P K T H M T	H H P I S D H E A T	L R C W 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

MHC I: SEQUENCE ALIGNMENT

	181	191	201	211	221	231
Consensus	R a d p K T H v T	H H p v S D H E A T	L R C W 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
Conservation						
4NT6_1	R A E H P K T H V T	H H P V S D H E A T	L R C W 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
5VGD_1	R A E H P K T H V T	H H P V S D H E A T	L R C W 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
5XS3_1	R A E H P K T H V T	H H P V S D H E A T	L R C W A L G F Y P	A R 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
2BVO_1	R A D P P K T H V T	H H P I S D H E A T	L R C W 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 R T
2HJK_1	R A D P P K T H V T	H H P I S D H E A T	L R C W 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 R T
1K5N_1	R A D P P K T H V T	H H P I S D H E A T	L R C W 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 R T
3HLA_1	R T D A P K T H M T	H H A V S D H E A T	L R C W 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
4HWZ_1	R T D A P K T H M T	H H A V S D H E A T	L R C W 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
2XPG_1	R T D P P K T H M T	H H P I S D H E A T	L R C W 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
	241	251	261	271		
Consensus	F Q K W A A V V V P	S G e E Q R Y T C H	V Q H E G L P k P L	T L R W - - - -		
Conservation						
4NT6_1	F Q K W A A V V V P	S G E E Q R Y T C H	V Q H E G L P E P L	T L R W - - - -		
5VGD_1	F Q K W A A V V V P	S G E E Q R Y T C H	V Q H E G L P E P L	T L R W G P S S		
5XS3_1	F Q K W A A V V V P	S G E E Q R Y T C H	V Q H E G L P E P L	T L R W - - - -		
2BVO_1	F Q K W A A V V V P	S G E E Q R Y T C H	V Q H E G L P K P L	T L R W E P - -		
2HJK_1	F Q K W A A V V V P	S G E E Q R Y T C H	V Q H E G L P K P L	T L R W - - - -		
1K5N_1	F Q K W A A V V V P	S G E E Q R Y T C H	V Q H E G L P K P L	T L R W E P - -		
3HLA_1	F Q K W A A V V V P	S G Q E Q R Y T C H	V Q H E G L P K P L	- - - - - -		
4HWZ_1	F Q K W V A V V V P	S G Q E Q R Y T C H	V Q H E G L P K P L	T L R W - - - -		
2XPG_1	F Q K W A A V V V P	S G E E Q R Y T C H	V Q H E G L P K P L	T L R W - - - -		

MHC I: STRUCTURAL ALIGNMENT

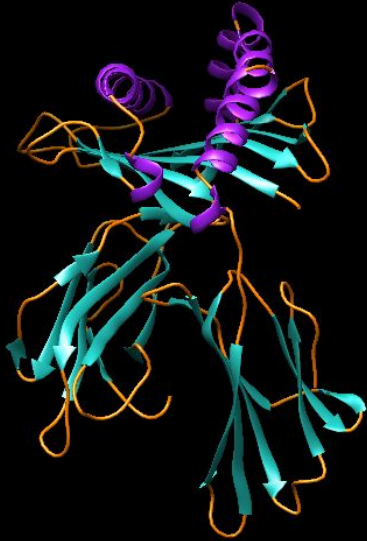
	1	11	21	31	41	51
Consensus	- s s H S M R Y F y	T a v S R P G R G E	P R F I a V G Y V D	D T Q F V r F D S D	A A S p r m e P R A	P W i E Q E G P E Y
Conservation						
5xs3AB	- S - H S M R Y F D	T A V S R - P - G E	P R F I S V G Y V D	D T Q F V R F D S D	A A S P R G E P R A	P W V E Q E G P E Y
5vgdAB	- S - H S M R Y F Y	T A V S R P G R G E	P R F I A V G Y V D	D T Q F V Q F D S D	A A S P R G E P R A	P W V E Q E G P E Y
2xpgAB	- G S H S M R Y F F	T S V S R P G R G E	P R F I A V G Y V D	D T Q F V R F D S D	A A S Q R M E P R A	P W I E Q E G P E Y
4nt6AB	- M S H S M R Y F Y	T A V S R P G R G E	P R F I A V G Y V D	D T Q F V Q F D S D	A A S P R G E P R A	P W V E Q E G P E Y
1k5nAB	- G S H S M R Y F H	T S V S R P G R G E	P R F I T V G Y V D	D T L F V R F D S D	A A S P R E E P R A	P W I E Q E G P E Y
2bvoAB	G S - H S M R Y F Y	T A M S R P G R G E	P R F I A V G Y V D	D T Q F V R F D S D	A A S P R M A P R A	P W I E Q E G P E Y
2hjkAB	G S - H S M R Y F Y	T A M S R P G R G E	P R F I A V G Y V D	D T Q F V R F D S D	A A S P R M A P R A	P W I E Q E G P E Y
3hiaAB	- G S H S M R Y F F	T S V S R P G R G E	P R F I A V G Y V D	D T Q F V R F D S D	A A S Q R M E P R A	P W I E Q E G P E Y
4hwzAB	- G S H S M R Y F Y	T S V S R P G R G E	P R F I A V G Y V D	D T Q F V R F D S D	A A S Q R M E P R A	P W I E Q E G P E Y
	61	71	81	91	101	111
Consensus	W D R E T r k y K a	q a Q T d R v d L r	t l r g Y Y N Q S E	A G S H t i Q r M Y	G C D v G p D G R l	L R G y n Q y A Y D
Conservation						
5xs3AB	W D R E T Q K Y K R	Q A Q A D R V N L R	K L R G Y Y N Q S E	D G S H T L O W M Y	G C D L G P D G R L	L R G Y D S S A Y D
5vgdAB	W D R E T Q K Y K R	Q A Q T D R V N L R	K L R G Y Y N Q S E	A G S H T L O R M Y	G C D L G P D G R L	L R G Y N Q F A Y D
2xpgAB	W D Q E T R N V K A	Q S Q T D R V D L G	T L R G Y Y N Q S E	A G S H T I Q I M Y	G C D V G S D G R F	L R G Y R Q D A Y D
4nt6AB	W D R E T Q K Y K R	Q A Q T D R V S L R	N L R G Y Y N Q S E	A G S H T L O R M Y	G C D L G P D G R L	L R G Y N Q F A Y D
1k5nAB	W D R E T Q I C K A	K A Q T D R E D L R	T L L R Y Y N Q S E	A G S H T L O N M Y	G C D V G P D G R L	L R G Y H Q H A Y D
2bvoAB	W D G E T R N M K A	S A Q T Y R E N L R	I A L R Y Y N Q S E	A G S H I I Q V M Y	G C D V G P D G R L	L R G H N Q Y A Y D
2hjkAB	W D G E T R N M K A	S A Q T Y R E N L R	I A L R Y Y N Q S E	A G S H I I Q V M Y	G C D V G P D G R L	L R G H D Q S A Y D
3hiaAB	W D G E T R K V K A	H S Q T H R V D L G	T L R G Y Y N Q S E	A G S H T V Q R M Y	G C D V G S D W R F	L R G Y H Q Y A Y D
4hwzAB	W D R N T R N V K A	Q S Q T D R V D L G	T L R G Y Y N Q S E	A G S H T I Q M M Y	G C D V G S D G R F	L R G Y R Q D A Y D
	121	131	141	151	161	171
Consensus	G K D Y I A L n E D	L r S W T A A D t A	A Q I T q r K W E A	A r v A E Q I R A Y	L E G t C V E W L R	R Y L E N G K e T L
Conservation						
5xs3AB	G K D Y I A L N E D	L R S W T A A D T A	A Q I T Q R K W E A	A R E A E Q W R A Y	L E G T C V E W L R	R Y L E N G K E T L
5vgdAB	G K D Y I A L N E D	L R S W T A A D K A	A Q I T Q R K W E A	A R E A E Q R R A Y	L E G T C V E W L R	R Y L E N G K K T L
2xpgAB	G K D Y I A L N E D	L R S W T A A D M A	A Q I T K R K W E A	A H E A E Q L R A Y	L D G T C V E W L R	R Y L E N G K E T L
4nt6AB	G K D Y I A L N E D	L R S W T A A D T A	A Q I T Q R K W E A	A R T A E Q L R A Y	L E G T C V E W L R	R Y L E N G K K T L
1k5nAB	G K D Y I A L N E D	L S S W T A A D T A	A Q I T Q R K W E A	A R V A E Q L R A Y	L E G E C V E W L R	R Y L E N G K E T L
2bvoAB	G K D Y I A L N E D	L S S W T A A D T A	A Q I T Q R K W E A	A R V A E Q L R A Y	L E G L C V E W L R	R Y L E N G K E T L
2hjkAB	G K D Y I A L N E D	L S S W T A A D T A	A Q I I Q R K W E A	A R V A E Q L R A Y	L E G L C V E W L R	R Y L E N G K E T L
3hiaAB	G K D Y I A L K E D	L R S W T A A D M A	A Q T T K H K W E A	A H V A E Q L R A Y	L E G T C V E W L R	R Y L E N G K E T L
4hwzAB	G K D Y I A L K E D	L R S W T A A D M A	A Q T T K H K W E A	A H V A E Q W R A Y	L E G T C V E W L R	R Y L E N G K E T L
	181	191	201	211	221	231
Consensus	Q R a d p P K T H v	T H H p v S D H E A	T L R C W 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
Conservation						
5xs3AB	Q R A E H P K T H V	T H H P V S D H E A	T L R C W A L G F Y	P A R 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
5vgdAB	Q R A E H P K T H V	T H H P V S D H E A	T L R C W 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
2xpgAB	Q R T D P P K T H M	T H H P I S D H E A	T L R C W 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
4nt6AB	Q R A E H P K T H V	T H H P V S D H E A	T L R C W 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
1k5nAB	Q R A D P P K T H V	T H H P I S D H E A	T L R C W 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
2bvoAB	Q R A D P P K T H V	T H H P I S D H E A	T L R C W 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
2hjkAB	Q R A D P P K T H V	T H H P I S D H E A	T L R C W 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
3hiaAB	Q R T D A P K T H M	T H H A V S D H E A	T L R C W 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
4hwzAB	Q R T D A P K T H M	T H H A V S D H E A	T L R C W 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

MHC I: STRUCTURAL ALIGNMENT

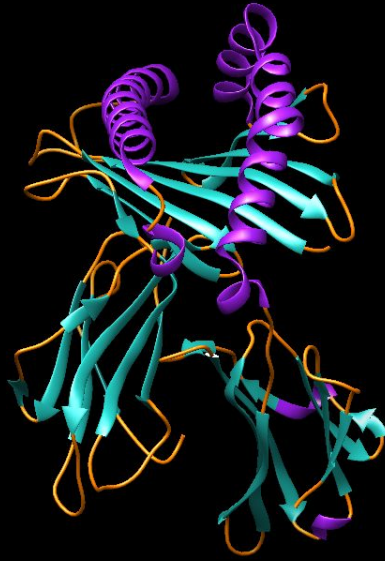
	241	251	261	271	281	291
Consensus	g T F Q K W A A V V	V P S G e E Q R Y T	C H V Q H E G L P k	P L - T L R - - w i	- Q R T P K I Q V Y	S R H P A E N G K S
Conservation						
5xs3AB	G T F Q K W A A V V	V P S G E E Q R Y T	C H V Q H E G L P E	P L - T L R - - W M	- Q R T P K I Q V Y	S R H P A E N G K S
5vgdAB	G T F Q K W A A V V	V P S G E E Q R Y T	C H V Q H E G L P E	P L - T L R - - W M	I Q R T P K I Q V Y	S R H P A E N G K S
2xpgAB	G T F Q K W A A V V	V P S G E E Q R Y T	C H V Q H E G L P K	P L - T L R - - W A	- Q R T P K I Q V Y	S R H P A E N G K S
4nt6AB	G T F Q K W A A V V	V P S G E E Q R Y T	C H V Q H E G L P E	P L - T L R - - W M	I Q R T P K I Q V Y	S R H P A E N G K S
1k5nAB	R T F Q K W A A V V	V P S G E E Q R Y T	C H V Q H E G L P K	P L - T L R W E P M	I Q R T P K I Q V Y	S R H P A E N G K S
2bvoAB	R T F Q K W A A V V	V P S G E E Q R Y T	C H V Q H E G L P K	P L - T L R - - W I	- Q R T P K I Q V Y	S R H P A E N G K S
2hjkAB	R T F Q K W A A V V	V P S G E E Q R Y T	C H V Q H E G L P K	P L - T L R - - W I	- Q R T P K I Q V Y	S R H P A E N G K S
3hlaAB	G T F Q K W A A V V	V P S G Q E Q R Y T	C H V Q H E G L P -	K P L - - - - - I	- Q R T P K I Q V Y	S R H P A E N G K S
4hwzAB	G T F Q K W V A V V	V P S G Q E Q R Y T	C H V Q H E G L P K	P L - T L R - - W I	- Q R T P K I Q V Y	S R H P A E N G K S
	301	311	321	331	341	351
Consensus	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 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
Conservation						
5xs3AB	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 E	H S D L S F S G D W	S F Y L L Y Y T E F	T P T E K D E Y A C
5vgdAB	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 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
2xpgAB	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 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
4nt6AB	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 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
1k5nAB	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 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
2bvoAB	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 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
2hjkAB	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 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
3hlaAB	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 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
4hwzAB	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 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
	361	371				
Consensus	R V N H V T L S Q P	K I V K W D R D m				
Conservation						
5xs3AB	R V N H V T L S Q P	K I V K W D R D -				
5vgdAB	R V N H V T L S Q P	K I V K W D R D M				
2xpgAB	R V N H V T L S Q P	K I V K W D R D -				
4nt6AB	R V N H V T L S Q P	K I V K W D R D -				
1k5nAB	R V N H V T L S Q P	K I V K W D R D M				
2bvoAB	R V N H V T L S Q P	K I V K W D R D M				
2hjkAB	R V N H V T L S Q P	K I V K W D R D M				
3hlaAB	R V N H V T L S Q P	K I V K W D R D M				
4hwzAB	R V N H V T L S Q P	K I V K W D R D M				

MHC-I: CLASSICAL HLA-I

Classical



HLA-A



HLA-B



HLA-C

MHC I: STRUCTURAL SUPERIMPOSITION

Sc 9.77
RMS 0.76
Len 377
nfit 361

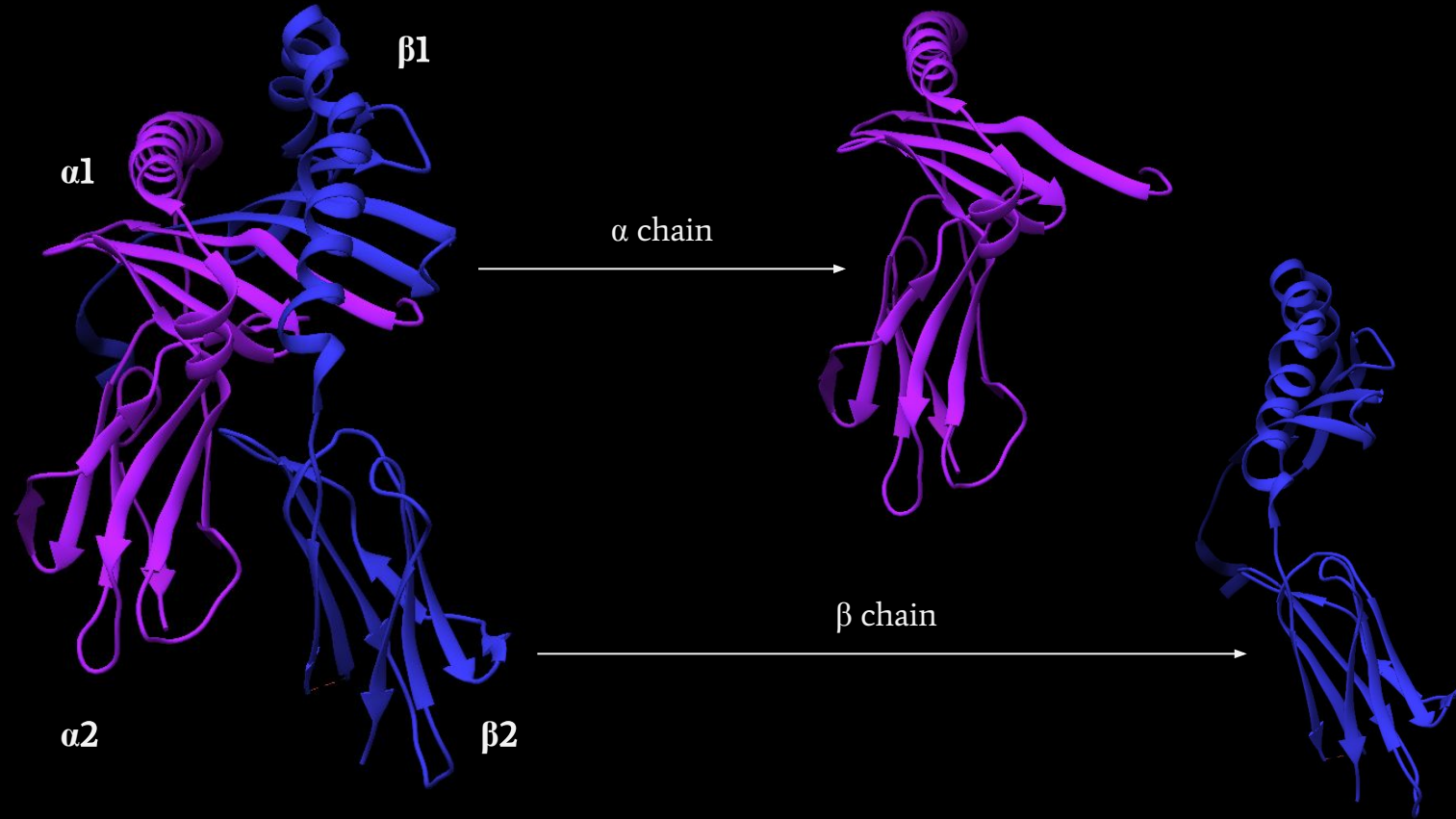


Cyan → HLA-A
Light sea green → HLA-A
Green → HLA-A
Yellow → HLA-B
Orange → HLA-B
Purple → HLA-B
Red → HLA-C
Blue → HLA-C
Hot pink → HLA-C

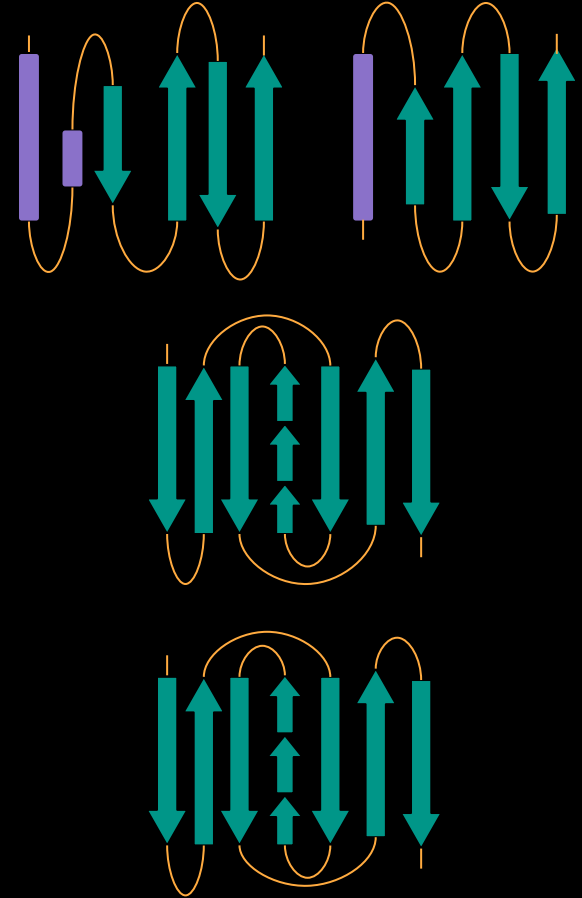
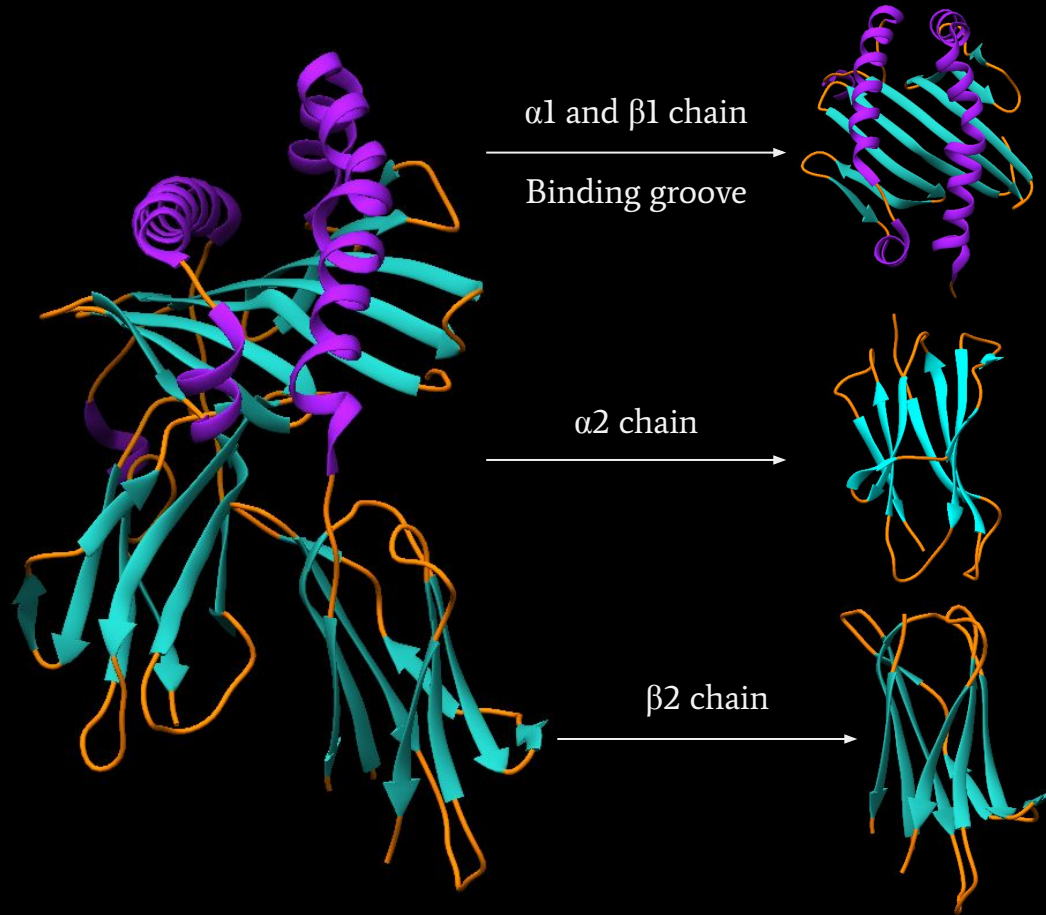
HLA-I superimposition made with STAMP and visualized with Chimera

MHC-II

MHC II: DOMAINS



MHC II: DOMAINS



MHC II: SEQUENCE ALIGNMENT CHAIN α

	1	11	21	31	41
Consensus	- - I k a d H V a i	y - a e f Y q s y d	p S G e f m f e F D	G D E i F y V D l a	k K E T V W r L e e
Conservation					
5KSV_1	ED I V A D H V A S	Y G V N L Y Q S Y G	P S G Q Y T H E F D	G D E Q F Y V D L G	R K E T V W C L P V
2NNA_1	ED I V A D H V A S	Y G V N L Y Q S Y G	P S G Q Y S H E F D	G D E E F Y V D L E	R K E T V W Q L P L
1KG0_1	- - - E H V I I	Q - A E F Y L N P D	Q S G E F M F D F D	G D E I F H V D M A	K K E T V W R L E E
1JWM_1	- - I K E H V I I	Q - A E F Y L N P D	Q S G E F M F D F D	G D E I F H V D M A	K K E T V W R L E E
3LQZ_1	- - I K A D H V S T	Y - A A F V Q T H R	P T G E F M F E F D	E D E M F Y V D L D	K K E T V W H L E E
	51	61	71	81	91
Consensus	F g r F a s F e a Q	g A L a N I A V I K	a N L n i m i K R S	N y T a a T N e p P	E V T V f s k S P V
Conservation					
5KSV_1	L R Q F R - F D P Q	F A L T N I A V L K	H N L N S L I K R S	N S T A A T N E V P	E V T V F S K S P V
2NNA_1	F R R F R R F D P Q	F A L T N I A V L K	H N L N I V I K R S	N S T A A T N E V P	E V T V F S K S P V
1KG0_1	F G R F A S F E A Q	G A L A N I A V D K	A N L E I M T K R S	N Y T P I T N V P P	E V T V L T N S P V
1JWM_1	F G R F A S F E A Q	G A L A N I A V D K	A N L E I M T K R S	N Y T P I T N V P P	E V T V L T N S P V
3LQZ_1	F G Q A F S F E A Q	G G L A N I A I L N	N N L N T L I Q R S	N H T Q A T N D P P	E V T V F P K E P V
	101	111	121	131	141
Consensus	e L g q P N t L I C	I l D k f f P P V V	N v T W L s N G h p	V T e G V S E T s F	L p r s D H s F r K
Conservation					
5KSV_1	T L G Q P N I L I C	L V D N I F P P V V	N I T W L S N G H S	V T E G V S E T S F	L S K S D H S F F K
2NNA_1	T L G Q P N T L I C	L V D N I F P P V V	N I T W L S N G H S	V T E G V S E T S F	L S K S D H S F F K
1KG0_1	E L R E P N V L I C	F I D K F T P P V V	N V T W L R N G K P	V T T G V S E T V F	L P R E D H L F R K
1JWM_1	E L R E P N V L I C	F I D K F T P P V V	N V T W L R N G K P	V T T G V S E T V F	L P R E D H L F R K
3LQZ_1	E L G Q P N T L I C	H I D K F F P P V L	N V T W L C N G E L	V T E G V A S L F	L P R T D Y S F H K
	151	161	171	181	191
Consensus	f h Y L t F L P S a	E d v Y D C r V E H	W G L D e P L L K H	W E p e - - - -	- - - - -
Conservation					
5KSV_1	I S Y L T L L P S A	E E S Y D C K V E H	W G L D K P L L K H	W E P E T P A P M S	E L T E V D I E G R
2NNA_1	I S Y L T F L P S A	D E I Y D C K V E H	W G L D E P L L K H	W E P E - - - -	- - - - -
1KG0_1	F H Y L P F L P S T	E D V Y D C R V E H	W G L D E P L L K H	W E F D A - - - -	- - - - -
1JWM_1	F H Y L P F L P S T	E D V Y D C R V E H	W G L D E P L L K H	W E F D A - - - -	- - - - -
3LQZ_1	F H Y L T F V P S A	E D F Y D C R V E H	W G L D Q P L L K H	W E A Q - - - -	- - - - -

MHC II: SEQUENCE ALIGNMENT CHAIN β

	1	11	21	31	41
Consensus	-----	-----sperF	lyQlKgeCyF	fNGTERVRLl	eRyIYNrEEs
Conservation					
5ksvB	-----	-----SPEDF	VYQFKGMCYF	TNGTERVRLV	SRSIYNREET
2nnaB	-----	-GSRDSPEDF	VYQFKGMCYF	TNGTERVRLV	TRYIYNREEFY
3lqzB	RKFHYLPFLP	STGGSSPENY	LFQGRQECYA	FNGTQ--RFL	ERYIYNREEFY
1kg0B	-----	-----TRPRF	LWQLKFECFH	FNGTERVRLl	ERCIYNQEEs
1jwmB	-----	-----GDTRPRF	LWQLKFECFH	FNGTERVRLl	ERCIYNQEEs
	51	61	71	81	91
Consensus	VRFDSDVGEy	RAVTeLGRPd	AEYWNSQKD i	LEqrRAavDt	yCRHNYqlge
Conservation					
5ksvB	VRFDSDVGEF	RAVTLLGLPA	AEYWNSQKDI	LERKRAAVDR	VCRHNYQLEL
2nnaB	ARFDSDVGVY	RAVTPLGPPA	AEYWNSQKEV	LERTRAELDT	VCRHNYQLEL
3lqzB	VRFDSDVGEF	RAVTELGRPD	EEYWNSQKDI	LEEERAVPDR	MCRHNYELGG
1kg0B	VRFDSDVGEY	RAVTELGRPD	AEYWNSQKDL	LEORRAAVDT	YCRHNYGVGE
1jwmB	VRFDSDVGEY	RAVTELGRPD	AEYWNSQKDL	LEORRAAVDT	YCRHNYGVGE
	101	111	121	131	141
Consensus	stTlQRRVEP	kVTvsPSk--	---hNLLVC	SVtdFYpgsI	kVRWFRNgQE
Conservation					
5ksvB	RTTLQRRVEP	TVTISPS---	---NLLVC	SVTDFYPAQI	KVRWFRNDQE
2nnaB	RTTLQRRVEP	TVTISPS---	---NLLVC	SVTDFYPAQI	KVRWFRNDQE
3lqzB	MTLQRRVQP	RVNVSPSKKG	---HNLLVC	HVTDFYPGSI	QVRWFLNGQE
1kg0B	SFTVQRRVEP	KVTIVPSKTQ	PLQHNNLLVC	SVSGFYPGSI	EVRWFRNGQE
1jwmB	SFTVQRRVEP	KVTIVPSKTQ	---HNLLVC	SVSGFYPGSI	EVRWFRNGQE
	151	161	171	181	191
Consensus	EtAGVVSTpL	I rNGDWTFO i	LVMLEmtPqs	GdVYTCqVEH	PSlqSPiTVE
Conservation					
5ksvB	ETAGVVSTPL	IRNGDWTFOI	LVMLEMTpQR	GDVYTCHVEH	PSLQSPITVE
2nnaB	ETTGVVSTPL	IRNGDWTFOI	LVMLEMTpQR	GDVYTCHVEH	PSLQNPITVE
3lqzB	ETAGVVSTNL	IRNGDWTFOI	LVMLEMTpQQ	GDVYTCQVEH	TSLDSPITVE
1kg0B	EKAGVVSTGL	IQNGDWTFOI	LVMLETVPRS	GEVYTCQVEH	PSVTSPLTVE
1jwmB	EKAGVVSTGL	IQNGDWTFOI	LVMLETVPRS	GEVYTCQVEH	PSVTSPLTVE
	201				
Consensus	WRA -				
Conservation					
5ksvB	WRA -				
2nnaB	WRA -				
3lqzB	WKAQ				
1kg0B	WRA -				
1jwmB	WRA -				

MHC II: STRUCTURAL ALIGNMENT

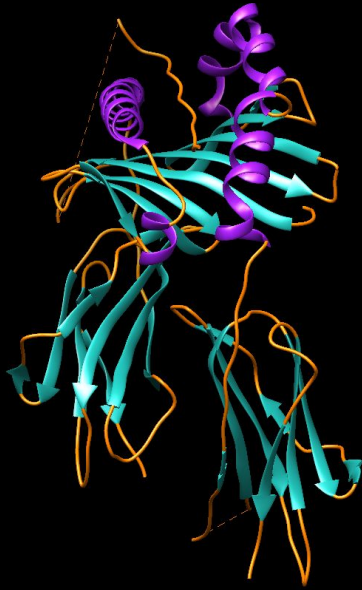
	1	11	21	31	41
Consensus	- i - a d H V i i y	- a e f Y q s y d -	q S G e f m f e F D	G D E i F y V D l a	k K E T V W r L e e
Conservation					
3lqzAB	- I K A D H V S T Y	- A A F V Q T H R P	T - G E F M F E F D	E D E M F Y V D L D	K K E T V W H L E E
1kg0AB	- - - E E H V I I Q	- A E F Y L N P D -	Q S G E F M F D F D	G D E I F H V D M A	K K E T V W R L E E
1jwmAB	- - - E E H V I I Q	- A E F Y L N P D -	Q S G E F M F D F D	G D E I F H V D M A	K K E T V W R L E E
5ksvAB	- I V A D H V A S Y	G V N L Y Q S Y G -	P S G Q Y T H E F D	G D E Q F Y V D L G	R K E T V W C L P V
2nnaAB	D I V A D H V A S Y	G V N L Y Q S Y G -	P S G Q Y S H E F D	G D E E F Y V D L E	R K E T V W Q L P L
	51	61	71	81	91
Consensus	F g r f a s F e a Q	g A L a N I A V I K	a N L n i m i K R S	N y T p a T N e p P	E V T V f s k S P V
Conservation					
3lqzAB	F G Q A F S F E A Q	G G L A N I A I L N	N N L N T L I Q R S	N H T Q A T N D P P	E V T V F P K E P V
1kg0AB	F G R F A S F E A Q	G A L A N I A V D K	A N L E I M T K R S	N Y T P I T N V P P	E V T V L T N S P V
1jwmAB	F G R F A S F E A Q	G A L A N I A V D K	A N L E I M T K R S	N Y T P I T N V P P	E V T V L T N S P V
5ksvAB	L R - Q F R F D P Q	F A L T N I A V L K	H N L N S L I K R S	N S T A A T N E V P	E V T V F S K S P V
2nnaAB	F R R F R R F D P Q	F A L T N I A V L K	H N L N I V I K R S	N S T A A T N E V P	E V T V F S K S P V
	101	111	121	131	141
Consensus	e L g q P N t L I C	l i D k f f P P V V	N v T W L r N G h p	V T e G V S E T s F	L p r s D H s F r K
Conservation					
3lqzAB	E L G Q P N T L I C	H I D K F F P P V L	N V T W L C N G E L	V T E G V A E S L F	L P R T D Y S F H K
1kg0AB	E L R E P N V L I C	F I D K F T P P V V	N V T W L R N G K P	V T T G V S E T V F	L P R E D H L F R K
1jwmAB	E L R E P N V L I C	F I D K F T P P V V	N V T W L R N G K P	V T T G V S E T V F	L P R E D H L F R K
5ksvAB	T L G Q P N I L I C	L V D N I F P P V V	N I T W L S N G H S	V T E G V S E T S F	L S K S D H S F F K
2nnaAB	T L G Q P N T L I C	L V D N I F P P V V	N I T W L S N G H S	V T E G V S E T S F	L S K S D H S F F K
	151	161	171	181	191
Consensus	f h Y L t F L P S a	E d v Y D C r V E H	W G L D e P L L K H	W E - - - - -	- - - - -
Conservation					
3lqzAB	F H Y L T F V P S A	E D F Y D C R V E H	W G L D Q P L L K H	W E A Q R K F H Y L	P F L P S T G G S S
1kg0AB	F H Y L P F L P S T	E D V Y D C R V E H	W G L D E P L L K H	W E F - - - - -	- - - - -
1jwmAB	F H Y L P F L P S T	E D V Y D C R V E H	W G L D E P L L K H	W E F - - - - -	- - - - -
5ksvAB	I S Y L T L L P S A	E E S Y D C K V E H	W G L D K P L L K H	W E - - - - -	- - - - -
2nnaAB	I S Y L T F L P S A	D E I Y D C K V E H	W G L D E P L L K H	W E - - - - -	- - - - -

MHC II: STRUCTURAL ALIGNMENT

	201	211	221	231	241
Consensus	- a g - - - - p e	r F l y Q I K g e C	y F f N G T E R V R	L l e r y I Y N r E	E s V R F D S D V G
Conservation					
3lqzAB	- - - - - - P E	N Y L F Q G R Q E C	Y A F N - G - T Q R	F L E R Y I Y N R E	E F V R F D S D V G
1kg0AB	D A T - - - - R P	R F L W Q L K F E C	H F F N G T E R V R	L L E R C I Y N Q E	E S V R F D S D V G
1jwmAB	D A G D - - - T R P	R F L W Q L K F E C	H F F N G T E R V R	L L E R C I Y N Q E	E S V R F D S D V G
5ksvAB	- P S - - - - P E	D F V Y Q F K G M C	Y F T N G T E R V R	L V S R S I Y N R E	E I V R F D S D V G
2nnaAB	- P G - S R D S P E	D F V Y Q F K G M C	Y F T N G T E R V R	L V T R Y I Y N R E	E Y A R F D S D V G
	251	261	271	281	291
Consensus	E y R A V T e L G r	P d A E Y W N S Q K	D i L E q r R A a v	D t y C R H N Y q l	g e s t T I Q R R V
Conservation					
3lqzAB	E F R A V T E L G R	P D E E Y W N S Q K	D I L E E E R A V P	D R M C R H N Y E L	G G P M T L Q R R V
1kg0AB	E Y R A V T E L G R	P D A E Y W N S Q K	D L L E Q R R A A V	D T Y C R H N Y G V	G E S F T V Q R R V
1jwmAB	E Y R A V T E L G R	P D A E Y W N S Q K	D L L E Q R R A A V	D T Y C R H N Y G V	G E S F T V Q R R V
5ksvAB	E F R A V T L L G L	P A A E Y W N S Q K	D I L E R K R A A V	D R V C R H N Y Q L	E L R T T L Q R R V
2nnaAB	V Y R A V T P L G P	P A A E Y W N S Q K	E V L E R T R A E L	D T V C R H N Y Q L	E L R T T L Q R R V
	301	311	321	331	341
Consensus	E P k V T v s P - s	- - - - - - N L	L V C S V t d F Y P	g s I k V R W F R N	g Q E E t A G V V S
Conservation					
3lqzAB	Q P R V N V S P - S	K K G - - H - - N L	L V C H V T D F Y P	G S I Q V R W F L N	G Q E E T A G V V S
1kg0AB	E P K V T V Y P S K	T Q - P L Q H H N L	L V C S V S G F Y P	G S I E V R W F R N	G Q E E K A G V V S
1jwmAB	E P K V T V Y P S K	T Q - - H - H N L	L V C S V S G F Y P	G S I E V R W F R N	G Q E E K A G V V S
5ksvAB	E P T V T I S P - S	- - - - - - N L	L V C S V T D F Y P	A Q I K V R W F R N	D Q E E T A G V V S
2nnaAB	E P T V T I S P - -	- - - - - - L -	L V C S V T D F Y P	A Q I K V R W F R N	D Q E E T T G V V S
	351	361	371	381	391
Consensus	T p L I r N G D W T	F Q i L V M L E m t	P q s G d V Y T C q	V E H P S l q S P i	T V E W R A -
Conservation					
3lqzAB	T N L I R N G D W T	F Q I L V M L E M T	P Q Q G D V Y T C Q	V E H T S L D S P V	T V E W K A Q
1kg0AB	T G L I Q N G D W T	F Q T L V M L E T V	P R S G E V Y T C Q	V E H P S V T S P L	T V E W R A -
1jwmAB	T G L I Q N G D W T	F Q T L V M L E T V	P R S G E V Y T C Q	V E H P S V T S P L	T V E W R A -
5ksvAB	T P L I R N G D W T	F Q I L V M L E M T	P Q R G D V Y T C H	V E H P S L Q S P I	T V E W R A -
2nnaAB	T P L I R N G D W T	F Q I L V M L E M T	P Q R G D V Y T C H	V E H P S L Q N P I	I V E W R A -

MHC-II: CLASSICAL HLA-II

Classical



HLA-DP



HLA-DQ



HLA-DR

MHC II: STRUCTURAL SUPERIMPOSITION

Sc 9.16
RMS 1.20
Len 395
nfit 347



hot pink → HLA-DP
cyan → HLA-DR
orange → HLA-DR
green → HLA-DQ
purple → HLA-DQ

HLA-II superimposition made with STAMP and visualized with Chimera

MODES OF EVOLUTION

MHC I: STRUCTURAL SUPERIMPOSITION SPECIES



hot pink	→	<i>Ctenopharyngodon idella</i>	(5Y9I) 1.90 Å
cyan	→	<i>Homo sapiens</i>	(3HLA) 2.60 Å
orange	→	<i>Pteropus alecto</i>	(6ILF) 2.70 Å
green	→	<i>Mus musculus</i>	(1BII) 2.40 Å
purple	→	<i>Macaca mulatta</i>	(3RWI) 2.01 Å
red	→	<i>Sus scrofa</i>	(6KWO) 1.80 Å
yellow	→	<i>Oryctolagus cuniculus</i>	(6M2J) 2.20 Å
grey	→	<i>Anas platyrhynchos</i>	(6KYU) 1.50 Å
dark blue	→	<i>Gallus gallus</i>	(6LHH) 2.71 Å

Sc 8.93
RMS 1.73
Len 405
nfit 328

MHC I: STRUCTURAL ALIGNMENT SPECIES

Consensus Conservation	1 - g s H S I r Y f y	11 T a v S r p g - g -	21 e p - - - - - r f	31 I a V G Y V D d t q	41 F v r f D S d a - s	51 p R a e P R a p W i	61 e q - e - - - g p e	71 Y W d r e T r i a k	81 d a a Q t f r v d L	91 g t l r r y Y N Q S	101 e a G S H T I Q I M
6kwoAB	- - P H S L S Y F Y	T A V S R P D - R G	D S - - - - - R F	I A V G Y V D D T Q	F V R F D N Y A P N	P R M E P R V P W I	Q Q - E - - - G Q D	Y W D E E T R K V K	D N A Q T Y G V G L	N T L R G Y Y N Q S	E A G S H T L Q S M
6iIfAB	- G F H S L R Y F Y	T A W S R P G S G -	E P - - - - - R F	V A V G Y V D D T Q	F V R F D S D N A S	P R A E P R A P W M	D L - V E Q Q D P Q	Y W D R N T R N A R	D A A Q T Y R V G L	D N V R G Y Y N Q S	E A G S H T I Q R M
6mj2AB	- G S H S M R Y F Y	T S V S R P G L G -	E P - - - - - R F	I I V G Y V D D T Q	F V R F D S D A A S	P R M E Q R A P W M	Q Q - V - - - E P E	Y W D Q Q T Q I A K	D T A Q T F R V N L	N T A L R Y Y N Q S	A A G S H T F Q T M
1biIfAB	- G S H S L R Y F Y	T A V S R P G F G -	E P - - - - - R Y	M E V G Y V D N T E	F V R F D S D A E N	P R Y E P R A R W I	E Q - E - - - G P E	Y W D E T R R A K	E N S Q S F R V D L	R T A L R Y Y N Q S	A A G S H T L Q W M
3hlaAB	- G S H S M R Y F Y	T S V S R P G R G -	E P - - - - - R F	I S V G Y V D D T Q	F V R F D S D A E S	Q R M E P R A P W I	E Q - E - - - G P E	Y W D G E T R K V K	A H S Q T F R V D L	G T L R G Y Y N Q S	E A G S H T V Q M L
3rwiAB	- G S H S M K Y F Y	T S V S R P G R G -	E P - - - - - R F	I S V G Y V D D T Q	F V R F D S D A E S	P R A E P R A P W V	E Q - E - - - G P E	Y W E A T R R A K	E A A Q T H R E N L	R T A L R Y Y N Q S	E A G S H T I Q K M
5y91AB	- G T H S L K Y V Y	T G V S R - - - - -	- G I - D F - P E F	T A V G M V D D G Q	F M Y F D S N S - -	M K A V P K T E W I	R Q N E - - - G A D	Y W D R Q T Q V L I	G A H Q V F K D S I	Q I V M E R F N Q S	- K G V H T W Q N M
6kyuAB	- E P H S L R Y F D	T G V S D - - - - -	- P S - P G V P R F	V S V G Y V D G H L	I D H Y D S E T - -	Q R T E P R A D W F	A A N T - - - D Q Q	Y W D R Q T E I S R	G A E Q I F R L D L	E T L R E R F N Q S	- R G S H T W Q L M
6lhhAB	E L - H T L R Y I S	T A M T D - - - - -	- P G P G Q - P W Y	D V G Y V D G E L	F T H Y N S T A - -	R R A V P R T E W I	A A N T - - - D Q Q	Y W D S E T Q T S Q	R T E Q I D R D G L	G T L Q R R Y N Q T	- G G S H T V Q L M
Consensus Conservation	111 y G C d l g p D g r	121 l l r G y r Q y A Y	131 D G a D y i A l n e	141 d l r - s w T A A d	151 m a A q i t k r K W	161 E a a - g y A E r d	171 r a Y L e g e C v E	181 w L r r y l e n g k	191 e t L q R a d p P k	201 t h v t h h - - p a	211 s - d - e a T l R c
6kwoAB	F G C Y L G P D G L	L L H G Y R Q D A Y	D G A D Y I A L N E	D L R - S W T A A D	M A A Q I T K R K W	E A A - N V A E R R	R S Y L Q G L C V E	S L R R Y L E M G K	D T L Q R A E P P K	T H V T R H - - P S	S - D L G V T L R C
6iIfAB	Y G C D Y G P H G R	L L H G Y D Q L A Y	D G A D Y I A L N E	D L R - S W T A A D	K A A Q I T R R K W	E A A - G Y A E R D	R A Y L E G E C V E	W L L K H L E N G R	E T L L R A D P P K	T H I T H - - P I	S - D R E V T L R C
6mj2AB	F G C E Y W A D G R	F F H G Y R Q Y A Y	D G A D Y I A L N E	D L R - S W T A A D	T A A Q N T Q R K W	E A A - G E A E R H	R A Y L E R E C V E	W L R R Y L E M G K	E T L Q R A D P P K	A H V T H - - P A	S - D R E A T L R C
1biIfAB	A G C D V E S D G R	L L R G Y W Q F A Y	D G C D Y I A L N E	D L K - T W T A A D	M A A Q I T R R K W	Q A - G A A E R D	R A Y L E G E C V E	W L R R Y L K N G K	A T L L R T D P P K	A H V T H - - P R	P E G - D V T L R C
3hlaAB	Y G C D Y G S D W R	F L R G Y H Q Y A Y	D G K D Y I A L K E	D L R - S W T A A D	M A A Q T T K H K W	E A A - H V A E R L	R A Y L E G T C V E	W L R R Y L E N G K	E T L Q R T D A P K	T H M T H - - A V	S - D H E A T L R C
3rwiAB	Y G C D L G P D G R	L L R G Y H Q S A Y	D G K D Y I A L N G	D L R - S W T A A D	M A A Q N T Q R K W	E G N - R Y A E R L	R A Y L E G E C L E	W L R R Y L E N G K	E T L Q R A D P P K	T H V T H - - P V	S - D H E A T L R C
5y91AB	Y G C E L N D G G -	T T Q G Y Q Y A Y	D G E D F V S L D -	K N T L T W T A A N	P A A V I T K H K W	E A L - A V A E R W	K G Y L E N T C I E	W L K K Y V A Y G K	D T L R K V S P Q	V S L L Q K D P S -	- - - - - S P V T C
6kyuAB	Y G C D L L E D G -	T S T R G F R Q Y G Y	E G R D F V A F D -	K D T L T F T A A D	A G A Q I T K R K W	Q E G T D A E R W	K F Y L E N T C I E	G L R K Y V S Y G K	D V L E R R E R D E	V Q V S G M - E A	D - K - I L T L S C
6lhhAB	Y G C D I L E D G -	T I R G Y S Q D A Y	D G R D F I A F D -	K D T M T F T A A V	P E A V P T K R K W	E E G - D Y A E G L	K Q Y L E T C V E	W L R R Y V Y G K	A E L G R R E R P E	V R V W G K - E A	D - G - I L T L S C
Consensus Conservation	221 w A I G F Y P a e I	231 t l t W q r d - G e	241 d q t q d t e l v e	251 t r P n g D G t f q	261 k W a a v v P s p G	271 e e - q r y t C h v	281 q H e g L p e p l -	291 - t l r - - - - -	301 - - - w - - - q - r	311 t P K i Q V Y S r h	321 P a e n G k p n f L
6kwoAB	W A L G F Y P K E I	S L T W O R E G Q D	Q S Q - D M E L V E	T R P S G D G T F Q	K W A A L V V P P G	E E - Q S Y T C H V	Q H E G L Q E P L -	- T L - - - - -	- - - R A - - - R	P P K V Q V Y S R H	P A E N G K P N Y L
6iIfAB	W A L G F Y P E E I	S L T W O H D - G E	D Q T O E M E L V E	T R P D G N G A F Q	K W A A L V V P S G	E E - Q R Y T C H V	Q H E G L P Q P L -	- T L R W E - - -	- - - P E - - - P - R	T P K I Q V Y S R H	P A E N G K P N Y L
6mj2AB	W A L G F Y P A E I	S L T W O R D - G E	D Q T O D T L V L V E	T R P G G D G T F Q	K W A A V V V P S G	E E - Q R Y T C R V	Q H E G L P E P L -	- T L T - - - - -	- - - W M - I Q - R	T P K I Q V Y S R H	P A E N G K S N F L
1biIfAB	W A L G F Y P A D I	T L T W O L N - G E	E L T O E M E L V E	T R P A G D G T F Q	K W A S V V V P L G	K E - Q K Y T C H V	E H E G L P E P L -	- T L R - - - - -	- - - W I - O - K	T P K I Q V Y S R H	P P E N G K P N I L
3hlaAB	W A L S F Y P A E I	T L T W O R D - G E	D Q T O D T L V L V E	T R P A G D G T F Q	K W A A V V V P S G	Q E - Q R Y T C H V	Q H E G L - P K P L	- - - - - - - - -	- - - - - - - - -	T P K I Q V Y S R H	P A E N G K S N F L
3rwiAB	W A L G F Y P A E I	T L T W O R D - G E	E Q T O D T F E F V E	T R P G G D G T F Q	K W A S V V V P S G	E E - Q R Y T C H V	Q H E G L P E P L -	- T L R W E - - -	- - - P I - O - R	T P K I Q V Y S R H	P P E N G K P N F L
5y91AB	H A T G F Y P S G V	T I T W Q K N - G Q	D H D E V D L G E	L L P N E D G S F Q	R M S T L N V G - P	W K N N R F S C V V	E H - Q - D K T I	- R K T E D D I I T	N F D - K - - V - S	S P K I Q V Y S H Y	P G G Y K E N T L
6kyuAB	R A H G F Y P R P I	S I S W L K D - G M	V Q E Q E T K R G S	T V P N S D G T Y H	I W A T I D V L P G	E R - D K Y Q C R V	E H A S L P Q P G -	- L F S - - - - -	- - - W G Q A K - A	A P K V Q V Y S R H	P A T A G T E N I L
6lhhAB	R A H G F Y P R P I	A V S W L K D - G A	V Q G Q D A O S G G	I V P N G D G T Y H	T W V T I D A Q P G	D G - D K Y Q C R V	E H A S L P Q P G -	- L Y S - - - - -	- - - W - - - - D L	T P K V Q V Y S R F	P A S A G T K N V L
Consensus Conservation	331 N C Y V s G F H P p	341 d I e i d L L K N G	351 e k m e k v e q s D	361 I S F s k D w s F y	371 L l v y t e F T P t	381 e k D e Y a C r V n	391 H v t l s e P k i v	401 k W d r d m -			
6kwoAB	N C Y V S G F H P P	Q I E I D L L K N G	E K M - N A E Q S D	L S F S K D W S F Y	L L V H T E F T P N	A V D Q Y S C R V K	H V T L D K P K I V	K W D R D H -			
6iIfAB	N C Y V Y G F H P P	Q I E I D L L K N G	Q K M - K T E Q S D	L S F S K D W S F Y	L L V H T D F T P S	T V D E Y S C R V N	H S S L A A P H M V	K W D R N N -			
6mj2AB	N C Y V S G F H P S	D I E I V D L L K N G	E R I E K V 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 -			
1biIfAB	N C Y V T Q F H P P	H I E I Q M L K N G	K K I P K V E M S D	M S F S K D W S F Y	I L A H T E F T P T	E T D T Y A C R V K	H D S M A E P K T V	Y W D R D M -			
3hlaAB	N C Y V S G F H P S	D I E I V D L L K N G	E R I E K V 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 -			
3rwiAB	N C Y V S G F H P S	D I E I V D L L K N G	E K M K V E H S D	L S F S K D W S F Y	L L Y Y T E F T P N	E K D E Y A C R V N	H V T L S G P R T V	K W D R D M -			
5y91AB	I C Y V S G F H P P	D I S I E L L K N G	E V I A D A Q O T D	L A F E K W Q S F H	L T K S V S F K P E	K S D E Y S C S V R	H M - - - S K T K K I	V W E S - N M			
6kyuAB	N C Y V E G F H P P	K I D I A L L K N G	E P M K D V K Y N D	M S F G D D W T F Q	R L V Y A P F T P T	K S D V Y T C R V D	H E A F T E P Q S F	R W E P - - -			
6lhhAB	N C F A E G F H P P	K I S I T L M K D G	V P M E G A Q Y S D	M S F N D D W T F Q	R L V H A D F T P S	S G S T Y A C K V E	H E T L K E P Q V Y	K W D P E F -			

MHC I: SEQUENCE ALIGNMENT SPECIES

	1	11	21	31	41	51	61	71	81	91
Consensus			gsHSLr	YfyTavSRPg	rGePrfiaVG	YVDDtdqFvrf	DSdaasPrae	PRapWie---	qegpeYWdre	TriakdaaQT
Conservation										
3HLA_1			GSHSMR	YFFTYSVSRPG	RGEPRFIAVG	YVDDTQFVRF	DSDAASQRME	PRAPWIE---	QEGPEYWDGE	TRKVKASHOT
3RWL_1			GSHSMK	YFYTSVSRPG	RGEPRFISVG	YVDDTQFVRF	DSDAESPREE	PRAPWVE---	QEGPEYWEAE	TRRAKEAAGT
6MJ2_1			GSHSMR	YFYTSVSRPG	LGEPRFIIVG	YVDDTQFVRF	DSDAASPRME	QRAPWMG---	QVEPEYWDQG	TQIAKDTAQT
6ILF_1			GFHSLR	YFYTAWSRPG	SGEPRFVAVG	YVDDTQFVRF	DSDNASPRAE	PRAPWMDLVE	QDDPEYWDQN	TRNARDAAQT
6KWO_1			PHLSLS	YFYTAWSRPG	RQDSRFIAVG	YVDDTQFVRF	DNYAPNPRME	PRVPWIIQ---	QEGQDYWDGE	TRKYKDNAQT
1BI1_1	MGAMAPRTLL	LLLAALALGPT	QTRAGSHSLR	YFVTAWSRPG	FGEPRFMEVG	YVDNTEFVRF	DSDAENPRYE	PRAPWIE---	QEGPEYWEAE	TRRAKNEQQT
6KYU_1			EPHSLR	YFDTGVSDPS	PGVPFRFVSVG	YVDGHLIDHY	DS--ETQRTT	PRADWFA--A	NTDQQYWDRO	TEISRGAEQI
6LHH_1			ELHTLR	YISTAMTDGP	PGQPWYVDVG	YVDGELFTHY	NS--TARRAV	PRTEWIA--A	NTDQQYWDSE	TQTSQRTQEI
5Y91_1			GTHSLK	YVYTGVSRRG	IDFPFFTAVG	MVDDGQFMYF	DS--NSMKAV	PKTEWIR--Q	NEGADYWDRO	TQVLIQAHQV
Consensus	101	111	121	131	141	151	161	171	181	191
Conservation										
3HLA_1	HRVDLGLTLRG	YYNQSEAGSH	TVORMYGCdV	GSDFWFLRLGY	HQYAYDGKDY	IALKEDLRSW	TAADMAAQIT	KHKWE--AAHV	AEQLRAYLEG	TCVEWLRRYL
3RWL_1	HRLENLRTALR	YYNQSEAGSH	TIQKMYGCdL	GPDRGLRLGY	HQSAYDGKDY	IALNGDLRSW	TAADMAAQNT	QRKWE--GNRY	AERFRAYLEG	ECLEWLRRYL
6MJ2_1	FRVNLNTALR	YYNQSAAGSH	TFQTFMFGCV	WADGRFFHGY	RQYAYDGADY	IALNEDLRSW	TAADTAQNT	QRKWE--AAGE	AERHRAYLER	ECVEWLRRYL
6ILF_1	YRVGLDNVRG	YYNQSEAGSH	TIQRMYGCdV	GPGRLLRLGY	DQLAYDGADY	IALNEDLRSW	TAADLAAQNT	RRKWE--EAGY	AERDRAYLEG	ECVEWLRLHL
6KWO_1	YRVGLNTLRG	YYNQSEAGSH	TLSMFGCYL	GPDGLLHGY	RQDAYDGADY	IALNEDLRSW	TAADMAAQIT	RRKWE--AANV	AERRRSYLEG	LCVESLRLHL
1BI1_1	FRVDLRTALR	YYNQSAAGSH	TLSMAGCGV	ESDGRLLHGY	WQFAYDGADY	IALNEDLKTW	TAADMAAQIT	RRKWE--QAGA	AERDRAYLER	ECVEWLRRYL
6KYU_1	FRDLDTLRLR	RYNQS--RGS	TWQLMYGCdL	LEDG--STRGF	RQYGYEGRDF	VAFDKDILTTF	TAADAAQAIT	RRKWE--QEGTD	AERWKFYLEN	TCIEGLRRYV
6LHH_1	DRDGLGLTLQR	RYNQT--GGSH	TWQLMYGCdI	LEDG--TIRGY	SQDAYVDGRDF	IAFDKDTMTF	TAAVPEAVPT	RRKWE--EGDY	AEGLKQYLEE	TCVEWLRRYV
5Y91_1	FKDSIQIVME	RFNQS--KGVH	TWQNMVGCdL	NDGG--TTQGF	YQYAYDGEDF	VSLKNTLTW	TAANPQAVIT	KHKWE--ALAV	AQNKGYLEN	TCIEWLKKYV
Consensus	201	211	221	231	241	251	261	271	281	291
Conservation										
3HLA_1	ENgKETLQRT	DAPKTHMTHH	AVSDHEATLR	CWALSFPAPAE	ITLTWQRDGE	DQTQDTLVE	TRPAGDGTFO	KWAADVVPSSG	--QEQRYTCH	VQHEG-----
3RWL_1	ENgKETLQRA	DPPKTHVTHH	PVSDHEATLR	CWALGFYPAPAE	ITLTWQRDGE	EQTQDTLVE	TRPGGDGTFO	KWAADVVPSSG	--EQRYTCH	VQHEG-----
6MJ2_1	EMGKETLQRA	DPPKAHVTHH	PASDREATLR	CWALGFYPAPAE	ISLTWQRDGE	DQTQDTLVE	TRPGGDGTFO	KWAADVVPSSG	--EQRYTCH	VQHEG-----
6ILF_1	ENgRETLLRA	DPPKTHIHTH	PISDREVTLR	CWALGFYPPEE	ITLTWQRDGE	DQTQDMLVE	TRPDGNGAFO	KWAADVVPSSG	--EQRYTCH	VQHEG-----
6KWO_1	EMGKDTLQRA	EPPKTHVTHH	PSSDLGVTLR	CWALGFYPKEE	ISLTWQRGEG	DQSQDMLVE	TRPDGNGAFO	KWAADVVPSSG	--EQRYTCH	VQHEG-----
1BI1_1	KNGNATLLRT	DPPKAHVTHH	RRPEGDVTLR	CWALGFYPAD	ITLTWQLNGE	ELTQDMLVE	TRPAGDGTFO	KWASVVPVPLG	--KEQKYTCH	VEHEG-----
6KYU_1	SYGKDLVLR	ERPEVQVSG	MEADKILTLS	CRAHGFPYRP	ISLSWLKDMG	VQEQETKRGS	TPVNSDGTTH	IWATIDVPLG	--ERDKYOCR	VEHAS-----
6LHH_1	EYGAELGRR	ERPEVRVWG	KEADGILTLS	CRAHGFPYRP	IAVSWLKDGA	VQGQDAQSGG	IVPNDDGTTH	TWYVIDAQPG	--PDGKYOCR	VEHAS-----
5Y91_1	AYGKDTLRR	VSPQVSLQLQ	--KPPSSPVT	CHATGFYPSG	VTITWQKNQG	DHDEDVDLGE	LLPNEDGSFO	RMSTLNVGPD	EWKNNRFSCV	VEHODKTIRK
Consensus	301	311	321	331	341	351	361	371		
Conservation										
3HLA_1	LPEPLTLRWE									
3RWL_1	LPEPLTLRWE									
6MJ2_1	LPEPLTLTW									
6ILF_1	LPEPLTLRWE									
6KWO_1	LQEPPLTLRWD									
1BI1_1	LPEPLTLRWG	KEEPPSSSTKT	NTVIIAVPVV	LGAVVILGAV	MAFV MKRRRN	TGGKGGDYAL	APGSQSSDMS	LPDCKV		
6KYU_1	LPOPGLFSW									
6LHH_1	LPOPGLYSW									
5Y91_1	TEDDIIINFD									

MHC I: DENDROGRAM SPECIES

Homo sapiens (3hla)

Macaca mulatta (3rwi)

Mus musculus (1bii)

Oryctolagus cuniculus (6m2j)

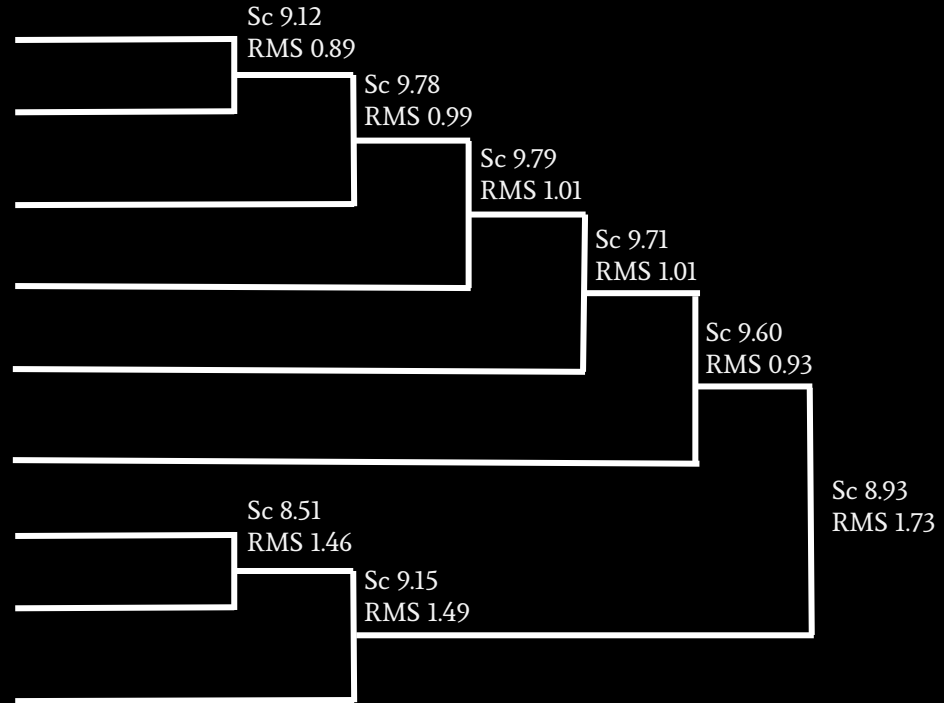
Pteropus alecto (6ilf)

Sus scrofa (6kwo)

Anas platyrhynchos (6kyu)

Gallus gallus (6lhh)

Ctenopharyngodon idella (5y91)



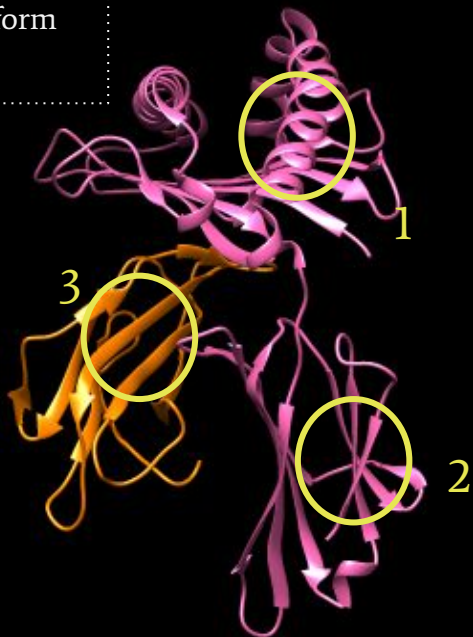
MHC-I phylogenetic tree made with ClustalW

MHC I INTERACTIONS

INNER INTERACTIONS

Disulfide bonds

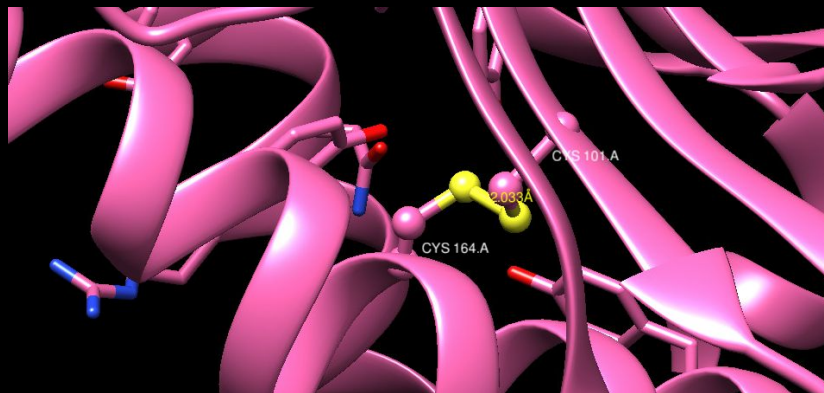
$\alpha 1$ domain does not contain any cysteine residues able to form disulfide bonds



HLA-I structure visualized with Chimera

1

$\alpha 2$ domain: Cys 101-Cys 164



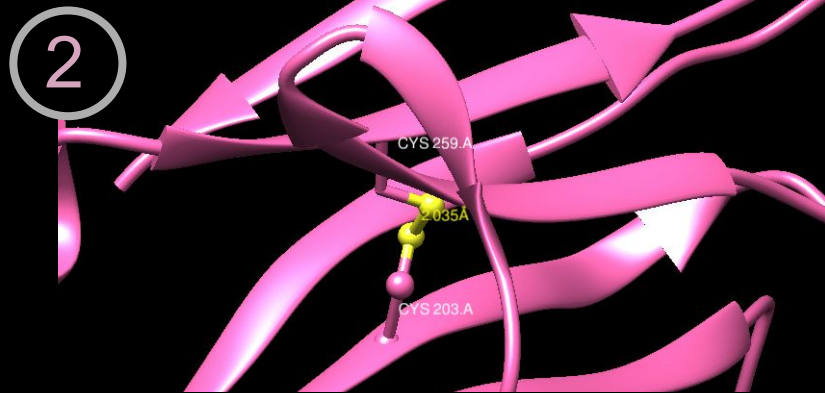
Disulfide bond

101
G C D v G p D G R I
G C D L G P D G R L
G C D L G P D G R L
G C D V G S D G R F
G C D L G P D G R L
G C D V G P D G R L
G C D V G P D G R L
G C D V G P D G R L
G C D V G S D W R F
G C D V G S D G R F

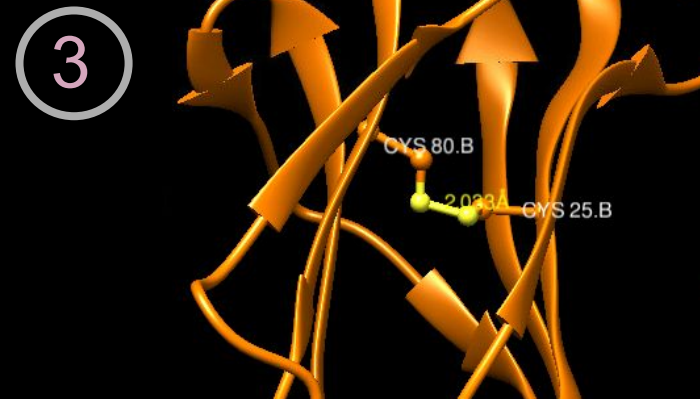
161
L E G t C V E W L R
L E G T C V E W L R
L E G T C V E W L R
L D G T C V E W L R
L E G T C V E W L R
L E G C V E W L R
L E G L C V E W L R
L E G L C V E W L R
L E G T C V E W L R
L E G T C V E W L R

Disulfide bonds

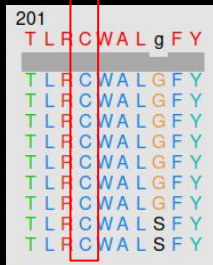
$\alpha 3$ domain: Cys 203-259



β2m: Cys 25- Cys 80



Disulfide bond



Disulfide bond



Disulfide bonds in evolution

Disulfide bond
($\alpha 2$ domain)

111

y	G	C	d	l	g	p	D	G	r
F	G	C	Y	L	G	P	D	G	L
Y	G	C	D	V	G	P	H	G	R
F	G	C	E	V	W	A	D	G	R
A	G	C	D	V	E	S	D	G	R
Y	G	C	D	V	G	S	D	W	R
Y	G	C	D	L	G	P	D	G	R
Y	G	C	E	L	N	D	D	G	-
Y	G	C	D	L	L	E	D	G	-
Y	G	C	D	I	L	E	D	G	-

171

r	a	Y	L	E	g	e	C	V	E
R	S	Y	L	Q	G	L	C	V	E
R	A	Y	L	E	G	E	C	V	E
R	A	Y	L	E	R	E	C	V	E
R	A	Y	L	E	G	E	C	V	E
R	A	Y	L	E	G	T	C	V	E
R	A	Y	L	E	G	E	C	L	E
K	G	Y	L	E	N	T	C	I	E
K	F	Y	L	E	N	T	C	I	E
K	Q	Y	L	E	E	T	C	V	E

Disulfide bond
($\alpha 3$ domain)

211

s	-	d	-	e	a	T	L	C	
S	-	D	L	G	V	T	L	R	C
S	-	D	R	E	V	T	L	R	C
S	-	D	R	E	A	T	L	R	C
P	E	G	-	D	V	T	L	R	C
S	-	D	H	E	A	T	L	R	C
S	-	D	H	E	A	T	L	R	C
-	-	-	-	S	P	V	T	C	
D	-	K	-	I	L	T	L	S	C
D	-	G	-	I	L	T	L	S	C

271

e	e	-	q	r	Y	t	C	h	V
E	E	-	Q	S	Y	T	C	H	V
E	E	-	Q	R	Y	T	C	H	V
E	E	-	Q	R	Y	T	C	R	V
K	E	-	Q	K	Y	T	C	H	V
Q	E	-	Q	R	Y	T	C	H	V
E	E	-	Q	R	Y	T	C	H	V
W	K	N	N	R	F	S	C	H	V
E	R	-	D	K	Y	Q	C	R	V
D	G	-	D	K	Y	Q	C	R	V

Disulfide bond
($\beta 2m$)

331

N	C	Y	V	s	G	F	H	P	p
N	C	Y	V	S	G	F	H	P	P
N	C	Y	V	Y	G	F	H	P	P
N	C	Y	V	S	G	F	H	P	S
N	C	Y	V	T	Q	F	H	P	P
N	C	Y	V	S	G	F	H	P	S
N	C	Y	V	S	G	F	H	P	S
I	C	Y	V	S	G	F	H	P	P
N	C	Y	V	E	G	F	H	P	P
N	C	F	A	G	F	H	P	P	

381

e	k	D	e	Y	a	C	r	V	n
A	V	D	Q	Y	S	C	R	V	K
T	V	D	E	Y	S	C	R	V	N
E	K	D	E	Y	A	C	R	V	N
E	T	D	T	Y	A	C	R	V	K
E	K	D	E	Y	A	C	R	V	N
E	K	D	E	Y	A	C	R	V	N
K	S	D	E	Y	S	C	S	V	R
K	S	D	V	Y	T	C	R	V	D
S	G	S	T	Y	A	C	K	V	E

Inner interactions $\alpha 1,2$ - $\beta 2m$

	$\beta 2m$		MHC		Hydrogen bond
	Residue	Atom	Residue	Atom	Length (Å)
1	Tyr 63	OH	Tyr 27	OH	3,515
2	His 31	NE2	Gln 96	OE1	2,871
3	Ile 1	N	Asp 119	O	3,465
4	Arg 3	NH1	Gly 120	O	3,813
5	Trp 60	NE1	Asp 122	OD1	2,659
6	Asp 53	OD2	Gln 32	NE2	2,619
7	Trp 60	O	Gln 96	NE2	2,952

	$\beta 2m$		MHC		Salt bridge
	Residue	Atom	Residue	Atom	Length (Å)
8	Asp 53	OD1	Arg 35	NH2	2,783
9	Asp 53	OD1	Arg 35	NE	2,786
10	Asp 53	OD2	Arg 35	NE	3,554

Inner interactions $\alpha 1,2 - \beta 2m$



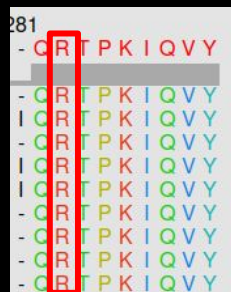
Interaction 1: Tyr 63 - Tyr 27



Interaction 2: His 31 - Gln 96



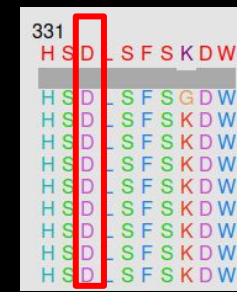
Interaction 3: Ile 1 - Asp 119



Interaction 4: Arg 3 - Gly 120



Interaction 5: Trp 60 - Asp 122



Interaction 6: Asp 53 - Gln 32

Inner interactions $\alpha_{1,2} - \beta_{2m}$



Interaction 7: Trp 60 - Gln 96



Interaction 8/9/10: Asp 53 - Arg 35

Inner interactions $\alpha 1,2$ - $\beta 2m$



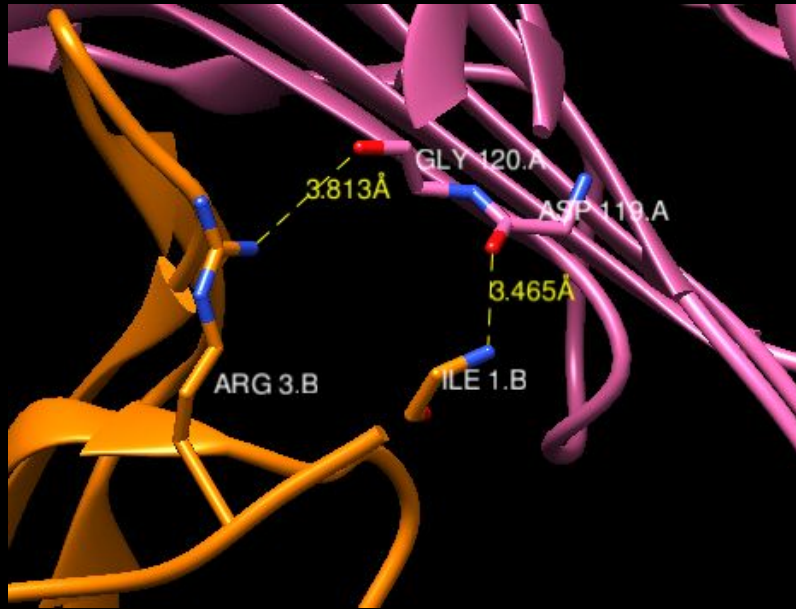
Asp53 - Gln32

Tyr63 - Tyr27



His 31 - Gln 96

Inner interactions $\alpha 1,2$ - $\beta 2m$



Arg 3 - Gly 120

Ile 1 - Asp 119

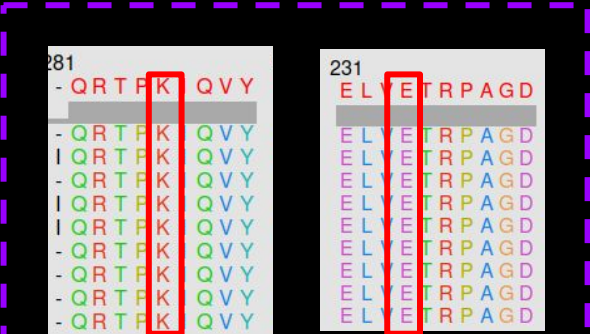


Trp 60 - Asp 122

Inner interactions $\alpha 1,2 - \beta 2m$ in evolution

	1	11	21	31	41	51	61	71	81	91	101
Consensus	- g s H S I r Y f y	T a v S r p g - g -	e p - - - - - r f	i a V G Y V d d t q	F v r F D S d a - s	p R a e P R a p W i	e q - e - - - g p e	Y W d r e T r i a k	d a a Q t f r v d L	g t l r r y Y N Q S	e a G S H T I Q I M
Conservation											
6kwoAB	- - P H S L S Y F Y	T A V S R P D - R G	D S - - - - - R F	I A V G Y V D D T Q	F V R F D N Y A P N	P R M E P R V P W I	Q Q - E - - - G Q D	Y W D E E T R K V K	D N A Q T Y G V G L	N T L R G Y Y N Q S	E A G S H T I Q S M
6iifAB	- G F H S L R Y F Y	T A W S R P G S G -	E P - - - - - R F	V A V G Y V D D T Q	F V R F D S D N A S	P R A E P R A P W M	D L - V E Q Q D P Q	Y W D R N T R N A R	D A A Q T Y R V G L	D N V R G Y Y N Q S	E A G S H T I Q R M
6mj2AB	- G S H S M R Y F Y	T S V S R P G L G -	E P - - - - - R F	I I V G Y V D D T Q	F V R F D S D A A S	P R M E Q R A P W M	Q Q - V - - - E P E	Y W D Q Q T Q I A K	D T A Q T F R V N L	N T A L R Y Y N Q S	A A G S H T I Q T M
1biifAB	- G S H S L R Y F Y	T A V S R P G F G -	E P - - - - - R Y	M E V G Y V D N T E	F V R F D S D A E N	F V R E P R A R W I	E Q - E - - - G P E	Y W D E T R R A K	E N Q S F R V D L	R T A L R Y Y N Q S	A A G S H T I Q W M
3hlaAB	- G S H S M R Y F Y	T S V S R P G R G -	E P - - - - - R F	I A V G Y V D D T Q	F V R F D S D A E S	Q R M E P R A P W I	E Q - E - - - G P E	Y W D G E T R K V K	A H S Q T F R V D L	G T L R Y Y Y N Q S	E A G S H T I Q R M
3rwiAB	- G S H S M K Y F Y	T S V S R P G R G -	E P - - - - - R F	I S V G Y V D D T Q	F V R F D S D A E S	P R A E P R A P W V	E Q - E - - - G P E	Y W E E T R R A K	E A A Q T H R E N L	R T A L R Y Y N Q S	E A G S H T I Q K M
5y91AB	- G T H S L K Y V Y	T G V S R - - - - -	- G I - D F - P E F	T A V G M V D D G Q	F N Y F D S N S - -	M K A V P K T E W I	R Q N E - - - G A D	Y W D R Q T Q V L I	G A H Q V F K D S I	Q I V M E R F N Q S	- K G V H T V Q N M
6kyuAB	- E P H S L R Y F D	T G V S D - - - - -	- P S - P G V P R F	V S V G Y V D G H L	I D H Y F D S E T -	Q R T E P R A D W F	A A N T - - - D Q Q	Y W D R Q T E I S R	G A E Q I F R L D L	E T L R Y Y Y N Q S	- R G S H T V Q L M
6lhhAB	E L - H T L R Y I S	T A M T D - - - - -	- G P G Q - P W Y	D V G Y V D G E L	F T H Y N S T A - -	R R A V P R T E W I	A A N T - - - D Q Q	Y W D S E T Q T S Q	R T E Q I D R D G L	G T L Q R R Y N Q T	- G G S H T V Q L M
	111	121	131	141	151	161	171	181	191	201	211
Consensus	y G C d l g p D g r	l l r G y r Q y A Y	D G D D Y I a l n e	d l r - s w T A A d	m a A q i T k r K W	E a a - g y A E r d	r a Y L e g e C v E	w L r r y l e n g k	e t L q R a d p P k	t h v t h h - p a	s - d - e a T l R c
Conservation											
6kwoAB	F G C Y L G P D G L	L L H G Y R Q D A Y	D G D D Y I A L N E	D L R - S W T A A D	M A A Q I T K R K W	E A A - N V A E R R	R S Y L Q G L C V E	S L R R Y L E M G K	D T L Q R A E P P K	T H V T R H - - P S	S - D L G V T L R C
6iifAB	Y G C Y V G P H R	L L H G Y D Q L A Y	D G D D Y I A L N E	D L R - S W T A A D	L A A Q N T R R K W	E A A - G Y A E R D	R A Y L E G C V E	S L L R K H L E N G R	E T L L R A D P P K	T H T I H - - - P I	S - D R V T L R C
6mj2AB	F G C Y V A D G R	F F H G Y R Q Y A Y	D G D D Y I A L N E	D L R - S W T A A D	T A A Q N T R K W	E A A - G E A E R D	R A Y L E R E C V E	W L R R Y L E M G K	E T L Q R A D P P K	A H V T H - - - P A	S - D R E A T L R C
1biifAB	A G C D V E S D G R	L L R G Y W Q F A Y	D G D D Y I A L N E	D L K - T W T A A D	M A A Q I T R R K W	E Q A - G A A E R D	R A Y L E G C V E	W L R R Y L K N G K	A T L L R T D P P K	A H V T H - - - R R	P E G - D V T L R C
3hlaAB	Y G C D V G S D W R	F L R G Y H Q Y A Y	D E K D Y I A L K E	D L R - S W T A A D	M A A Q T T K H K W	E A A - H V A E Q L	R A Y L E G T C V E	W L R R Y L E N G K	E T L Q R T D A P K	T H M T H - - - A V	S - D H E A T L R C
3rwiAB	Y G C D L G P D G R	L L R G Y H Q S A Y	D E K D Y I A L N G	D L R - S W T A A D	M A A Q N T R K W	E G N - R Y A E R L	R A Y L E G C V E	W L R R Y L E N G K	E T L Q R A D P P K	T H V T H - - - P V	S - D H E A T L R C
5y91AB	Y G C L N D D G -	T T G Q Y Y Q Y A Y	E R D F V F S L D -	K N T L T W T A A N	P A V I T K H K W	E A L - A V A E Q L	K G Y L E N T C I E	W L K K Y V A Y G K	D T L R K V S P Q	V S L L Q K D P S -	- - - - - S P V T C
6kyuAB	Y G C D L L E D G -	T T R G F R Q Y G Y	E R D F V A F D -	K D T L T F T A A D	A G A Q I T K R K W	Q E G T D A E R W	K F Y L E N T C I E	G L R K Y V S Y G K	V L R R R E R P E	V Q V S G M - - E A	D - K - I L T L S C
6lhhAB	Y G C D I L E D G -	T I R G Y S Q D A Y	D E R F I A F D -	K D T M T F T A A V	P E A V P T K R K W	E E G - D Y A E G L	K Q Y L E T C V E	W L R R Y V E Y G K	A E L G R R E R P E	V R V W G K - - E A	D - G - I L T L S C
	221	231	241	251	261	271	281	291	301	311	321
Consensus	w A I 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 n g D G t f q	k W a a v v P s p G	e e - q r y T c h v	q H e g L p e p l -	- t l r - - - -	- - - w - - - q r	t P K i Q V Y S r h	P a e n G k p n f L
Conservation											
6kwoAB	W A L G F Y P K E I	S L T W O R E G Q D	Q S Q - D M E L V E	T R P S G D G T F Q	K W A A L V V P P G	E E - Q S Y T C H V	Q H E G L Q E P L -	- - - - - - - -	- - - R A - - -	P P K V Q V Y S R H	P A E N G K P N Y L
6iifAB	W A L G F Y P E E I	T L T W O H D - G E	D Q T O E M E L V E	T R P D G N G A F Q	K W A A L V V P S G	E E - Q R Y T C H V	Q H E G L P O P L -	- - - - - - - -	- - - P E - - -	T P K I Q V Y S R H	P A E N G K P N Y L
6mj2AB	W A L G F Y P A D I	S L T W O R D - G E	D Q T O D T L V E	T R P G G D G T F Q	K W A A V V V P S G	E E - Q R Y T C R V	Q H E G L P E P L -	- - - - - - - -	- - - W M - I Q	T P K I Q V Y S R H	P A E N G K S N F L
1biifAB	W A L G F Y P A D I	T L T W O L N - G E	E L T O E M E L V E	T R P A G D G T F Q	K W A S V V V P L G	K E - Q K Y T C H V	E H E G L P E P L -	- - - - - - - -	- - - W I - Q K	T P Q I Q V Y S R H	P P E N G K P N I L
3hlaAB	W A L S F Y P A E I	T L T W O R D - G E	D Q T O D T L V E	T R P A G D G T F Q	K W A A V V V P S G	Q E - Q R Y T C H V	Q H E G L - P K P L	- - - - - - - -	- - - - - - - -	T P K I Q V Y S R H	P A E N G K S N F L
3rwiAB	W A L G F Y P A E I	T L T W O R D - G E	E Q T O D T F E V E	T R P G G D G T F Q	K W A S V V V P S G	E E - Q R Y T C H V	Q H E G L P E P L -	- - - - - - - -	- - - P I - Q	T P K I Q V Y S R H	P P E N G K P N F L
5y91AB	H A T G F Y P S G V	T I T W Q K N - G Q	D H D E V D L G E	L L P N E D G S F Q	R M S T L N V G - P	W K N N R F S C V V	E H - Q - D K T I	- - - - - - - -	- - - - - - - -	S P K I Q V Y S H Y	P G G Y K E N T L
6kyuAB	R A H G F Y P R P I	S I S W L K D - G M	V Q E Q E T K R G S	T V P N S D G T Y H	I W A T I D V L P G	E R - D K Y Q C R V	E H A S L P Q P G -	- - - - - - - -	- - - W G Q A K	A P K V Q V Y S R H	P A T A G T E N I L
6lhhAB	R A H G F Y P R P I	A V S W L K D - G A	V Q G Q D A S G S G	I V P N G D G T Y H	T W V T I D A Q P G	D G - D K Y Q C R V	E H A S L P Q P G -	- - - - - - - -	- - - W - - - -	T P K V Q V Y S R F	P A S A G T K N V L
	331	341	351	361	371	381	391	401			
Consensus	N C Y V s G F H P p	d l e i d L L K N G	e k m e k v e q s D	I S F s k D w s F y	L l v y t e F T P t	e k D e Y a C r V n	H v t l s e P k i v	k W d r d m -			
Conservation											
6kwoAB	N C Y V S G F H P P	Q I E I D L L K N G	E K M - N A E Q S D	L S F S K D W S F Y	L L V H T E F T P N	A V D Q Y S C R V K	H V T L D K P K I V	K W D R D H -			
6iifAB	N C Y V Y G F H P P	Q I E I D L L K N G	Q K M - K T E Q S D	L S F S K D W S F Y	L L V H T D F T P S	T V D E Y S C R V N	H S S L A A P H M V	K W D R N N -			
6mj2AB	N C Y V S G F H P S	D I E I V D L L K N G	E R I E K V 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 -			
1biifAB	N C Y V T Q F H P P	H I E I Q M L K N G	K K I E K V E M S D	M S F S K D W S F Y	I L A H T E F T P T	E T D T Y A C R V N	H D S M A E P K T V	Y W D R D M -			
3hlaAB	N C Y V S G F H P S	D I E I V D L L K N G	E R I E K V 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 -			
3rwiAB	N C Y V S G F H P S	D I E I V D L L K N G	E K M K V E M S D	L S F S K D W S F Y	L L Y Y T E F T P N	E K D E Y A C R V N	H V T L S G P R T V	K W D R D M -			
5y91AB	I C Y V S G F H P P	D I S I E L L K N G	E V I A D A Q O T D	L A F E K W D F H	L T K S V S F K P E	K S D E Y S C S V R	H M - - - S K T K K I	V W E S - N M			
6kyuAB	N C Y V E G F H P P	K I D I A L L K N G	E P M K D V K Y N D	M S F G D D W T F Q	R L V Y A P F T P T	K S D V Y T C R V D	H E A F T E P Q S F	R W E P - - -			
6lhhAB	N C F A A G F H P P	K I S I T L M K D G	V P M E G A Q Y S D	M S F N D D W T F Q	R L V H A D F T P S	S G S T Y A C K V E	H E T L K E P Q V Y	K W D P E F -			

Inner interactions $\alpha 3$ - $\beta 2m$: salt bridges



Interaction 1: Lys 6 - Glu 232



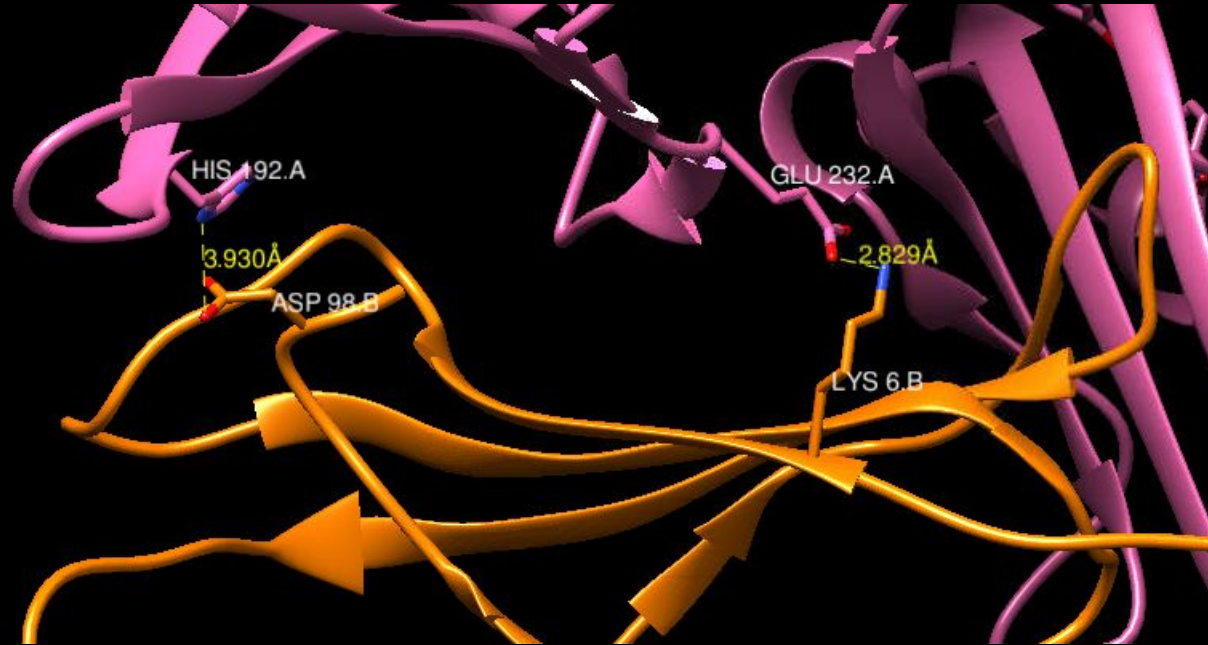
Interaction 2: Asp 98 - Hist 192

β2m		MHC		Salt bridge
Residue	Atom	Residue	Atom	Length (Å)
Lys 6	NZ	Glu 232	OE1	2,829
Asp 98	OD2	Hist 192	ND1	3,930
Met 99	O	Arg 234	NH1	2,674



Interaction 3: Met 99 - Arg 234

Inner interactions $\alpha 3$ - $\beta 2m$: salt bridges



Asp98 -His192

Lys6- Glu232

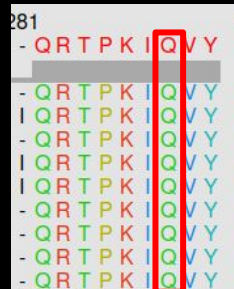
Inner interactions $\alpha 3$ - $\beta 2m$: salt bridges in evolution

Consensus Conservation	1 - g s H S I r Y f y	11 T a v S r p g - g -	21 e p - - - - - r f	31 I a V G Y V D d t q	41 F v r f D S d a - s	51 p R a e P R a p W i	61 e q - e - - - g p e	71 Y W d r e T r i a k	81 d a a Q t f r v d L	91 g t l r r y Y N Q S	101 e a G S H T I Q I M
6kwoAB	- - P H S L S Y F Y	T A V S R P D - R G	D S - - - - - R F	I A V G Y V D D T Q	F V R F D N Y A P N	P R M E P R V P W I	Q Q - E - - - G Q D	Y W D E E T R K V K	D N A Q T Y G V G L	N T L R G Y Y N Q S	E A G S H T L Q S M
6iifAB	- G F H S L R Y F Y	T A W S R P G S G -	E P - - - - - R F	V A V G Y V D D T Q	F V R F D S D N A S	P R A E P R A P W M	D L - V E Q Q D P Q	Y W D R N T R N A R	D A A Q T Y R V G L	D N V R G Y Y N Q S	E A G S H T I Q R M
6mj2AB	- G S H S M R Y F Y	T S V S R P G L G -	E P - - - - - R F	I I V G Y V D D T Q	F V R F D S D A A S	P R M E Q R A P W M	Q Q - V - - - E P E	Y W D Q Q T Q I A K	D T A Q T F R V N L	N T A L R G Y Y N Q S	A A G S H T F Q T M
1biifAB	- G S H S L R Y F Y	T A V S R P G F G -	E P - - - - - R Y	M E V G Y V D N T E	F V R F D S D A E N	Q R Y E P R A R W I	Q Q - E - - - G P E	Y W E R E T R R A K	E N Q S T F R V D L	R T A L R G Y Y N Q S	A A G S H T L Q W M
3hlaAB	- G S H S M R Y F Y	T S V S R P G R G -	E P - - - - - R F	I S V G Y V D D T Q	F V R F D S D A E S	P R M E P R A P W I	Q Q - E - - - G P E	Y W D G E T R K V K	A H S Q T F R V D L	G T A L R G Y Y N Q S	E A G S H T V O R M
3rwiAB	- G S H S M K Y F Y	T S V S R P G R G -	E P - - - - - R F	I S V G Y V D D T Q	F V R F D S D A E S	P R A E P R A P W V	Q Q - E - - - G P E	Y W E A T R R A K	E A A Q T F R E N L	R T A L R G Y Y N Q S	E A G S H T I Q K M
5y91AB	- G T H S L K Y V Y	T G V S R - - - - -	- G I - D F - P E F	T A V G M V D D G Q	F M Y F D S N S - -	M K A V P K T E W I	R Q N E - - - G A D	Y W D R Q T Q V L I	G A H Q V F K D S I	Q I V M E R F N Q S	- K G V H T W Q N M
6kyuAB	- E P H S L R Y F D	T G V S D - - - - -	- P S - P G V P R F	V S V G Y V D G H L	I D H Y D S E T - -	Q R T E P R A D W F	A A N T - - - D Q Q	Y W D R Q T E I S R	G A E Q I F R L D L	E T L R E R Y N Q S	- R G S H T W Q L M
6lhhAB	E L - H T L R Y I S	T A M T D - - - - -	- P G P G Q - P W Y	D V G Y V D G E L	F T H Y N S T A - -	R R A V P R T E W I	A A N T - - - D Q Q	Y W D S T Q T S Q	R T E Q I D R D G L	E T L Q R R Y N Q T	- G G S H T V Q L M
Consensus Conservation	111 y G C d l g p D g r	121 l l r G y r Q y A Y	131 D G a D y i A l n e	141 d l r - s w T A A d	151 m a A q i t k r K W	161 E a a - g y A E r d	171 r a Y L e g e C v E	181 w L r r y l e n g k	191 e t L q R a d p P k	201 t h v t h - - p a	211 s - d - e a T l R c
6kwoAB	F G C Y L G P D G L	L L H G Y R Q D A Y	D G A D Y I A L N E	D L R - S W T A A D	M A A Q I T K R K W	E A A - N V A E R R	R S Y L Q G L C V E	S L R R Y L E M G K	D T L Q R A E P P K	T H V T R H - - P S	S - D L G V T L R C
6iifAB	F G C Y V G P H G R	L L H G Y D Q L A Y	D G A D Y I A L N E	D L R - S W T A A D	M A A Q I T R R K W	E A A - G Y A E R D	R A Y L E G C V E	W L L K H L E N G R	E T L L R A D P P K	T H I T H - - P I	S - D R E V T L R C
6mj2AB	F G C E Y W A D G R	F F H G Y R Q Y A Y	D G A D Y I A L N E	D L R - S W T A A D	T A A Q N T Q R K W	E A A - G E A E R D	R A Y L E R E C V E	W L R R Y L E M G K	E T L Q R A D P P K	A H V T H - - P A	S - D R E A T L R C
1biifAB	A G C D V E S D G R	L L R G Y W Q F A Y	D G C D Y I A L N E	D L K - T W T A A D	M A A Q I T R R K W	Q A - G A A E R D	R A Y L E G C V E	W L R R Y L K N G N	A T L L R T D P P K	A H V T H - - R R	P E G - D V T L R C
3hlaAB	Y G C D V G S D W R	F L R G Y H Q Y A Y	D G K D Y I A L K E	D L R - S W T A A D	M A A Q T T K H K W	E A A - H V A E R L	R A Y L E G T C V E	W L R R Y L E N G K	E T L Q R T D A P K	T H M T H - - A V	S - D H E A T L R C
3rwiAB	Y G C D L G P D G R	L L R G Y H Q S A Y	D G K D Y I A L N G	D L R - S W T A A D	M A A Q N T Q R K W	E G N - R Y A E R L	R A Y L E G C L V E	W L R R Y L E N G K	E T L Q R A D P P K	T H V T H - - P V	S - D H E A T L R C
5y91AB	Y G C E L N D G G -	T T G Q Y Y Q Y A Y	D G E D F V S L D -	K N T L T W T A A N	P A A V I T K H K W	E A L - A V A E R L	K G Y L E N T C I E	W L K K Y V A Y G K	D T L R K V S P Q	V S L L Q K D P S -	- - - - - S P V T C
6kyuAB	Y G C D L L E D G -	T T R G F R Q Y G Y	E G R D F V A F D -	K D T L T F T A A D	A G A Q I T K R K W	Q E G T D A E R W	K F Y L E N T C I E	G L R K Y V S Y G K	D V L E R R E R P E	V Q V S G M - E A	D - K - I L T L S C
6lhhAB	Y G C D I L E D G -	T I R G Y S Q D A Y	D G R D F I A F D -	K D T M T F T A A V	P E A V P T K R K W	E E G - D Y A E G L	K Q Y L E T C V E	W L R R Y V E Y G K	A E L G R R E R P E	V R V W E K - E A	D - G - I L T L S C
Consensus Conservation	221 w A I G F Y P a e i	231 t l t W q r d - G e	241 d q t q d t e l v e	251 r n g D G t f q	261 k W a a v v P s p G	271 e e - q r y t C h v	281 q H e g L p e p l -	291 - t l r - - - - -	301 - - - w - - - q - r	311 t P K I Q V Y S R h	321 P a e n G k p n f L
6kwoAB	W A L G F Y P K E I	S L T W O R E G Q D	Q S Q - D M E L V E	T R P S G D G T F Q	K W A A L V V P P G	E E - Q S Y T C H V	Q H E G L Q E P L -	- T L - - - - -	- - - R A - - - R	P P K I Q V Y S R H	P A E N G K P N Y L
6iifAB	W A L G F Y P E E I	T L T W O H D - G E	D Q T O E M E L V E	T R P D G N G A F Q	K W A A L V V P S G	E E - Q R Y T C H V	Q H E G L P O P L -	- T L R W E - - -	- - - P E - - - P	T P K I Q V Y S R H	P A E N G K P N Y L
6mj2AB	W A L G F Y P A E I	S L T W O R D - G E	D Q T O D T L E V E	T R P G G D G T F Q	K W A A V V V P S G	E E - Q R Y T C R V	Q H E G L P E P L -	- T L T - - - - -	- - - W M - I Q - R	T P K I Q V Y S R H	P A E N G K S N F L
1biifAB	W A L G F Y P A D I	T L T W O L N - G E	E L T O E M E L V E	T R P A G D G T F Q	K W A S V V V P L G	K E - Q K Y T C H V	E H E G L P E P L -	- T L R - - - - -	- - - W I - O - K	T P K I Q V Y S R H	P P E N G K P N I L
3hlaAB	W A L S F Y P A E I	T L T W O R D - G E	D Q T O D T L E V E	T R P A G D G T F Q	K W A A V V V P S G	Q E - Q R Y T C H V	Q H E G L - P K P L	- - - - - - - -	- - - - - - - -	T P K I Q V Y S R H	P A E N G K S N F L
3rwiAB	W A L G F Y P A E I	T L T W O R D - G E	E Q T O D T F E V E	T R P G G D G T F Q	K M S T L N V G - P	E E - Q R Y T C H V	Q H E G L P E P L -	- T L R W E - - -	- - - P I - O - R	T P K I Q V Y S R H	P P E N G K P N F L
5y91AB	H A T G F Y P S G V	T I T W Q K N - G Q	D H D E V D L G E	L L P N E D G S F Q	R W S T L N V G - P	W K N N R F S C V V	E H - Q - D K T I	- R K T E D D I I T	N F D - K - - V - S	S P K I Q V Y S H Y	P G G Y K E N T L
6kyuAB	R A H G F Y P R P I	S I S W L K D - G M	V Q E Q E T K R G S	L V P N S D G T Y H	I W A T I D V L P G	E R - D K Y Q C R V	E H A S L P Q P G -	- L F S - - - - -	- - - W G Q A K - A	A P K V Q V Y S R H	P A T A G T E N I L
6lhhAB	R A H G F Y P R P I	A V S W L K D - G A	V Q G D A Q S G S	L V P N G D G T Y H	T W V T I D A Q P G	D G - D K Y Q C R V	E H A S L P Q P G -	- L Y S - - - - -	- - - W - - - - D L	T P K V Q V Y S R F	P A S A G T K N V L
Consensus Conservation	331 N C Y V s G F H P p	341 d I e i d L L K N G	351 e k m e k v e q s D	361 I S F s k D W s F y	371 L l v y t e F T P t	381 e k D e Y a C r V n	391 H v t l s e P k i v	401 k W d r d m			
6kwoAB	N C Y V S G F H P P	Q I E I D L L K N G	E K M - N A E Q S D	L S F S K D W S F Y	L L V H T E F T P N	A V D Q Y S C R V K	H V T L D K P K I V	K W D R D F			
6iifAB	N C Y V Y G F H P P	Q I E I D L L K N G	Q K M - K T E Q S D	L S F S K D W S F Y	L L V H T D F T P S	T V D E Y S C R V N	H S S L A A P H M V	K W D R F N N			
6mj2AB	N C Y V S G F H P S	D I E I V D L L K N G	E R I E K V 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			
1biifAB	N C Y V T Q F H P P	H I E I Q M L K N G	K K I P K V E M S D	M S F S K D W S F Y	I L A H T E F T P T	E T D T Y A C R V K	H D S M A E P K T V	Y W D R D W			
3hlaAB	N C Y V S G F H P S	D I E I V D L L K N G	E R I E K V 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 V			
3rwiAB	N C Y V S G F H P S	D I E I V D L L K N G	E K M K V E H S D	L S F S K D W S F Y	L L Y Y T E F T P N	E K D E Y A C R V N	H V T L S G P R T V	K W D R D V			
5y91AB	I C Y V S G F H P P	D I S I E L L K N G	E V I A D A Q Q T D	L A F E K W Q S F H	L T K S V S F K P E	K S D E Y S C S V R	H M - - - S K T K K I	V W E S - N M			
6kyuAB	N C Y V E G F H P P	K I D I A L L K N G	E P M K D V K Y N D	M S F G D D W T F Q	R L V Y A P F T P T	K S D V Y T C R V D	H E A F T E P Q S F	R W E R - - -			
6lhhAB	N C F A A G F H P P	K I S I T L M K D G	V P M E G A Q Y S D	M S F N D D W T F Q	R L V H A D F T P S	S G S T Y A C K V E	H E T L K E P Q V Y	K W D R E F			

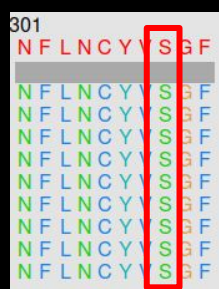
Inner interactions $\alpha 3$ - $\beta 2m$: hydrogen bonds

		β2m		MHC		Hydrogen Bond			β2m		MHC		Hydrogen bond
		Residue	Atom	Residue	Atom	Length (Å)			Residue	Atom	Residue	Atom	Length (Å)
1		Gln 8	NE2	Glu 232	O	3,019	10		Arg 12	O	Gln 242	NE2	3,007
2		Ser 28	OG	Glu 232	OE1	2,936	11		Asp 98	O	Arg 202	NH1	3,152
3		Tyr 26	OH	Glu 232	OE2	3,099	12		Met 99	O	Trp 244	NE1	3,367
4		Tyr 10	OH	Pro 235	O	2,622							
5		Arg 12	NE	Ala 236	O	3,162							
6		Asn 24	ND2	Ala 236	O	2,871							
7		Arg 12	NH2	Gly 237	O	3,718							
8		Gln 8	OE1	Arg 234	NH1	2,942							
9		Ser 11	O	Gln 242	NE2	3,823							

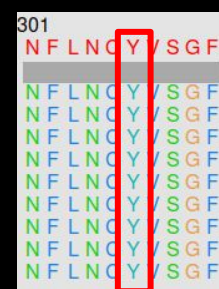
Inner interactions $\alpha 3$ - $\beta 2m$: hydrogen bonds



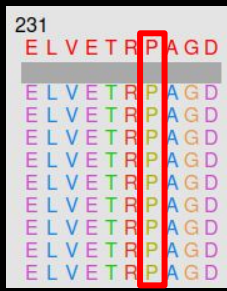
Interaction 1: Gln 8 - Glu 232



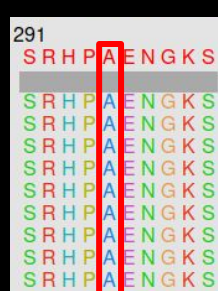
Interaction 2: Ser 28 - Glu 232



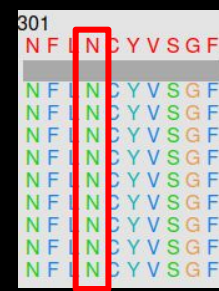
Interaction 3: Tyr 26 - Glu 232



Interaction 4: Tyr 10 - Pro 235

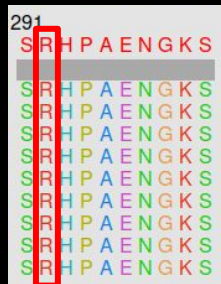


Interaction 5: Arg 12 - Ala 236



Interaction 6: Asn 24 - Ala 236

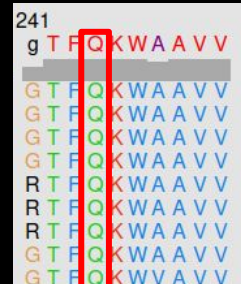
Inner interactions $\alpha 3$ - $\beta 2m$: hydrogen bonds



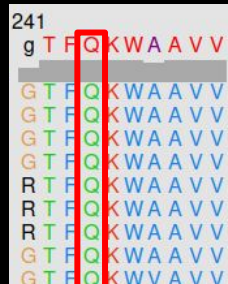
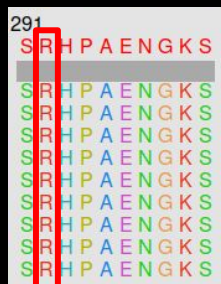
Interaction 7: Arg 12 - Gly 237



Interaction 8: Gln 8 - Arg 234



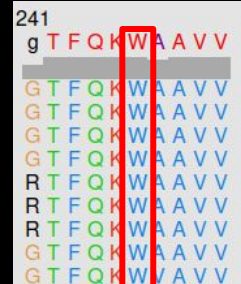
Interaction 9: Ser 11 - Gln 242



Interaction 10: Arg 12 - Gln 242

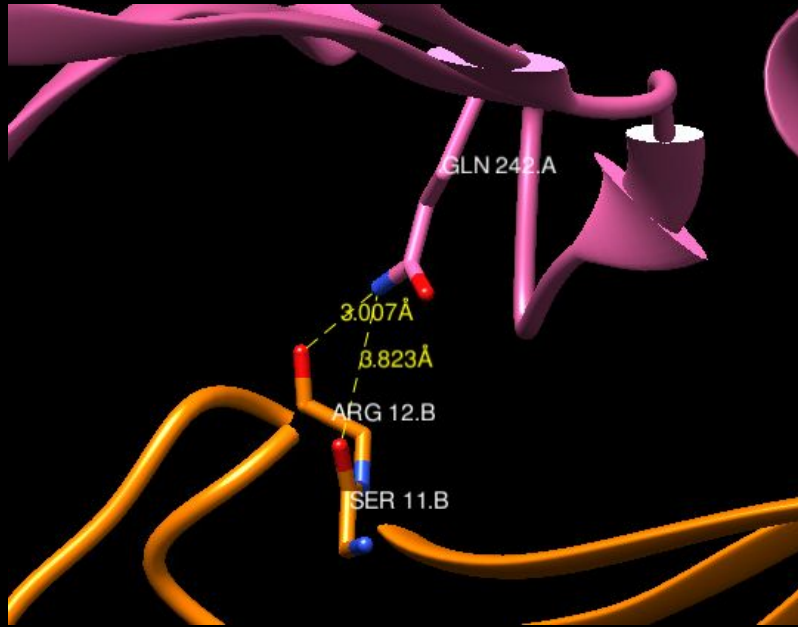


Interaction 11: Asp 98 - Arg 202



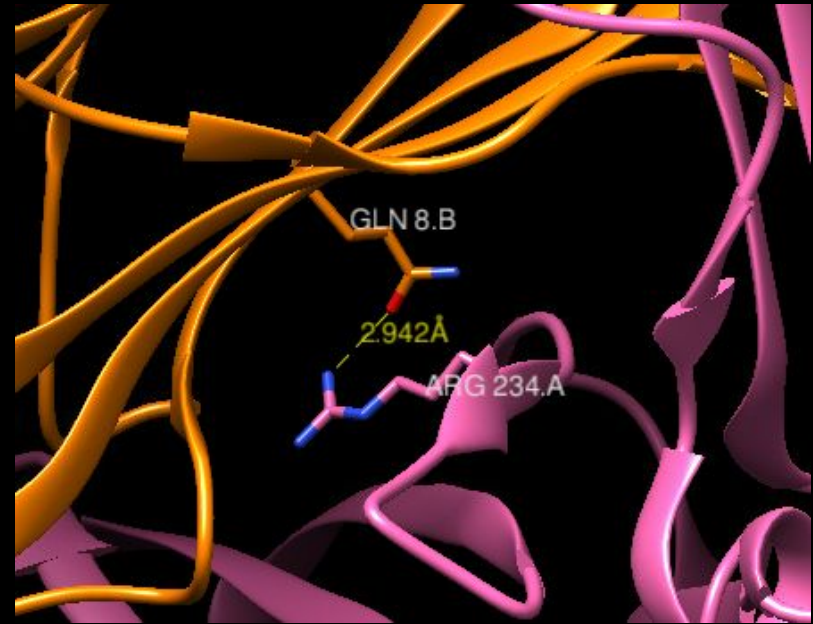
Interaction 12: Met 99 - Trp 244

Inner interactions $\alpha 3$ - $\beta 2m$: hydrogen bonds



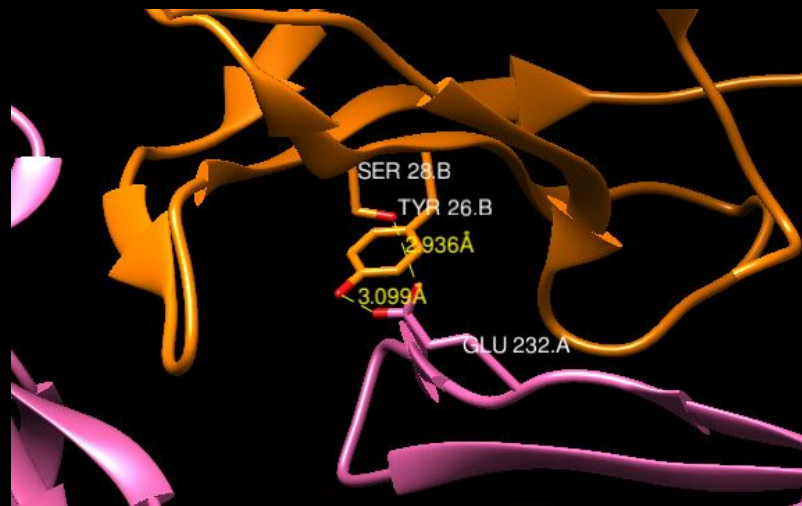
Arg 12 - Gln 242

Ser 11 - Gln 242



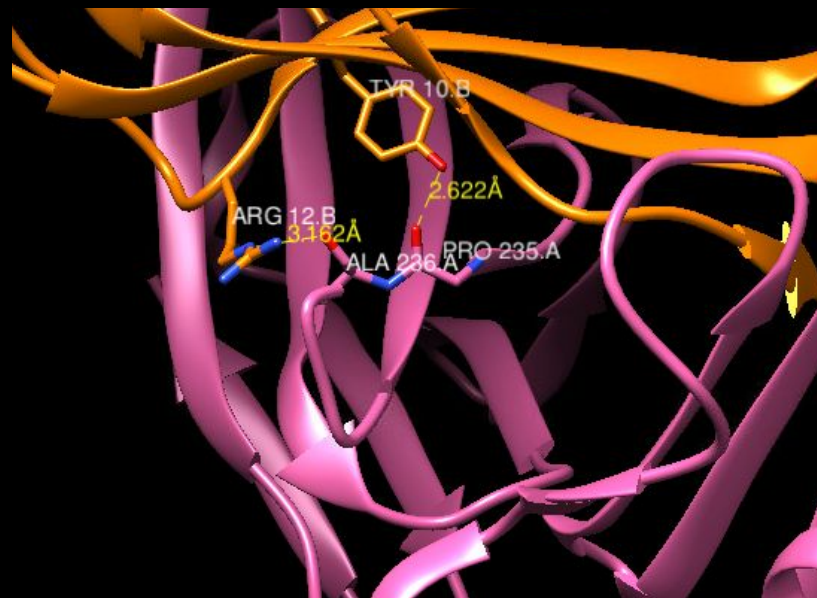
Gln 8 - Arg 234

Inner interactions $\alpha 3$ - $\beta 2m$: hydrogen bonds



Ser 28 - Glu 232

Tyr 26 - Glu 232



Arg 12 - Ala 236

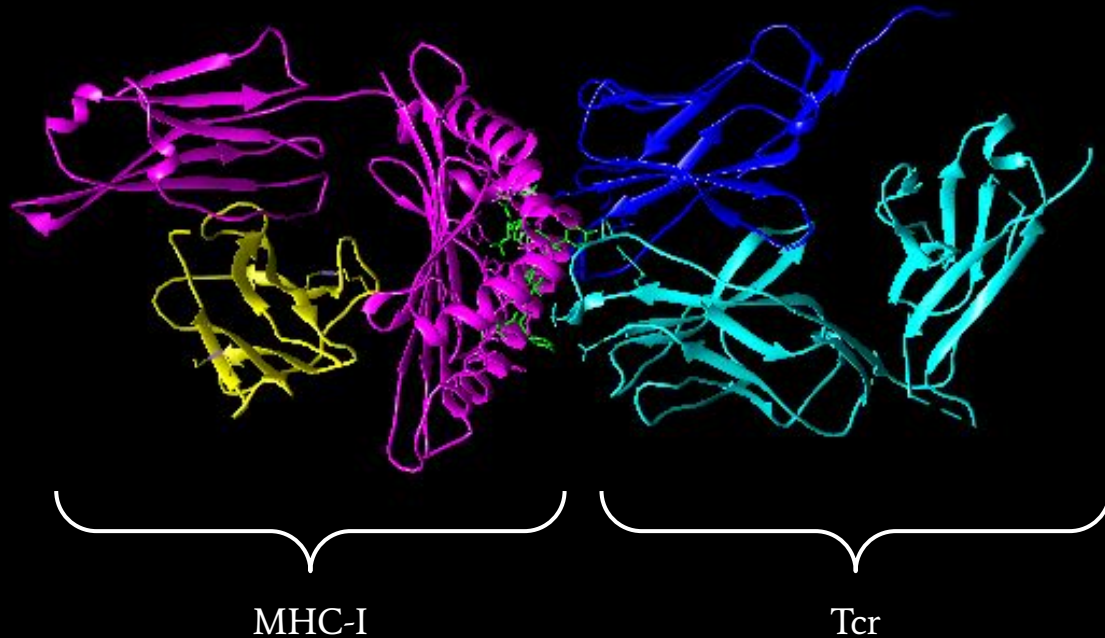
Tyr 10 - Pro 235

Inner interactions $\alpha 3$ - $\beta 2m$: hydrogen bonds in evolution

Consensus Conservation	1 -gsHSIrYfy	11 TavSrpg-g-	21 ep-----rf	31 IaVGyVDDtq	41 FvrFDSDa-s	51 pRaePRapWi	61 eq-e---gpe	71 YWdreTriak	81 daaQtrfvdL	91 gtlrryYnQS	101 eaGSHTIQIM
6kwoAB	-PHSLSYFY	TAVSRPD-RG	DS-----RF	IAGVYVDDTQ	FVRFDNYAPN	PRMEPRVPWI	QQ-E---GQD	YWDEETRKVK	DNAQTYGVGL	NTLRGYYNQS	EAGSHTLOSM
6lilAB	-GFHSIRYFY	TAVSRPGSG-	EP-----RF	IAVGYVDDTQ	FVRFDSDNAS	PRAEPRAPWM	DL-VEQQDPQ	YWDRNTRNAR	DAQAQTYRVGL	DNVRGYNNQS	EAGSHTIORM
6mj2AB	-GSHSMRYFY	TSVSRPGLG-	EP-----RF	IIVGYVDDTQ	FVRFDSDAAS	PRMEQRPAPWM	QQ-V---EPE	YWDQQTQIAK	DTAQTFRVNL	NTALRGYYNQS	AAGSHTFOTM
1biiAB	-GSHSLRYFY	TAVSRPGFG-	EP-----RY	MEVGYVDNTE	FVRFDSDAEN	PRVEPRAPWI	EQ-E---GPE	YWERETRRAK	ENQSTFRVDL	RTLARGYYNQS	AAGSHTLOWM
3hlaAB	-GSHSMRYFY	TSVSRPGRG-	EP-----RF	IAVGYVDDTQ	FVRFDSDAAS	PRMEPRAPWI	EQ-E---GPE	YWDGETRKVK	AHSQSTRVDL	GTLARGYYNQS	EAGSHTVORM
3rwiAB	-GSHSMKYFY	TSVSRPGRG-	EP-----RF	ISVGYVDDTQ	FVRFDSDAES	PRAEPRAPWV	EQ-E---GPE	YWEATRRAK	EAAQTHRENL	RTLARGYYNQS	EAGSHTIQKM
5y91AB	-GTHSLKYFY	TGVSR-----	-GI-DF-PEF	TAVMVDGGO	FMYFDSNS--	MKAVPKTEWI	RQN-E---GAD	YWDRQTQVLI	GAHQVKDSI	QIVMERFNQS	-KGVHTWQNM
6kyuAB	-EPHSLRYFY	TGVSD-----	-PS-PGVPRF	VSVGYVDGHL	IDHYDSEI--	QRTQPRADWF	AANT---DQO	YWDRQTEISR	GAEQIFRLDL	ETLRLMERFNQS	-RGSHTWQNM
6lhhAB	EL-HTLRYIS	TAMTD-----	-GGPGQ-PWY	VDVGyVVGEL	FDHYNSTA--	RRAVPRTTEWI	AANT---DQO	YWDSQTQSG	RTEQIDRDGL	ETLQRRYNQT	-GGSHTVQLM
Consensus Conservation	111 yGCdIlgpDGr	121 llrGyrQyAY	131 DGaDyIAlne	141 dlr-swTAAAd	151 maAqITkrKW	161 Eaa-gyAERd	171 raYLEgcCvE	181 wLrrylenGk	191 etLqRadpPk	201 thvthh--pa	211 s-d-eaTLrC
6kwoAB	FGCYLGPDGL	LLHYGRQDAY	DGADYIALNE	DLR-SWTAAD	MAAQITKRKW	EAA-NVAERR	RSYLQGLCvE	SLRRYLEMGK	DTLQRAEPK	THVTRH--PS	S-DLGVTLRC
6lilAB	FGCYVGPGR	LLHYGRQDAY	DGADYIALNE	DLR-SWTAAD	MAAQITKRKW	EAA-GYAEER	RAYLEGEcV	WLLKHLNENR	ETLLRADPPK	THITHH--PI	S-DREVTLRC
6mj2AB	FGCYVWADGR	FFHYGRQYAY	DGADYIALNE	DLR-SWTAAD	TAAQNTQRKW	EAA-GAEARR	RAYLEGEcV	WLLRRYLEMGK	ETLQRAEPK	AHVTHH--PA	S-DREVTLRC
1biiAB	AGCDVSDGR	LLRGYQWQAY	DGCDYIALNE	DLK-SWTAAD	MAAQITKRKW	QA-GAAERD	RAYLEGEcV	WLLRRYLEMGK	ATLLRTDPPK	AHVTHH--AV	PEG-DVTLRC
3hlaAB	YGCDVSDGR	FLRGYQWQAY	DGCDYIALNE	DLR-SWTAAD	MAAQITKRKW	EAA-HVAERL	RAYLEGEcV	WLLRRYLEMGK	ETLQRAEPK	THVTHH--AV	S-DHEATLRC
3rwiAB	YGCDVSDGR	LLRGYQWQAY	DGCDYIALNE	DLR-SWTAAD	MAAQITKRKW	EGN-RYAEQL	RAYLEGEcV	WLLRRYLEMGK	ETLQRAEPK	THVTHH--PV	S-DHEATLRC
5y91AB	YGCDLNDGD	TTQGYQYAY	DGEDFVSLD-	KNTLTWTAAN	PAVITKRKW	EAL-AVAERL	KGYLENTCIE	WLLKKYVAYGK	DTLKRKVSPO	VSLLLQKDP-	-SPVTC
6kyuAB	YGCDLNDGD	STRGFQYQY	EGRDFVAFD-	KDNTLTFAAV	AGAQITKRKW	QEGTDAAERW	KGYLENTCIE	GLRKYVSYGK	DTLKRKVSPO	VQVSGM--EA	D-K-I-LTLC
6lhhAB	YGCDLNDGD	TIRGYSQDAY	DGRDFVAFD-	KDNTLTFAAV	PEAVPTKRKW	EEG-DYAEGL	KGYLENTCIE	WLLRRYVYSGK	AELGRRERPE	VRVWGK4-EA	D-G-I-LTLC
Consensus Conservation	221 wAIGFYPaeI	231 tlTWqrD-Ge	241 dqtqdtelVe	251 trngDGtftq	261 kWaavvVpsG	271 ee-qrytChV	281 qHegLpepl-	291 -tlr-----	301 --w---q-r	311 tPKiQVYSrh	321 PaenGkpNfL
6kwoAB	WALGFYKPEI	SLTWOREGQD	QSQ-DMELVE	TRNGDGDTFO	KWAALVVPVG	EE-QSYTCHV	QHEGLQEPPL	-TL-----	--RA---R	PPKVQVYSRH	PAENKPNYL
6lilAB	WALGFYKPEI	SLTWOREGQD	QSQ-DMELVE	TRNGDGDTFO	KWAALVVPVG	EE-QRYTCHV	QHEGLQEPPL	-TLWE---	--PE--P-R	TPKVQVYSRH	PAENKPNYL
6mj2AB	WALGFYKPEI	SLTWOREGQD	QSQ-DMELVE	TRNGDGDTFO	KWAALVVPVG	EE-QRYTCHV	QHEGLQEPPL	-TL---	--WM-IO-R	TPKVQVYSRH	PAENKPNYL
1biiAB	WALGFYKPEI	SLTWOREGQD	QSQ-DMELVE	TRNGDGDTFO	KWAALVVPVG	KE-QRYTCHV	QHEGLQEPPL	-TL---	--WI--O-K	TPKVQVYSRH	PAENKPNYL
3hlaAB	WALGFYKPEI	SLTWOREGQD	QSQ-DMELVE	TRNGDGDTFO	KWAALVVPVG	KE-QRYTCHV	QHEGLQEPPL	-TL---	--WI--O-K	TPKVQVYSRH	PAENKPNYL
3rwiAB	WALGFYKPEI	SLTWOREGQD	QSQ-DMELVE	TRNGDGDTFO	KWAALVVPVG	KE-QRYTCHV	QHEGLQEPPL	-TL---	--WI--O-K	TPKVQVYSRH	PAENKPNYL
5y91AB	HATGFYKPEI	SLTWOREGQD	QSQ-DMELVE	TRNGDGDTFO	KWAALVVPVG	KE-QRYTCHV	QHEGLQEPPL	-TL---	--WI--O-K	TPKVQVYSRH	PAENKPNYL
6kyuAB	RHAGFYKPEI	SLTWOREGQD	QSQ-DMELVE	TRNGDGDTFO	KWAALVVPVG	KE-QRYTCHV	QHEGLQEPPL	-TL---	--WI--O-K	TPKVQVYSRH	PAENKPNYL
6lhhAB	RHAGFYKPEI	SLTWOREGQD	QSQ-DMELVE	TRNGDGDTFO	KWAALVVPVG	KE-QRYTCHV	QHEGLQEPPL	-TL---	--WI--O-K	TPKVQVYSRH	PAENKPNYL
Consensus Conservation	331 NCYsGFHPp	341 diEidLLKNG	351 ekmekveqsD	361 ISFSKdWsfY	371 LlvyteFTPt	381 ekDeYaCrVn	391 HvtlsePkiv	401 kWdrdm-			
6kwoAB	NCYsGFHPp	QIEIDLKNG	EKM-NAEQSD	LSFSKdWsfY	LLVHTFTPTN	AVDQYSCRVK	HVTLDPKPKIV	KWDRDMN			
6lilAB	NCYsGFHPp	QIEIDLKNG	EKM-NAEQSD	LSFSKdWsfY	LLVHTFTPTN	TVDEYSCRVN	HSSLAAPHMV	KWDRDMN			
6mj2AB	NCYsGFHPp	QIEIDLKNG	EKM-NAEQSD	LSFSKdWsfY	LLVHTFTPTN	EKDEYACRVN	HVTLSPKPKIV	KWDRDMN			
1biiAB	NCYsGFHPp	QIEIDLKNG	EKM-NAEQSD	LSFSKdWsfY	LLVHTFTPTN	ETDTYACRVN	HDSMAEPKTV	KWDRDMN			
3hlaAB	NCYsGFHPp	QIEIDLKNG	EKM-NAEQSD	LSFSKdWsfY	LLVHTFTPTN	EKDEYACRVN	HVTLSPKPKIV	KWDRDMN			
3rwiAB	NCYsGFHPp	QIEIDLKNG	EKM-NAEQSD	LSFSKdWsfY	LLVHTFTPTN	EKDEYACRVN	HVTLSPKPKIV	KWDRDMN			
5y91AB	NCYsGFHPp	QIEIDLKNG	EKM-NAEQSD	LSFSKdWsfY	LLVHTFTPTN	EKDEYACRVN	HVTLSPKPKIV	KWDRDMN			
6kyuAB	NCYsGFHPp	QIEIDLKNG	EKM-NAEQSD	LSFSKdWsfY	LLVHTFTPTN	EKDEYACRVN	HVTLSPKPKIV	KWDRDMN			
6lhhAB	NCYsGFHPp	QIEIDLKNG	EKM-NAEQSD	LSFSKdWsfY	LLVHTFTPTN	EKDEYACRVN	HVTLSPKPKIV	KWDRDMN			

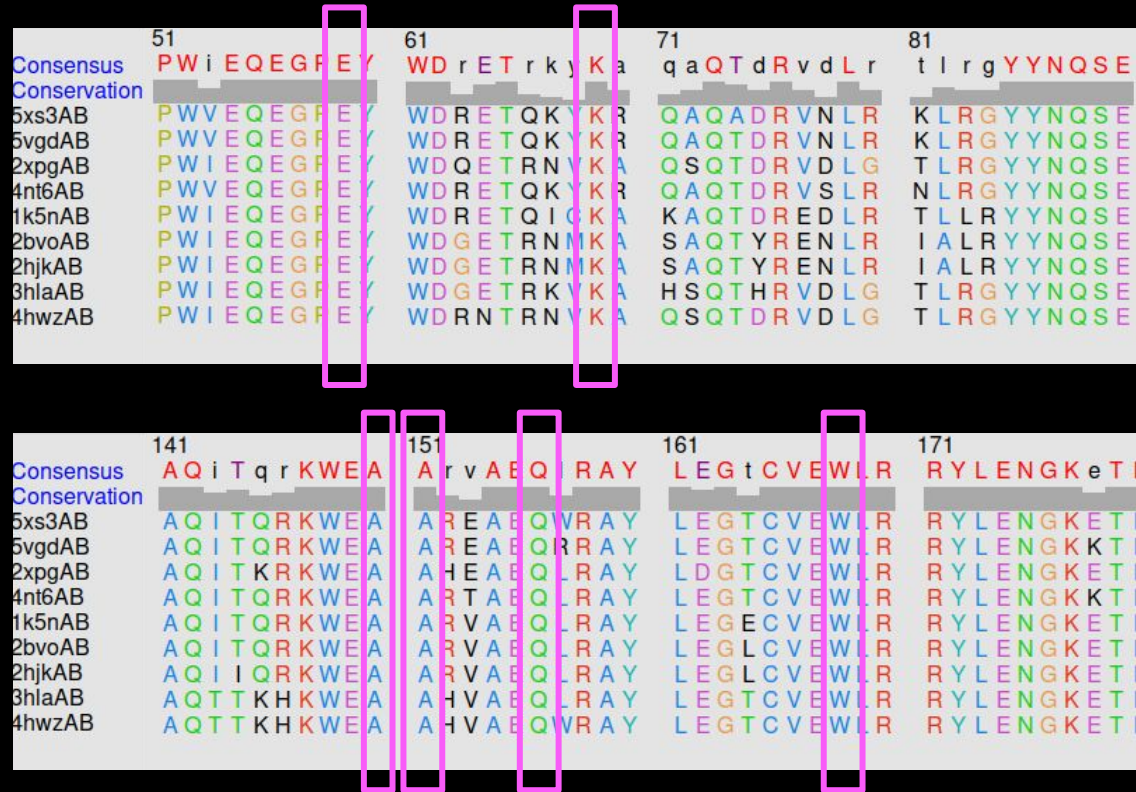
INTERACTIONS WITH OTHER MOLECULES

Interactions MHC I - Tcr



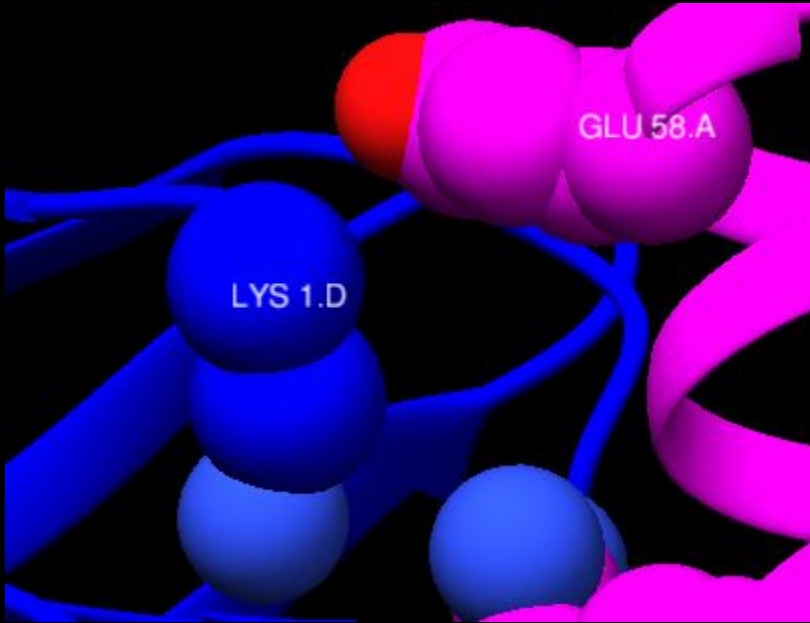
Magenta → MHC I
Blue → Tcr α
cyan → Tcr β
Yellow → Beta 2
microglobulin
Green → TAX
peptide

Interactions MHC I - Tcr: Structural alignment



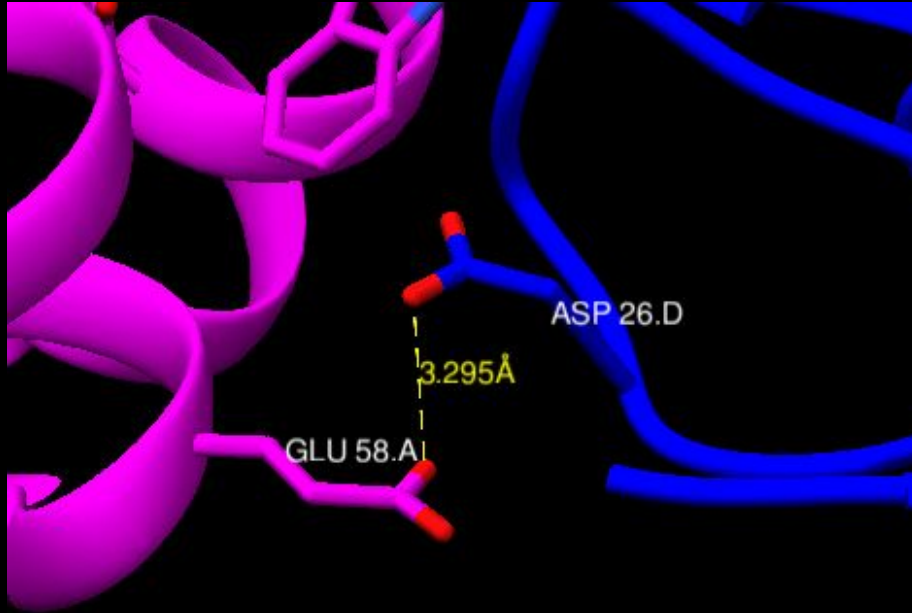
Structural alignment made with Stamp and visualized with Chimera

MHC I - Tcr (CDR1 α)



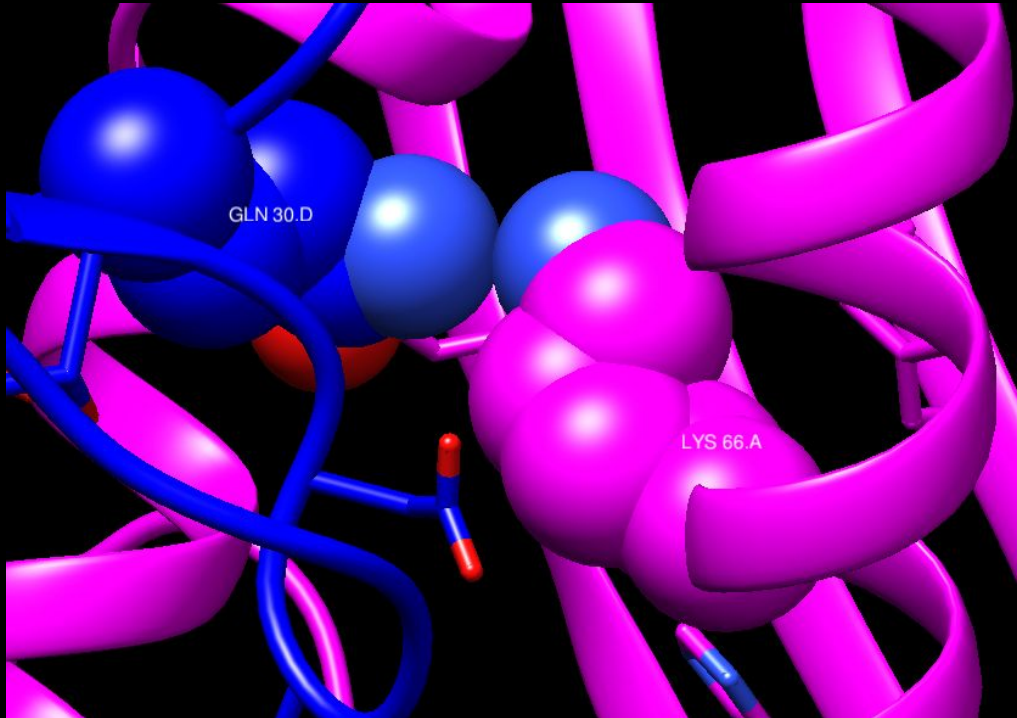
MHC I		Tcr (CDR1 α)	
Residue	Atom	Residue	Atom
Glu58	OE2	Lys1	N

MHC I - Tcr (CDR1 α)



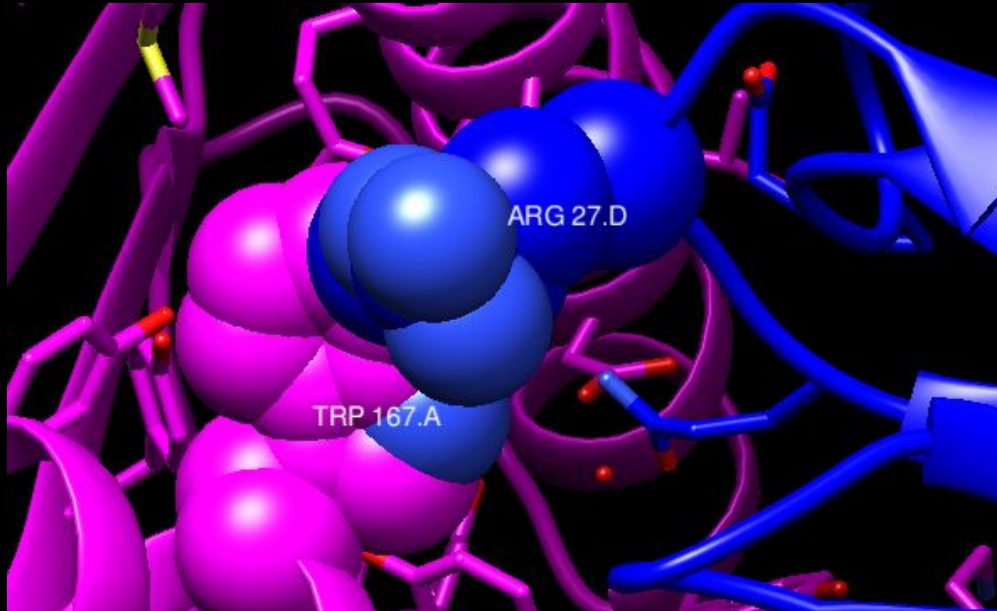
MHC I		Tcr (CDR1 α)		Hydrogen Bond
Residue	Atom	Residue	Atom	Length (Å)
Glu58	OE1	Asp26	OD2	3,295

MHC I - Tcr (CDR1 α)



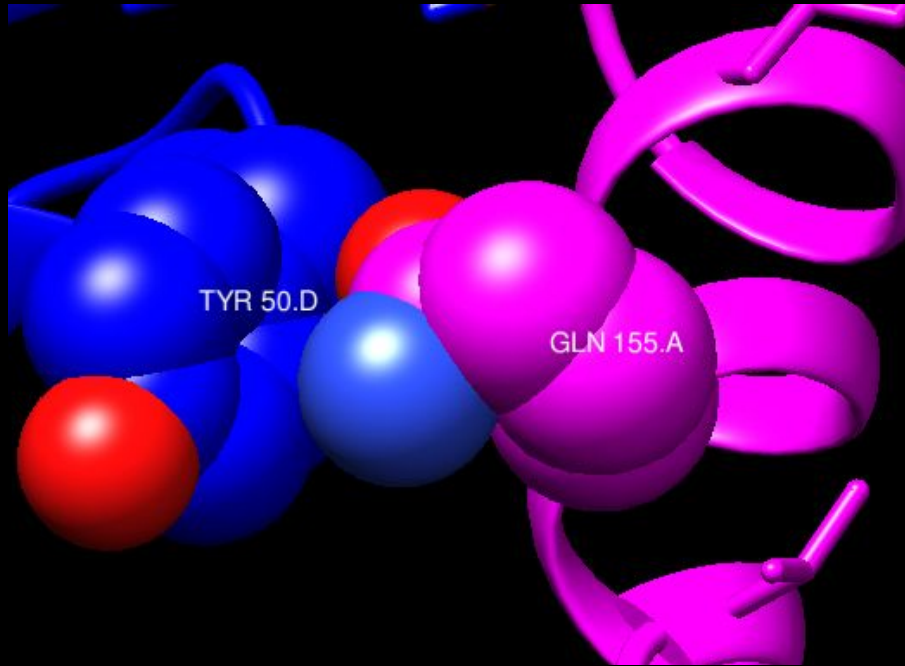
MHC I		Tcr (CDR1 α)	
Residue	Atom	Residue	Atom
Lys66	NZ	Gly30	NE2

MHC I - Tcr (CDR1 α)



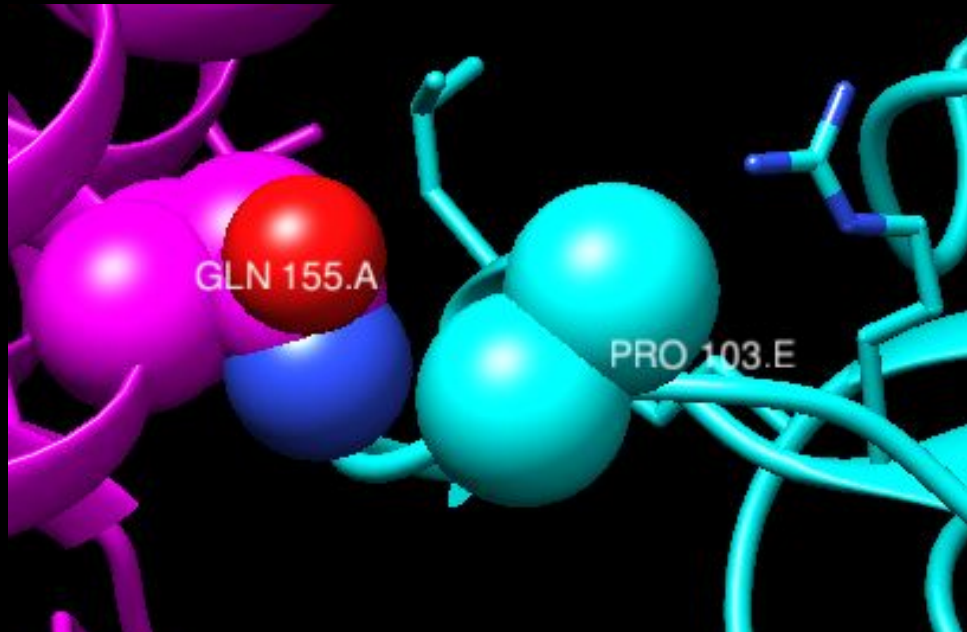
MHC I		Tcr (CDR1 α)	
Residue	Atom	Residue	Atom
Trp167	CZ2	Arg27	CG

MHC I - Tcr (CDR2 α)



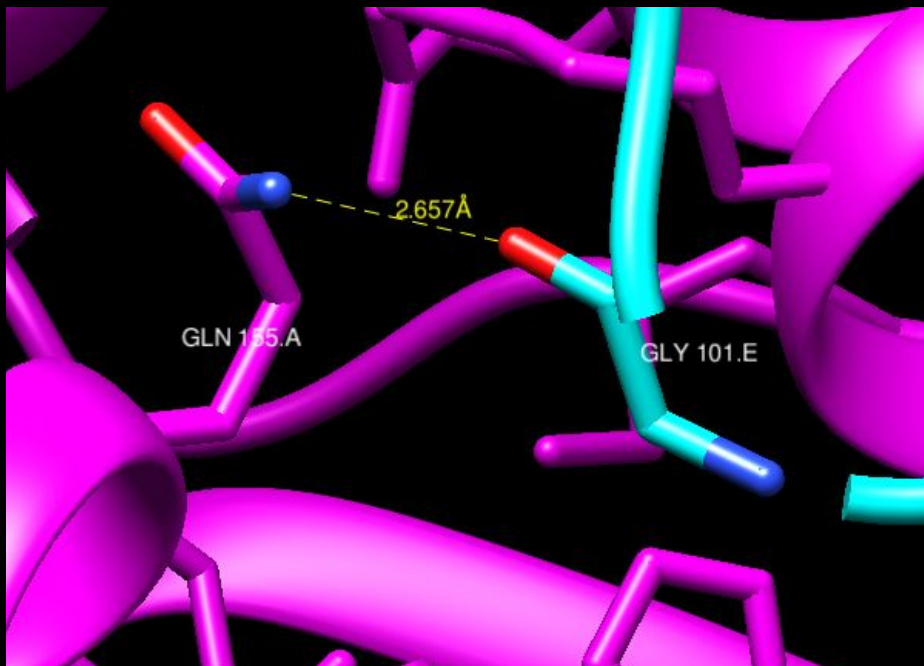
MHC I		Tcr (CDR2 α)	
Residue	Atom	Residue	Atom
Gln155	OE1	Tyr50	CG

MHC I - Tcr (CDR3 β)



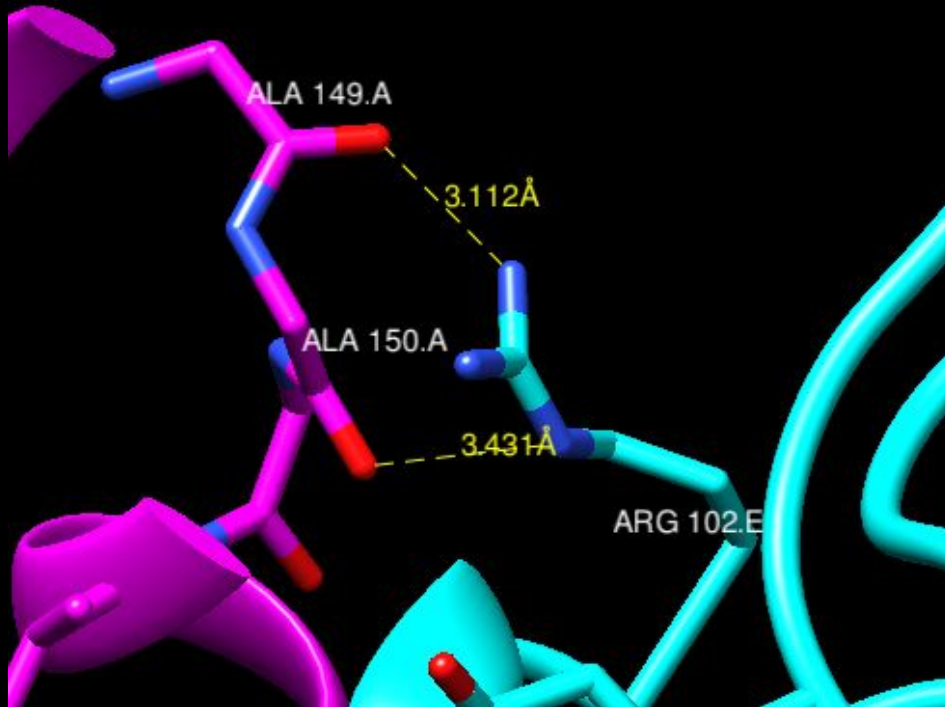
MHC I		Tcr (CDR3 β)	
Residue	Atom	Residue	Atom
Gln155	NE2	Pro103	CD

MHC I - Tcr (CDR3 β)



MHC I		Tcr (CDR3 β)		Hydrogen Bond
Residue	Atom	Residue	Atom	Length (Å)
Gln155	NE2	Gly101	O	2,657

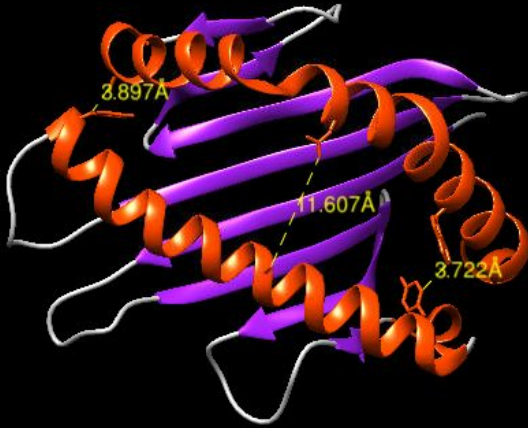
MHC I - Tcr (CDR3 β)



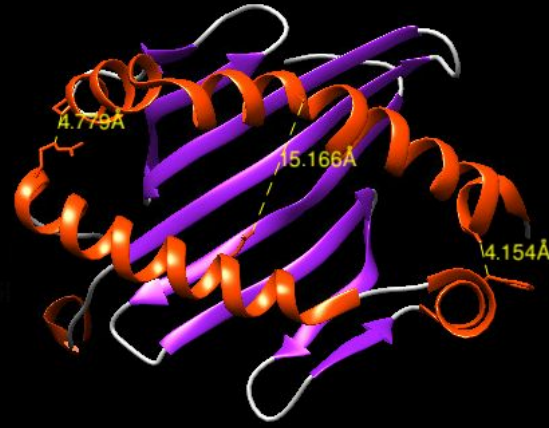
MHC I		Tcr (CDR3 β)		Hydrogen Bond
Residue	Atom	Residue	Atom	Length (Å)
Ala149	O	Arg102	NH1	3,112
Ala150	O	Arg102	NE	3,431

POCKETS

POCKETS: MHC I - MHC II comparison



HLA I



HLA II

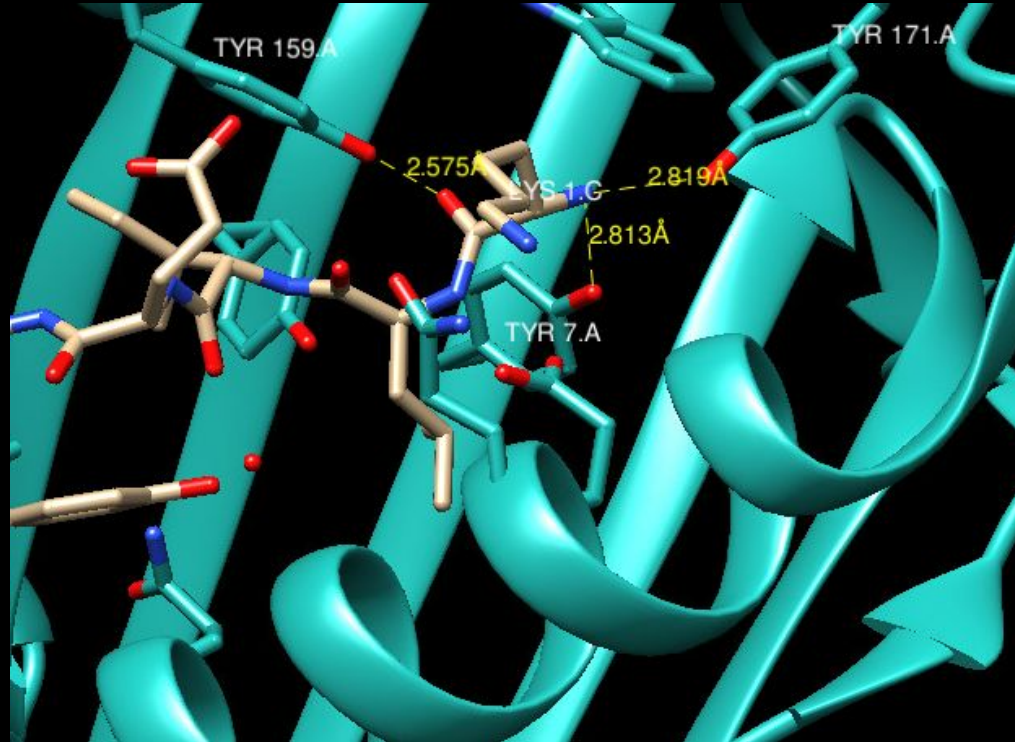
POCKETS: MHC I - MHC II comparison

	MHC I	MHC II
Binding domains	$\alpha 1$ and $\alpha 2$ domains form two α helices topping a sheet of 8 β strands.	Binding domain formed by $\alpha 1$ and $\beta 1$. Each chain provides 4 β strands and an α helix
Binding cleft ends	Closed at the N and C terminal ends due to the presence of aromatic residues blocking both end.	Both ends are open-ended.
Peptide size	Restricted to an optimal length of 8-11 residues	12-25 residues
Anchoring residues	Mainly located in the ends of the groove	More random distribution
Number of pockets	6	9

MHC I POCKETS: Types

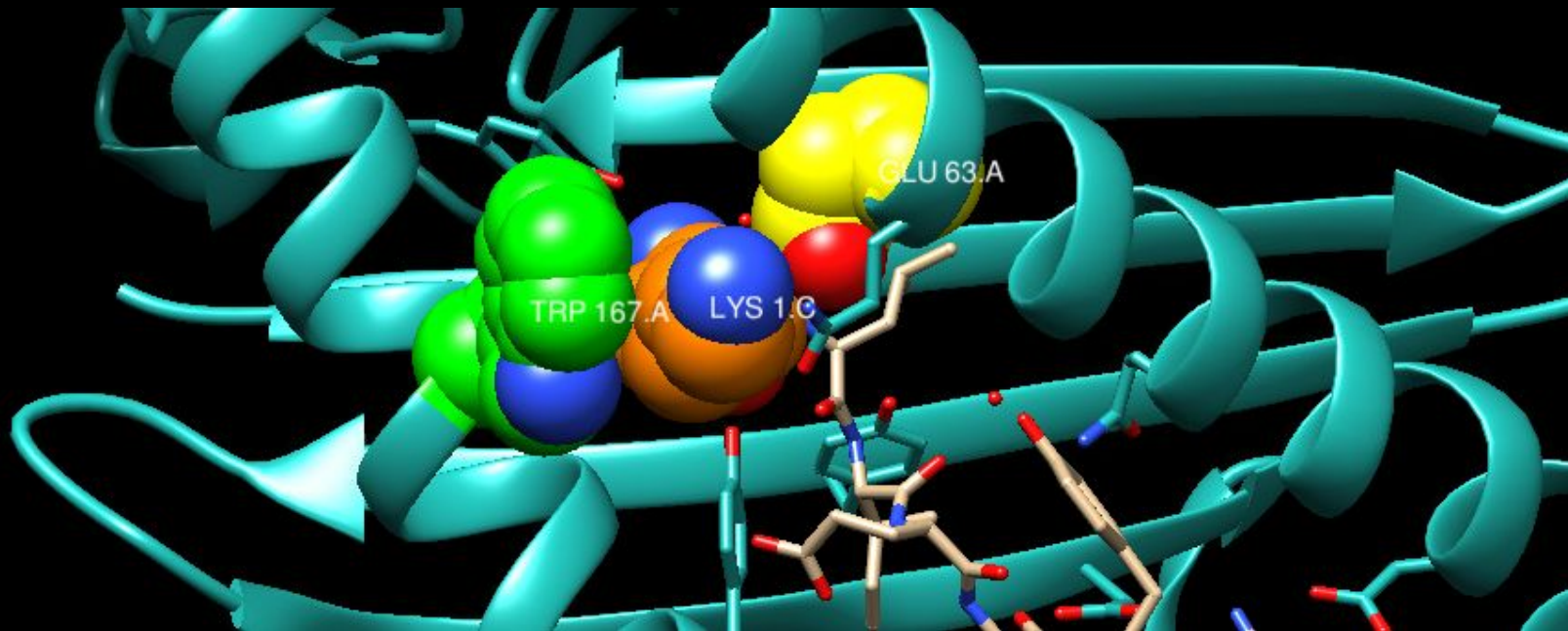
Pocket A	Pocket B	Pocket C
5, 7, 59, 63, 66, 159, 163, 167, 171	7, 9, 24, 34, 45, 63, 66, 67, 70, 99	9, 70, 73, 74, 97
- Anchors the N - terminal group of the peptide, P1 residue. - Closure of the end of the cleft with the formation of a “wall”. Binds shorter peptides	- Binds to position 2 (P2) of the peptide. - Main pocket of peptide anchoring	-Bind residues at P3 and/or P5/6 depending on the peptide. -Against the $\alpha 1$ helix facing pocket D
Pocket D	Pocket E	Pocket F
99, 114, 155, 156, 159, 160	97, 114, 147, 152, 156	77, 80, 81, 84, 95, 123, 143, 146, 147
-Bind residues at P3 and/or P5/6 depending on the peptide. -Against the $\alpha 2$ helix facing pocket D	-Mainly hydrophobic pocket	- Binds primary PΩ residues - Closes the cleft in the C-terminal part

POCKET A



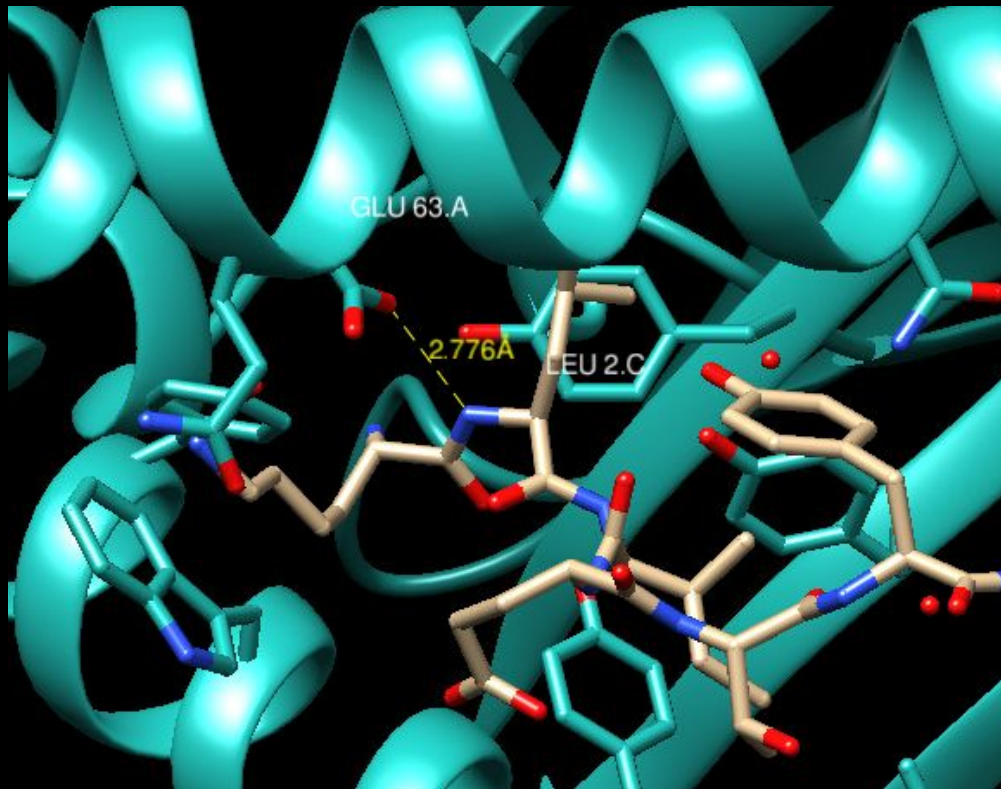
Peptide		MHC		Hydrogen Bond
Residue	Atom	Residue	Atom	Length (Å)
Lys (P1)	O	Tyr159	OH	2,575
	N	Tyr171	OH	2,819
	N	Tyr7	OH	2,813

POCKET A



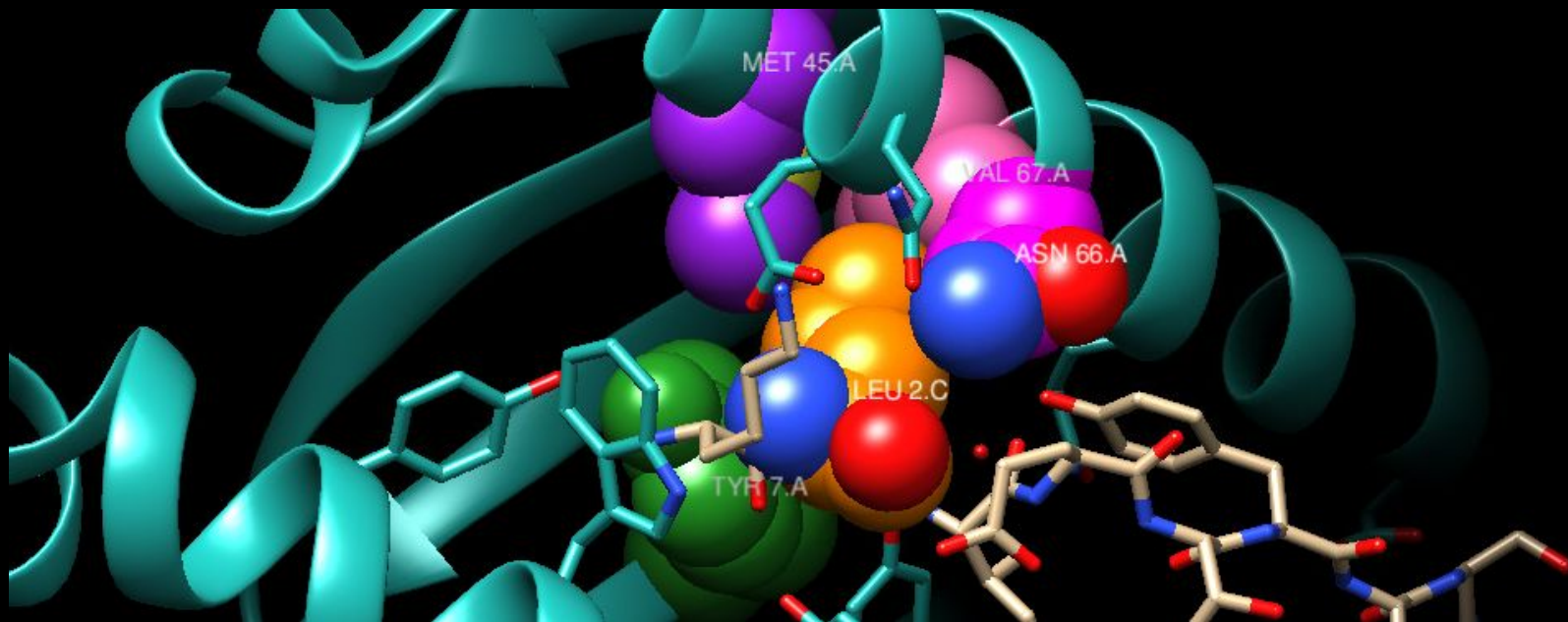
Lys (P1)	
Glu63	Trp167

POCKET B



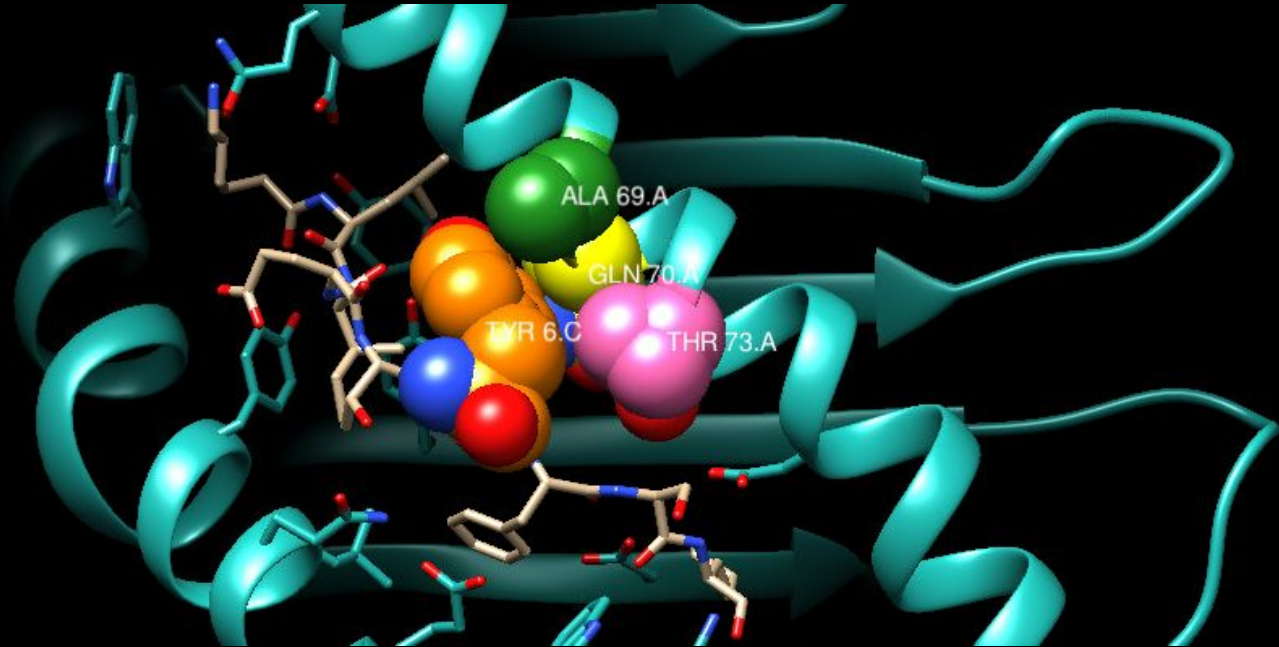
Peptide		MHC		Hydrogen Bond
Residue	Atom	Residue	Atom	Length (Å)
Leu (P2)	N	Glu63	OE1	2,776

POCKET B



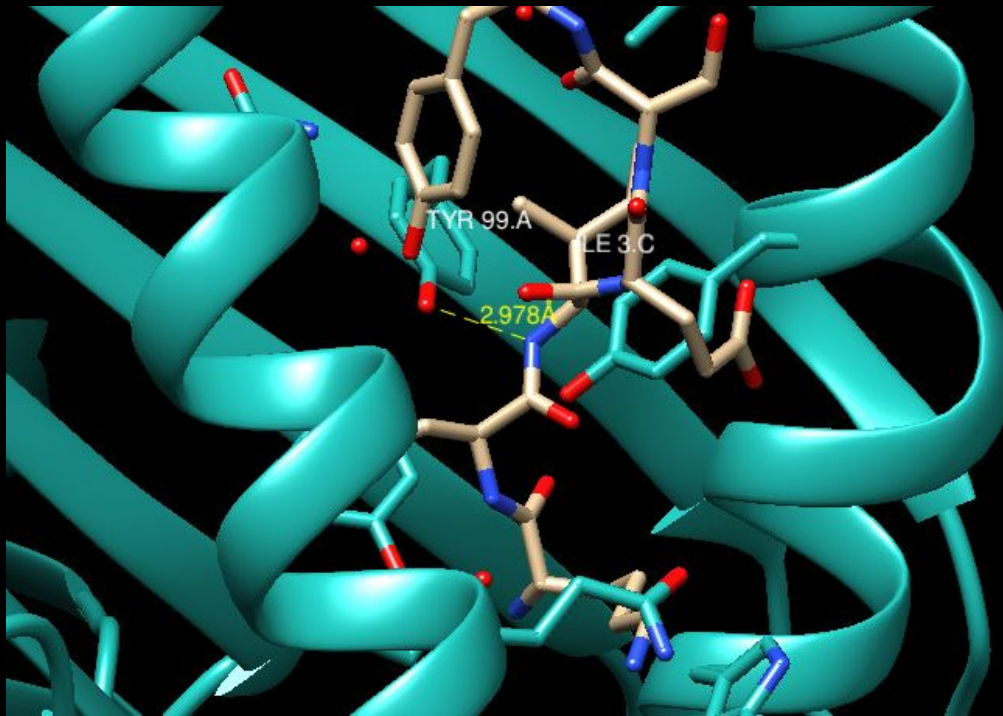
Leu (P2)			
Tyr7	Met45	Asn66	Val67

POCKET C



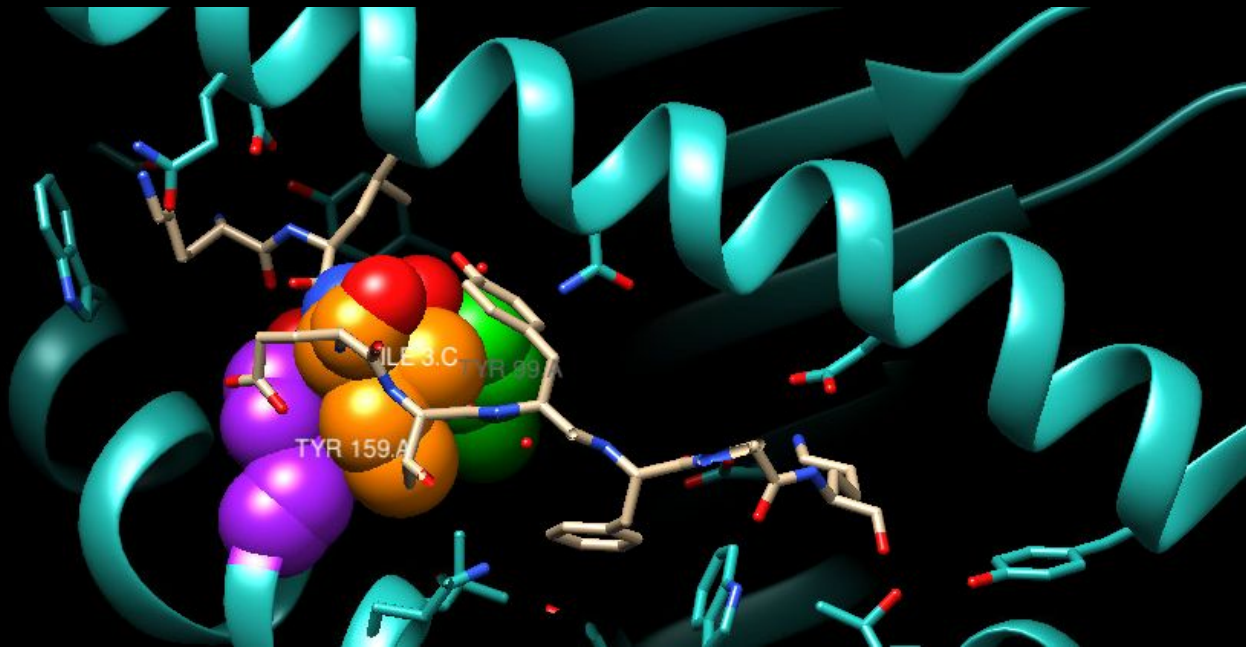
Tyr (P6)		
Ala69	Thr73	Gln70

POCKET D



Peptide		MHC		Hydrogen Bond
Residue	Atom	Residue	Atom	Length (Å)
Ile (P3)	N	Tyr99	OH	2,978

POCKET D

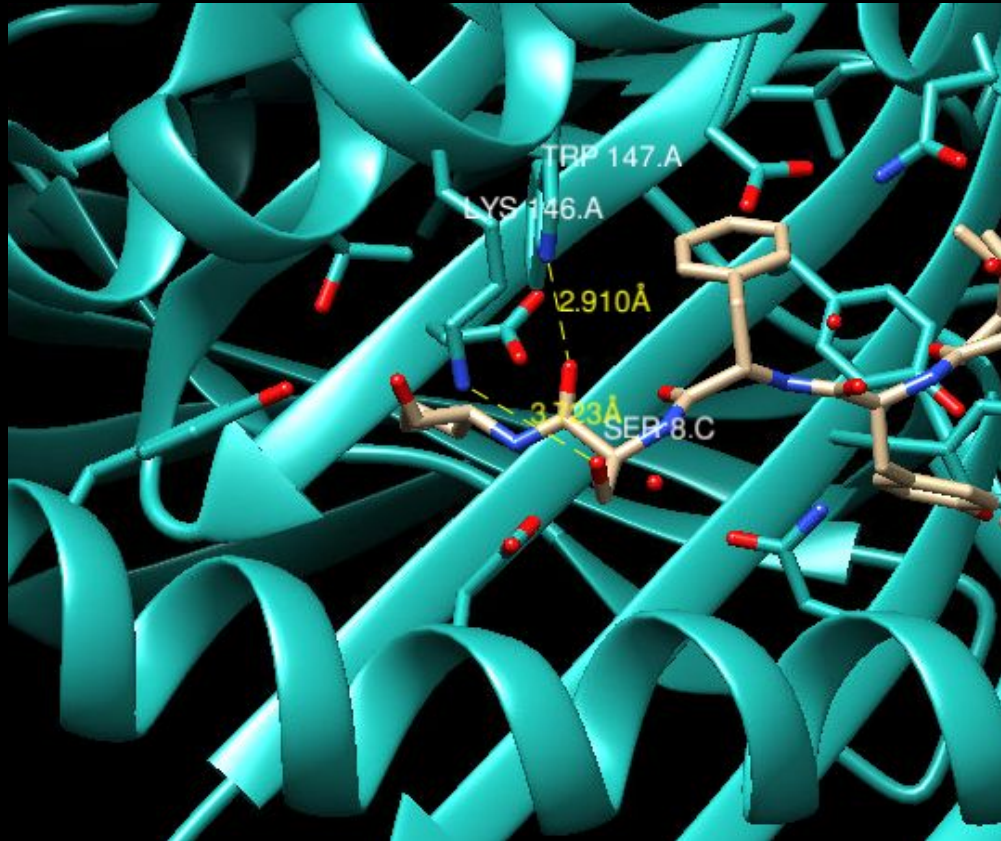


Ile (P3)

Tyr99

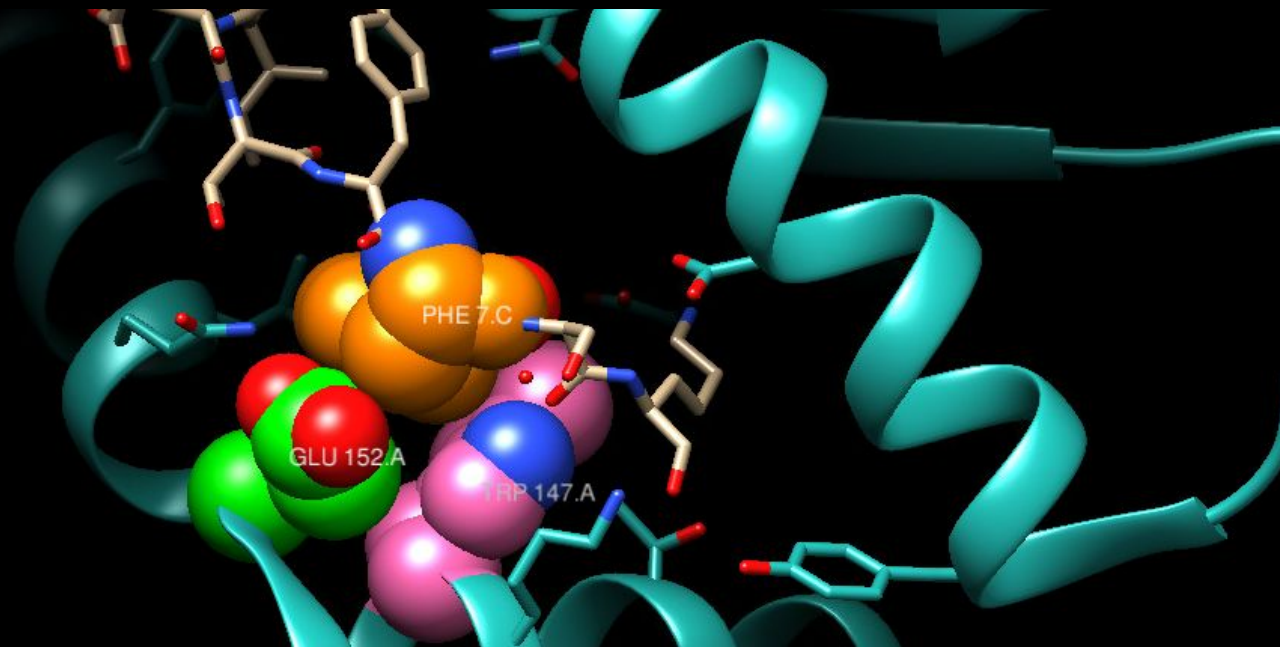
Tyr159

POCKET E



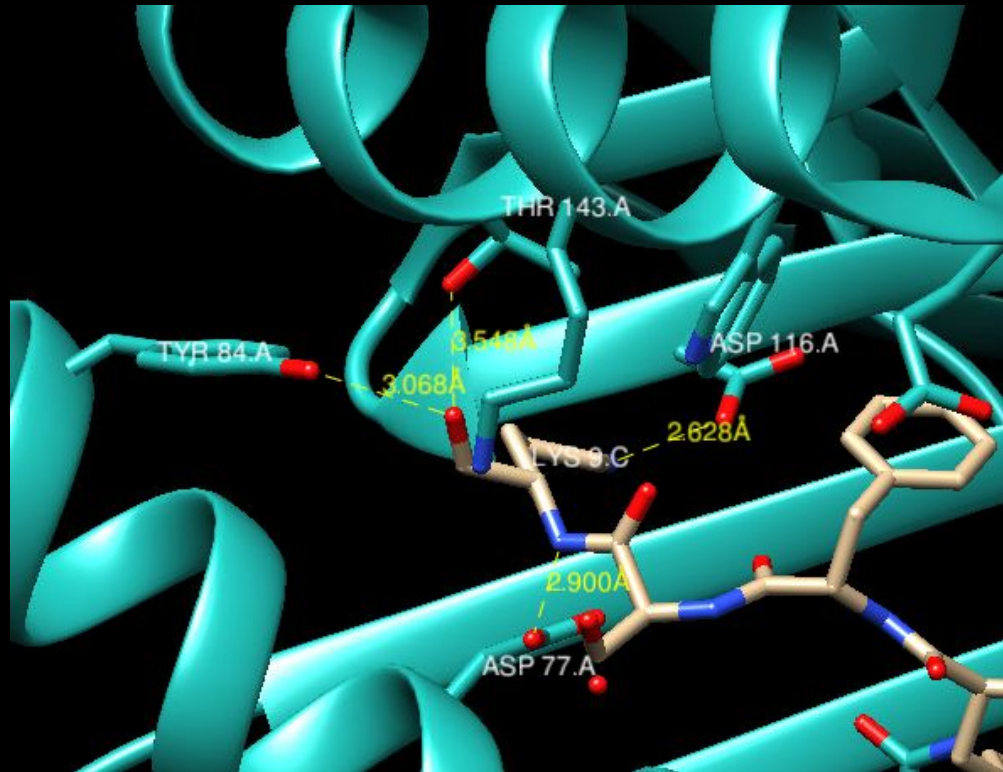
Peptide		MHC		Hydrogen Bond
Residue	Atom	Residue	Atom	Length (Å)
Ser (P8)	O	Trp147	NE1	2,910
	OG	Lys146	NZ	3,723

POCKET E



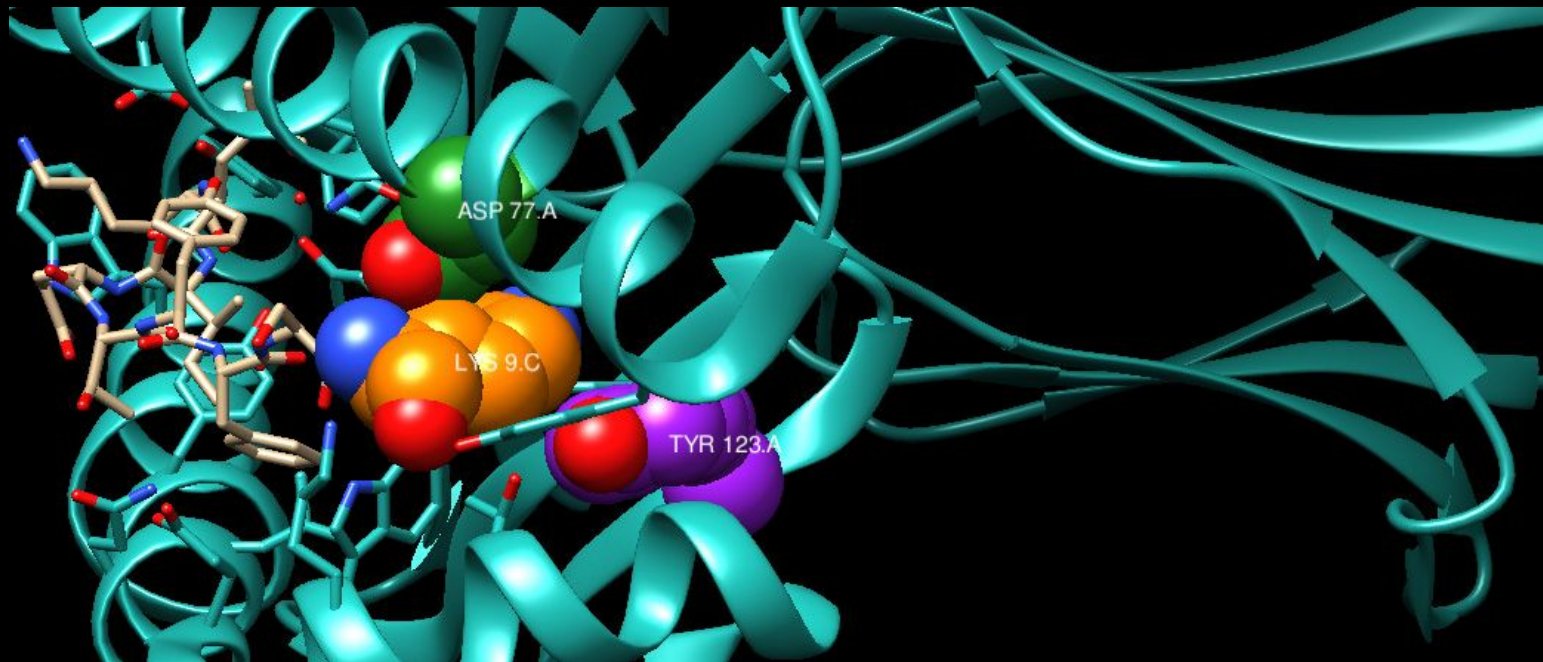
Phe (P7)	
Trp147	Glu152

POCKET F



Peptide		MHC		Hydrogen Bond
Residue	Atom	Residue	Atom	Length (Å)
Lys (P9)	O	Tyr84	OH	3,068
	O	Thr143	OG1	3,548
	N	Asp77	OD1	2,900
	NZ	Asp116	OD2	2,628

POCKET F



Lys (P9)		
Asp77	Tyr123	Tyr147

Conclusions

MHC: cell-surface proteins that present peptides to T-cell receptors

Conservation

Sequence, structural and functional conservation between:

Classical HLA-I

Classical HLA-II

Different species

Mammals > birds > fish

Polymorphism

Specially found in the regions that belong to the binding groove

Wide variety of peptides to bind

Higher protection from the immune system

PEM questions

- Which of the following domains does NOT participate in the formation of any disulfide bond in MHC I?
 - a. $\alpha 1$ domain in chain A
 - b. $\alpha 2$ domain in chain A
 - c. $\alpha 3$ domain in chain A
 - d. $\beta 2$ -microglobulin
 - e. None of the above

- Regarding, the binding groove in MHC I, choose the CORRECT answer
 - a. It is composed of 9 pockets
 - b. The anchoring residues are situated in the ends of the groove
 - c. Both a and b are correct
 - d. The binding cleft is open in one end and closed in the other
 - e. The optimal peptide length that it can bind is less than 7 residues

- Choose the correct answer related to the MHC-II classification
 - a. Classical MHC-II: HLA-DO and HLA-DM. Non classical MHC-II: HLA-DP, HLA-DQ and HLA-DR
 - b. Classical MHC-II: HLA-DP, HLA-DM and HLA-DQ. Non classical MHC-II: HLA-DO and HLA-DR
 - c. Classical MHC-II: HLA-DP and HLA-DR. Non classical MHC-II: HLA-DO, HLA-DQ and HLA-DM
 - d. Classical MHC-II: HLA-DQ and HLA-DP. Non classical MHC-II: HLA-DO, HLA-DR and HLA-DM
 - e. Classical MHC-II: HLA-DP, HLA-DQ and HLA-DR. Non classical MHC-II: HLA-DO and HLA-DM

- Which are the two most important pockets in the anchoring of the peptide in MHC-I?
 - a. Pockets A and C
 - b. Pockets B and E
 - c. Pockets B and F
 - d. Pockets A and F
 - e. Pockets D and E

PEM questions

- Regarding the SCOP classification of the MHC, to which class of the mentioned below does the MHC belong to?
 - a. All alpha proteins
 - b. All beta proteins
 - c. Alpha and beta proteins (a/b)
 - d. Alpha and beta proteins (a+b)
 - e. None of the above

- Which of the following domains participate in the formation of the binding groove in MHC II?
 - a. $\alpha 1$ and $\alpha 2$
 - b. $\alpha 2$ and $\beta 2$ -microglobulin
 - c. $\alpha 2$ and $\beta 2$
 - d. $\alpha 1$ and $\beta 1$
 - e. $\alpha 1$ and $\beta 2$

- Which of the following statements regarding the MHC is/are TRUE?
 - a. The MHC I is composed exclusively by a α -chain
 - b. The MHC II is composed by a α -chain and the domain of the $\beta 2$ -microglobulin
 - c. Both a and b are true
 - d. There are three classes of MHC, all of which are found on chromosome 6 in humans
 - e. All of them are true

- Which of the following statements regarding the MHC is/ are TRUE?
 - a. There are only two types of MHC molecules: MHC I and MHC II.
 - b. Both MHC I and MHC II can be found on nucleated cell types.
 - c. Both A and b are true.
 - d. MHC I binds TCD8+ cells and MHC II binds TCD4+ cells.
 - e. All of them are true.

PEM questions

- Regarding the MHC homology between species, choose the correct answer
 - a. Not all vertebrates have MHC.
 - b. *The more similar sequences to Homo sapiens are the ones that come from mammals.*
 - c. Both a and b are true.
 - d. The more similar sequences to Homo sapiens are the ones that come from birds.
 - e. All of them are true.

- From the following associations, choose the correct one:
 - a. MHC I - peptide size of 12-25 aa
 - b. MHC II - peptide size of 8-1 aa
 - c. Both a and b are true
 - d. *MHC I - mostly expressed in nucleated cell types*
 - e. MHC I - MHC II

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9. Wu Y, Zhang N, Hashimoto K, et al. Structural Comparison Between MHC Classes I and II; in Evolution, a Class-II-Like Molecule Probably Came First. *Front Immunol*. 2021;12:1–24.

The image features a black background with two large, intricate, and colorful abstract shapes on the left and right sides. These shapes are composed of many thin, flowing ribbons in shades of green, blue, purple, and yellow, creating a complex, organic, and somewhat chaotic appearance. In the center of the image, the text "THANK YOU FOR YOUR ATTENTION!" is written in a bold, white, serif font.

THANK YOU FOR YOUR ATTENTION!



MAJOR HISTOCOMPATIBILITY COMPLEX

Elaia Bercianos, Alba Carús and Claudia Gomariz