

# Simulation of Major Histocompatibility Complex (MHC) Structure and Peptide Loading into an MHC Binding Pocket with Teachers' Hands

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## Abstract

Molecular understanding of three-dimensional (3D) peptide: MHC models require both basic knowledge of computational modeling and skilled visual perception, which are not possessed by all students. The present model aims to simulate MHC molecular structure with the hands and make a profound impression on the students.

**Keywords:** Binding pocket, Hand, MHC molecules, Physical model using hands, Simulation

Currently, lecturers can use many instructional models to enhance teaching of molecular structures to undergraduate students. However, we sometimes find it necessary to present an immunological concept with a touchable model to create a more understandable and profound image than can be found in books. The realization of paratope-epitope interaction with both hands and an apple is one example of this simulation in immunology teaching (1). MHC class I and II structures and MHC peptide-loading compartments are considered to be fundamental concepts in immunology. Molecular understanding of 3D peptide: MHC models require both basic knowledge of computational modeling and skilled visual perception, which are not possessed by all audiences. However, no models are more accessible, efficient, and affordable than teachers' hands. This simulation aims to simplify perception of MHC molecular structures and provide an enduring image of MHC-peptide interactions.

### *Simulation of MHC class I structure and its peptide loading compartment*

To imitate MHC class I structure with the hands, bend the index, middle, and ring fingers toward the palm and then touch the thumb with the little finger as shown in Fig. 1. The three bent fingers and the

connected thumb and little finger simulate the pair of parallel  $\alpha$ -helices that form the peptide binding groove. One helix belongs to the  $\alpha 1$  domain and the other to the  $\alpha 2$  domain. The palm represents the beta-pleated sheet structure, which forms the base of the groove. The narrow groove between the bent and connected fingers represents the peptide-loading compartment. A flexible rod inserted into this groove can be imagined as an antigenic peptide located in the closed groove of the MHC class I molecule. The rod must bend in the middle to simulate the loaded peptide. Introduce your left hand to the students as an  $\alpha$ -chain of MHC class I structure, which is encoded on chromosome 6 in humans. Then, introduce your watch as a  $\beta 2$ -microglobulin chain that is non-covalently associated with the  $\alpha$ -chain and encoded on chromosome 15 in humans. It should be emphasized that the polypeptide chains are encoded by genes on different chromosomes. The MHC class I  $\alpha$ -chain is inserted into the cell membrane, indicated by the shirt sleeve in our simulation (2, 3).

### *Simulation of MHC class II structure and its peptide loading compartment*

To demonstrate MHC class II structure, bend all the fingers of both hands toward the palms and then close both hands from the forearms as shown in Fig. 2. Try

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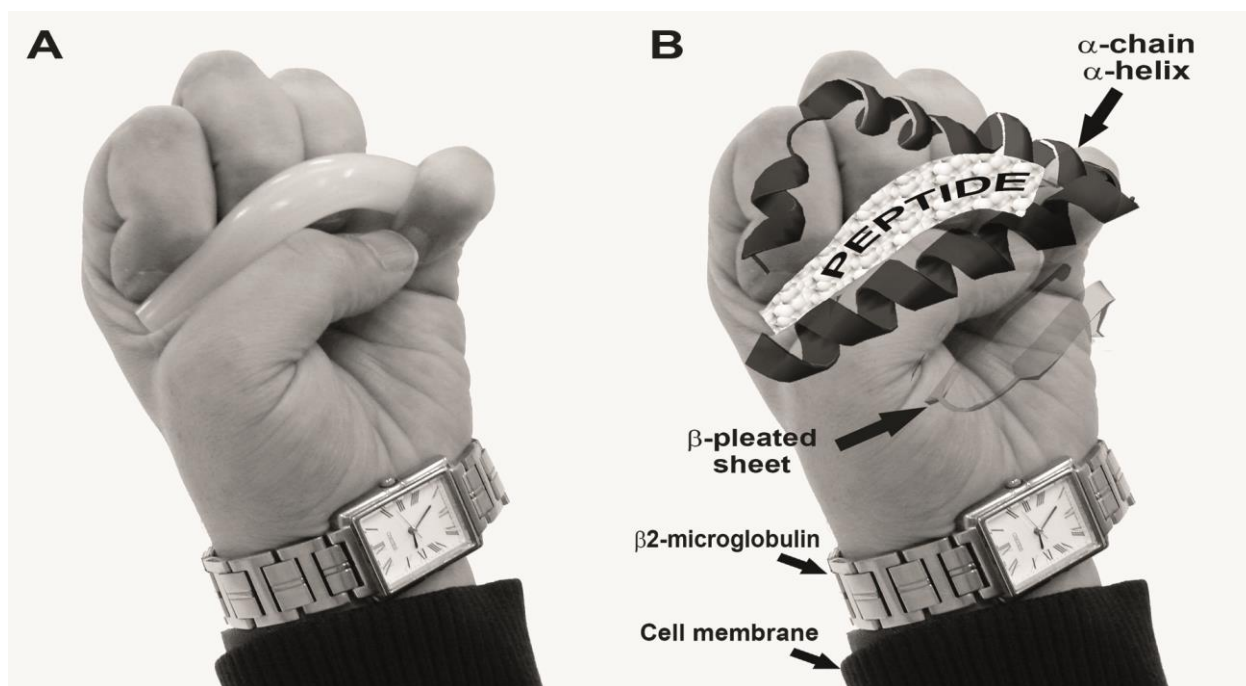
to hide your watch, which represented  $\beta$ 2-microglobulin. The bent fingers and palm of the left hand represent the  $\alpha$ -helix and  $\beta$ -pleated sheet of the  $\alpha$ -chain, respectively (Fig. 2), and the same status could be imagined for the right hand as a  $\beta$ -chain of MHC class II. The open space between the bent fingers of both hands represents the peptide anchoring site, which is an open-ended groove in MHC class II. A flexible rod with overhanging portions projecting from both sides of groove inserted in this space simulates an antigenic peptide that has been located in an open-ended groove of the MHC class II molecule. MHC class II molecules bind peptides of 13-25 amino acids, which is considerably longer than MHC class I-binding peptides of 8-11 amino acids. The two chains of MHC class II molecules are inserted into the cell membrane, represented by the shirt sleeves in our simulation. In this simulation, the two chains of the MHC class II molecules are represented by the two hands, while the MHC class I molecule was modeled by a hand and a watch. This is a good time

to remind the students that both chains of MHC class II molecules, in contrast to class I molecules, are encoded by the MHC gene cluster on chromosome 6 in humans, and that the two chains associate non-covalently (2, 3).

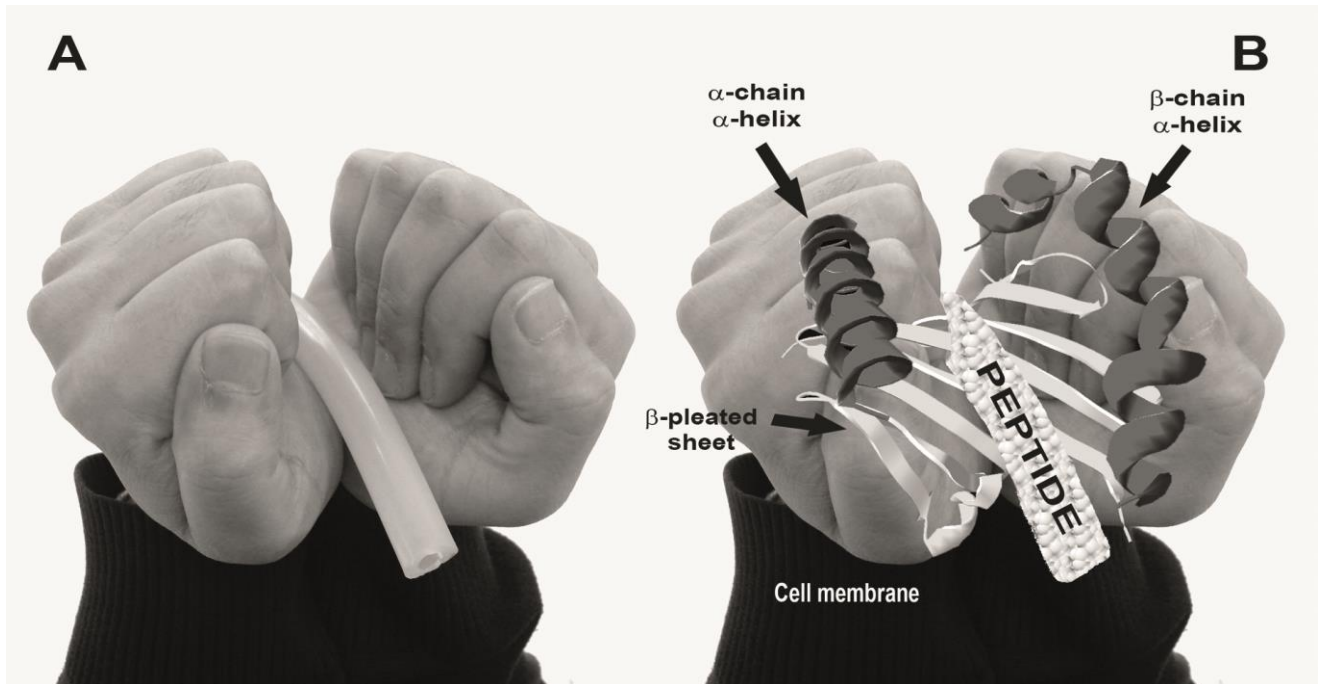
Certainly, some MHC structural features are not completely duplicated with this model, but this visualization of a molecular structure makes a profound impression on the students.

## References

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**Fig. 1.** Simulation of MHC class I structure and its peptide loading compartment (A). In B this simulation has been superimposed with two  $\alpha$ -helices and a beta-pleated sheet of the  $\alpha$ -chain from a 3D view of human class I MHC HLA-A2 (3PWJ).



**Fig. 2.** Simulation of MHC class II structure and its peptide loading compartment (A). This simulation has been superimposed with two  $\alpha$ -helices and two beta-pleated sheets of  $\alpha$ -chain and  $\beta$ -chain from the crystal structure of HLA-DR1 (3PDO) (B).