# IMMUNOLOGY

http://www.lehigh.edu/~sk08/Courses/Bios328/mainpage.htm

# Immunogen, antigen, epitope, hapten

- Immunogen:  a stimulus that produces a humoral or cell-mediated immune response
- Antigen: any substance that binds specifically to an antibody or a T-cell receptor

Immunogen, antigen, epitope, hapten

- All immunogens are antigens but not all antigens are immunogens
  - Some very small molecules called haptens can bind to Ab's or TCR's but they cannot initiate an immune response…

# Immunogen, antigen, epitope, hapten

- Immunogen:  a stimulus that produces a humoral or cell-mediated immune response

- Antigen: any substance that binds specifically to an antibody or a T-cell receptor

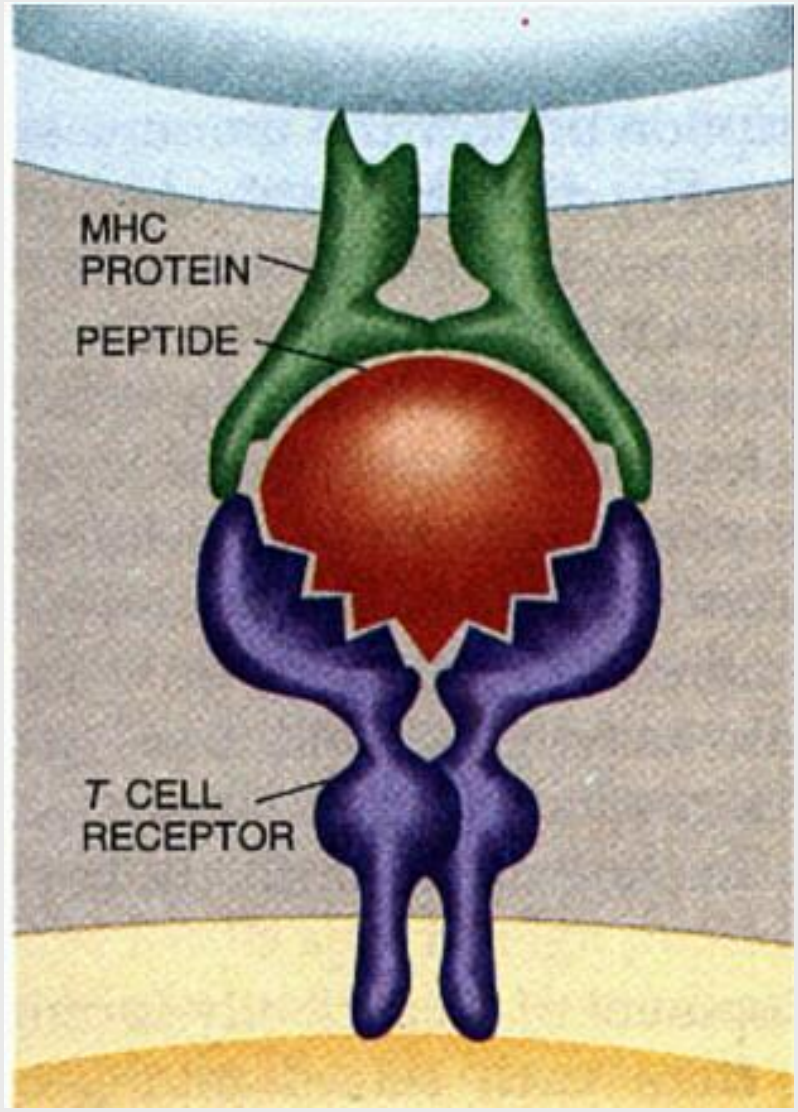
- Epitope: the portion of an antigen that is recognized and bound by an Ab or TCR/MHC complex (aka antigenic determinant)

- Hapten: a low molecular weight molecule that can be made immunogenic by conjugation to a suitable carrier

Immunogen, antigen, epitope, hapten

- Paratope…
- Paratope: “The site in the variable (V) domain of an antibody or T-cell receptor that binds to an epitope on an antigen

# The key event…



# The basis of immunogenicity…

- Foreignness
- Molecular size
- Chemical composition and heterogeneity
- Degradability

# The key event…

A processed antigen in an MHC is seen by a TCR.

The TCR asks the MHC, “Are you me?” and receives an affirmative answer, “Yes.”

The TCR asks the processed antigen, “Are you me?” and receives the negative answer, “No!”

Thus, the processed antigen is seen as “not-self,” *i. e.,* “foreign.”

# The key event…

A processed antigen in an MHC is seen by a TCR. This "viewing" occurs in the ***ternary complex.***

The TCR asks the MHC, "Are you me?" and receives an affirmative answer, "Yes." Here the TCR looks at the MHC ***histotope.***

The TCR asks the processed antigen, "Are you me?" and receives the negative answer, "No!" Here the TCR uses its ***paratope*** and looks at the ***epitope.***

# The key event…

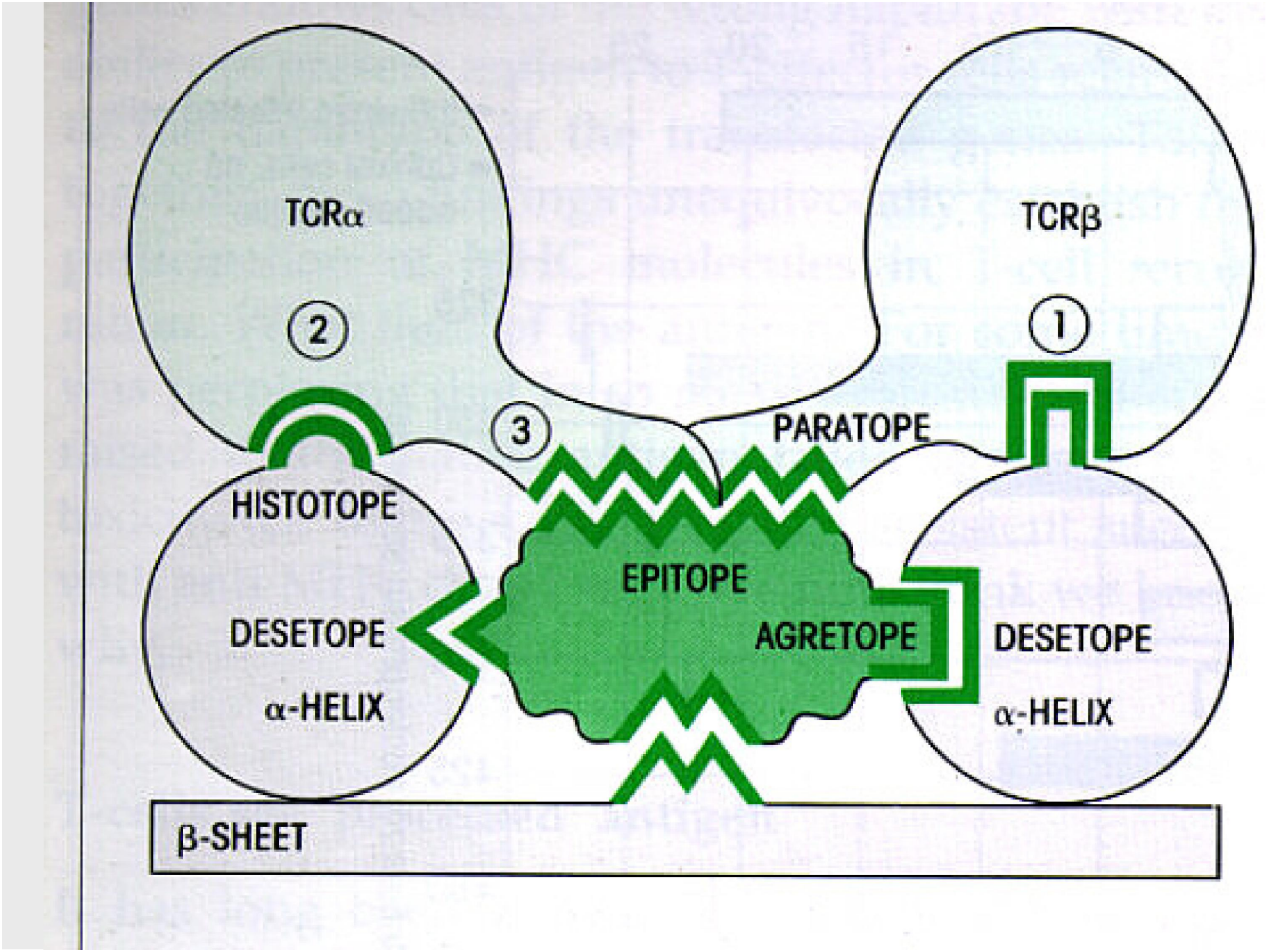
A processed antigen in an MHC is seen by a TCR.

The TCR asks the MHC, “Are you me?” and receives an affirmative answer, “Yes.”

The TCR asks the processed antigen, “Are you me?” and receives the negative answer, “No!”

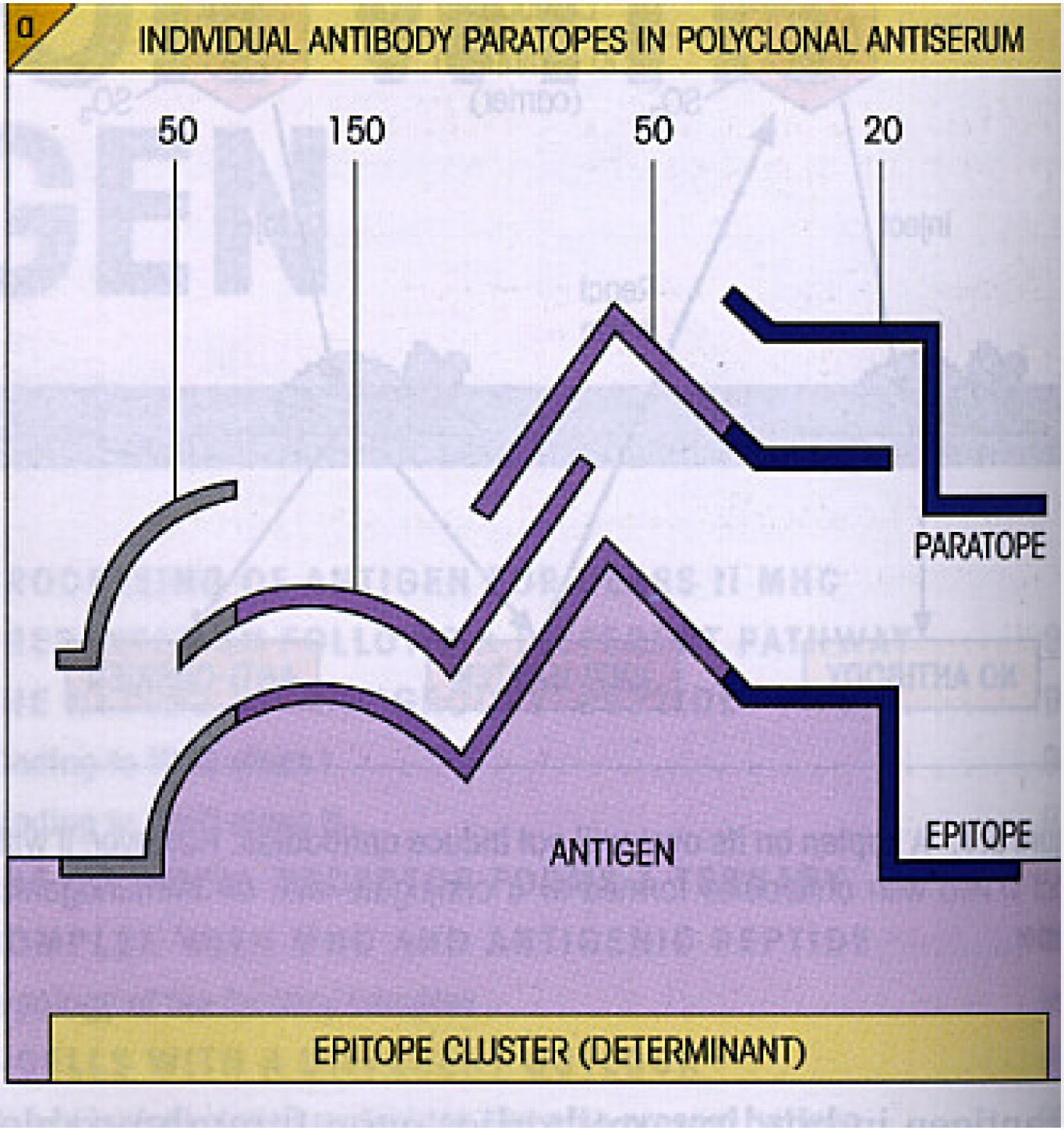
But what if the TCR asks the processed antigen, “Are you me?” and receives the answer, “Yes.” TCR’s which can see “self” are *eliminated* in a process called clonal deletion.

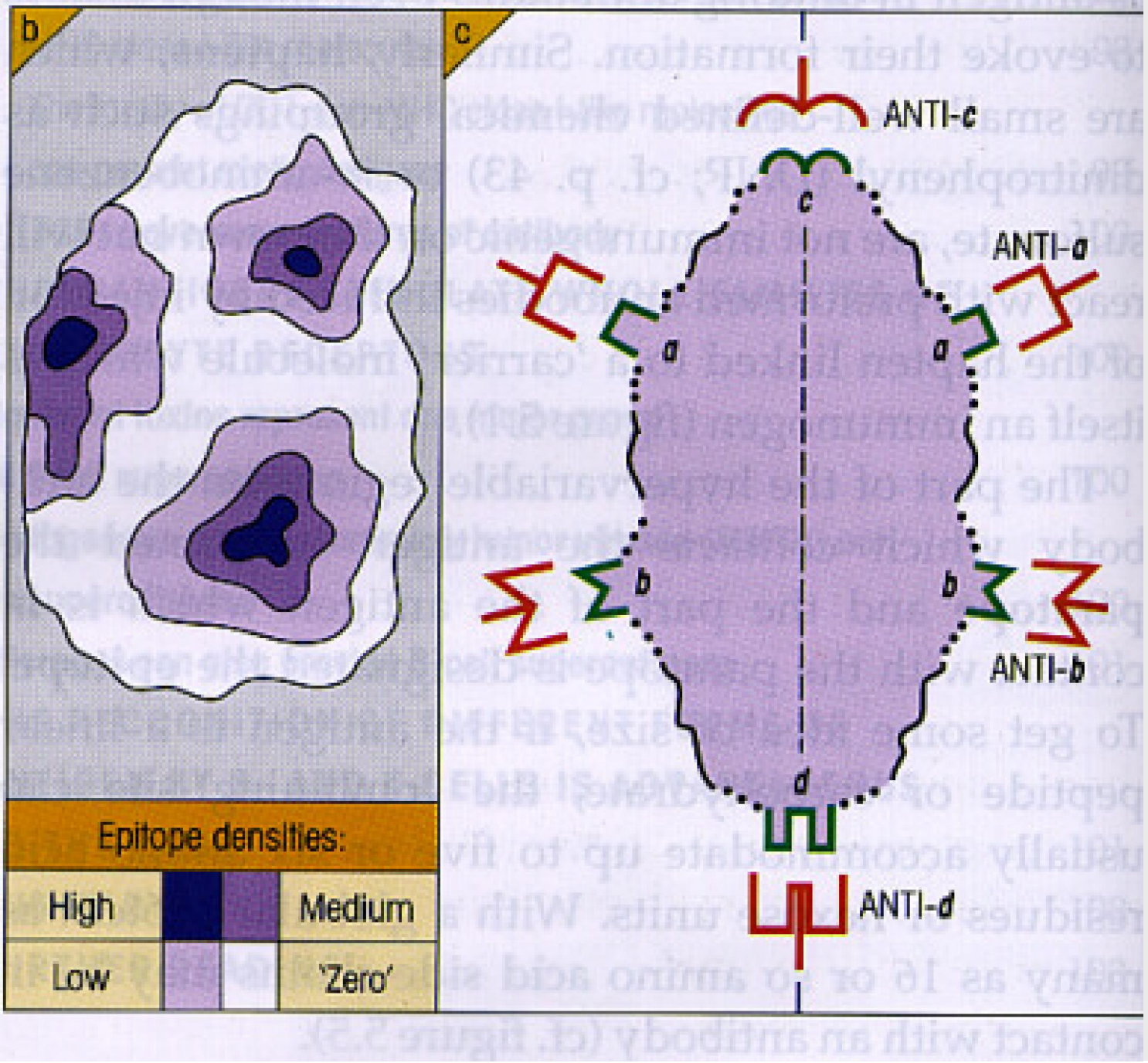
Clonal deletion assures that TCR’s don’t see “self.”


TCRα
TCRβ
2
1
3
PARATOPE
HISTOTOPE
EPITOPE
DESETOPE
AGRETOPE
DESETOPE
α-HELIX
α-HELIX
β-SHEET

# The basis of immunogenicity…

- Foreignness
- Molecular size
- Chemical composition and heterogeneity
- Degradability


a
INDIVIDUAL ANTIBODY PARATOPES IN POLYCLONAL ANTISERUM
50
150
50
20
PARATOPE
ANTIGEN
EPITOPE
EPITOPE CLUSTER (DETERMINANT)

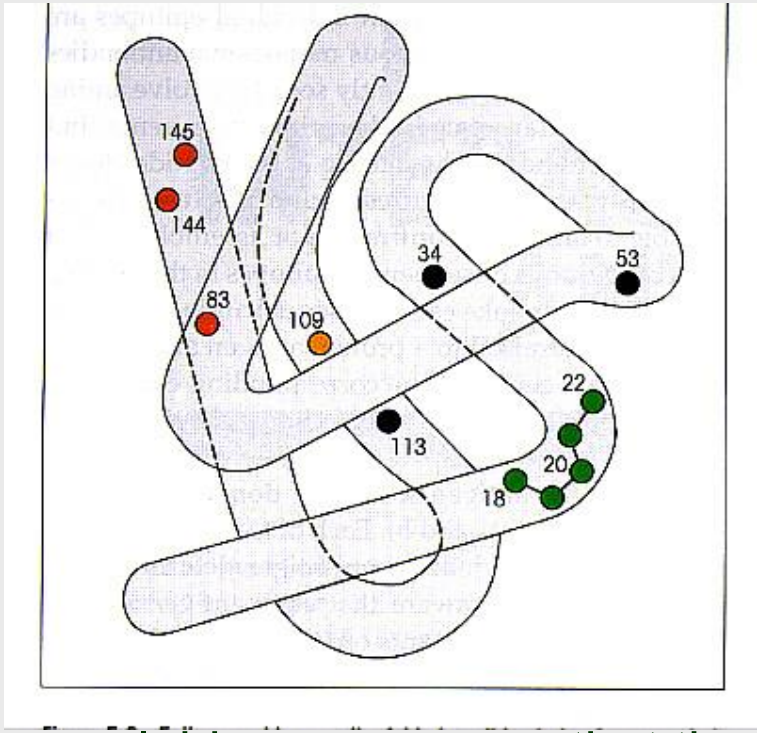

b
c
ANTI-c
ANTI-a
ANTI-b
ANTI-d
c
a
a
b
b
d
Epitope densities:
High
Medium
Low
'Zero'

# Experimental systems…

**TABLE 3-1 MOLECULAR WEIGHT OF SOME COMMON EXPERIMENTAL ANTIGENS USED IN IMMUNOLOGY**

| Antigen | Approximate molecular mass (Da) |
|---|---|
| Bovine gamma globulin (BGG) | 150,000 |
| Bovine serum albumin (BSA) | 69,000 |
| Flagellin (monomer) | 40,000 |
| Hen egg-white lysozyme (HEL) | 15,000 |
| Keyhole limpet hemocyanin (KLH) | >2,000,000 |
| Ovalbumin (OVA) | 44,000 |
| Sperm whale myoglobin (SWM) | 17,000 |
| Tetanus toxoid (TT) | 150,000 |

# Epitopes for B-cells *versus* T-cells




By examining myoglobin one can see that the Ag's seen by B-cells and T-cells are different. B-cells see a continuous or discontinuous series of amino acids; by some circumstance, amino acid residue 109 has *never* been a part of an epitope for any monoclonal antibody; yet residue 109 is *always* part of the processed antigen seen by a TCR.

# Presentation of processed antigen…

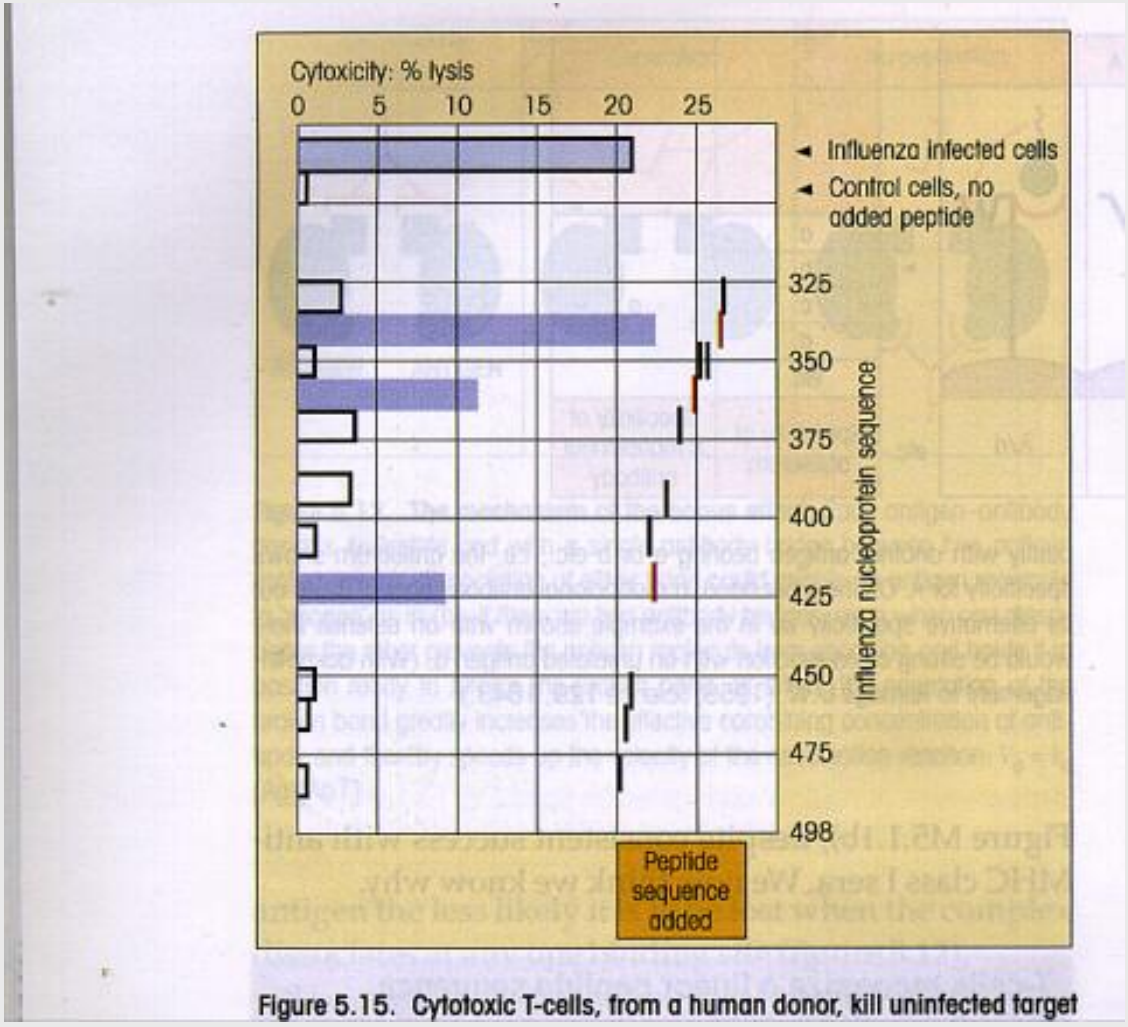
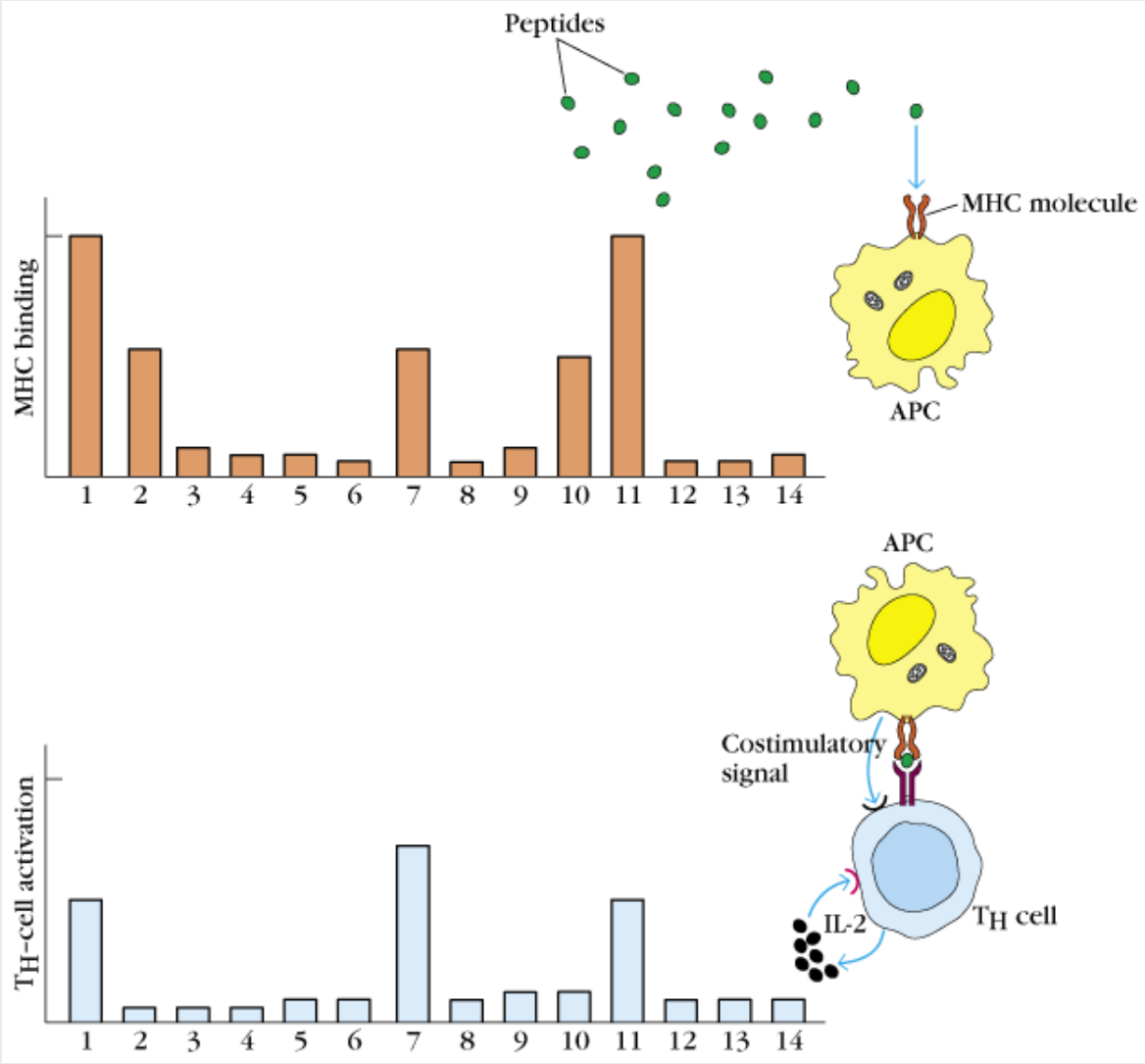



Figure 5.15. Cytotoxic T-cells, from a human donor, kill uninfected target

# Presentation of processed antigen…



There are two general classes of antigens

Exogenous (external)

Endogenous (internal)

# There are two general classes of antigens

Exogenous: presented by Antigen Presenting Cells (APC's). These are macrophages, B-cells, and some dendritic cells

Endogenous: typically peptides derived from *any* protein; an infected cell displays "not-self" proteins and is, thus, an "altered self cell"

# There are two general classes of antigens

Exogenous: these antigens are presented in MHC-II; they are seen by T-cells with a TCR *and* an associated protein called CD4

Endogenous: these antigens are presented by MHC-I; they are seen by T-cells with a TCR *and* an associated protein called CD8

There are two classes of T-cells

- $T_H$ have **CD4** which interacts with MHC-II; thus, $CD4^+$ T-cells are "MHC-II restricted."
- $T_H$ cells are "helper cells" that send signals (via cytokines and surface proteins) to other cells of the immune system. The $T_H$ cells function as the "brain" of the immune system.

There are two classes of T-cells

- $T_C$ have **CD8** which interacts with MHC-I; thus, $CD8^+$ T-cells are "MHC-I restricted."
- $T_C$ cells become *cytotoxic T lymphocytes* (CTL's) which attack "altered self-cells (*e. g.,* infected cells.) "Altered self-cells" are also called "target cells." They are the targets for the CTL's cytotoxicity.

# Experimental systems… *viz.* “haptens”

Hapten: a low molecular-weight molecule that can be made immunogenic by conjugation to a suitable carrier…

# Haptens…

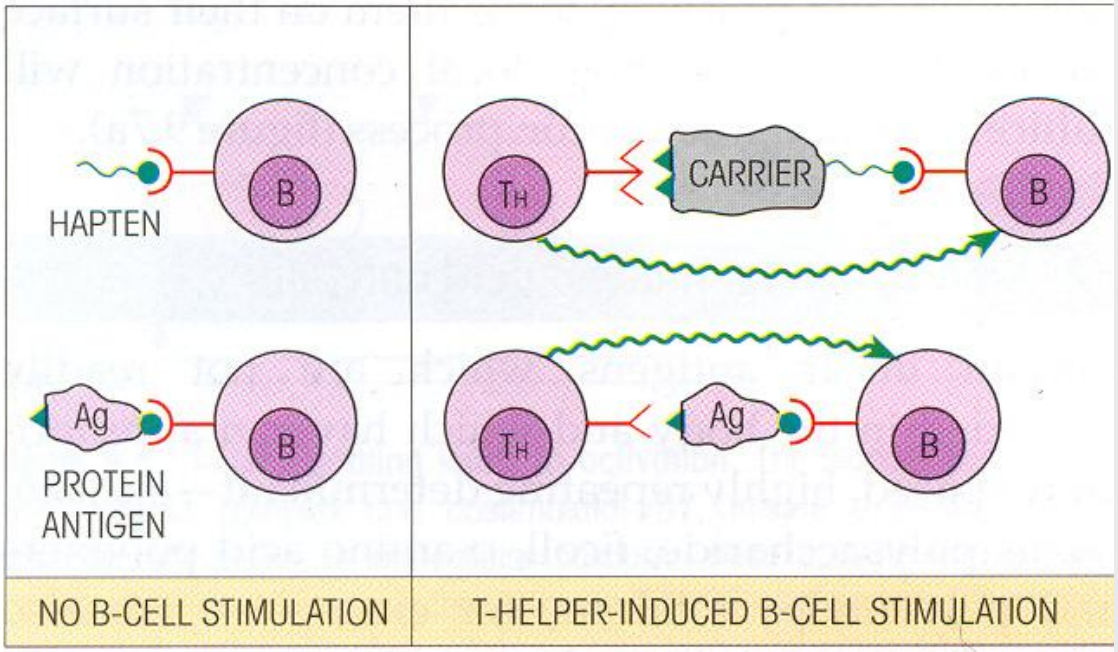



**Figure 9.8. T-helper cells cooperate through protein carrier determinant to help B-cells respond to hapten or equivalent determinants on antigen by providing accessory signals.** (For simplicity we are ignoring the MH component and epitope processing in T-cell recognition, but we won't forge it.)

# Haptens…

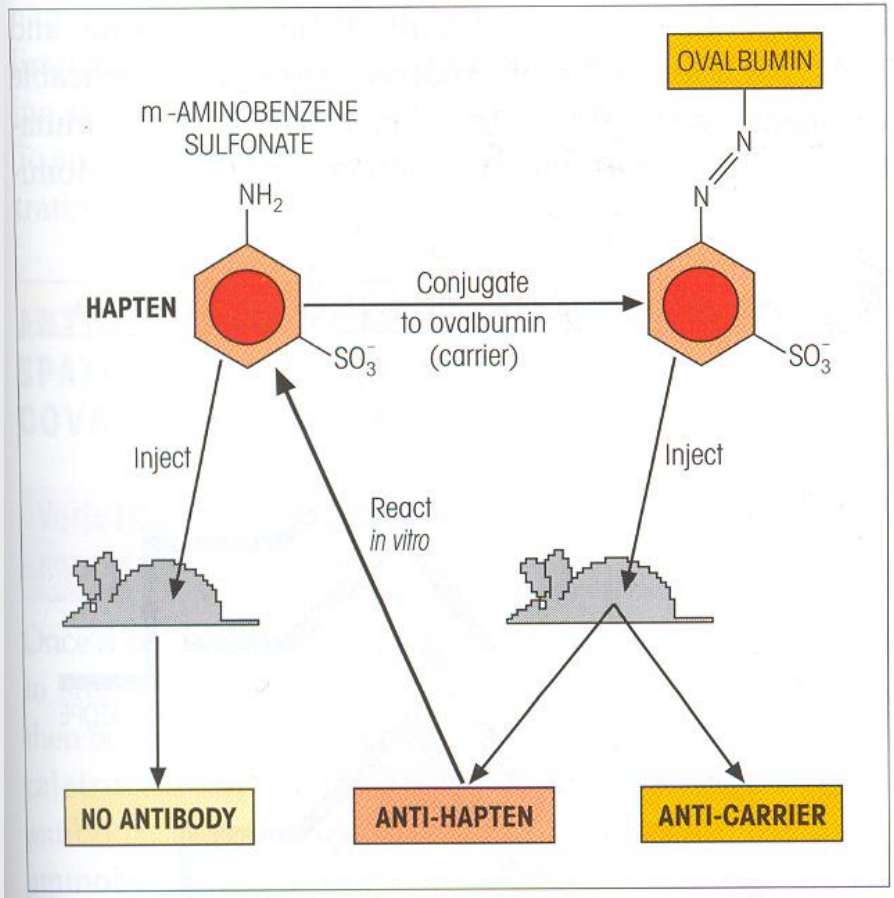



Figure 5.1. **A hapten on its own will not induce antibodies.** However, it will react *in vitro* with antibodies formed to a conjugate with an immunogenic carrier.

# Summary…

- Immunogen
- Antigen
- Epitope
- Hapten
- Foreignness
- Molecular size
- Chemical composition and heterogeneity
- Degradability

# Experimental systems… *viz.* “adjuvants”

Adjuvants: A substance that non-specifically enhances the immune response to an antigen

- Prolong the presence of the antigen
- Enhance production of “co-stimulatory” signals
- Induce granuloma formation (*i.e.,* an accumulation of macrophages)
- Non-specifically stimulate lymphocytes