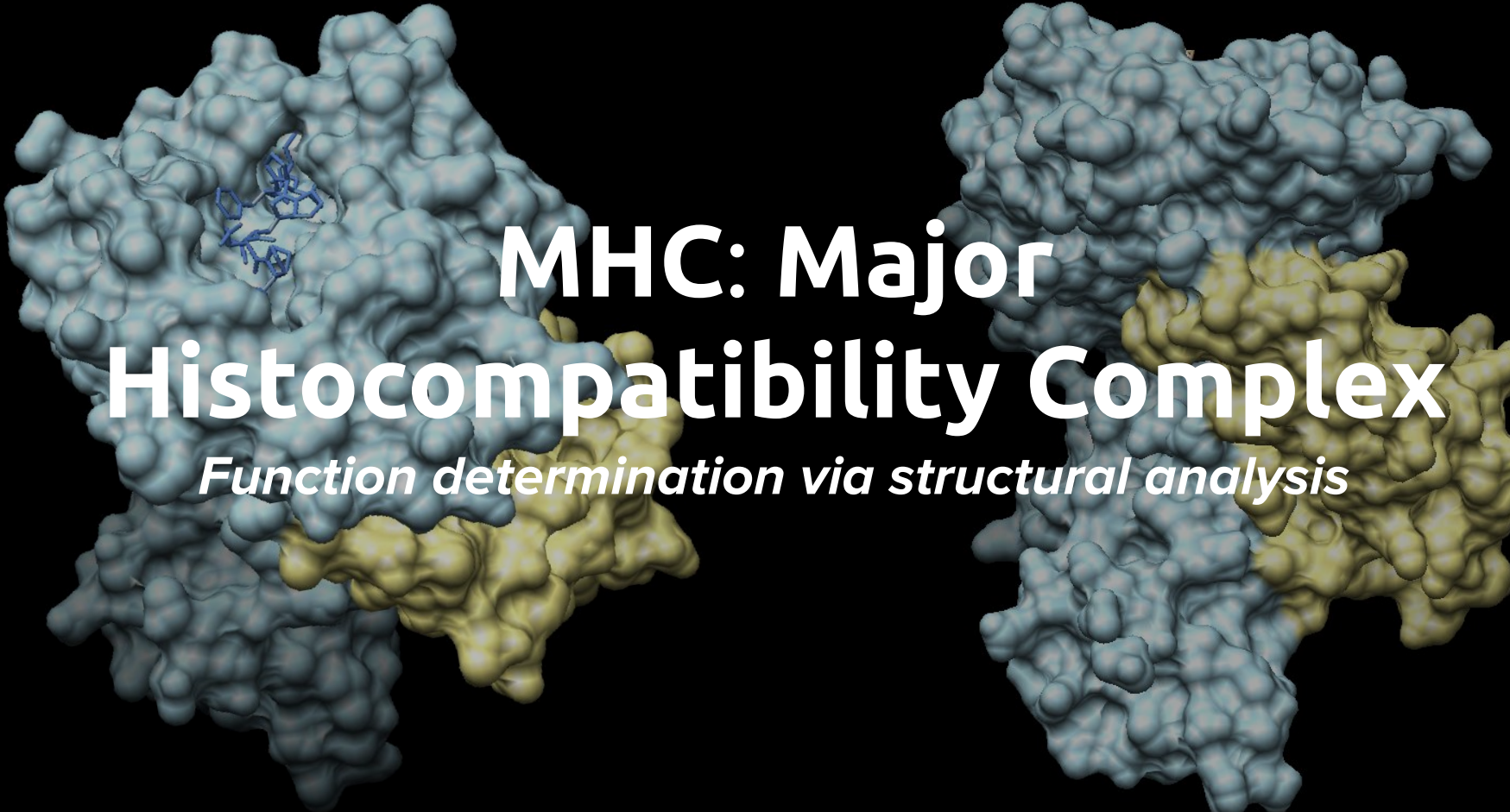


A 3D surface model of the Major Histocompatibility Complex (MHC) is shown against a black background. The complex is composed of several subunits, with some colored in light blue and others in yellow. A small, blue, stick-model structure representing an antigen is bound within the groove of one of the blue subunits. The text 'MHC: Major Histocompatibility Complex' is overlaid in large white font.

# MHC: Major Histocompatibility Complex

*Function determination via structural analysis*

Jana Rovira, Berta Sabariego, Martina Serrat i Laia Vila

# INDEX

## 1. INTRODUCTION

Description

Structure and function

## 2. EVOLUTION

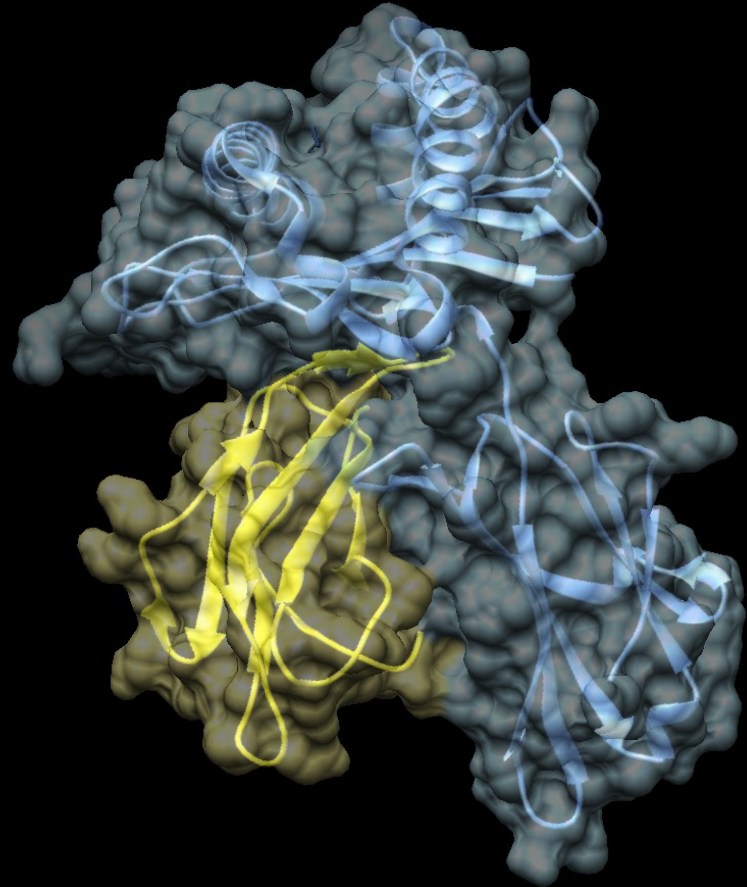
## 3. MHC CLASS I

- Inner interactions

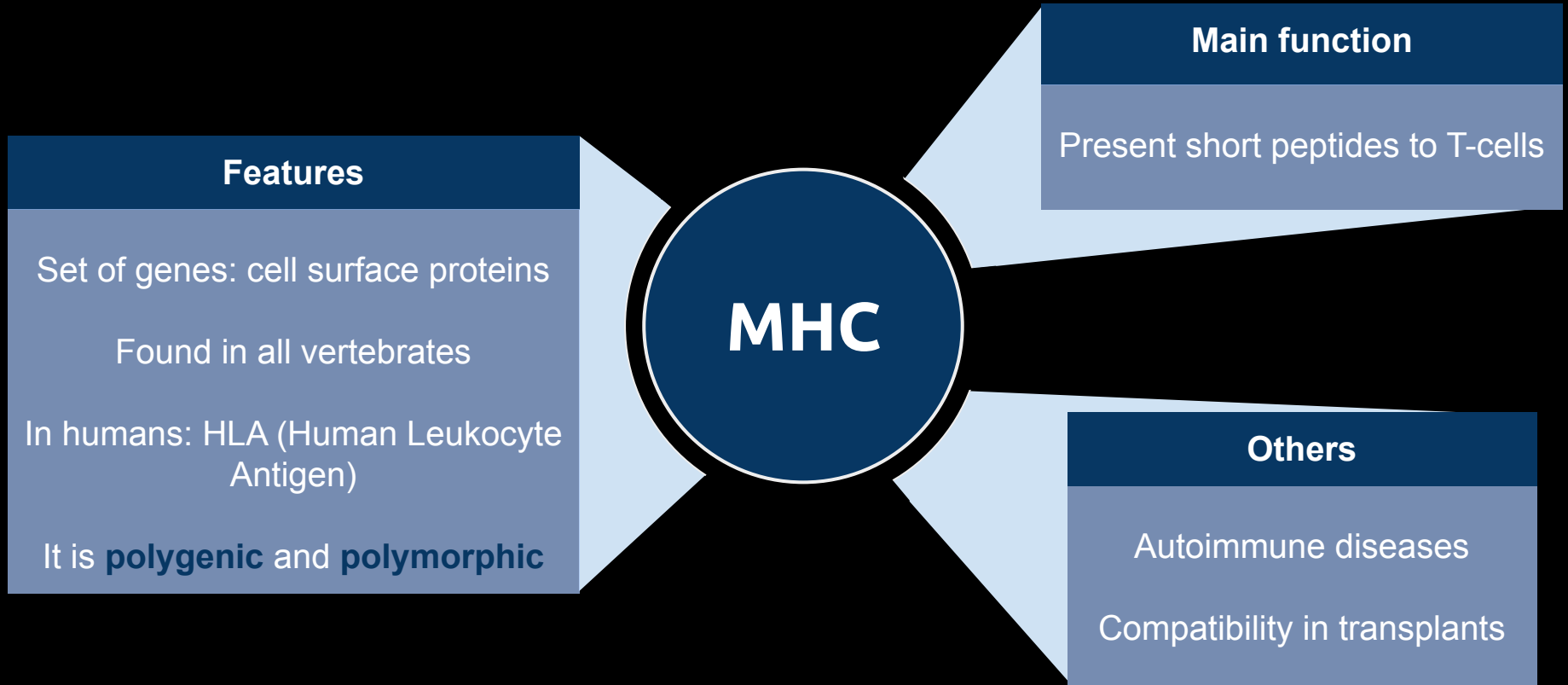
- Interactions with other structures

## 4. POCKETS

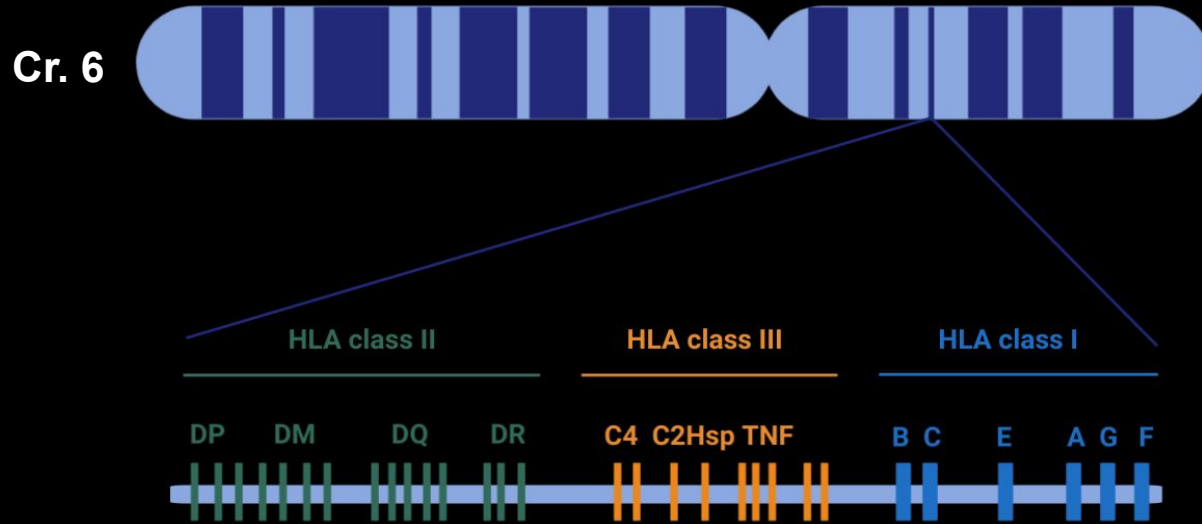
## 5. CONCLUSIONS



# 1. INTRODUCTION



# 1. INTRODUCTION



|               | Class I             | Class II               |
|---------------|---------------------|------------------------|
| Classical     | HLA-A, HLA-B, HLA-C | HLA-DP, HLA-DQ, HLA-DR |
| Non-classical | HLA-E, HLA-F, HLA-G | HLA-DO, HLA-DM         |

# 1. INTRODUCTION

## SCOP classification

**CLASS**

Alpha and beta

**FAMILY**

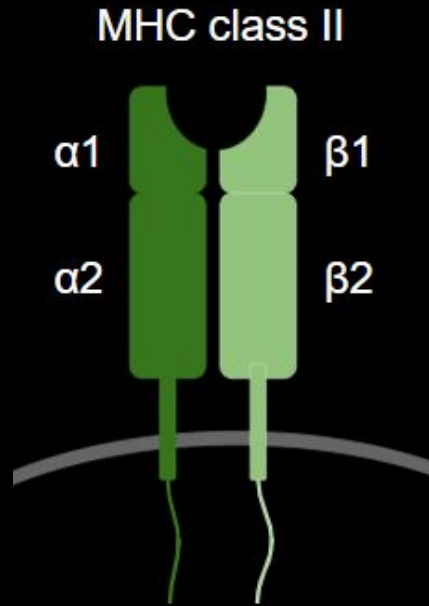
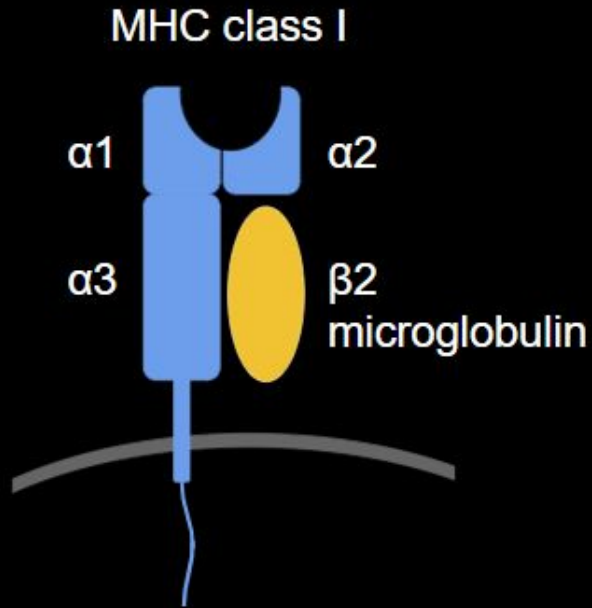
MHC antigen-recognition domain

**SUPERFAMILY**

MHC antigen-recognition domain

# 1. INTRODUCTION

## Structure and function MHC



Extracellular peptide binding site

Immunoglobulin like domain

Transmembrane segment

Cytoplasmic segment

# 1. INTRODUCTION

## Structure and function MHC



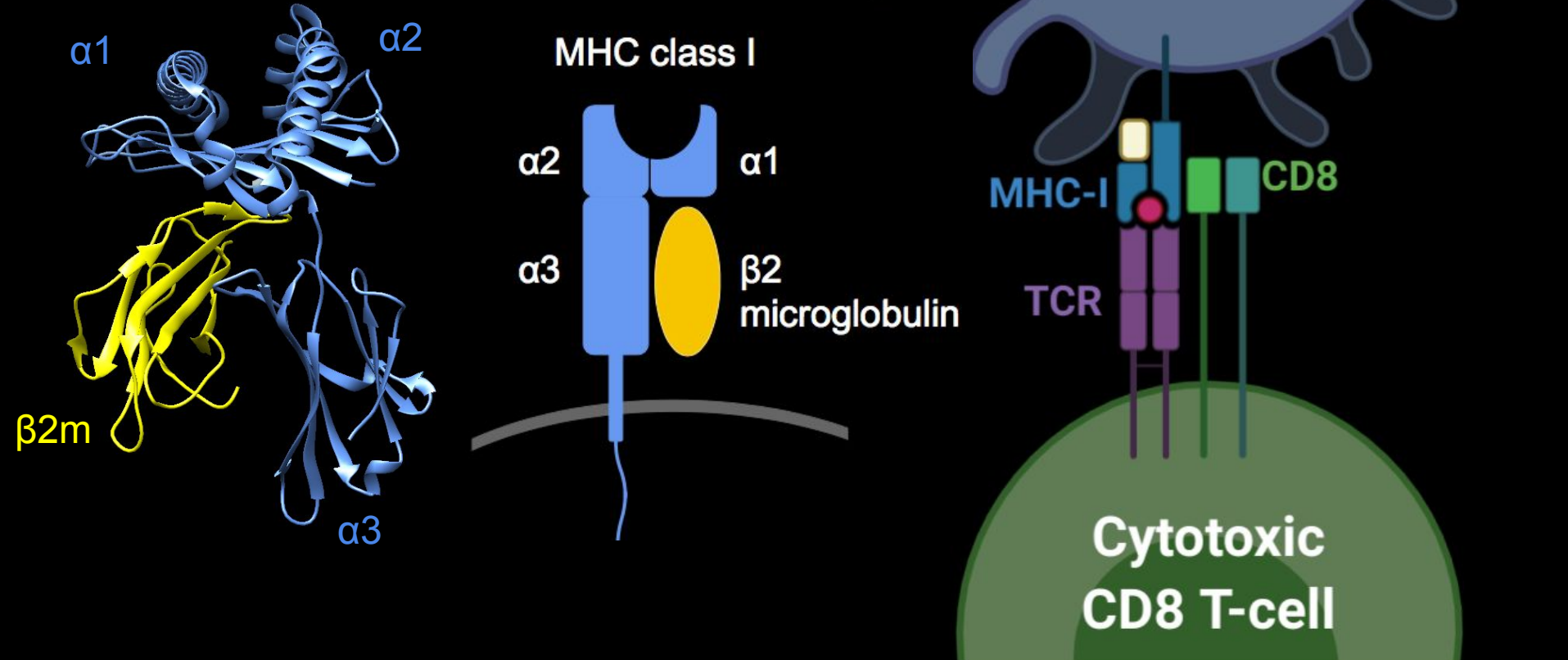
MHC class I



MHC class II

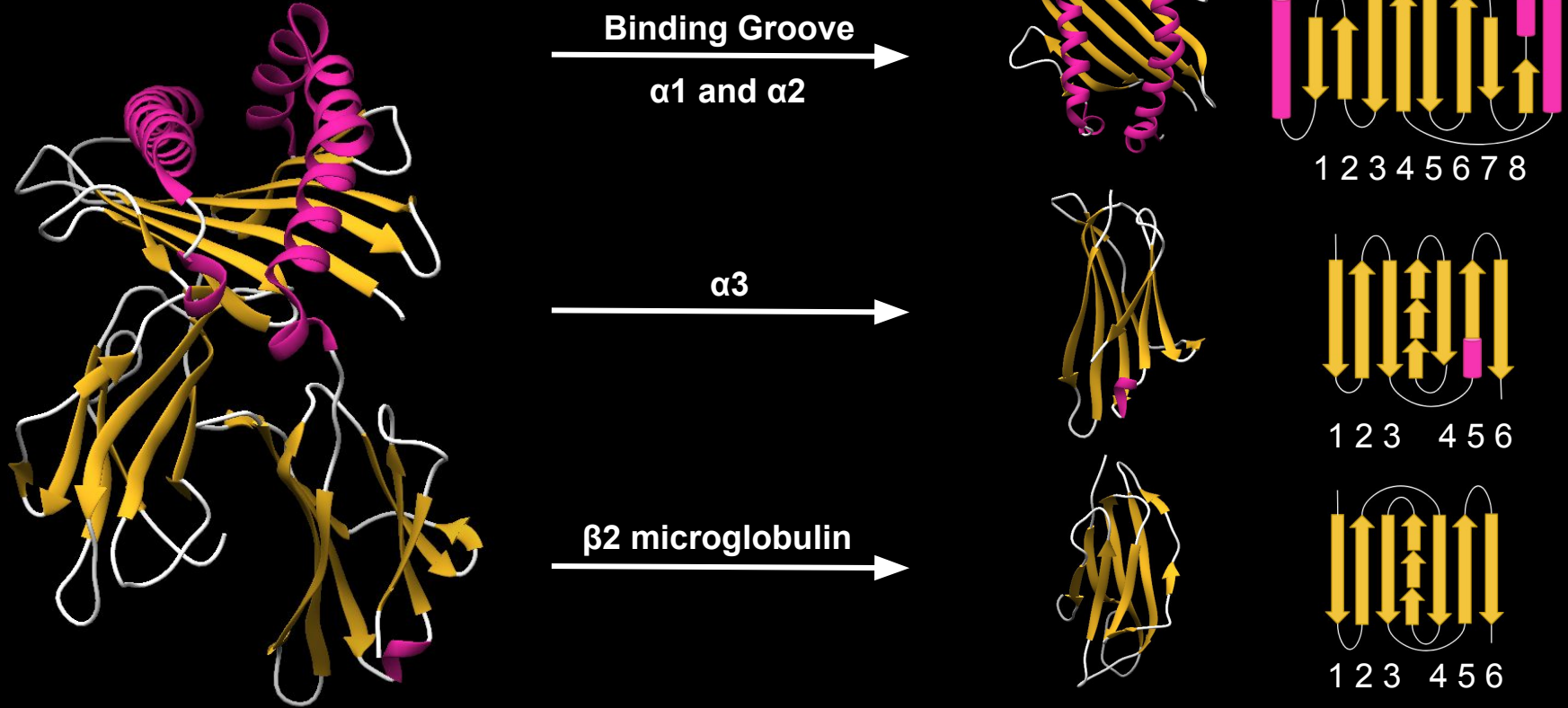
# 1. INTRODUCTION

## Structure and function MHC I



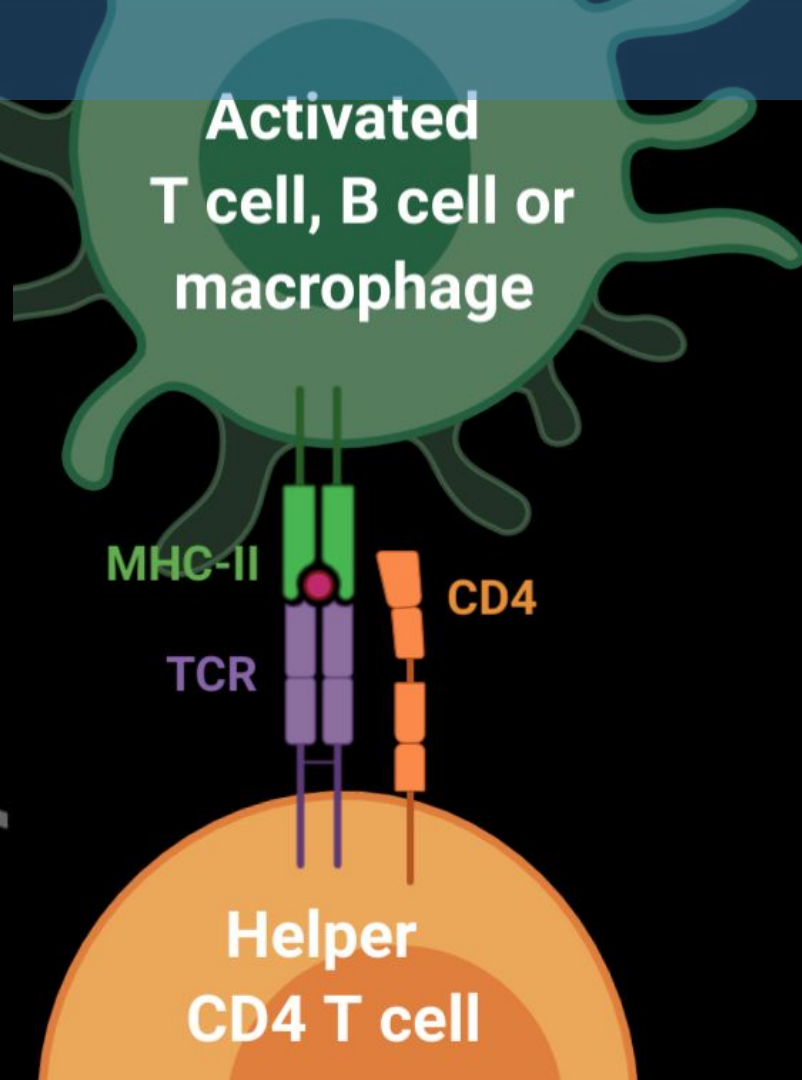
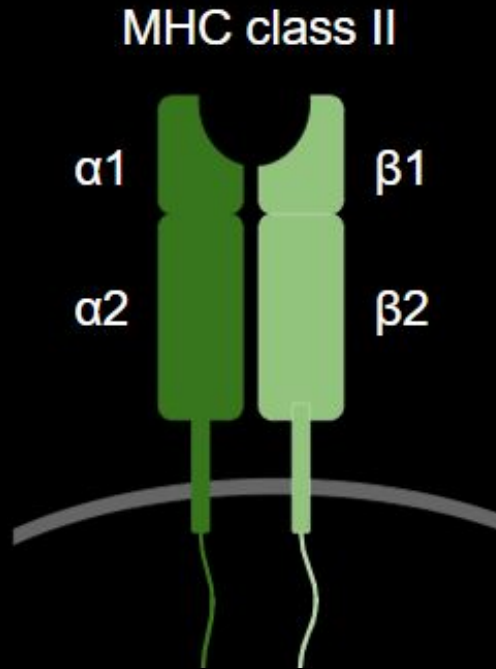
# 1. INTRODUCTION

## Structure and function MHC I



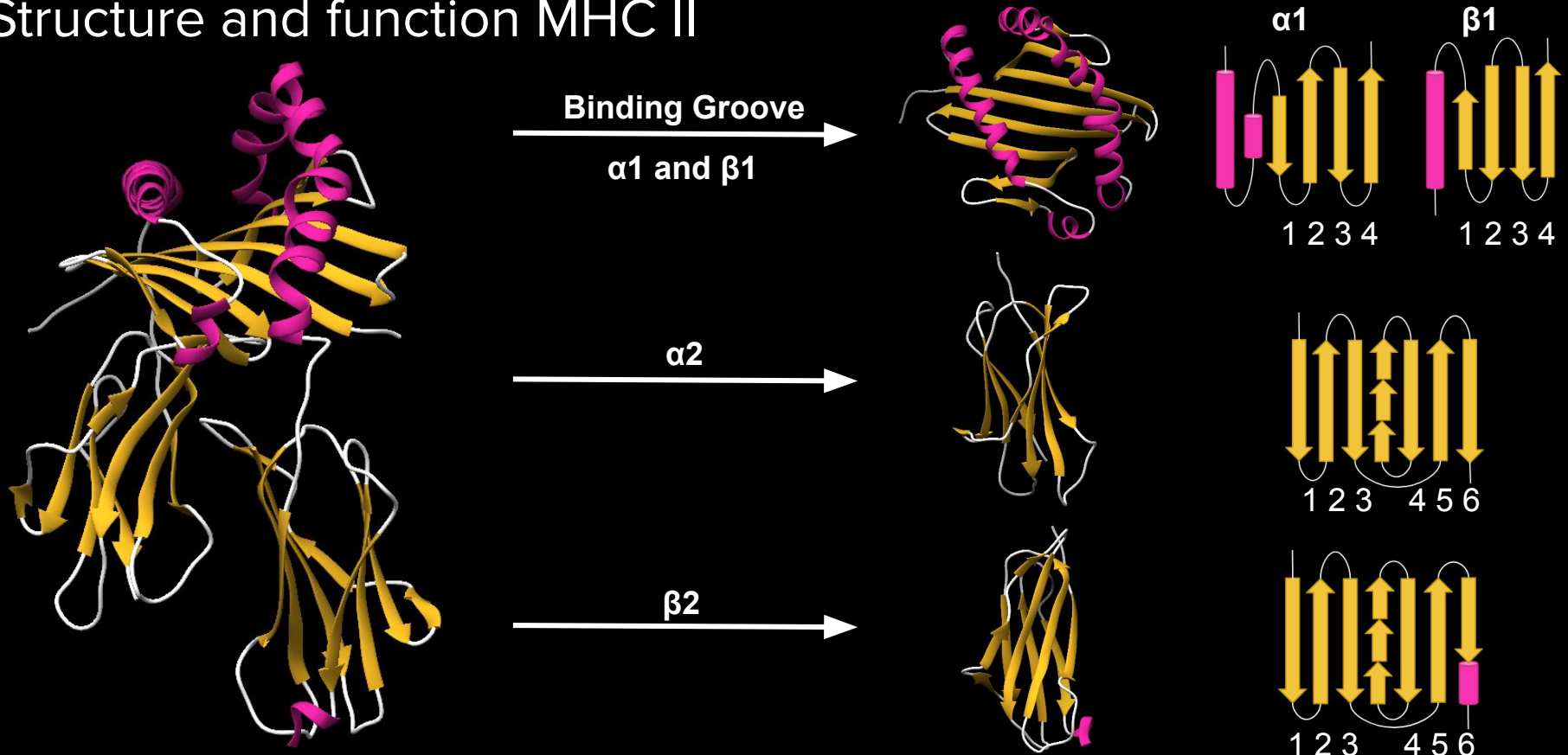
# 1. INTRODUCTION

## Structure and function MHC II



# 1. INTRODUCTION

## Structure and function MHC II



# 1. INTRODUCTION

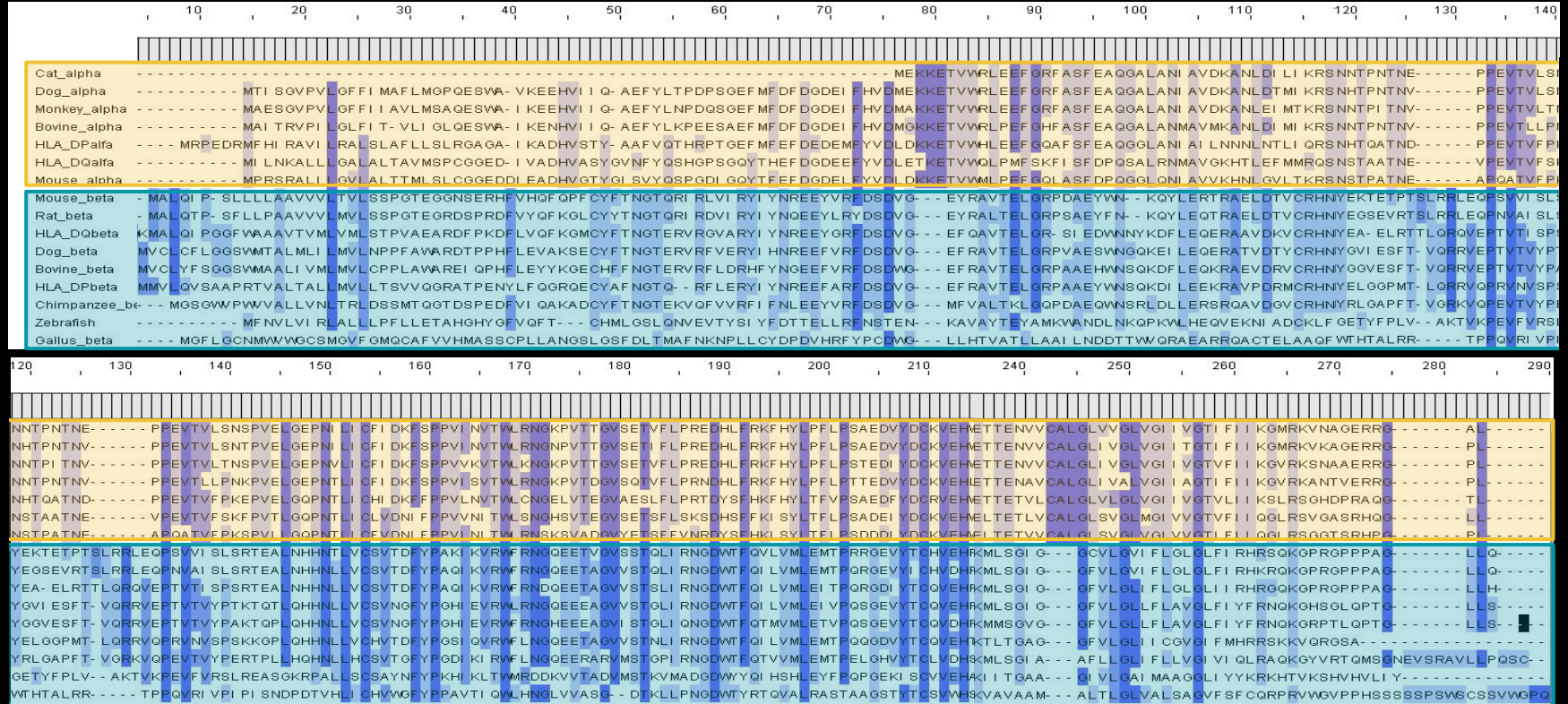
## MHC I vs MHC II

|                        | MHC I                                     | MHC II                                   |
|------------------------|-------------------------------------------|------------------------------------------|
| Chains                 | Alpha + Beta 2 microglobulin              | Alpha + Beta                             |
| Binding Groove domains | Alpha 1 + Alpha 2                         | Alpha 1 + Beta 1                         |
| Interactions           | CD8 - Alpha 3 and<br>TCR - Binding groove | CD4 - Beta 2 and<br>TCR - Binding Groove |
| Localization           | All nucleated cells                       | Antigen Presenting Cells (APCs)          |
| Peptide size           | 8-10 amino acids                          | 12-25 amino acids                        |

# **MODES OF EVOLUTION**

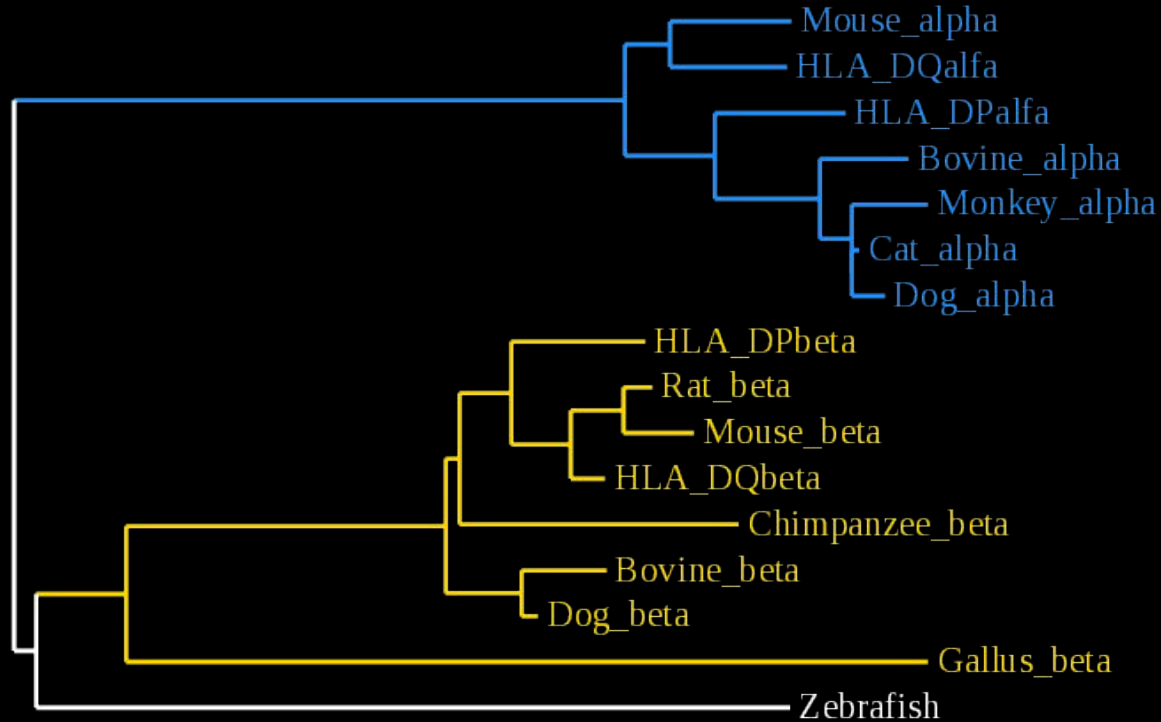
# 2. EVOLUTION: MHC II

## Sequence alignment



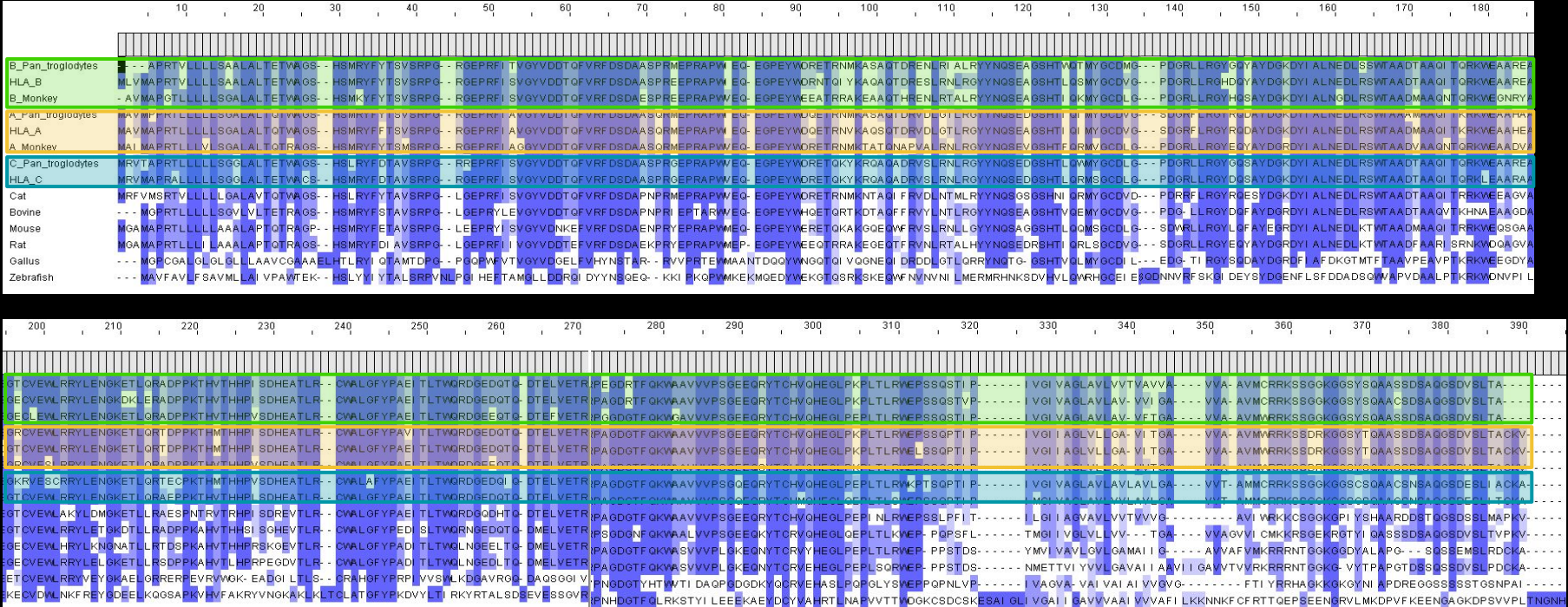
## 2. EVOLUTION: MHC II

### Phylogenetic tree



# 2. EVOLUTION: MHC I

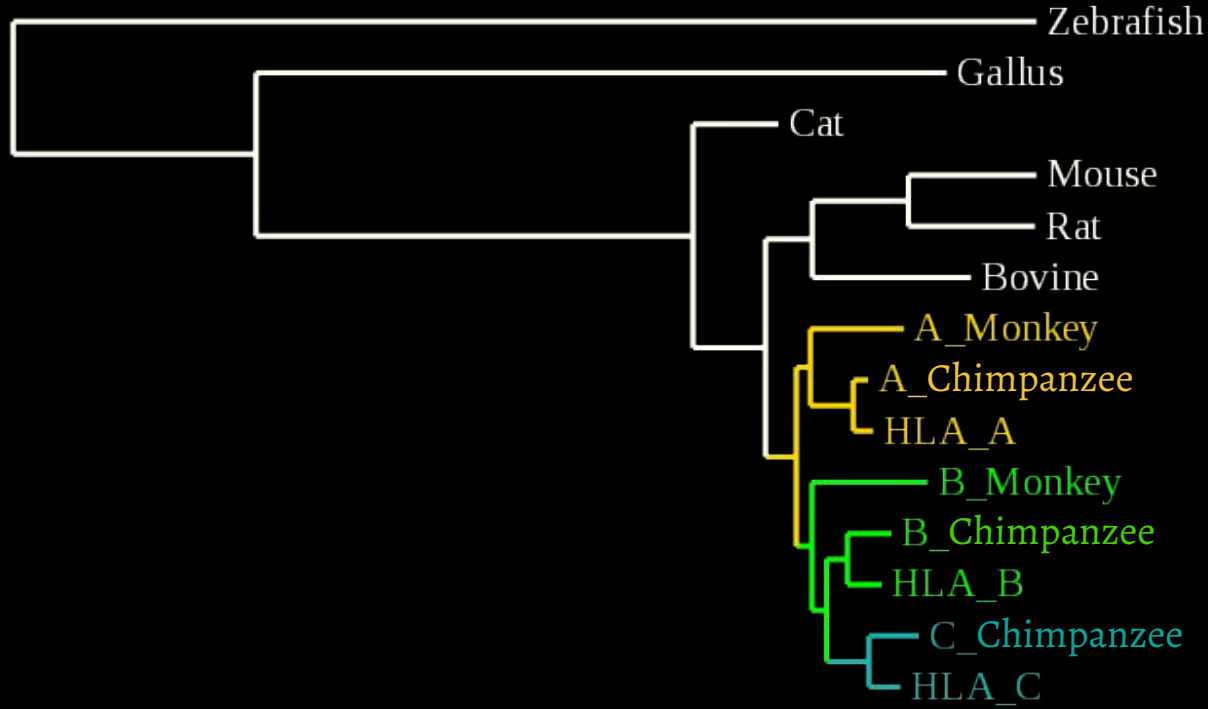
## Sequence alignment



Sequence alignment made with ClustalW and visualized with Pfalt

## 2. EVOLUTION: MHC I

### Phylogenetic tree



# 2. EVOLUTION: MHC I

## Structural alignment

|              |   |    |    |    |    |    |    |    |    |    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
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| Consensus    | 1 | 11 | 21 | 31 | 41 | 51 | 61 | 71 | 81 | 91 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Conservation | g | s  | r  | f  | t  | a  | w  | d  | q  | t  | r | v | d | l | r | t | l | r | y | n | q | s | e | g | s | t | i | q | r | m | y |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| hlaA         | G | S  | H  | S  | M  | R  | Y  | F  | Y  | T  | S | V | S | R | P | G | R | G | E | P | R | F | 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 | D | R | 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 | D | G | S | H | T | I | Q | I | M | Y |   |   |
| hlaB         | G | S  | H  | S  | M  | R  | Y  | F  | D  | T  | A | M | S | R | P | G | R | G | E | P | R | F | F | I | A | 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 | I | E | Q | - | E | G | P | E | Y | W | D | R | 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 | D | G | S | H | T | I | Q | I | M | Y |   |   |
| hlaC         | - | S  | H  | S  | M  | R  | Y  | F  | S  | T  | - | S | V | S | R | P | G | R | G | E | P | R | F | F | I | A | 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 | I | E | Q | - | E | G | P | E | Y | W | D | R | 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 | D | G | S | H | T | I | Q | I | M | Y |   |
| primat       | G | S  | H  | S  | M  | R  | Y  | F  | T  | -  | R | Y | S | V | S | R | P | G | R | G | E | P | R | F | F | I | A | 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 | I | E | Q | - | E | G | P | E | Y | W | D | R | 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 | D | G | S | H | T | I | Q | I | M | Y |
| mouse        | G | S  | H  | S  | M  | R  | Y  | F  | T  | -  | R | Y | S | V | S | R | P | G | R | G | E | P | R | F | F | I | A | 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 | I | E | Q | - | E | G | P | E | Y | W | D | R | 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 | D | G | S | H | T | I | Q | I | M | Y |
| rat          | G | S  | H  | S  | M  | R  | Y  | F  | T  | -  | R | Y | S | V | S | R | P | G | R | G | E | P | R | F | F | I | A | 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 | I | E | Q | - | E | G | P | E | Y | W | D | R | 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 | D | G | S | H | T | I | Q | I | M | Y |
| cat          | G | S  | H  | S  | M  | R  | Y  | F  | T  | -  | R | Y | S | V | S | R | P | G | R | G | E | P | R | F | F | I | A | 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 | I | E | Q | - | E | G | P | E | Y | W | D | R | 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 | D | G | S | H | T | I | Q | I | M | Y |
| gallus       | E | L  | H  | T  | L  | R  | Y  | I  | Q  | T  | - | A | M | T | D | P | G | P | G | Q | Q | W | F | V | T | 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 | I | E | Q | - | E | G | P | E | Y | W | D | R | 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 | D | G | S | H | T | I | Q | I | M | Y |   |   |

|              |     |     |     |     |     |     |     |     |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
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| Consensus    | 101 | 111 | 121 | 131 | 141 | 151 | 161 | 171 | 181 | 191 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Conservation | G   | C   | D   | V   | g   | p   | D   | g   | R   | I   | L | R | G | y | n | Q | d | A | Y | D | G | K | D | Y | I | A | L | N | e | D | L | R | s | W | T | A | A | D | m | a | A | Q | I | T | q | R | K | W | e | A | A | r | a | A | E | q | f | r | a | y | L | E | G | T | C | v | E | W | L | r | R | Y | L | e | n | G | K | e | T | L | R | A | d | p | P | k | t | h | v | t | h | P | i | s | d | h | e | a |
| hlaA         | G   | C   | D   | V   | G   | P   | D   | G   | R   | I   | L | R | G | N | Q | d | A | Y | D | G | K | D | Y | I | A | L | N | e | D | L | R | s | W | T | A | A | D | m | a | A | Q | I | T | q | R | K | W | e | A | A | r | a | A | E | q | f | r | a | y | L | E | G | T | C | v | E | W | L | r | R | Y | L | e | n | G | K | e | T | L | R | A | d | p | P | k | t | h | v | t | h | P | i | s | d | h | e | a |   |
| hlaB         | G   | C   | D   | V   | G   | P   | D   | G   | R   | I   | L | R | G | N | Q | d | A | Y | D | G | K | D | Y | I | A | L | N | e | D | L | R | s | W | T | A | A | D | m | a | A | Q | I | T | q | R | K | W | e | A | A | r | a | A | E | q | f | r | a | y | L | E | G | T | C | v | E | W | L | r | R | Y | L | e | n | G | K | e | T | L | R | A | d | p | P | k | t | h | v | t | h | P | i | s | d | h | e | a |   |
| hlaC         | G   | C   | D   | L   | G   | P   | D   | G   | R   | L   | L | R | G | N | Q | d | A | Y | D | G | K | D | Y | I | A | L | N | e | D | L | R | s | W | T | A | A | D | m | a | A | Q | I | T | q | R | K | W | e | A | A | r | a | A | E | q | f | r | a | y | L | E | G | T | C | v | E | W | L | r | R | Y | L | e | n | G | K | e | T | L | R | A | d | p | P | k | t | h | v | t | h | P | i | s | d | h | e | a |   |
| primat       | G   | C   | D   | L   | G   | P   | D   | G   | R   | L   | L | R | G | N | Q | d | A | Y | D | G | K | D | Y | I | A | L | N | e | D | L | R | s | W | T | A | A | D | m | a | A | Q | I | T | q | R | K | W | e | A | A | r | a | A | E | q | f | r | a | y | L | E | G | T | C | v | E | W | L | r | R | Y | L | e | n | G | K | e | T | L | R | A | d | p | P | k | t | h | v | t | h | P | i | s | d | h | e | a |   |
| mouse        | G   | C   | D   | L   | G   | P   | D   | G   | R   | L   | L | R | G | N | Q | d | A | Y | D | G | K | D | Y | I | A | L | N | e | D | L | R | s | W | T | A | A | D | m | a | A | Q | I | T | q | R | K | W | e | A | A | r | a | A | E | q | f | r | a | y | L | E | G | T | C | v | E | W | L | r | R | Y | L | e | n | G | K | e | T | L | R | A | d | p | P | k | t | h | v | t | h | P | i | s | d | h | e | a |   |
| rat          | S   | C   | E   | V   | G   | P   | D   | G   | R   | L   | L | R | G | N | Q | d | A | Y | D | G | K | D | Y | I | A | L | N | e | D | L | R | s | W | T | A | A | D | m | a | A | Q | I | T | q | R | K | W | e | A | A | r | a | A | E | q | f | r | a | y | L | E | G | T | C | v | E | W | L | r | R | Y | L | e | n | G | K | e | T | L | R | A | d | p | P | k | t | h | v | t | h | P | i | s | d | h | e | a |   |
| cat          | G   | C   | D   | V   | E   | G   | P   | D   | G   | R   | L | L | R | G | N | Q | d | A | Y | D | G | K | D | Y | I | A | L | N | e | D | L | R | s | W | T | A | A | D | m | a | A | Q | I | T | q | R | K | W | e | A | A | r | a | A | E | q | f | r | a | y | L | E | G | T | C | v | E | W | L | r | R | Y | L | e | n | G | K | e | T | L | R | A | d | p | P | k | t | h | v | t | h | P | i | s | d | h | e | a |
| gallus       | G   | C   | D   | I   | L   | E   | D   | G   | -   | T   | L | R | G | N | Q | d | A | Y | D | G | K | D | Y | I | A | L | N | e | D | L | R | s | W | T | A | A | D | m | a | A | Q | I | T | q | R | K | W | e | A | A | r | a | A | E | q | f | r | a | y | L | E | G | T | C | v | E | W | L | r | R | Y | L | e | n | G | K | e | T | L | R | A | d | p | P | k | t | h | v | t | h | P | i | s | d | h | e | a |   |

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| Consensus    | 201 | 211 | 221 | 231 | 241 | 251 | 261 | 271 | 281 | 291 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Conservation | 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 | O | D | T | E | L | V | E | T | R | P | a | G | D | 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 | e | - | - | I | Q | R | T | P | K | I | Q | V | Y | S | R | H | P | A | E | N | G | K | P | n | f |
| hlaA         | 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 | O | D | T | E | L | V | E | T | R | P | a | G | D | 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 | e | - | - | I | Q | R | T | P | K | I | Q | V | Y | S | R | H | P | A | E | N | G | K | P | n | f |
| hlaB         | 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 | O | D | T | E | L | V | E | T | R | P | a | G | D | 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 | e | - | - | I | Q | R | T | P | K | I | Q | V | Y | S | R | H | P | A | E | N | G | K | P | n | f |
| hlaC         | 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 | O | D | T | E | L | V | E | T | R | P | a | G | D | 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 | e | - | - | I | Q | R | T | P | K | I | Q | V | Y | S | R | H | P | A | E | N | G | K | P | n | f |
| primat       | 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 | O | D | T | E | L | V | E | T | R | P | a | G | D | 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 | e | - | - | I | Q | R | T | P | K | I | Q | V | Y | S | R | H | P | A | E | N | G | K | P | n | f |
| mouse        | 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 | O | D | T | E | L | V | E | T | R | P | a | G | D | G | T | F | Q | K | W | a | a | V | V | V | P | S |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

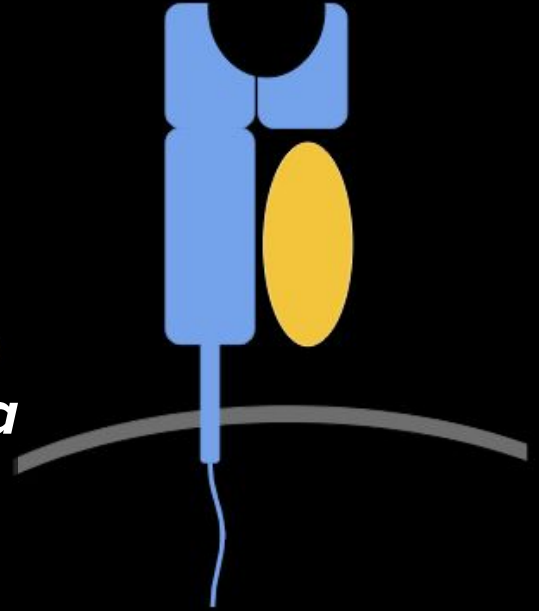
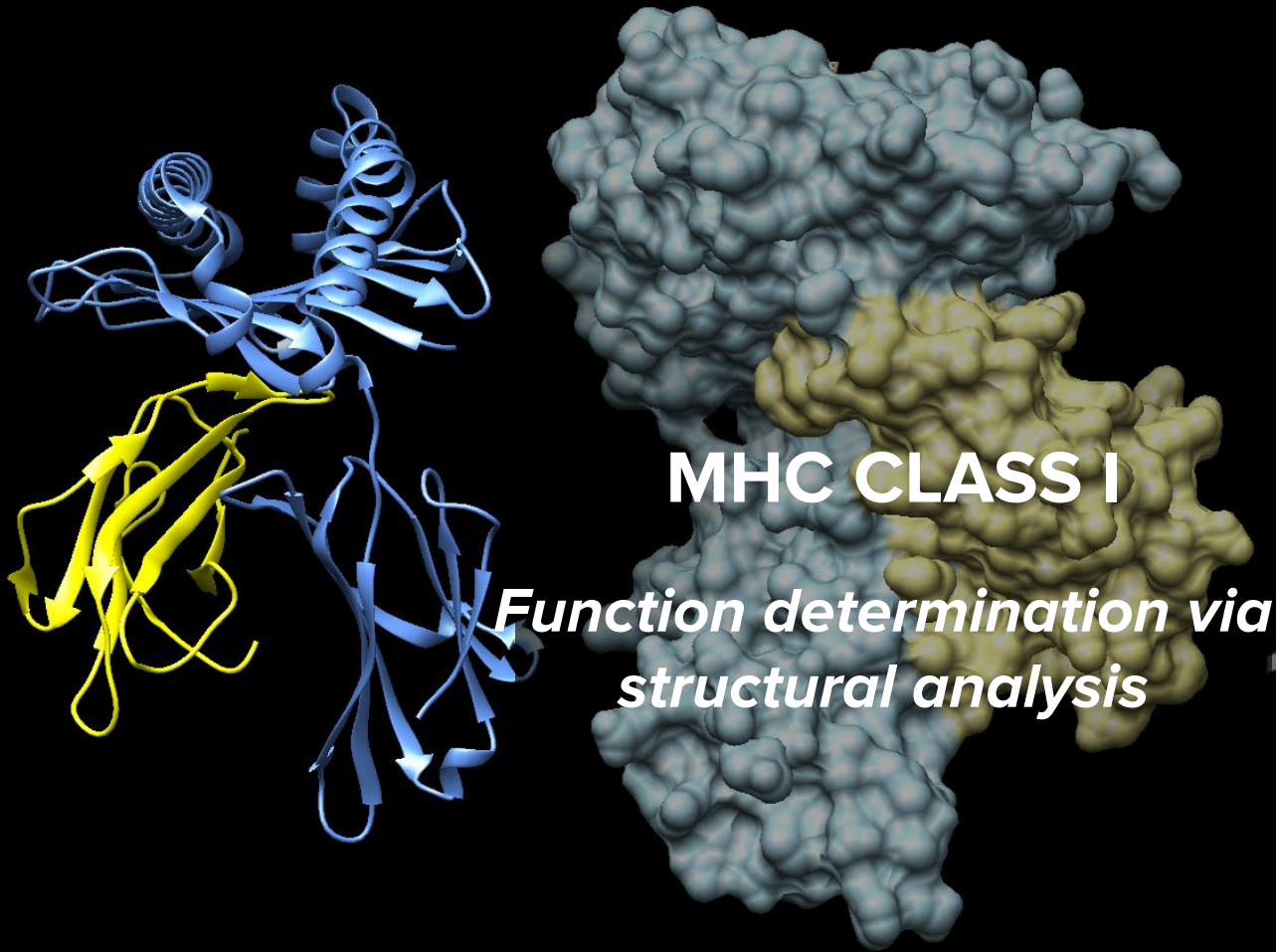
## 2. EVOLUTION: MHC I

### Superimposition

→ **Score:** 9.68  
→ **RMSD:** 0.84  
→ **Length:** 379  
→ **N-fit:** 348

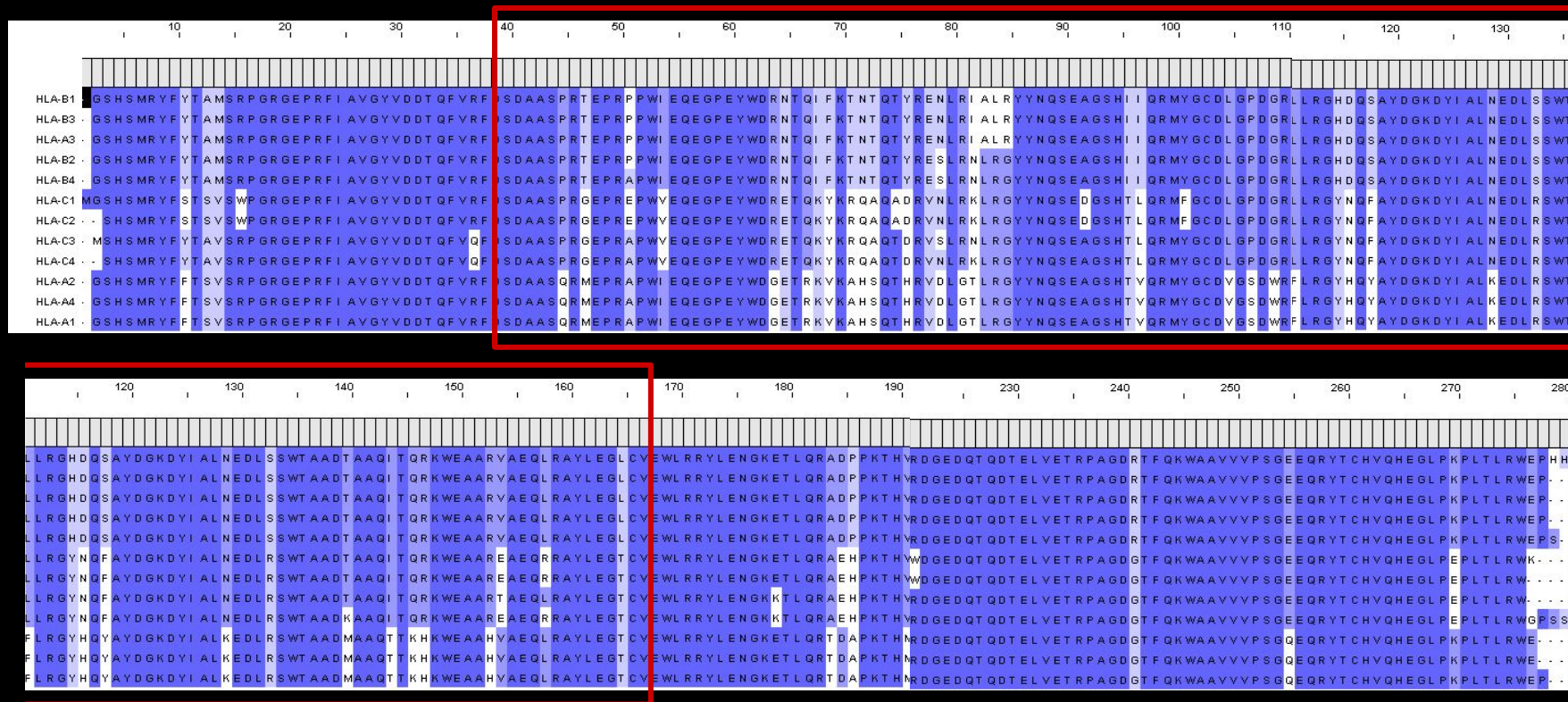


Light green: HLA-A  
Dark green: HLA-B  
Light blue: HLA-C  
Cyan: cat  
Magenta: rat  
Yellow: mouse  
Red: chicken  
Orange: ape



# 3. MHC CLASS I

## HLA-A, HLA-B and HLA-C sequence alignment



# 3. MHC CLASS I

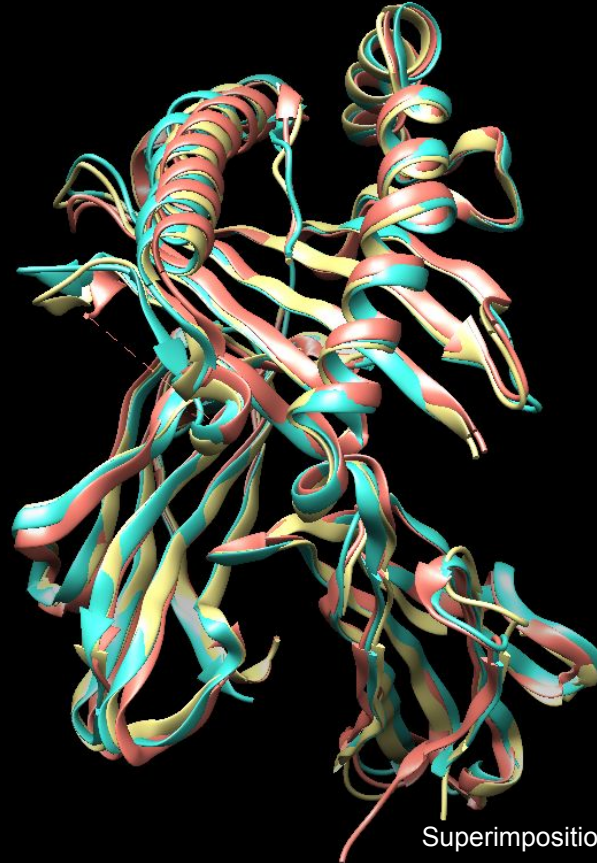
## HLA-A, HLA-B and HLA-C structural alignment

|              |                     |                     |                     |                     |                     |                     |                     |                     |                       |                     |
|--------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|-----------------------|---------------------|
|              | 1                   | 11                  | 21                  | 31                  | 41                  | 51                  | 61                  | 71                  | 81                    | 91                  |
| 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 D r e T q k y K a | q a Q T y R v n L r | t L R G Y Y N Q S E   | A G S H t i Q R M Y |
| Conservation |                     |                     |                     |                     |                     |                     |                     |                     |                       |                     |
| HLA-A1       | - 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 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 |
| HLA-C4       | - - 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 G E P R A | P W V E Q E G P E Y | 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 Q R M Y |
| HLA-B4       | 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 T E P R A | P W I E Q E G P E Y | W D R N T Q I F K T | N T Q T Y R E S L R | N L R G Y Y N Q S E   | A G S H I L Q R M Y |
| HLA-A2       | - 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 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 |
| HLA-C3       | - 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 R F D S D | A A S Q R M E P R A | P W V E Q E G P E Y | 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 Q R M Y |
| HLA-A3       | - 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 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 |
| HLA-A4       | - 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 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 |
| HLA-B1       | - 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 T E P R P | P W I E Q E G P E Y | W D R N T Q I F K T | N T Q T Y R E N L R | I A L R G Y Y N Q S E | A G S H T V Q R M Y |
| HLA-B2       | 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 T E P R P | P W I E Q E G P E Y | W D R N T Q I F K T | N T Q T Y R E N L R | I A L R G Y Y N Q S E | A G S H I I Q R M Y |
| HLA-B3       | 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 T E P R P | P W I E Q E G P E Y | W D R N T Q I F K T | N T Q T Y R E N L R | I A L R G Y Y N Q S E | A G S H I I Q R M Y |
| HLA-C1       | - G S H S M R Y F S | T S V S W 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 G E P R E | P W V E Q E G P E Y | 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 Q R M F |
| HLA-C2       | - - S H S M R Y F S | T S V S W 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 G E P R E | P W V E Q E G P E Y | 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 Q R M F |
|              | 101                 | 111                 | 121                 | 131                 | 141                 | 151                 | 161                 | 171                 | 181                   | 191                 |
| Consensus    | G C D I G p D g R I | L R G y h Q y A Y D | 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 | Q R a d a P K T H v   | T H H p V S D H E A |
| Conservation |                     |                     |                     |                     |                     |                     |                     |                     |                       |                     |
| HLA-A1       | 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 I 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 H A V S D H E A |
| HLA-C4       | G C D L G P D G R L | L R G Y N Q F A Y D | G K D Y I A L N E D | L R S W T A A D K A | A Q I T O 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 E T L | Q R A E H P K T H V   | T H H P V S D H E A |
| HLA-B4       | G C D L G P D G R L | L R G H D Q F A Y D | G K D Y I A L N E D | L S S W T A A D T A | A Q I T O R 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 A D P P K T H V   | T H H P V S D H E A |
| HLA-A2       | 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 I 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 H A V S D H E A |
| HLA-C3       | G C D L G P D G R L | L R G Y N Q F A Y D | G K D Y I A L N E D | L R S W T A A D T A | A Q I T O 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 E T L | Q R A E H P K T H V   | T H H P V S D H E A |
| HLA-A3       | 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 I 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 H A V S D H E A |
| HLA-A4       | 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 I 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 H A V S D H E A |
| HLA-B1       | G C D L G P D G R L | L R G H D Q S A Y D | G K D Y I A L N E D | L S S W T A A D T A | A Q I T O 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 R A D P P K T H V   | T H H P V S D H E A |
| HLA-B2       | G C D L G P D G R L | L R G H D Q S A Y D | G K D Y I A L N E D | L S S W T A A D T A | A Q I T O 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 R A D P P K T H V   | T H H P V S D H E A |
| HLA-B3       | G C D L G P D G R L | L R G H D Q S A Y D | G K D Y I A L N E D | L S S W T A A D T A | A Q I T O 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 R A D P P K T H V   | T H H P V S D H E A |
| HLA-C1       | G C D L G P D G R L | L R G Y N Q F A Y D | G K D Y I A L N E D | L R S W T A A D T A | A Q I T O 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 E T L | Q R A E H P K T H V   | T H H P V S D H E A |
| HLA-C2       | G C D L G P D G R L | L R G Y N Q F A Y D | G K D Y I A L N E D | L R S W T A A D T A | A Q I T O 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 E T L | Q R A E H P K T H V   | T H H P V S D H E A |
|              | 201                 | 211                 | 221                 | 231                 | 241                 | 251                 | 261                 | 271                 |                       |                     |
|              | 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 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 - - -   |                       |                     |
|              | 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 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 L R W E P - -   |                       |                     |
|              | 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 F Q K W A A V V V | P S G E Q R Y T C   | H V Q H E G L P E P | L T L R W - - -     |                       |                     |
|              | 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 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 L R W - - -     |                       |                     |
|              | 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 F Q K W A A V V V | P S G E Q R Y T C   | H V Q H E G L P E P | L T L R W - - -     |                       |                     |
|              | 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 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 L R W E - - -   |                       |                     |
|              | 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 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 L R W E - - -   |                       |                     |
|              | 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 F Q K W A A V V V | P S G E Q R Y T C   | H V Q H E G L P E P | L T L R W E P H H   |                       |                     |
|              | 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 F Q K W A A V V V | P S G E Q R Y T C   | H V Q H E G L P E P | L T L R W E P - -   |                       |                     |
|              | T L R C W A L G F Y | P A E I T L T W Q W | D G E D Q T Q D T E | L V E T R P A G D G | T F Q K W A A V V V | P S G E Q R Y T C   | H V Q H E G L P E P | L T L R W K - - -   |                       |                     |
|              | T L R C W A L G F Y | P A E I T L T W Q W | D G E D Q T Q D T E | L V E T R P A G D G | T F Q K W A A V V V | P S G E Q R Y T C   | H V Q H E G L P E P | L T L R W - - -     |                       |                     |

### 3. MHC CLASS I

#### HLA-A, HLA-B and HLA-C superimposition

- Score: 9.67
- **RMSD: 0.95**
- Length: 388
- N-fit: 367

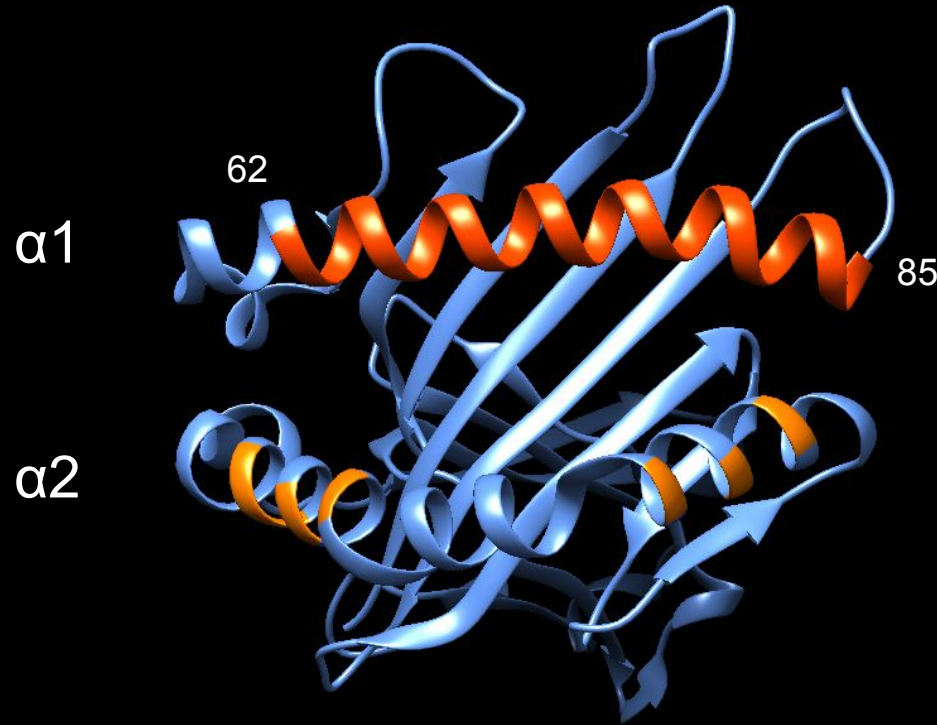


pink: HLA-A  
blue: HLA-B  
yellow: HLA-C

Superimpositions made with Stamp and visualized with Chimera

### 3. MHC CLASS I

#### HLA-A, HLA-B and HLA-C variability



Alpha helices:

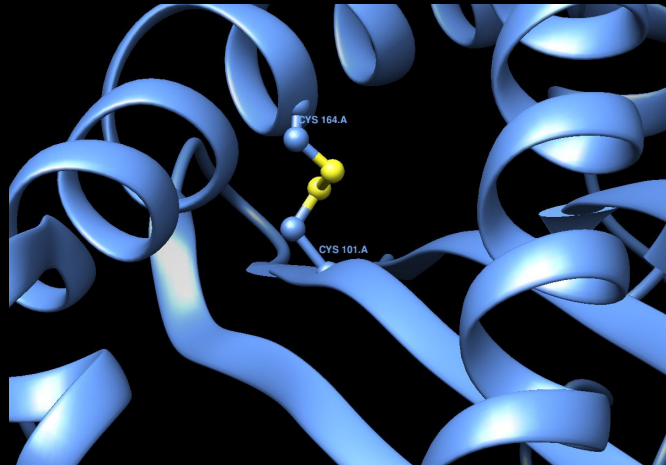
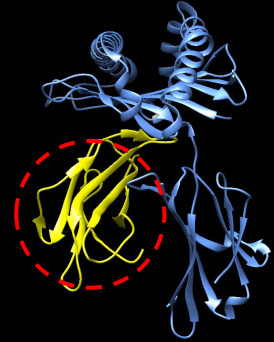
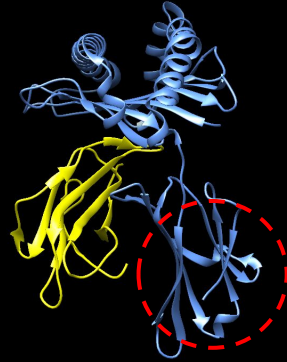
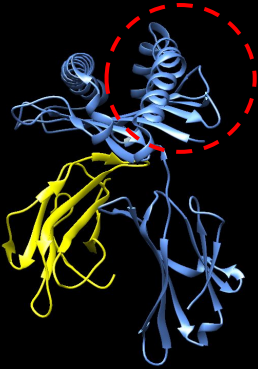
- Interaction with the peptide
- Interaction with TCR
- Part of the binding pockets

Variability between HLA-A, B and C visualized with Chimera

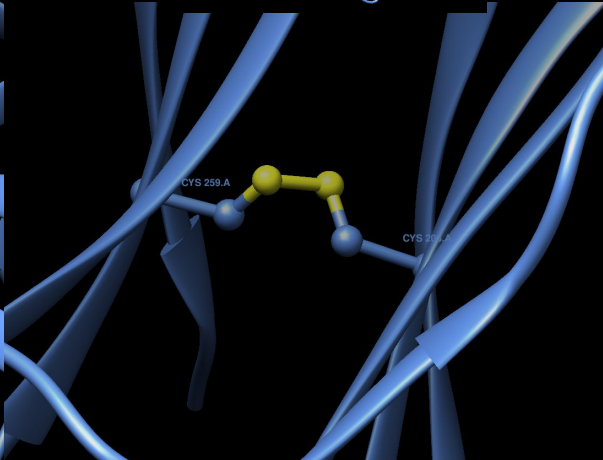
# **INNER INTERACTIONS**

### 3. MHC CLASS I

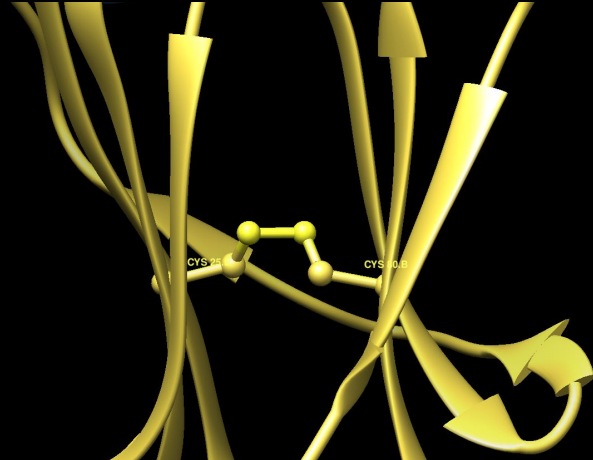
#### Inner interactions MHC I: Disulfide bonds



$\alpha 2$  chain 164 - 101



$\alpha 3$  chain 259 - 208

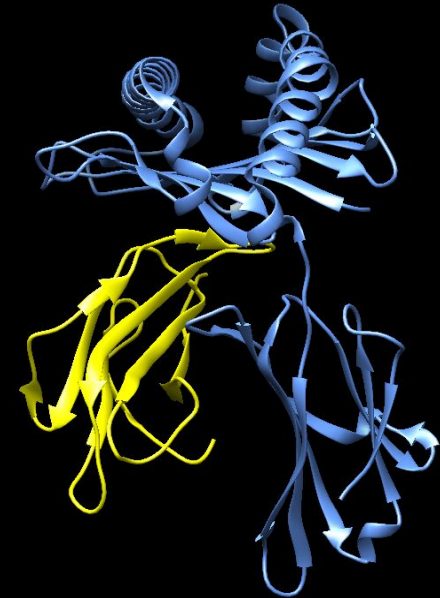


$\beta 2m$  25 - 80

# 3. MHC CLASS I

## Inner interactions MHC I: $\beta 2m$ - $\alpha 3$

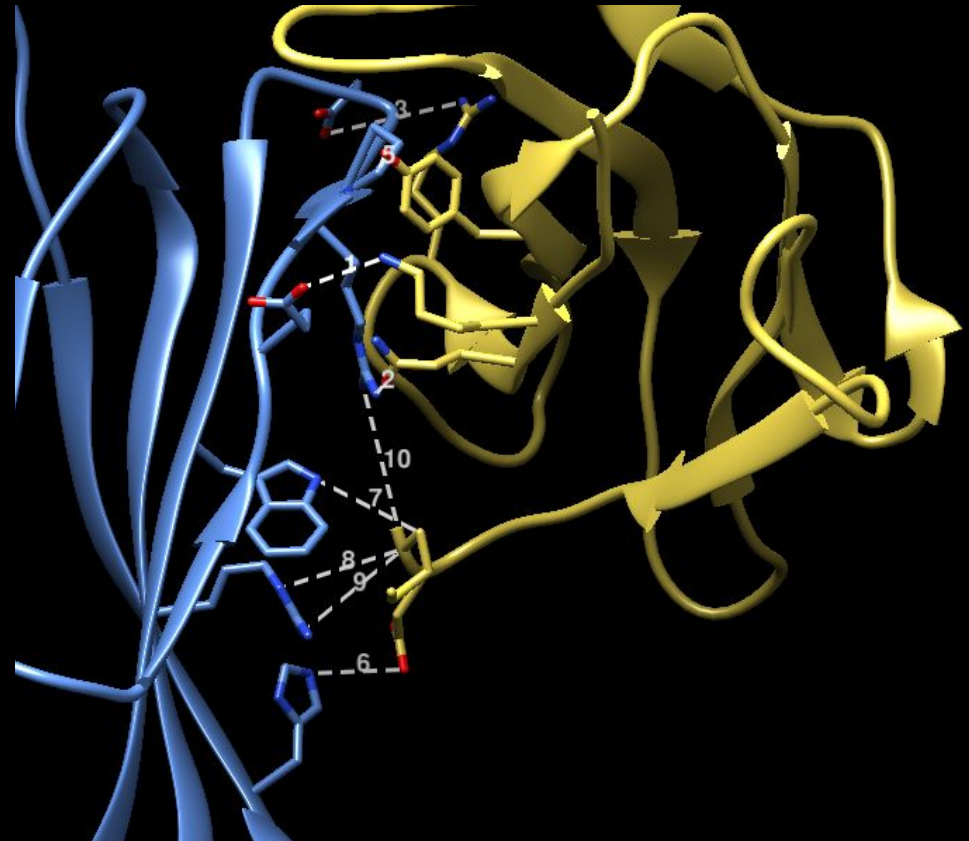
|              | 201        | 211        | 221        | 231        | 241       | 251        | 261        | 271   |
|--------------|------------|------------|------------|------------|-----------|------------|------------|-------|
| Consensus    | TLRCWALgFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDg | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| Conservation |            |            |            |            |           |            |            |       |
| HLA-A1       | TLRCWALSFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDG | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-C4       | TLRCWALGFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDG | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-B4       | TLRCWALGFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDR | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-A2       | TLRCWALSFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDG | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-C3       | TLRCWALGFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDG | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-A3       | TLRCWALSFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDG | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-A4       | TLRCWALSFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDG | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-B1       | TLRCWALGFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDR | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-B2       | TLRCWALGFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDR | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-B3       | TLRCWALGFY | PAEITLTWQR | DGEDQTQDTE | LVETRPAGDR | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-C1       | TLRCWALGFY | PAEITLTWQW | DGEDQTQDTE | LVETRPAGDG | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |
| HLA-C2       | TLRCWALGFY | PAEITLTWQW | DGEDQTQDTE | LVETRPAGDG | TFQKWAADV | PSGEEQRYTC | HVQHEGLPKP | LTLRW |



### 3. MHC CLASS I

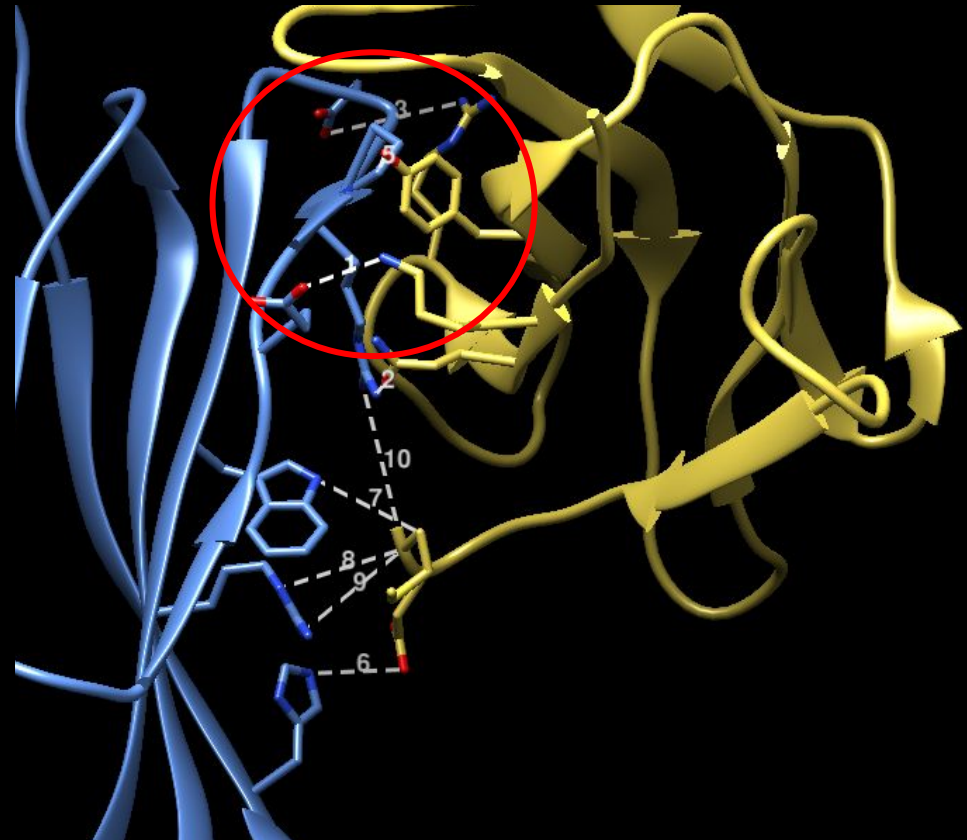
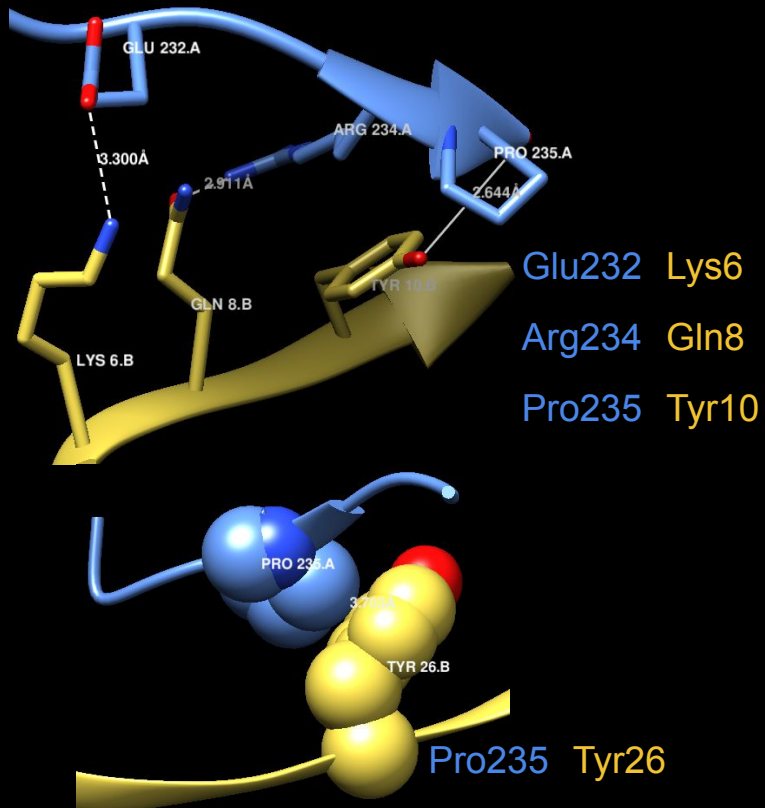
#### Inner interactions MHC I: $\beta 2m$ - $\alpha 3$

| $\alpha 3$ | $\beta 2m$ | Length (Å) |
|------------|------------|------------|
| Glu232     | Lys6       | 3.03       |
| Arg234     | Gln8       | 2.91       |
| Pro235     | Tyr10      | 2.644      |
|            | Tyr26      |            |
| Ala236     | Arg12      | 3.012      |
| Ala236     | Asn24      | 3.004      |
| His192     | Asp98      | 3.69       |
| Arg234     | Met99      | 3.692      |
| Trp244     | Cterm      | 2.793      |



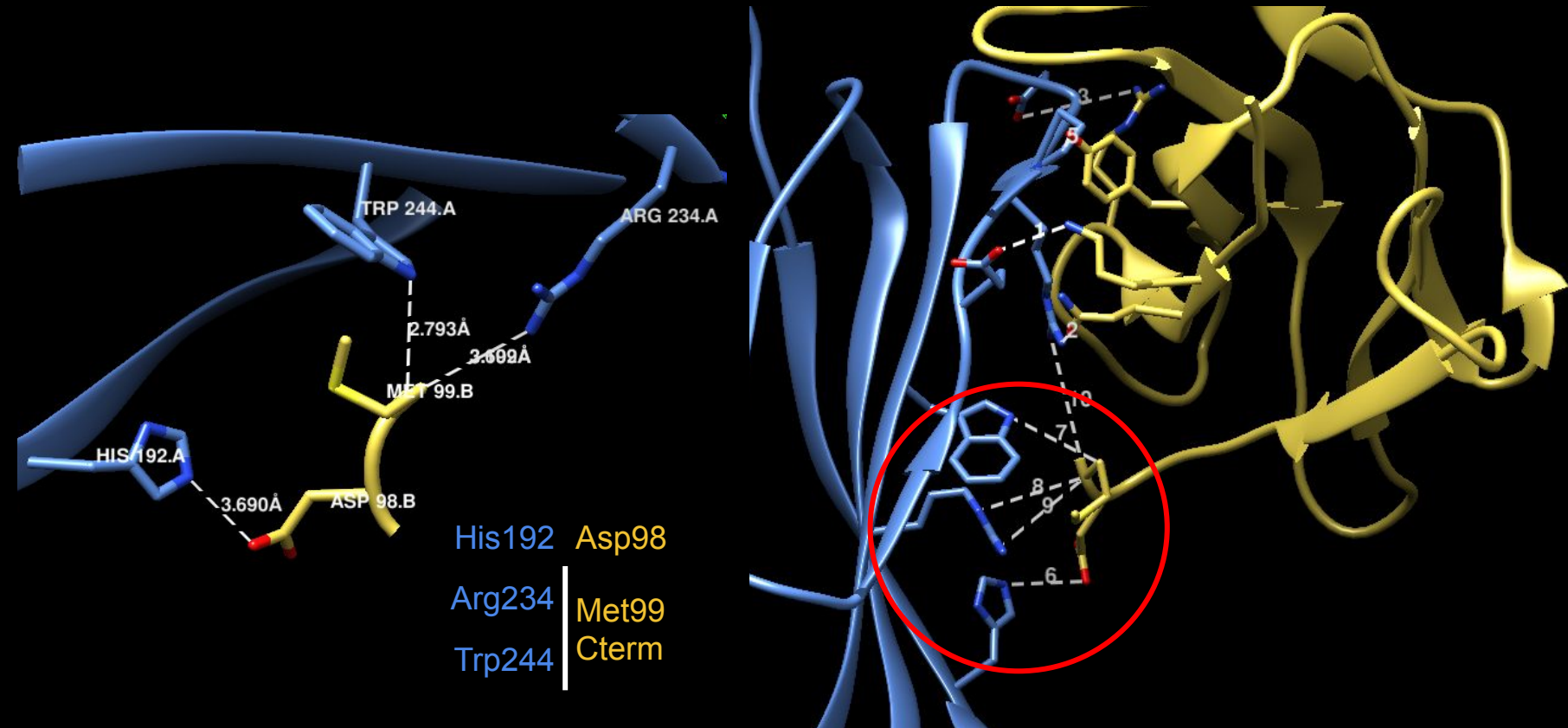
# 3. MHC CLASS I

## Inner interactions MHC I: $\beta 2m$ - $\alpha 3$



### 3. MHC CLASS I

#### Inner interactions MHC I: $\beta 2m$ - $\alpha 3$



# 3. MHC CLASS I

## Inner interactions MHC I: $\beta 2m$ - $\alpha 1,2$

| Consensus    | 31         | 41          | 51         | 61           | 71           | 81         |
|--------------|------------|-------------|------------|--------------|--------------|------------|
| Conservation | DTQFVRFDS  | AASpRmEPra  | PWIEQEGPEY | WDreTqkyKa   | qaQTyRvnLr   | tLRGYYNQSE |
| HLA-A1       | DTQFVRFDS  | AASQRMPEPRA | PWIEQEGPEY | WDGETRKVKAKR | HSQTHRVDLGL  | TLRGYYNQSE |
| HLA-C4       | DTQFVQFDSD | AASPRGEPRA  | PWVEQEGPEY | WDRNETQIKTKR | QAQTDNRVNLRL | KLRGYYNQSE |
| HLA-B4       | DTQFVRFDS  | AASPRTEPRA  | PWIEQEGPEY | WDRNTQIFKTKR | NTQTYRESLRL  | NLRGYYNQSE |
| HLA-A2       | DTQFVRFDS  | AASQRMPEPRA | PWIEQEGPEY | WDGETRKVKAKR | HSQTHRVDLGL  | TLRGYYNQSE |
| HLA-C3       | DTQFVQFDSD | AASPRGEPRA  | PWVEQEGPEY | WDRNETQIKTKR | QAQTDNRVNLRL | NLRGYYNQSE |
| HLA-A3       | DTQFVRFDS  | AASQRMPEPRA | PWIEQEGPEY | WDGETRKVKAKR | HSQTHRVDLGL  | TLRGYYNQSE |
| HLA-A4       | DTQFVRFDS  | AASQRMPEPRA | PWIEQEGPEY | WDGETRKVKAKR | HSQTHRVDLGL  | TLRGYYNQSE |
| HLA-B1       | DTQFVRFDS  | AASPRTEPRA  | PWIEQEGPEY | WDRNETQIKTKR | NTQTYRESLRL  | TLRGYYNQSE |
| HLA-B2       | DTQFVRFDS  | AASPRTEPRA  | PWIEQEGPEY | WDRNETQIKTKR | NTQTYRESLRL  | TLRGYYNQSE |
| HLA-B3       | DTQFVRFDS  | AASPRTEPRA  | PWIEQEGPEY | WDRNETQIKTKR | NTQTYRESLRL  | TLRGYYNQSE |
| HLA-C1       | DTQFVRFDS  | AASPRGEPRE  | PWVEQEGPEY | WDRNETQIKTKR | QAQADRVNLRL  | KLRGYYNQSE |
| HLA-C2       | DTQFVRFDS  | AASPRGEPRE  | PWVEQEGPEY | WDRNETQIKTKR | QAQADRVNLRL  | KLRGYYNQSE |



### 3. MHC CLASS I

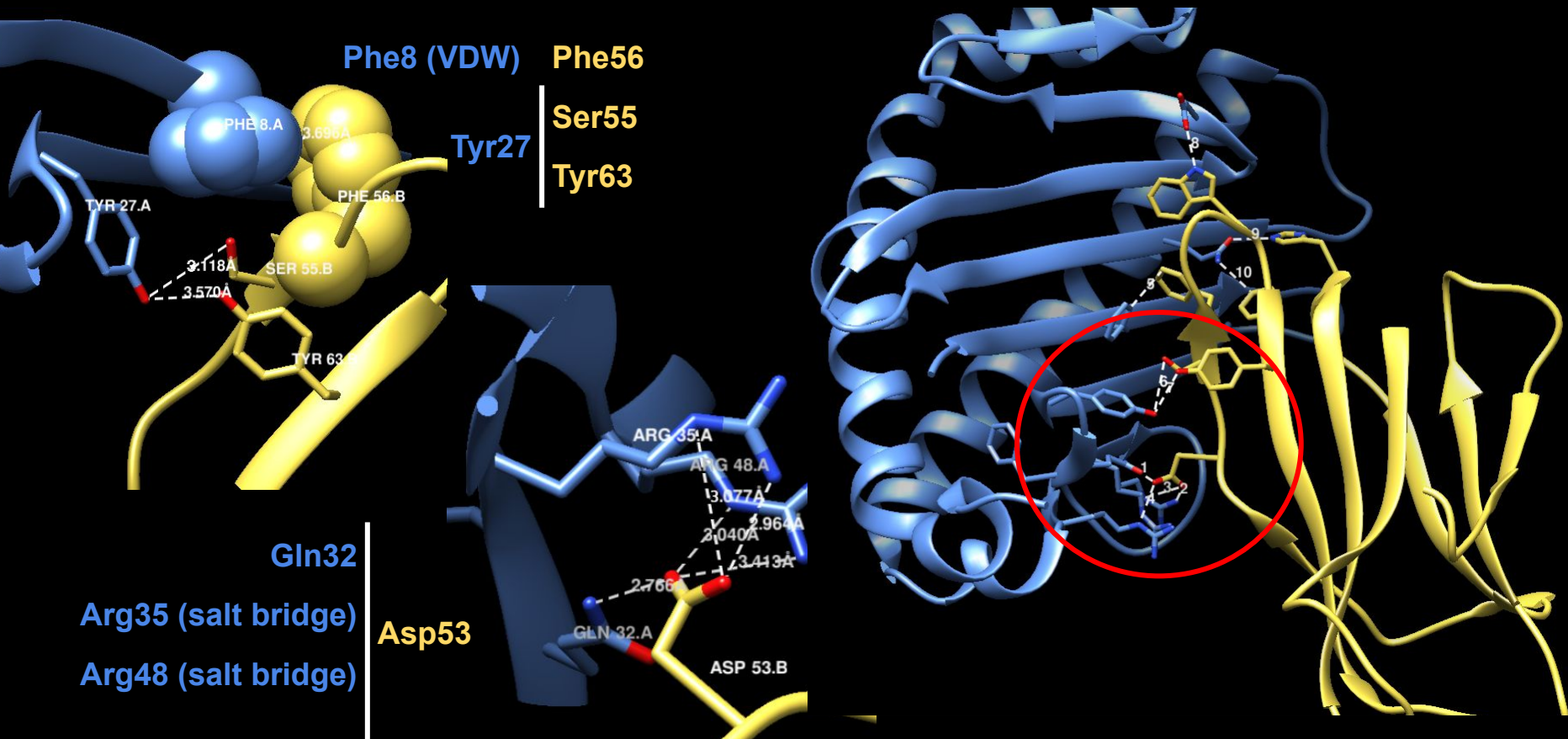
#### Inner interactions MHC I: $\beta 2m$ - $\alpha 1,2$

| $\alpha 1$ | $\beta 2m$ | Length (Å)    |
|------------|------------|---------------|
| Gln32      |            | 2,766         |
| Arg35      | Asp53      | 2.964 / 3.077 |
| Arg48      |            | 3.04 / 3.41   |
| Phe8       | Phe56      |               |
| Tyr27      | Ser55      | 3.118         |
|            | Tyr63      | 3.57          |
| $\alpha 2$ | $\beta 2m$ | Length (Å)    |
| Gln96      | His31      | 2.85          |
|            | Phe62      | 3.52          |
| Asp120     | Trp60      | 2.859         |



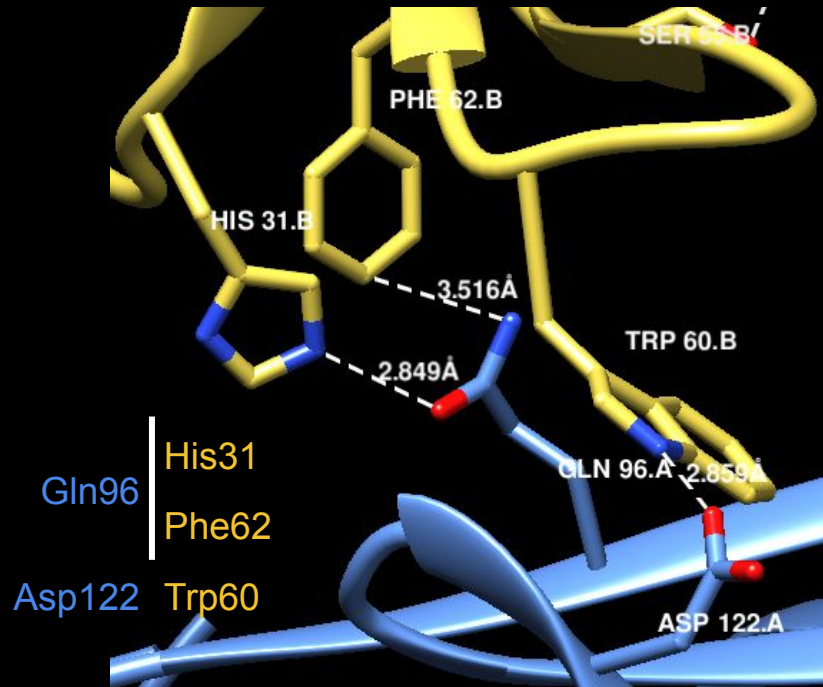
# 3. MHC CLASS I

## Inner interactions MHC I: $\beta 2m$ - $\alpha 1,2$



### 3. MHC CLASS I

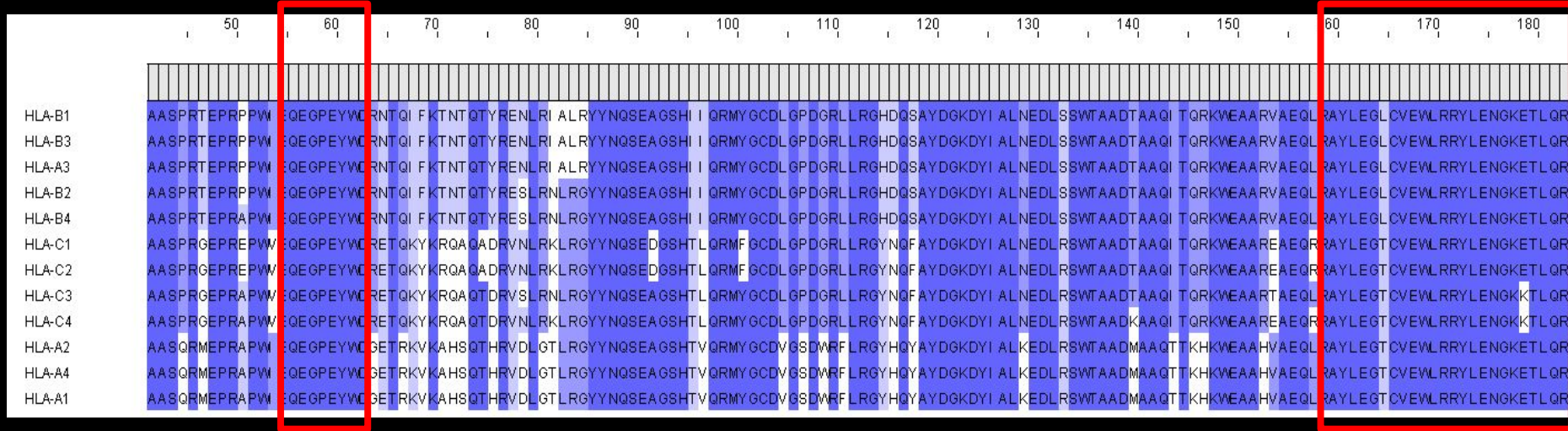
#### Inner interactions MHC I: $\beta 2m$ - $\alpha 1,2$



# **INTER INTERACTIONS**

# 3. MHC CLASS I

## Interactions MHC I - TCR: sequence alignment



Sequence alignment made with ClustalW  
and visualized with Pfaff

# 3. MHC CLASS I

## Interactions MHC I - TCR: structural alignment

|              |    |             |    |            |    |            |
|--------------|----|-------------|----|------------|----|------------|
|              | 61 | EYWDreTqi y | 71 | KaqaQTdRes | 81 | LrnlrgYYNQ |
| Consensus    |    |             |    |            |    |            |
| Conservation |    |             |    |            |    |            |
| HLA2         |    | EYWDGETRNM  |    | KASAQTYREN |    | LRIALRYYNQ |
| HLA1         |    | EYWDRETQIS  |    | KTNTQTYREN |    | LRTALRYYNQ |
| HLA5         |    | EYWDRNTQIF  |    | KTNTQTYRES |    | LRNLRGYYNQ |
| HLA9         |    | EYWDRNTQIY  |    | KAAQQTDRS  |    | LRNLRGYYNQ |
| HLA11        |    | EYWDRNTQIY  |    | KAAQQTDRS  |    | LRNLRGYYNQ |
| HLA4         |    | EYWDRNTQAF  |    | KTNTQTDRES |    | LRNLRGYYNQ |
| HLA8         |    | EYWDRRETQKY |    | KRQAQTDREV |    | LRNLRGYYNQ |
| HLA3         |    | EYWDQETRNIV |    | KAQSQTDREV |    | LGTLRGYYNQ |
| HLA10        |    | EYWDGETRKNV |    | KAHSQTHREV |    | LGTLRGYYNQ |

|              |     |            |     |            |     |              |
|--------------|-----|------------|-----|------------|-----|--------------|
|              | 141 | tAAQITqRKW | 151 | EAArvAEQLR | 161 | AYLEGtCVEW   |
| Consensus    |     |            |     |            |     |              |
| Conservation |     |            |     |            |     |              |
| HLA2         |     | TAAQIIQRKW |     | EAArvAEQLR |     | AYLEGGLCWEW  |
| HLA1         |     | TAAQITQRKW |     | EAArvAEQDR |     | AYLEGGLCVES  |
| HLA5         |     | TAAQITQRKW |     | EAArvAEARR |     | AYLEGGLCWEW  |
| HLA9         |     | TAAQITQRKW |     | EAArEAEQRR |     | AYLEGGECEWEW |
| HLA11        |     | TAAQITQRKW |     | EAArEAEQRR |     | AYLEGGECEWEW |
| HLA4         |     | TAAQITQRKW |     | EAArvAEQDR |     | AYLEGGLTCWEW |
| HLA8         |     | TAAQITQRKW |     | EAArTAEQLR |     | AYLEGGLTCWEW |
| HLA3         |     | MAAQITKRKW |     | EAAHEAEQLR |     | AYLDGGLTCWEW |
| HLA10        |     | MAAQTTKHKW |     | EAAHVAEQLR |     | AYLEGGLTCWEW |

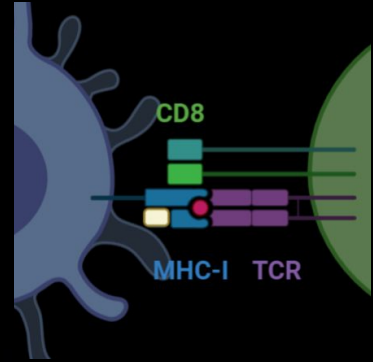
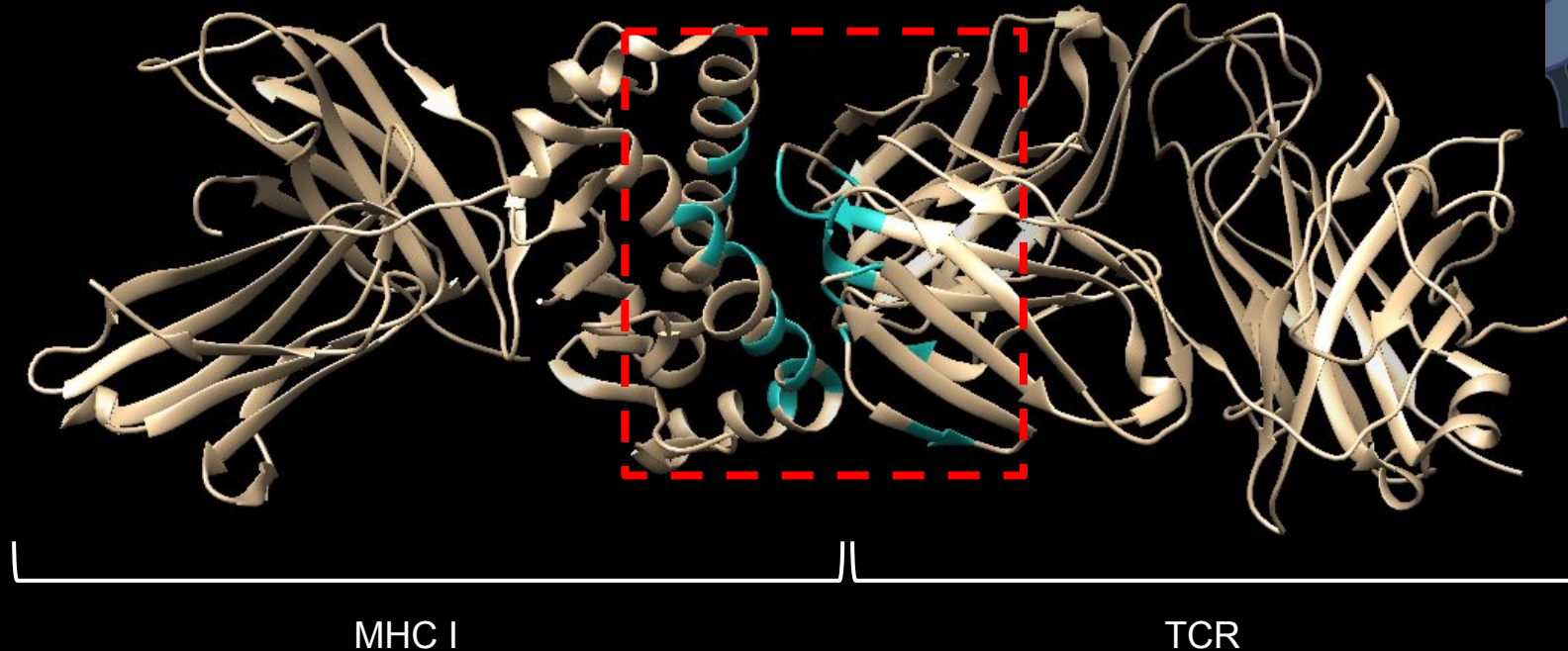


Structural alignment made with Stamp and visualized with Chimera

Conserved residues in MHC I visualized with Chimera

### 3. MHC CLASS I

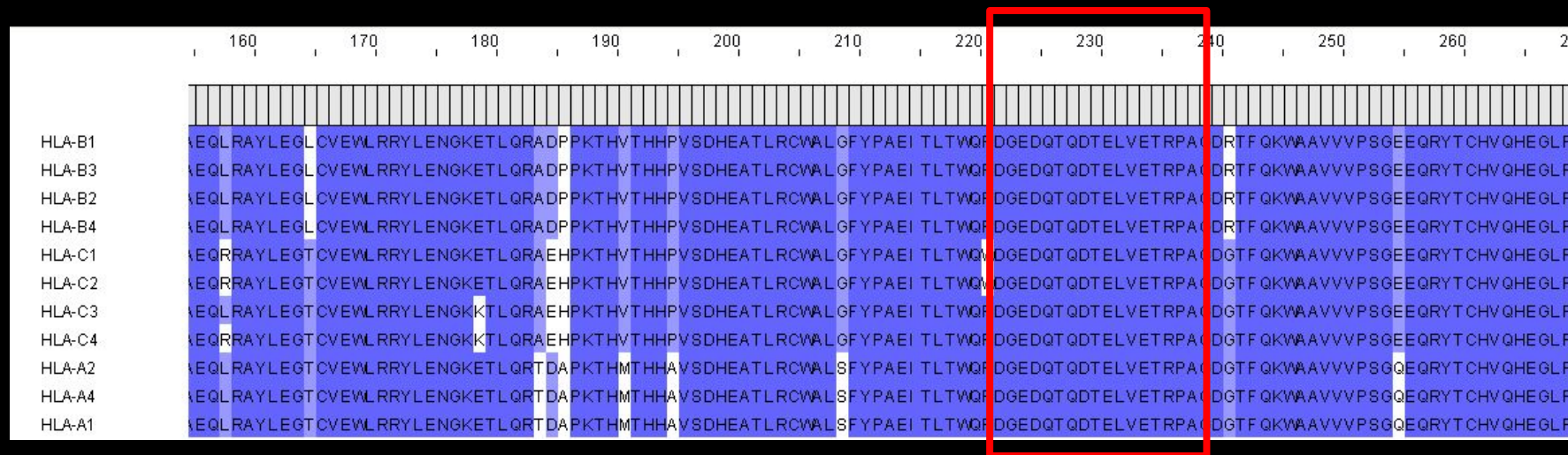
#### Interactions MHC I - TCR



Interaction between MHC I and TCR visualized with Chimera

### 3. MHC CLASS I

## Interactions MHC I - CD8: sequence alignment



Sequence alignment made with ClustalW  
and visualized with Pfaat

# 3. MHC CLASS I

## Interactions MHC I - CD8: structural alignment

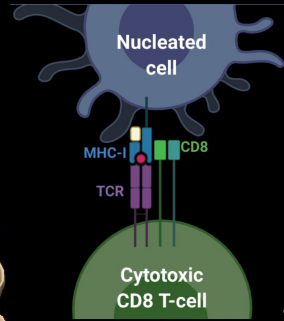
- Interactions between CD8 alpha 1 and 2 with MHC I alpha 3
- Highly conserved residues
- Tapasin: residues 221-229

|              | 211        | 221        | 231        | 241                 |
|--------------|------------|------------|------------|---------------------|
| Consensus    | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | D r T F Q K W A A V |
| Conservation |            |            |            |                     |
| HLA9         | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | DRTFQKWAAV          |
| HLA11        | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | DRTFQKWAAV          |
| HLA4         | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | DRTFQKWAAV          |
| HLA5         | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | DRTFQKWAAV          |
| HLA2         | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | DRTFQKWAAV          |
| HLA1         | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | DRTFQKWAAV          |
| HLA8         | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | DGT FQ KWAAV        |
| HLA3         | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | DGT FQ KWAAV        |
| HLA10        | FYPAEITLTW | QRDGEDQTQD | TELVETRPAG | DGT FQ KWAAV        |

Structural alignment made with Stamp and visualized with Chimera



Interaction between MHC I and CD8 visualized with Chimera

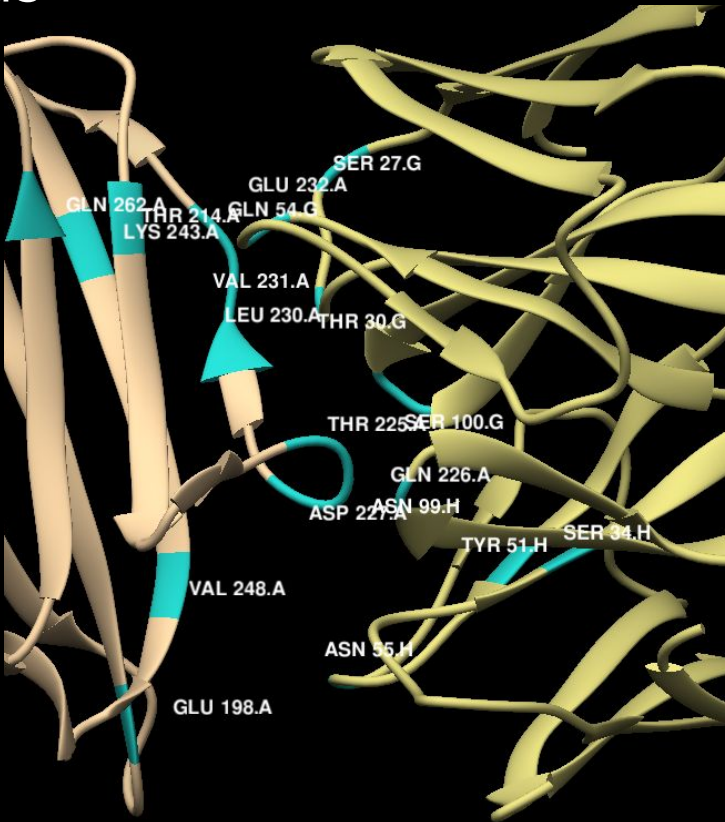


# 3. MHC CLASS I

## Interactions MHC I - CD8: hydrogen bonds

| MHC I                                | CD8 alpha 1 | Length (Å)                |
|--------------------------------------|-------------|---------------------------|
| Glu232                               | Ser27       | 3.36                      |
| Leu230<br>Val231<br>Glu232<br>Lys243 | Asn28       | 3.25, 3.26,<br>3.16, 3.24 |
| Thr225                               | Thr30       | 2.57                      |
| Gln262,<br>Thr214                    | Gln54       | 2.78, 2.61                |
| Leu230                               | Asn99       | 3.23                      |
| Gln226                               | Ser100      | 3.12                      |

| MHC I            | CD8 alpha 2 | Length (Å) |
|------------------|-------------|------------|
| Gln226           | Ser34       | 3.29       |
| Asp227           | Tyr51       | 3.03       |
| Glu198<br>Val248 | Asn55       | 3.36, 3.23 |
| Glu222           | Asn99       | 3.14       |

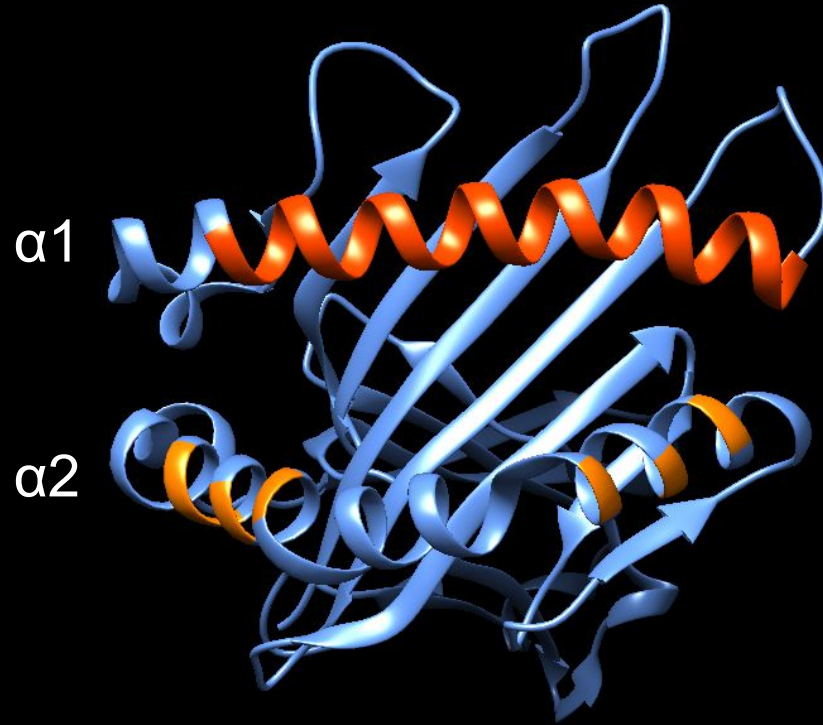


Interaction between MHC I and CD8 visualized with Chimera

**BINDING GROOVE: POCKETS**

## 4. POCKETS

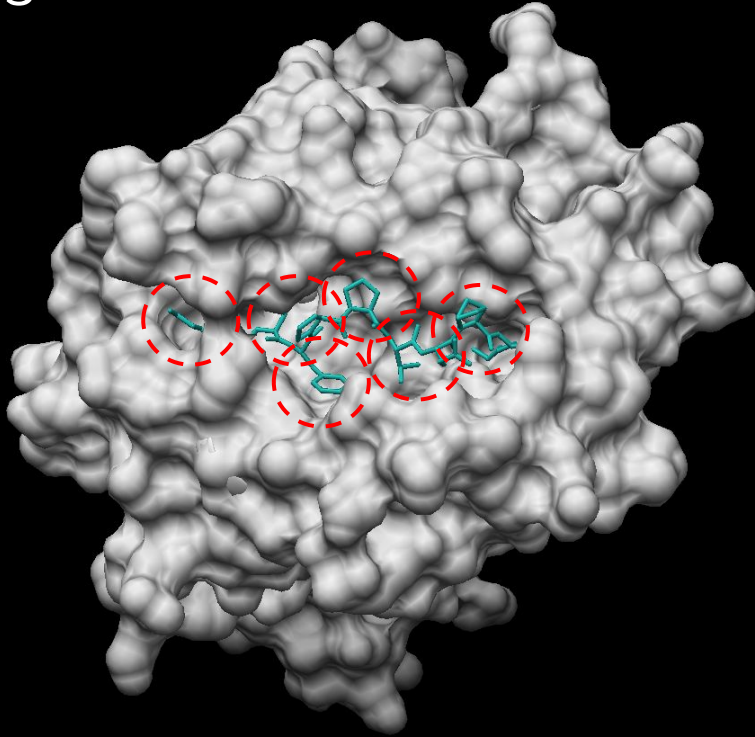
### Binding Groove



Variability between HLA-A, B and C visualized with Chimera

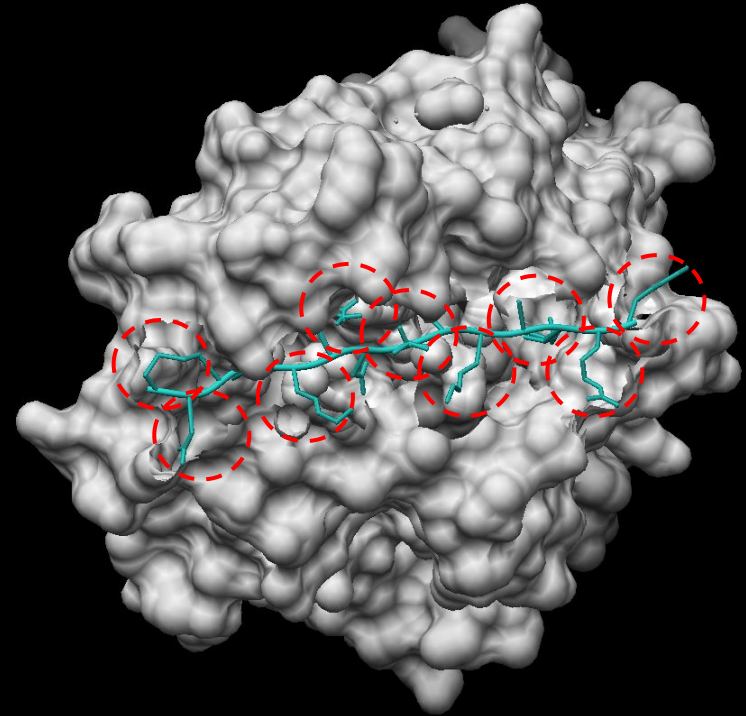
## 4. POCKETS

### Binding Groove



MHC class I: 6 pockets

Visualized with Chimera



MHC class II: 9 pockets

Visualized with Chimera

# 4. POCKETS

## Binding Groove comparison



Superimposition HLA I and HLA II

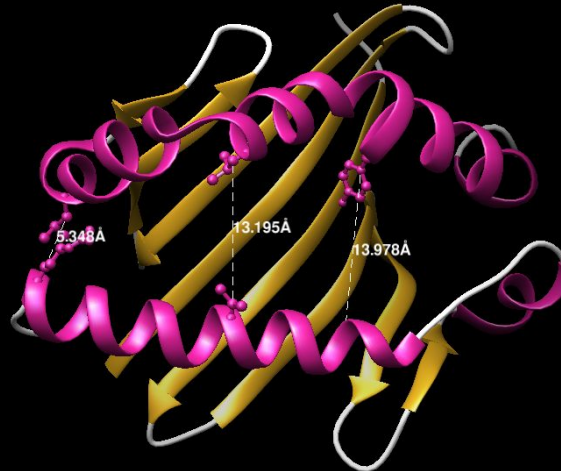
■ HLA I  
■ HLA II

Superimposition made with Stamp and visualized with Chimera



MHC class I

- $\alpha 1$  and  $\alpha 2$
- Closed ends with Tyr
- Peptides of 8-10 aa

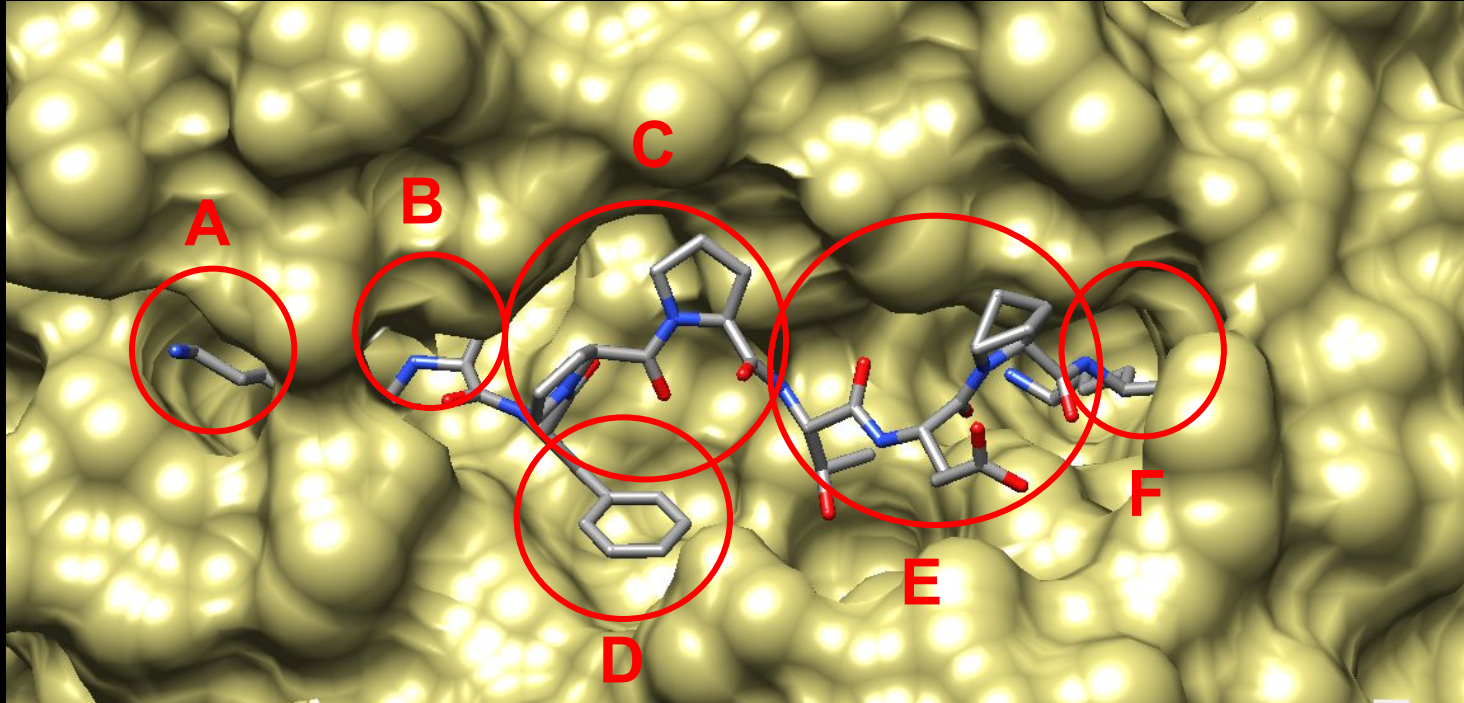


MHC class II

- $\alpha 1$  and  $\beta 1$
- Opened
- Peptides of 12-25 aa

## 4. POCKETS

### Binding Groove MHC I: HLA-A supertype 3



Visualized with Chimera

## 4. POCKETS

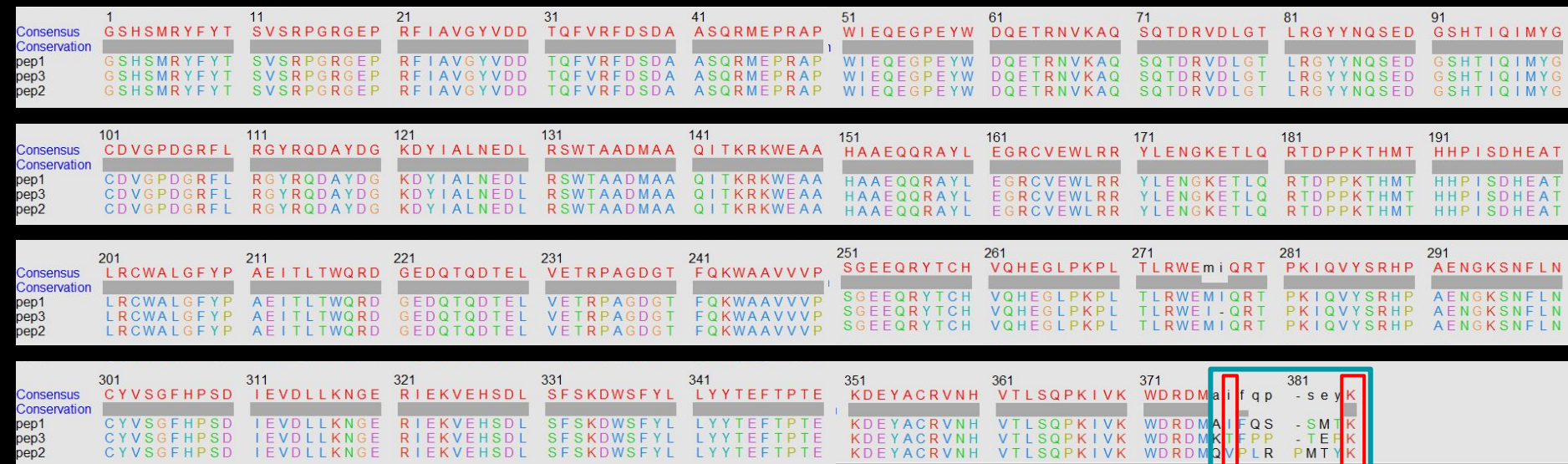
### Binding Groove MHC I: HLA-A supertype 3

| Pocket          | Characteristics                       | Residue                |
|-----------------|---------------------------------------|------------------------|
| Pocket A        | Open nature → broad range of residues | Lys 1                  |
| <b>Pocket B</b> | Small and/or hydrophobic              | Thr 2                  |
| Pocket C        | Open nature → broad range of residues | Pro 4 and Pro 5        |
| Pocket D        | Wide → few restrictions               | Phe 3                  |
| Pocket E        | Open nature → broad range of residues | Thr 6, Glu 7 and Pro 8 |
| <b>Pocket F</b> | Lysine or Arginine                    | Lys 9                  |

# 4. POCKETS

## Binding Groove MHC I: HLA-A supertype 3

| Pocket          | Characteristics                       |
|-----------------|---------------------------------------|
| Pocket A        | Open nature → broad range of residues |
| <b>Pocket B</b> | Small and/or hydrophobic              |
| Pocket C        | Open nature → broad range of residues |
| Pocket D        | Wide → few restrictions               |
| Pocket E        | Open nature → broad range of residues |
| <b>Pocket F</b> | Lysine or Arginine                    |



Structural alignment made with Stamp and visualized with Chimera

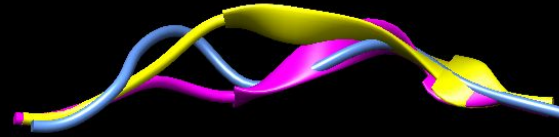
Peptide

Pocket B

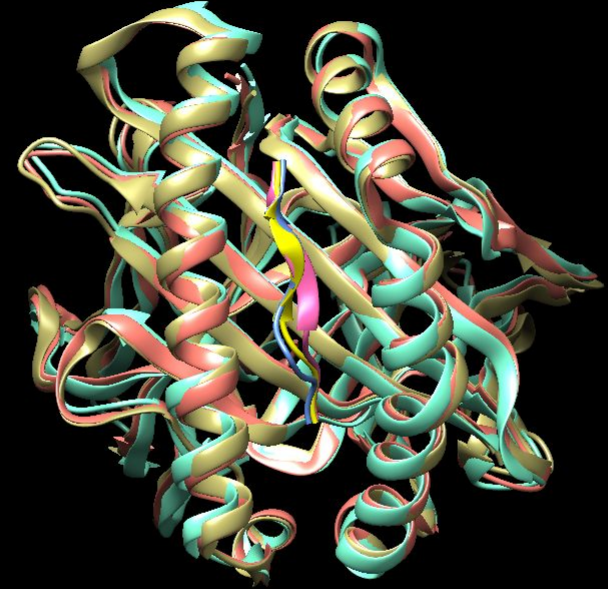
Pocket F

## 4. POCKETS

### Binding Groove MHC I

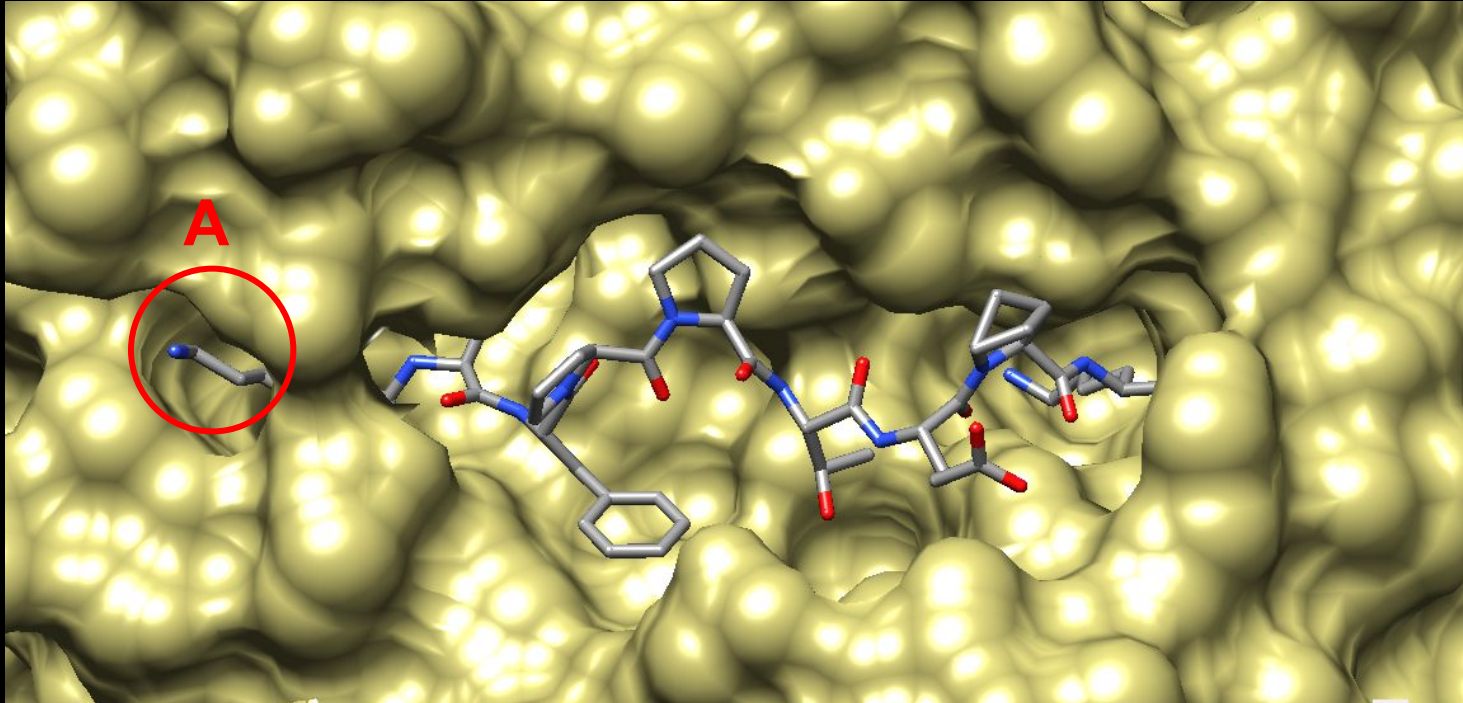


- SNP (Sars nucleocapside peptide)
- Nef (Negative factor)
- RT (Reverse transcriptase)



## 4. POCKETS

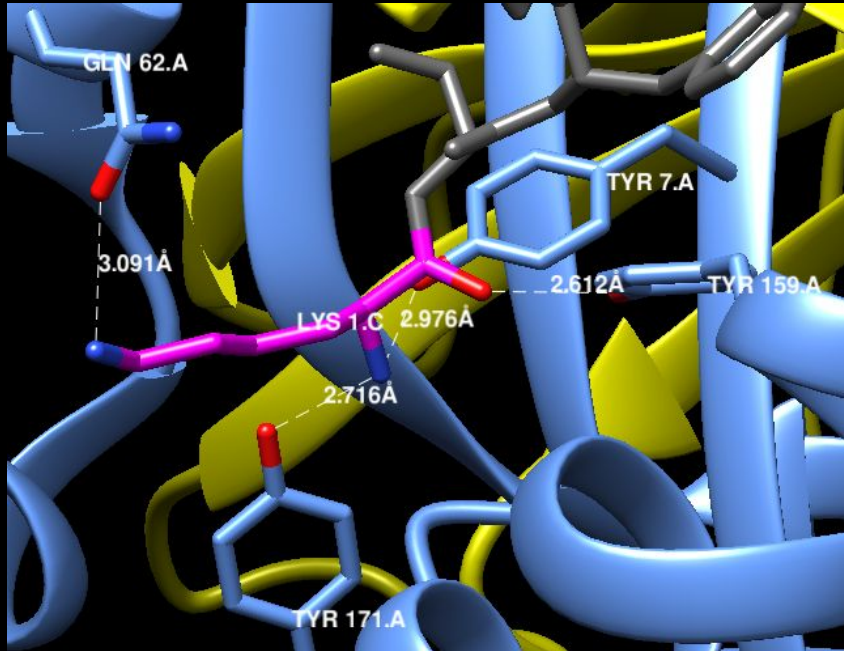
### Binding Groove MHC I: HLA-A supertype 3



Visualized with Chimera

## 4. POCKETS

### Binding Groove MHC I: Pocket A

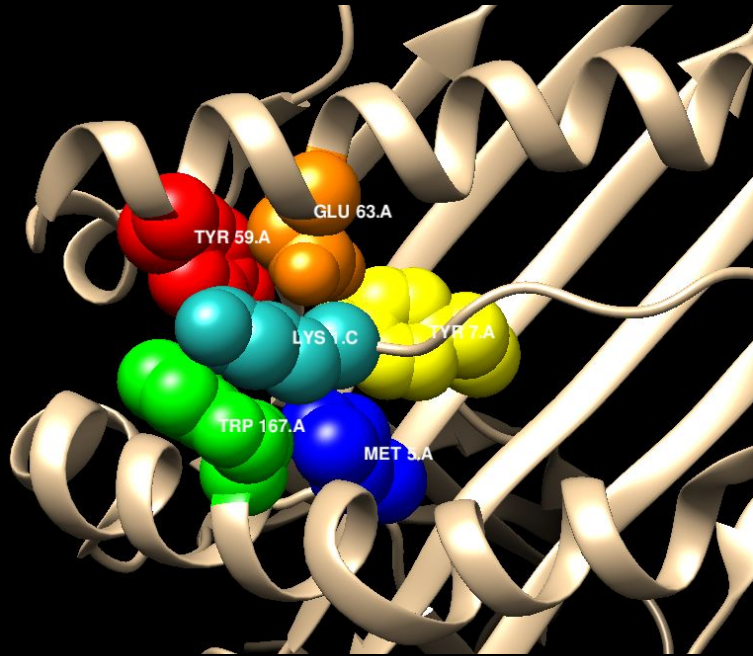


Hydrogen bonds

| Hydrogen Bonds |      |         |      |            |
|----------------|------|---------|------|------------|
| Peptide        | Atom | MHC I   | Atom | Length (Å) |
| Lys 1          | N    | Tyr 7   | OH   | 3          |
|                | N    | Tyr 171 | OH   | 2.7        |
|                | O    | Tyr 159 | OH   | 2.6        |
|                | N ζ  | Gln 62  | O ε  | 3.1        |

## 4. POCKETS

### Binding Groove MHC I: Pocket A

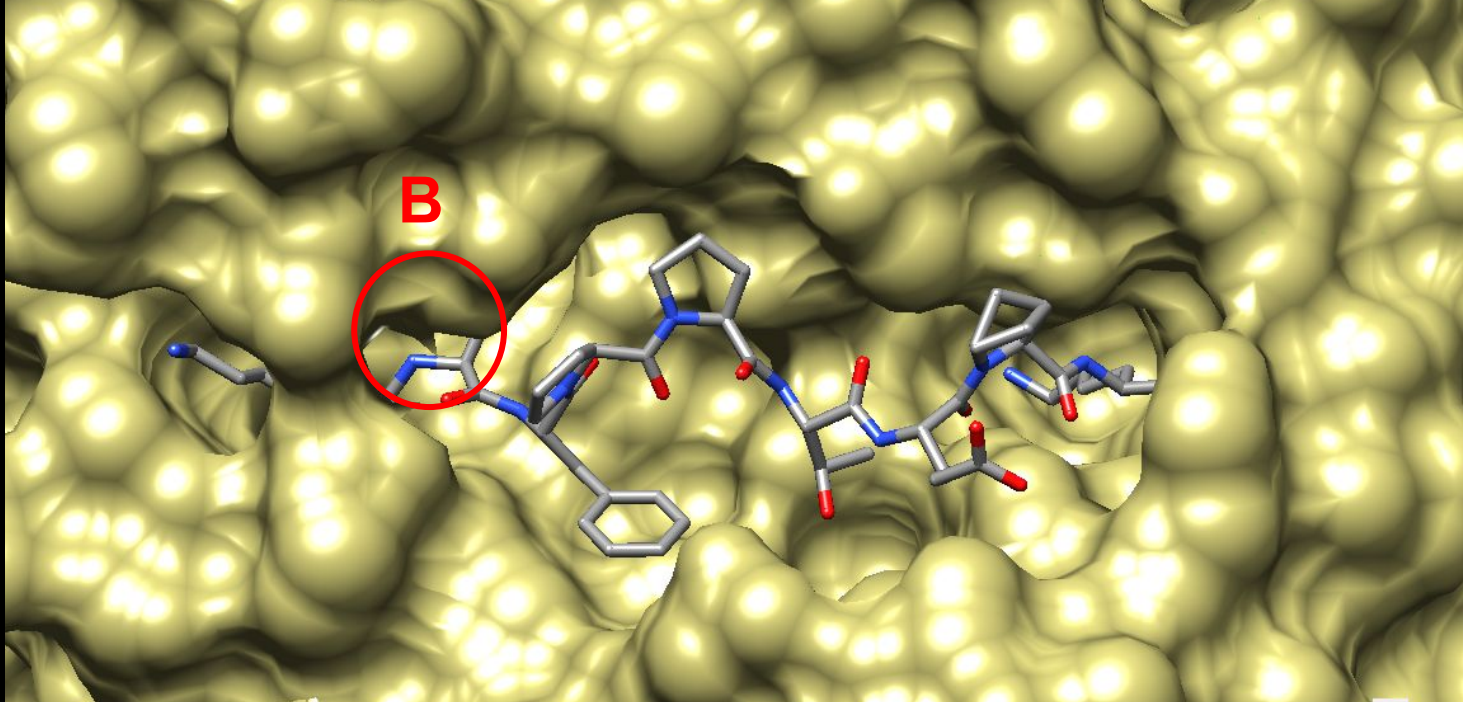


Van der Waals interaction

| Van der Waals |         |
|---------------|---------|
| MHC I         | Peptide |
| Lys 1         | Met 5   |
|               | Tyr 7   |
|               | Tyr 59  |
|               | Glu 63  |
|               | Trp 167 |

## 4. POCKETS

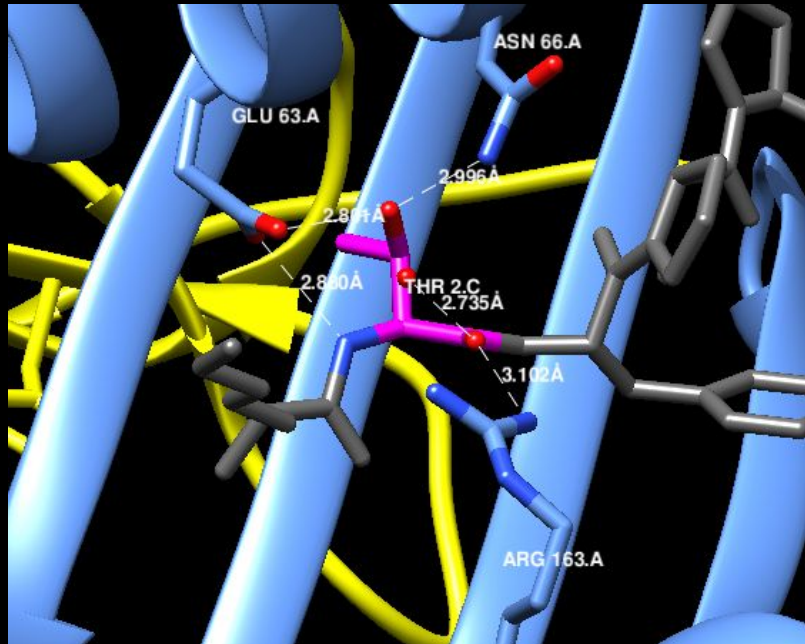
### Binding Groove MHC I: HLA-A supertype 3



Visualized with Chimera

## 4. POCKETS

### Binding Groove MHC I: Pocket B

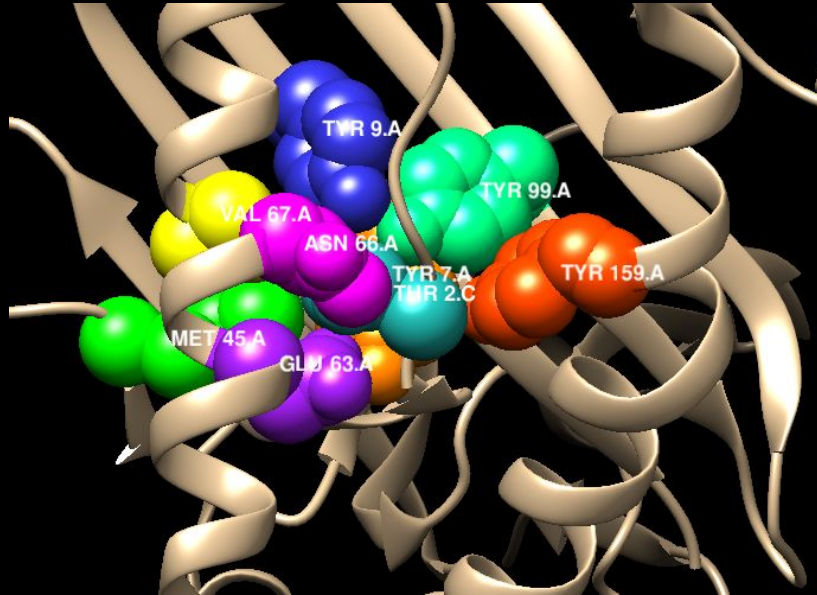


Hydrogen bonds

| Hydrogen Bonds |      |         |      |            |
|----------------|------|---------|------|------------|
| Peptide        | Atom | MHC I   | Atom | Length (Å) |
| Thr2           | N    | Glu63   | Oε1  | 2.9        |
|                | O    | Arg163  | NH2  | 3.1        |
|                | O    | Water 6 | O    | 2.7        |
|                | Oγ1  | Glu63   | Oε1  | 2.8        |
|                | Oγ1  | Asn66   | Nδ2  | 3.0        |

## 4. POCKETS

### Binding Groove MHC I: Pocket B

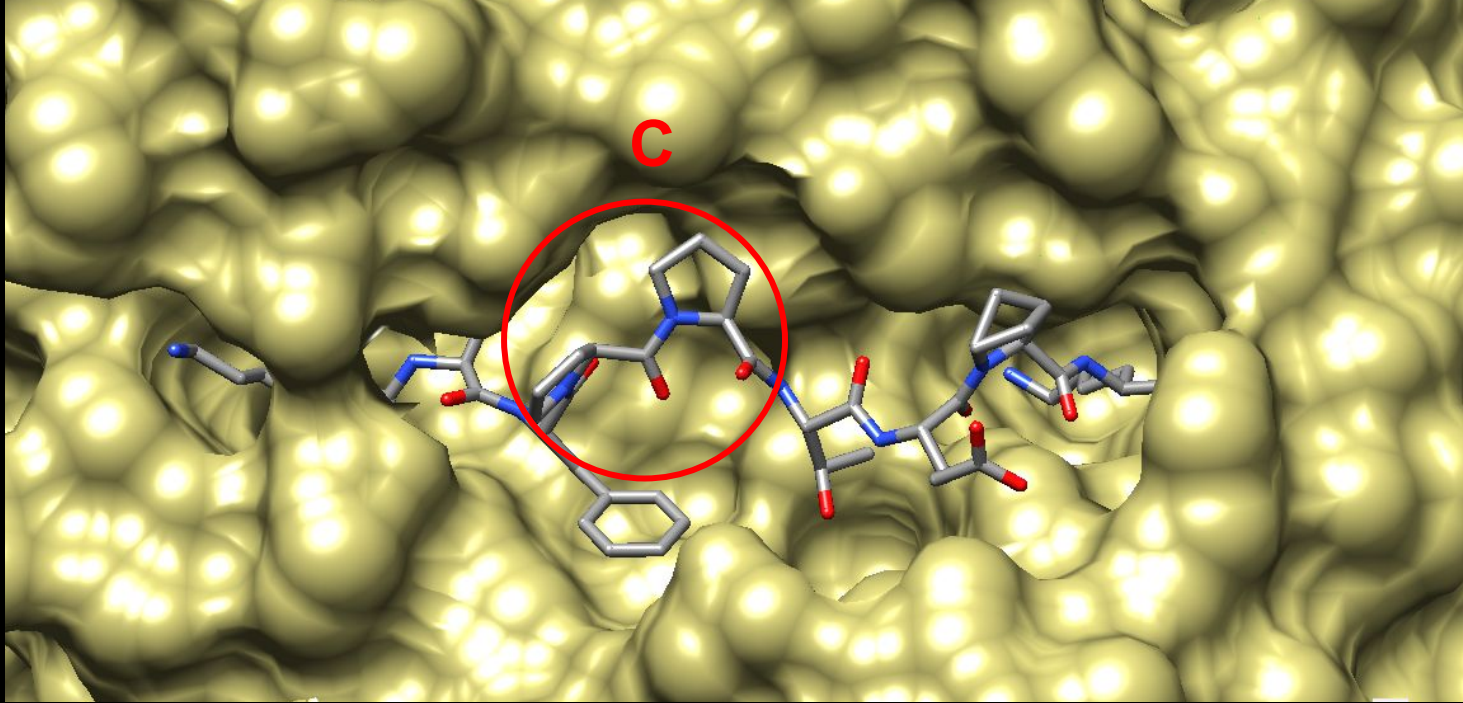


Van der Waals interaction

| Van der Waals |         |
|---------------|---------|
| Peptide       | MHC I   |
| Thr2          | Tyr 7   |
|               | Tyr 9   |
|               | Met 45  |
|               | Glu 63  |
|               | Asn 66  |
|               | Val 67  |
|               | Tyr 99  |
|               | Tyr 159 |

## 4. POCKETS

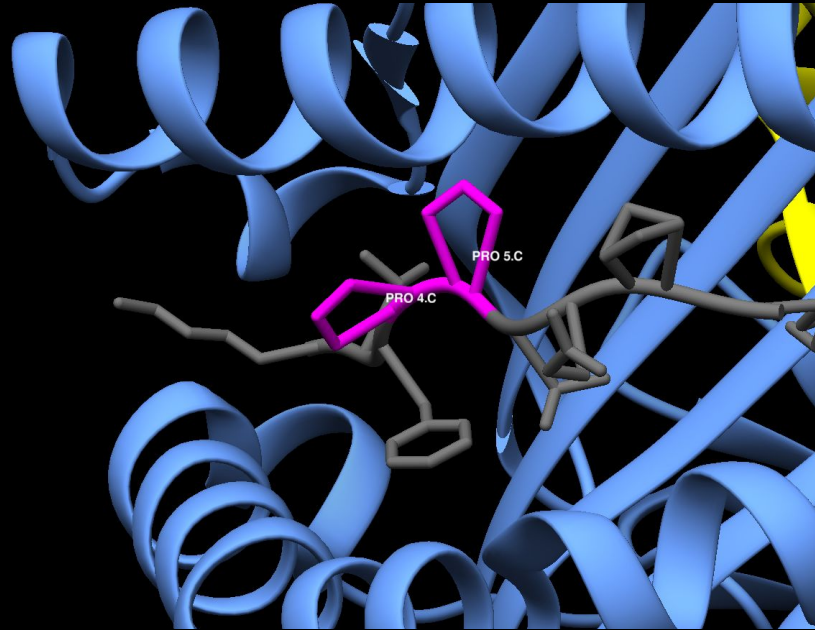
### Binding Groove MHC I: HLA-A supertype 3



Visualized with Chimera

## 4. POCKETS

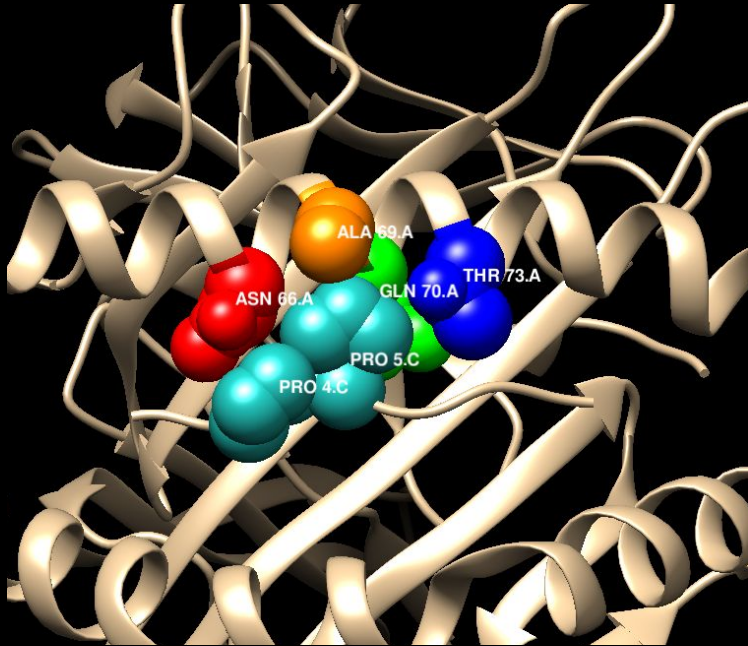
### Binding Groove MHC I: Pocket C



Hydrogen bonds

## 4. POCKETS

### Binding Groove MHC I: Pocket C

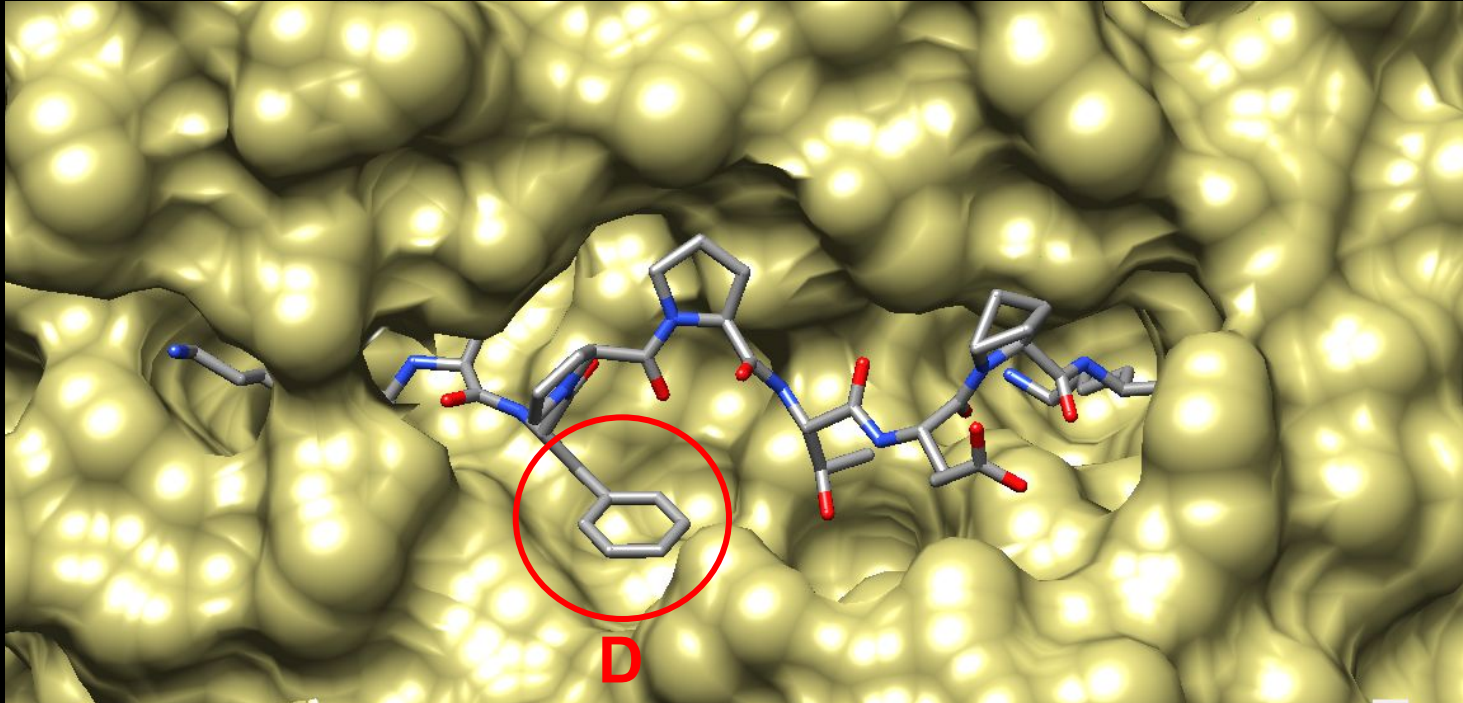


Van der Waals interactions

| Van der Waals |         |
|---------------|---------|
| MHC I         | Peptide |
| Pro 4         | Asn 66  |
| Pro 5         | Asn 66  |
|               | Ala 69  |
|               | Glu 70  |
|               | Thr 73  |

## 4. POCKETS

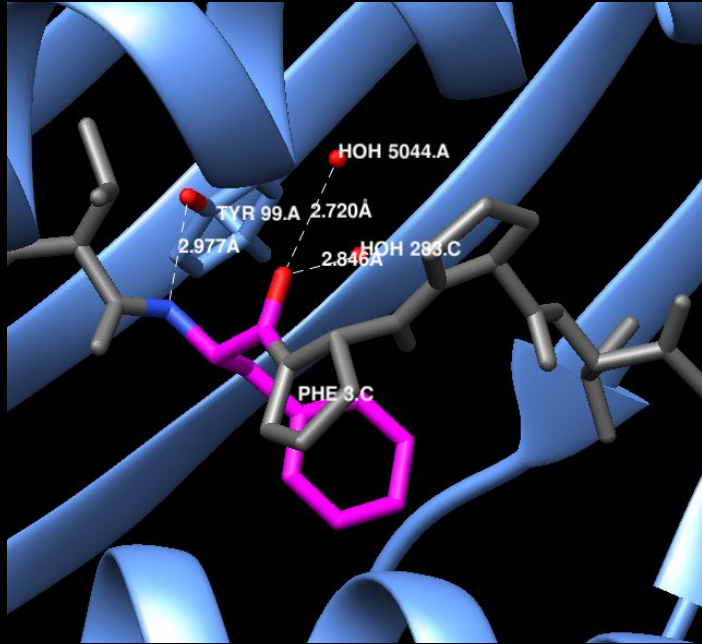
### Binding Groove MHC I: HLA-A supertype 3



Visualized with Chimera

## 4. POCKETS

### Binding Groove MHC I: Pocket D

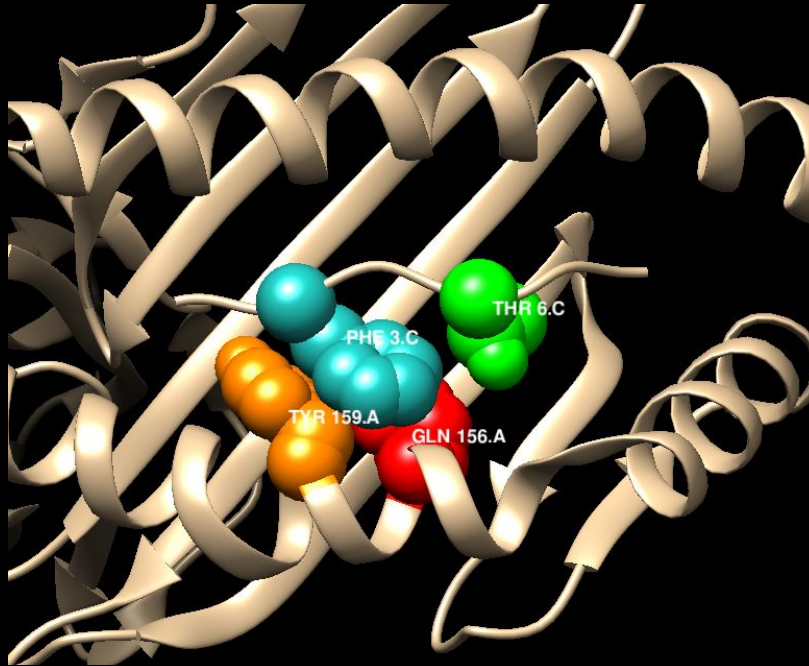


Hydrogen bonds

| Hydrogen Bonds |      |           |      |            |
|----------------|------|-----------|------|------------|
| Peptide        | Atom | MHC I     | Atom | Length (Å) |
| Phe 3          | N    | Tyr 99    | OH   | 3          |
|                | O    | Water 46  | O    | 2.7        |
|                | O    | Water 283 | O    | 2.9        |

## 4. POCKETS

### Binding Groove MHC I: Pocket D

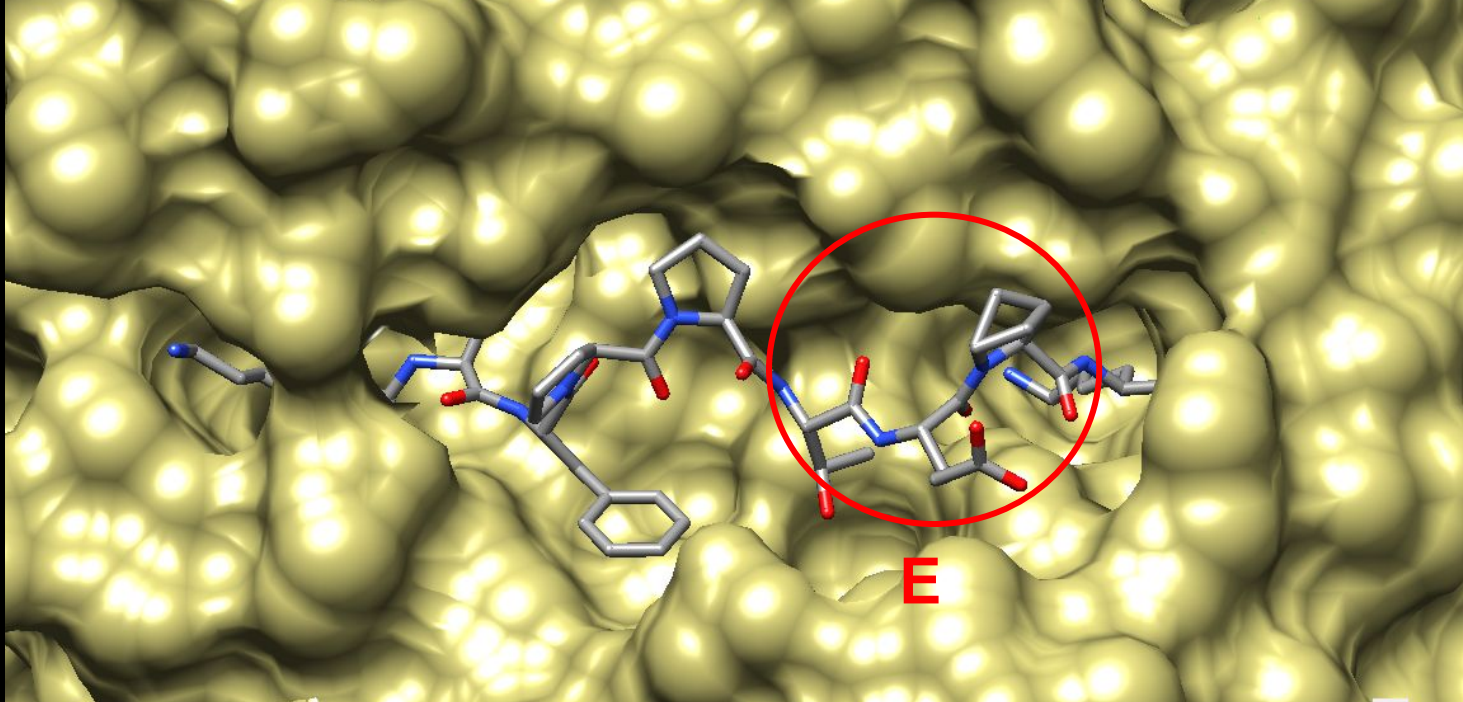


Van der Waals interaction

| Van der Waals |                 |
|---------------|-----------------|
| Peptide       | MHC I           |
| Phe 3         | Gln 156         |
|               | Tyr 159         |
|               | Thr 6 (peptide) |

## 4. POCKETS

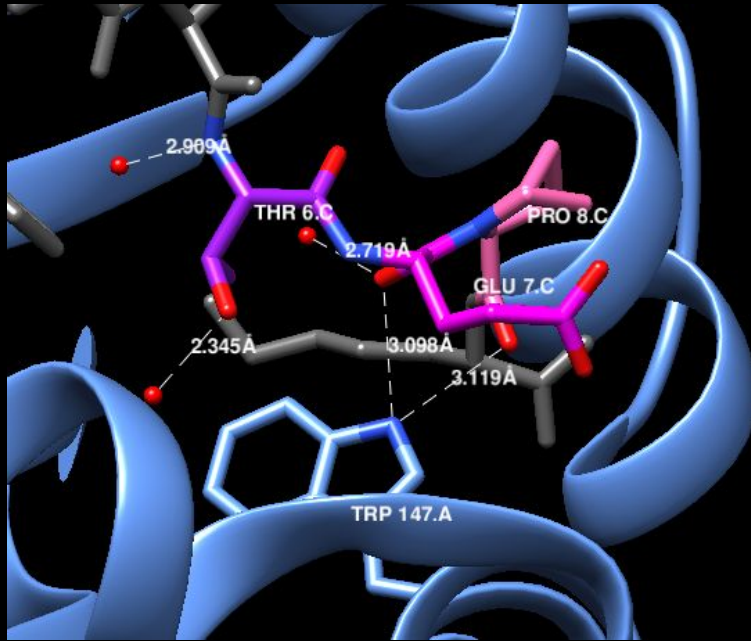
### Binding Groove MHC I: HLA-A supertype 3



Visualized with Chimera

## 4. POCKETS

### Binding Groove MHC I: Pocket E

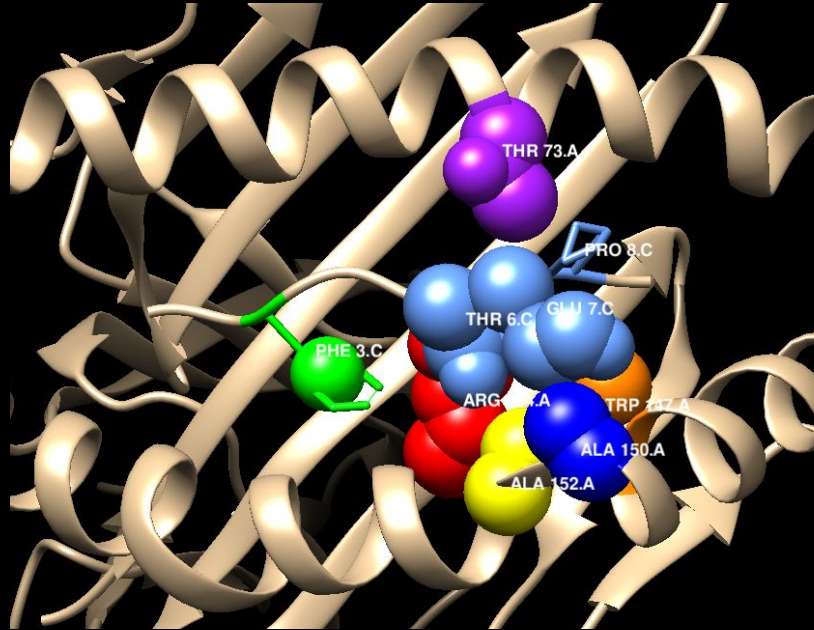


Hydrogen bonds

| Hydrogen Bonds |      |           |      |            |
|----------------|------|-----------|------|------------|
| Peptide        | Atom | MHC I     | Atom | Length (Å) |
| Thr 6          | N    | Water 159 | O    | 2.9        |
|                | O γ1 | Water 391 | O    | 2.3        |
| Glu 7          | O    | Trp 147   | N ε1 | 3.1        |
|                | O    | Water 87  | O    | 2.7        |
| Pro 8          | O    | Trp 147   | N ε1 | 3.1        |

## 4. POCKETS

### Binding Groove MHC I: Pocket E

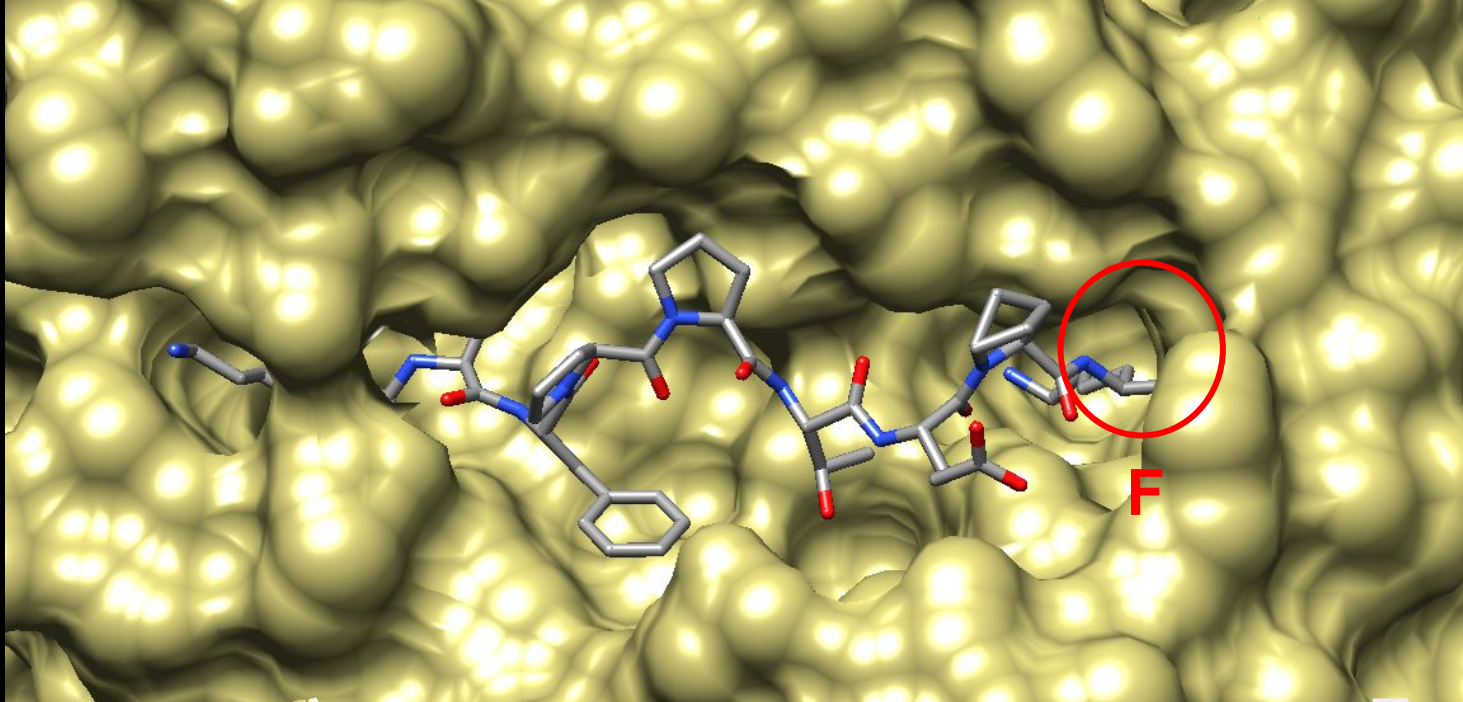


Van der Waals interaction

| Van der Waals |                 |
|---------------|-----------------|
| Peptide       | MHC I           |
| Thr 6         | Arg 114         |
|               | Trp 147         |
|               | Ala 152         |
|               | Phe 3 (peptide) |
| Glu 7         | Trp 147         |
|               | Ala 150         |
|               | Phe 3 (peptide) |
| Pro 8         | Thr 73          |
|               | Trp 147         |
|               | Glu 7 (peptide) |

## 4. POCKETS

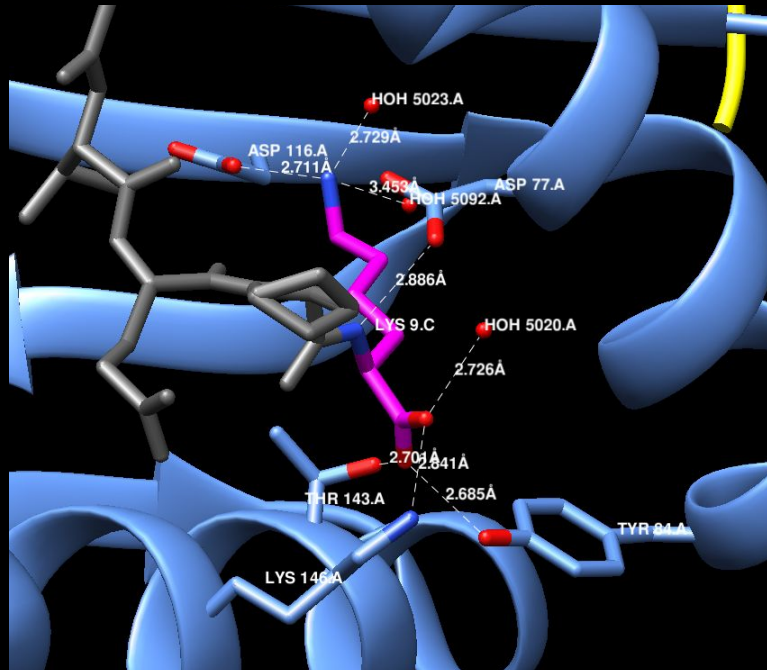
### Binding Groove MHC I: HLA-A supertype 3



Visualized with Chimera

## 4. POCKETS

### Binding Groove MHC I: Pocket F

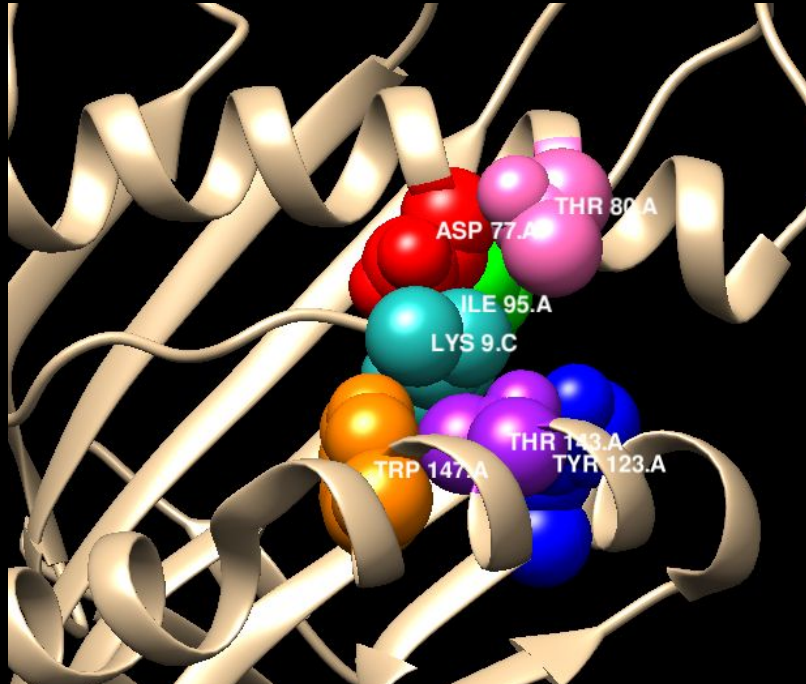


Hydrogen bonds

| Hydrogen Bonds |      |           |      |            |
|----------------|------|-----------|------|------------|
| Peptide        | Atom | MHC I     | Atom | Length (Å) |
| Lys 9          | N    | Asp 77    | O δ1 | 2.9        |
|                | O τ1 | Tyr 84    | OH   | 2.7        |
|                | O τ1 | Thr 143   | O γ1 | 2.7        |
|                | O τ2 | Lys 146   | N ζ  | 2.8        |
|                | O τ2 | Water 16  | O    | 2.7        |
|                | N ζ  | Asp 116   | O δ2 | 2.7        |
|                | N ζ  | Water 19  | O    | 2.7        |
|                | N ζ  | Water 121 | O    | 3.5        |

## 4. POCKETS

### Binding Groove MHC I: Pocket F



Van der Waals interaction

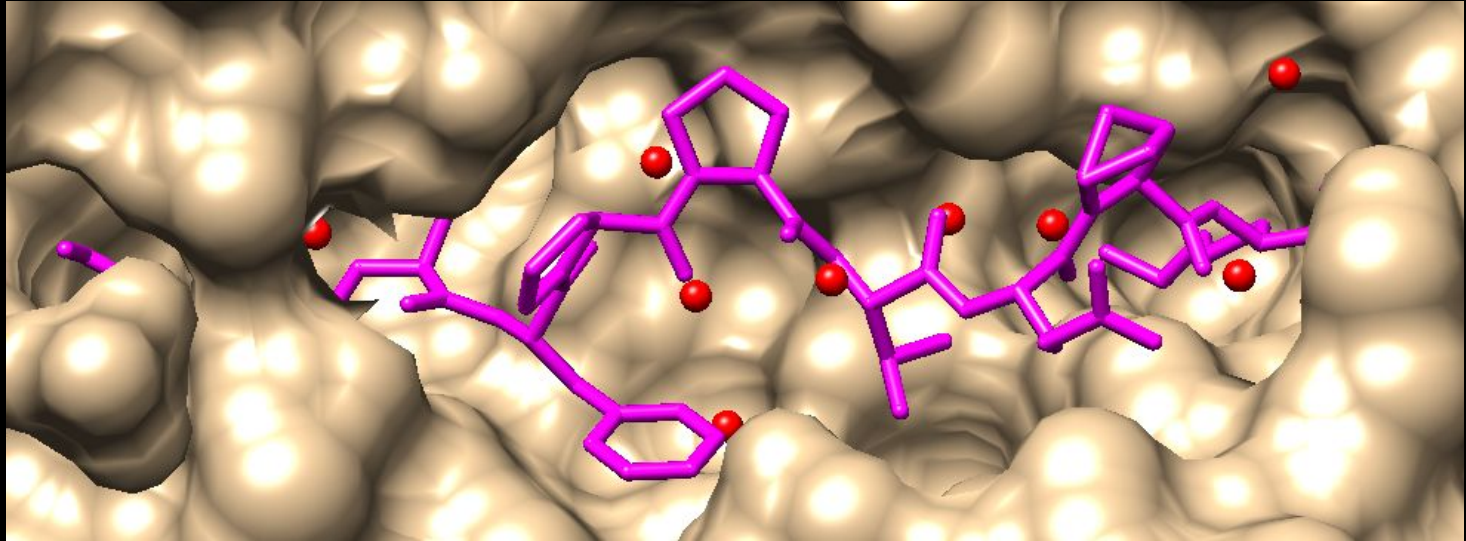
| Van der Waals |         |
|---------------|---------|
| Peptide       | MHC I   |
| Lys 9         | Asp 77  |
|               | Leu 81  |
|               | Ile 95  |
|               | Tyr 123 |
|               | Thr 143 |
|               | Trp 147 |

## 4. POCKETS

### HLA-A\*1101 SNP peptide complex

→ 16 Hydrogen bonds to the alpha chain residues

→ 9 Hydrogen bonds to water molecules

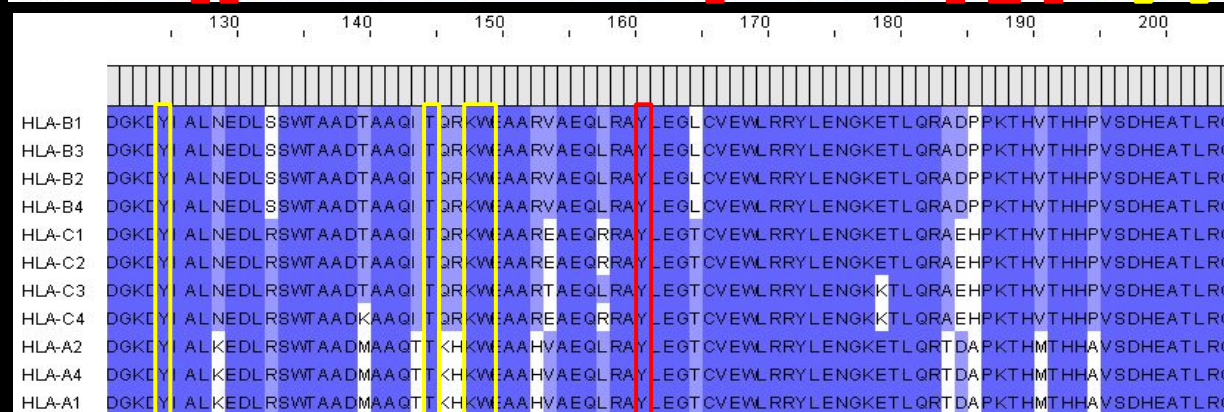
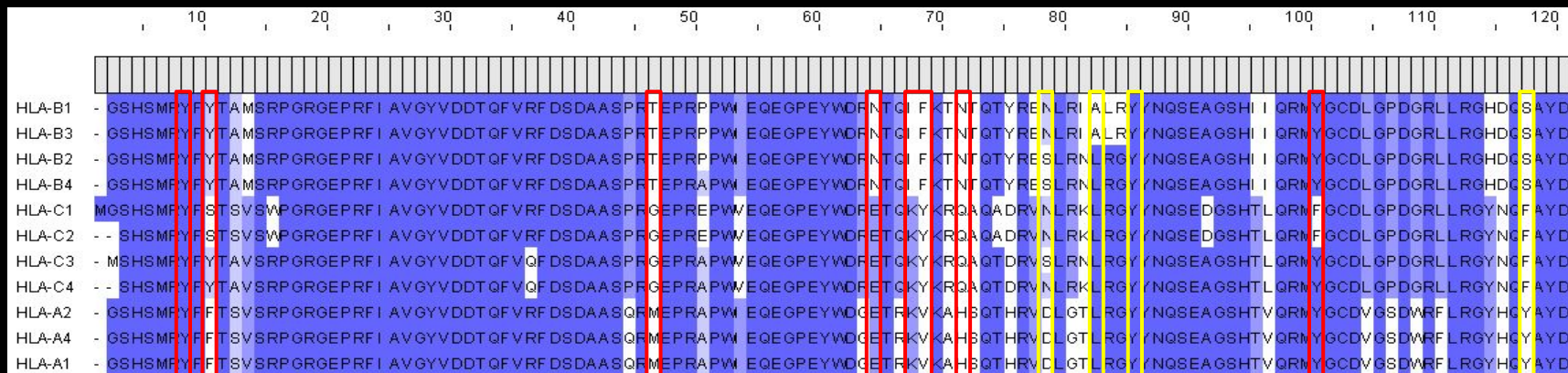


Visualized with Chimera

# 4. POCKETS

## Pockets B and F: HLA-A, HLA-B, HLA-C differences

■ B Pocket  
■ F Pocket



**POCKET B** { TYR 7  
TYR159

**POCKET F** { TYR 84  
TYR 123  
THR 143  
LYS 146  
TRP 147

Sequence alignment made with ClustalW and visualized with Pfadt

# 5. CONCLUSIONS

MHC complex presents foreign peptides to T-Cell receptors to fight potential infections.

## Residue conservation

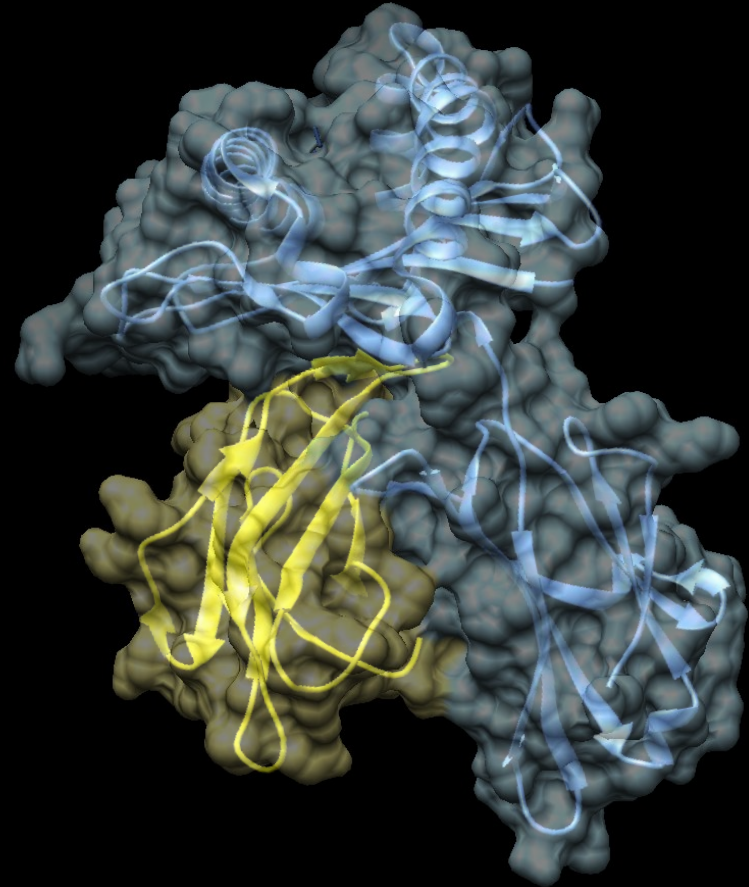
Structure and T-cell receptor interaction maintenance

## Residue variability

Mainly found in the binding groove (pocket B and F).

→ Detecting and fighting against any kind of danger

Polymorphism implies higher probability of immune surveillance



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A 3D surface model of the Major Histocompatibility Complex (MHC) is shown against a black background. The complex is composed of several subunits, with some colored in light blue and others in yellow. A small blue ribbon structure, representing an antigen, is visible within the binding groove of one of the blue subunits. The text 'MHC: Major Histocompatibility Complex' is overlaid in large white font.

# MHC: Major Histocompatibility Complex

*Function determination via structural analysis*

Thank you for your attention!!

# PEM QUESTIONS

1. Choose the correct answer about MHC class I and MHC class II:

- a) The structure of both MHC is identical
- b) The binding groove of MHC class I and MHC class II is formed by the same domains
- c) MHC class II is formed by 3 alpha domains and a B2-microglobulin
- d) The binding groove of MHC I is formed by the domains alpha 1 and alpha 2
- e) All are wrong

2. About HLA-A, HLA-B and HLA-C:

- a) Their sequence shows variability in some positions
- b) Regarding the structure, they are very similar
- c) a and b are correct
- d) The variable region interacts with the peptide
- e) All are correct

3. The MHC I interacts with:

- a) T-cell
- b) CD8
- c) a and b are correct
- d) CD4
- e) All are correct

# PEM QUESTIONS

4. Choose the correct answer about MHC class I and MHC class II binding groove:

- a) The MHC I has a 6 pockets' binding groove
- b) The MHC II has a 9 pockets' binding groove
- c) MHC I can present peptides of 8-10 amino acids
- d) MHC II can present peptides of 12-25 amino acids
- e) All are correct

5. The inner interactions of the MHC I and II are:

- a) Hydrogen bonds
- b) Disulphide bonds
- c) a and b are correct
- d) Van der Waals
- e) All are correct

6. Regarding the evolution of the MHC:

- a) MHC class I and MHC class II have evolved in the same way
- b) The human HLA-A is more similar to the human HLA-B than to the chimpanzee's MHC-A
- c) Alpha and beta chains present an orthologous relationship among distantly related mammals
- d) In the MHC I evolution, monkeys are apes and present MHC-C
- e) All are wrong

# PEM QUESTIONS

7. Regarding MHC classification:

- a) Both MHC I and MHC II have 3 classical subtypes and 3 non-classical subtypes
- b) HLA-A, HLA-B, HLA-C are non-classical subtypes of the MHC I
- c) HLA-DP, HLA-DQ, HLA-DR are classical subtypes of the MHC II
- d) HLA-E, HLA-F, HLA-G are classical subtypes of the MHC I
- e) HLA-DO, HLA-DM are classical subtypes of the MHC II

8. The secondary structure:

- a) MHC-I is formed by an alpha chain and a beta chain
- b) MHC II is formed by an alpha chain and a beta chain
- c) Both MHC I and MHC II have a microglobulin domain
- d) MHC II only has 1 cytoplasmic domain
- e) All are correct

9. In the MHC I binding groove:

- a) Pocket B and F are the most important ones for the peptide presentation
- b) All pockets can interact with a huge amount of residues
- c) All pockets have a really selective peptide nature
- d) Pocket F is the less restrictive one
- e) Pocket A is the most restrictive one

# PEM QUESTIONS

10. Regarding Major Histocompatibility complex evolution:

- a) Residue conservation and variability are crucial for MHC function
- b) MHC polymorphism enables the presentation of a wider range of peptides
- c) a and b are correct
- d) No residue variability is present in MHC
- e) All are correct