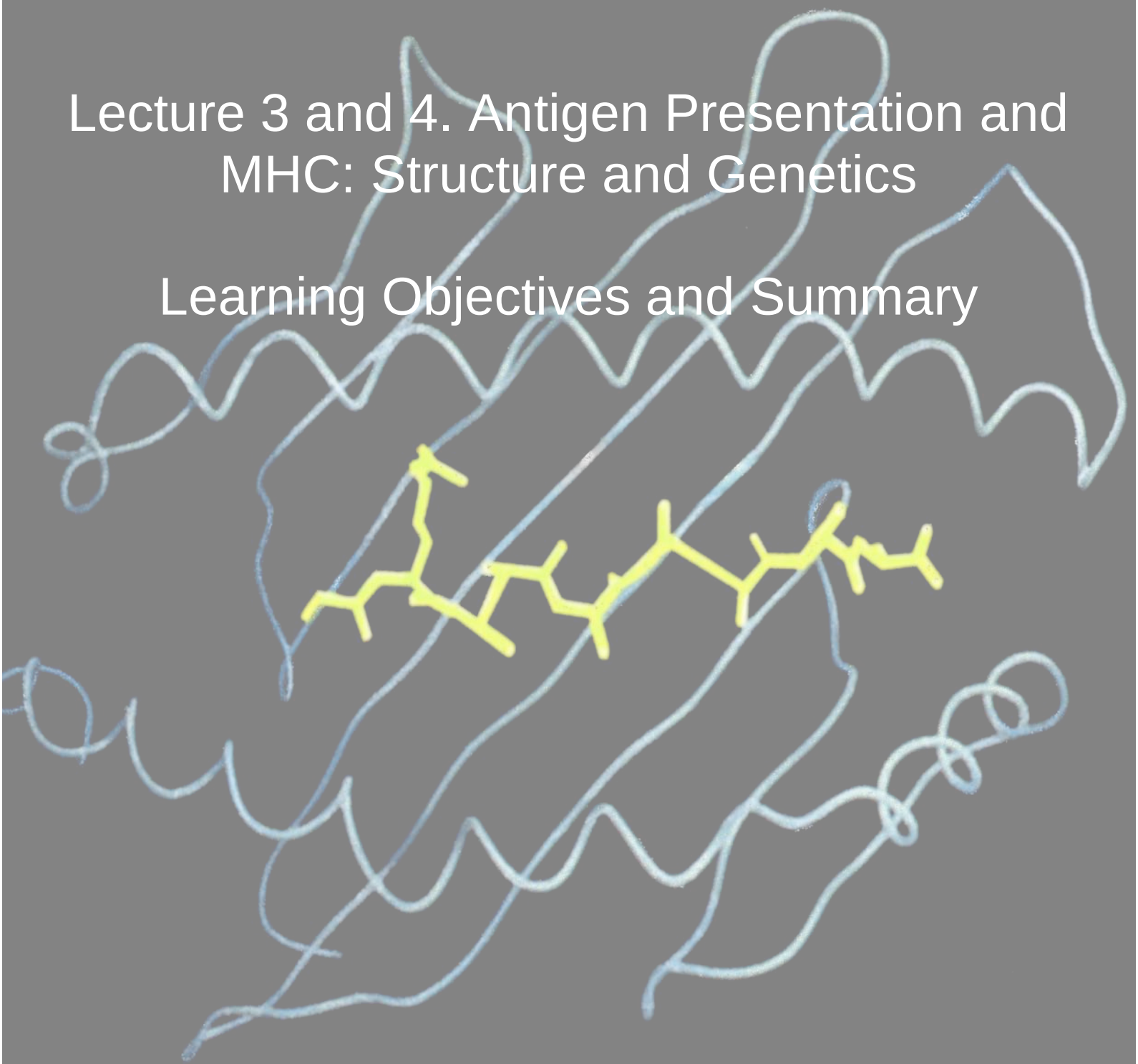
Lecture 3 and 4. Antigen Presentation and MHC: Structure and Genetics

Learning Objectives and Summary



Lectures 3 and 4. Antigen presentation and MHC: Structure and genetics

Learning objectives:

1. Understand how T cells recognize antigen and that the diversity of the peptides to be recognized requires an enormous repertoire of different T cell clones, distinguished by receptors of different specificity that react with MHC and peptide.
2. Understand that in order to prevent microbial pathogens mutating around a static antigen presenting MHC, the evolutionary strategy is to evolve many alternative MHC molecules that bind different peptides.
3. Appreciate that T cell clones specific for pathogen peptides must be developed before the individual encounters the pathogen and that the solution to this problem is the use of self-peptides as surrogates.
4. Consider that as a consequence of these first three points that a clonal selection process is required to select a different T cell repertoire appropriate for each individual's combination of MHC genes and self peptides, immunologic self.
5. Understand the two types of challenges pathogens present to the adaptive immune system, how each type of pathogen peptide is routed to either class I or class II, the different molecular mechanisms used to accomplish pathogen peptide recognition and pathogen elimination in different immune responses.
6. Appreciate the structure of class I and II MHC molecules, how they are genetically encoded, how they are expressed and how their polymorphisms enables them to bind different peptides.
7. Be able to explain how the T cell responses differ in two unrelated individual with different MHC genes that are responding to the same viral infection

SUMMARY

1. Later during an immune response these same T cells recognize "not quite self"/non self peptides presented on these MHC molecules and then clonally expand

2. MHC molecules are codominantly expressed, with class I molecules found on the surface of all nucleated cells and class II molecules on professional antigen presenting cells

3. The alleles of the MHC genes specify different amino acids in MHC pockets that bind peptide side chains, and this confers specificity on MHC molecules to bind different peptides

4. As a consequence individuals vary markedly in what particular peptides the T cell recognizes

5. During development ~16 T cell repertoires are separately selected on self-peptides presented by 3 types of class I and 3 types of class II MHC molecules

6. The presence of a “not quite self”/non self peptide on a MHC class I molecule renders the cell a target of a cytotoxic CD8 T cell, while a peptide in a class II molecule evokes macrophage activation and B cell help

7. Class I and class II MHC molecules differ markedly in the details of how they bind peptides and the biochemical pathways the peptides take to be loaded on the MHC. These differences assure that the correct CD4 or CD8 adaptive immune response is made to a peptide

8. The fact that class I MHC molecules bind the CD8 molecule and class II MHC molecules bind the CD4 molecules assists in the discrimination