# Cell mediated immune response

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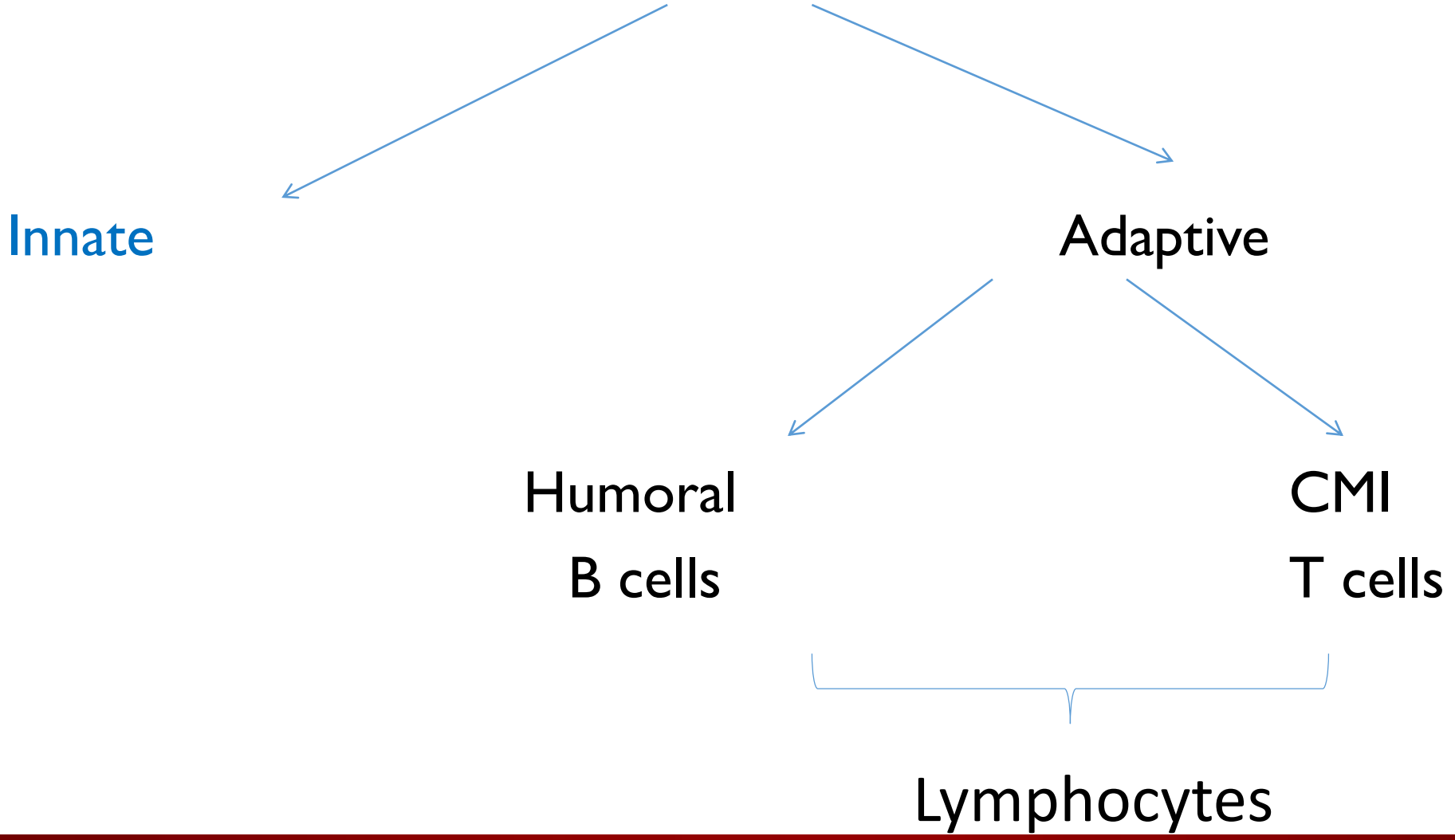
# Objectives

- Types of immune responses
- Lymphocyte subsets
- Antigens
- Antibodies
- MHC molecules
- Recognition of antigens by T lymphocytes
- Activation of T lymphocytes
- Effector mechanisms

# Immune Response

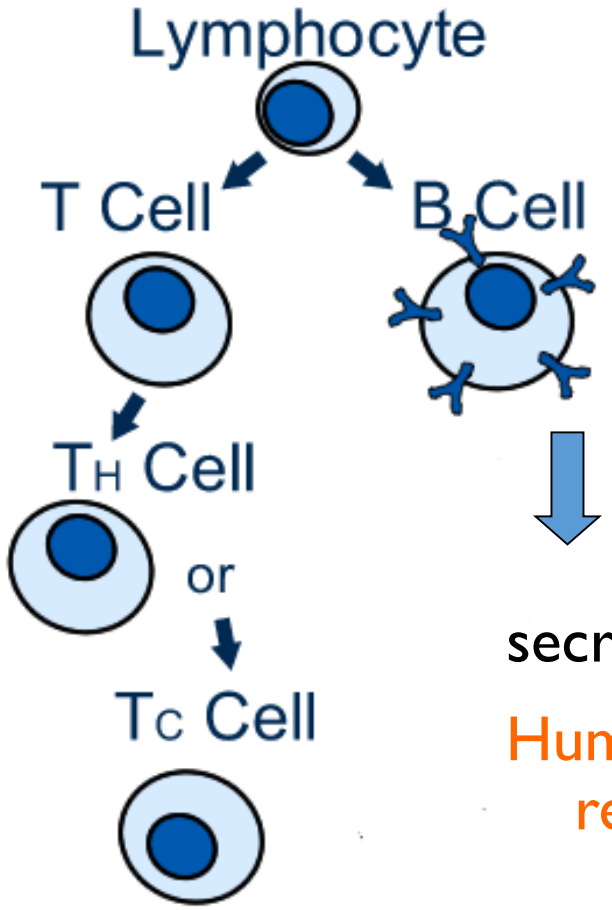


# Innate Vs. Adaptive

- Born with it
- 1st line- acts immediately
- Less specific
- No memory
- Only acts on foreign substances
- Recognize broad molecules on pathogens by a small set of rceptors
- Components
  - Barriers
  - Secretions
  - cells

- Stimulated by pathogens
- 2nd line- takes time
- Specific
- Memory
- Can act on self tissues

- Recognize specific molecules (Antigens) on pathogens by a vast array of receptors
- Components
  - Secretions
    - Antibodies, cytokines
  - Cells
    - Lymphocytes




secrete antibodies

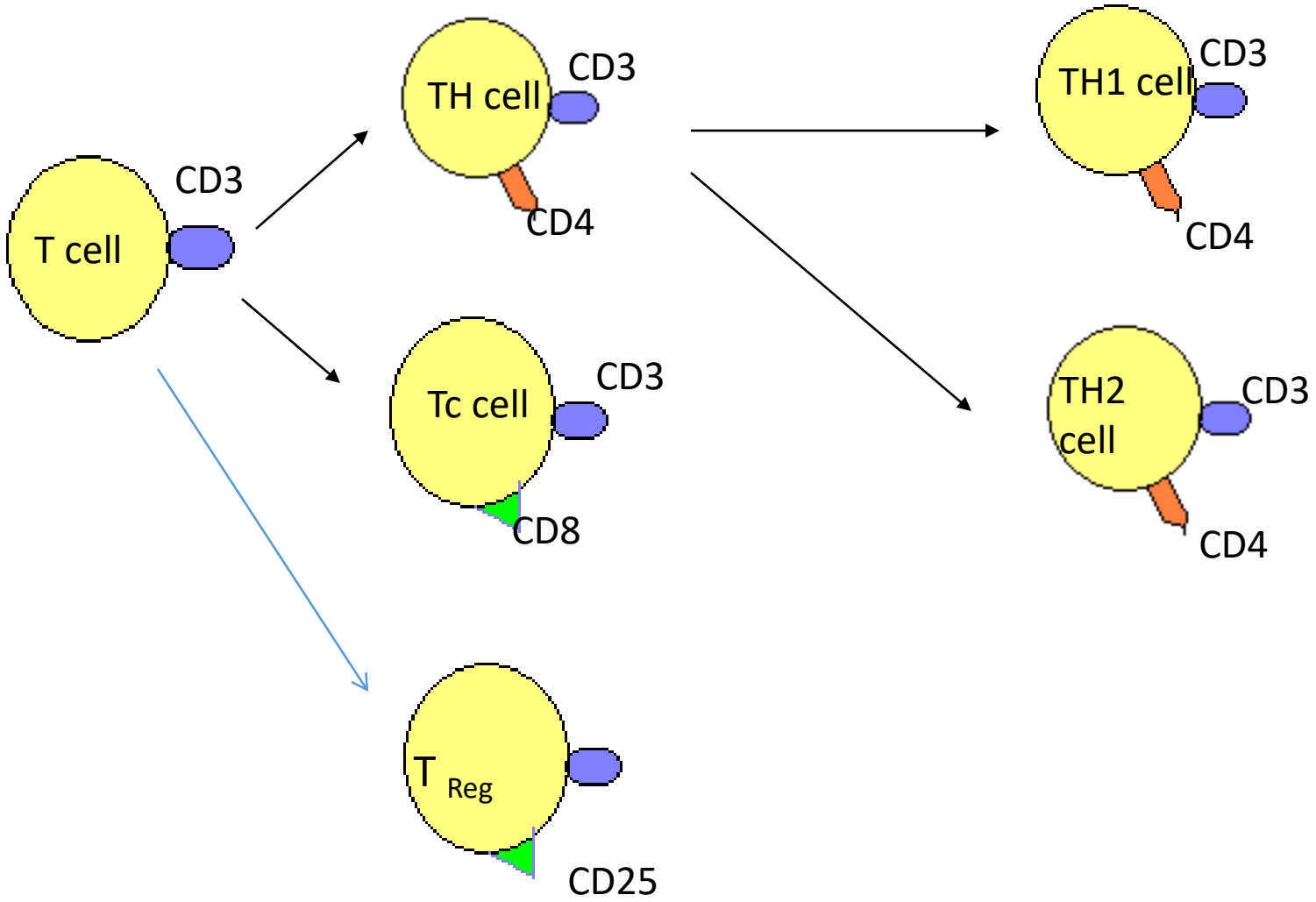
Humoral Immune response

Cell Mediated Immunity

# Lymphocyte subsets

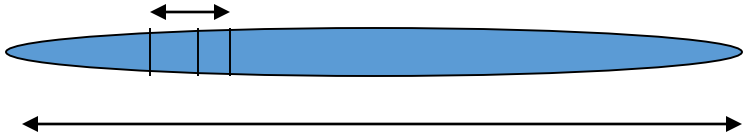
| Lymphocyte | Antigen receptor | Surface markers | Functions |
|---|---|---|---|
| T | T cell receptor (TCR) | CD3 | CMI ( cell mediated) |
| B | B cell receptor (Surface Ig) | CD19, CD20 | Humoral by secreting Abs |
| NK | None | CD56 | Innate |

# Types of T cells ( T cell Subsets)

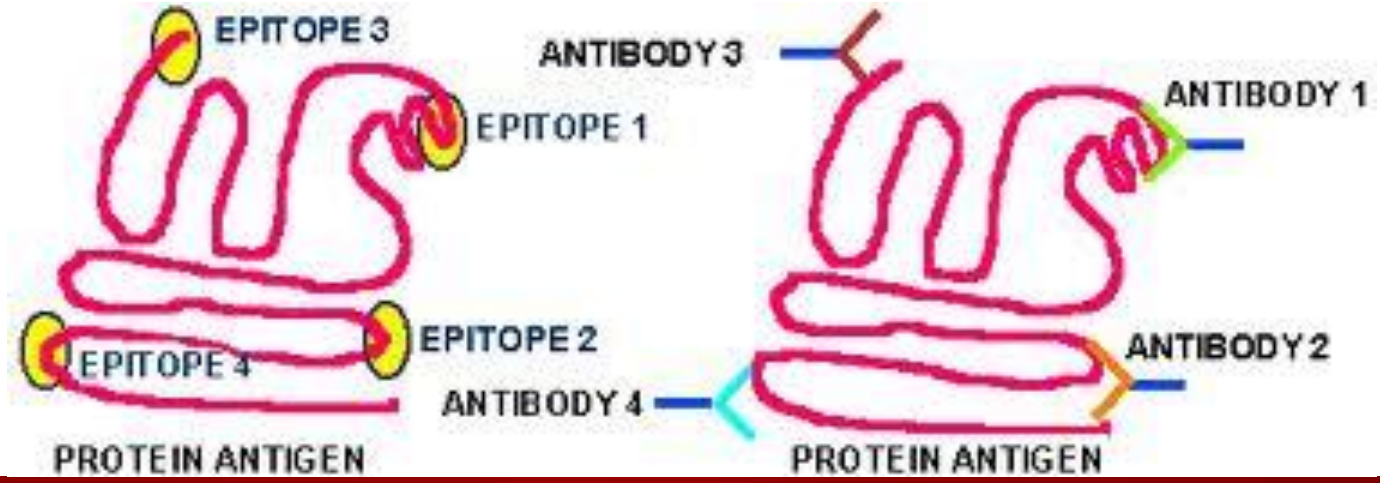


# Antigens and epitopes

epitope



antigen



# Adaptive response

- Recognition
- Activation
- Effector

# Ag Recognition in Adaptive immunity

- Highly specific and specialized
- B cells can recognize unprocessed Ags
- T cells only identifies peptide fragments of an Ag (processed Ag) displayed by a special unit called MHC molecules on APC/ nucleated cells

  "MHC restricted"

- Both T and B cells need two signals for activation

## B cell receptor

Can identify Ags that are,

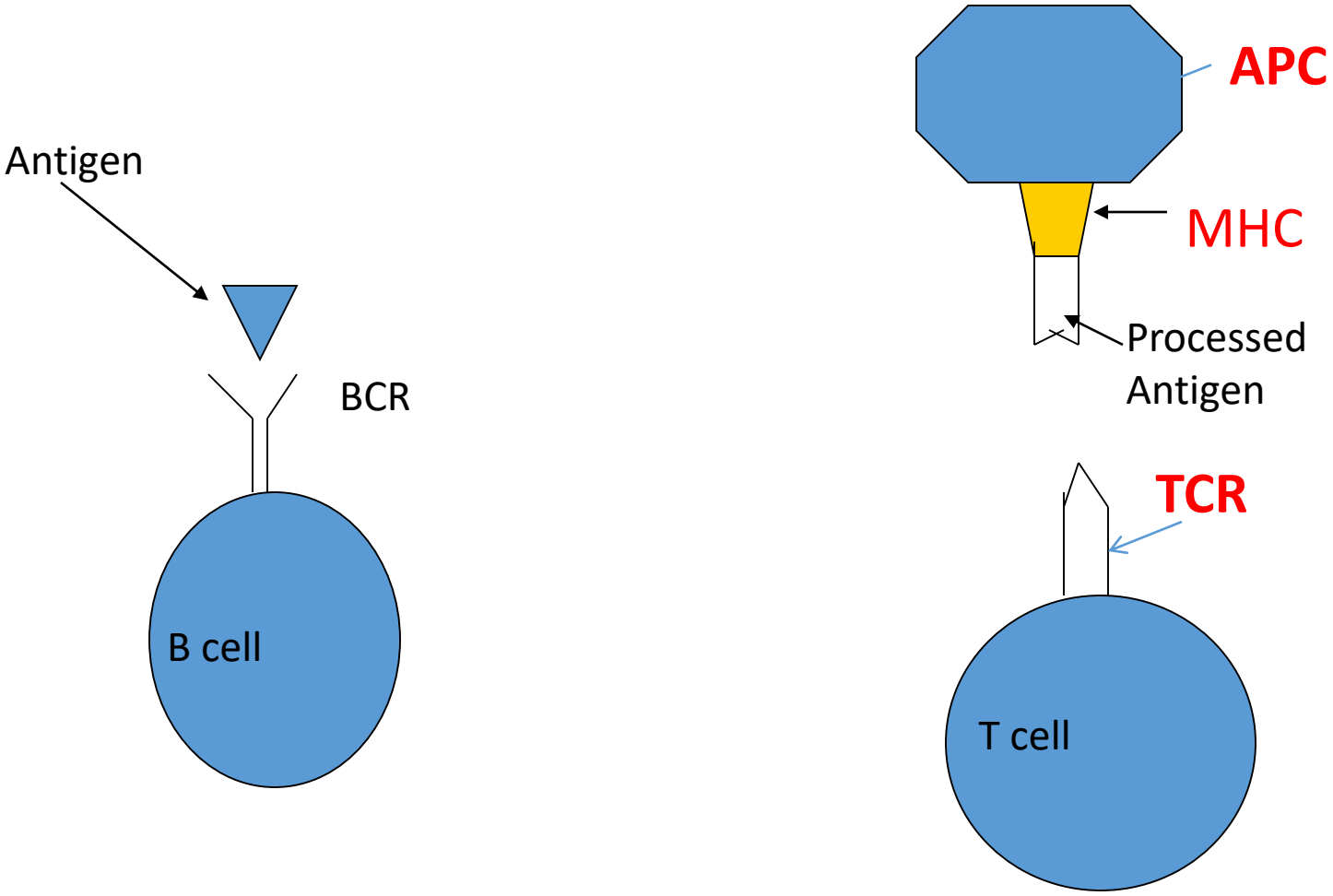
- unprocessed (native)
- Not combined with MHC
- proteins, CHO, lipids etc

## T cell receptor

Recognize Ags that are,

- Processed by APC
- Combined with MHC molecules
- Only peptides

"MHC restricted"


Antigen
BCR
B cell
APC
MHC
Processed
Antigen
TCR
T cell

# MHC molecules

| MHC class I | MHC class II |
| --- | --- |
| Membrane proteins | Membrane proteins |
| Coded by class I MHC genes | Coded by class II MHC genes |
| Expressed on all nucleated cells | Expressed on APC's only |
| Present peptides to $CD_8$ T cells | Present peptides to $CD_4$ T cells |

# Professional APC

- The immune system contains of three types of antigen presenting cells (APC's).

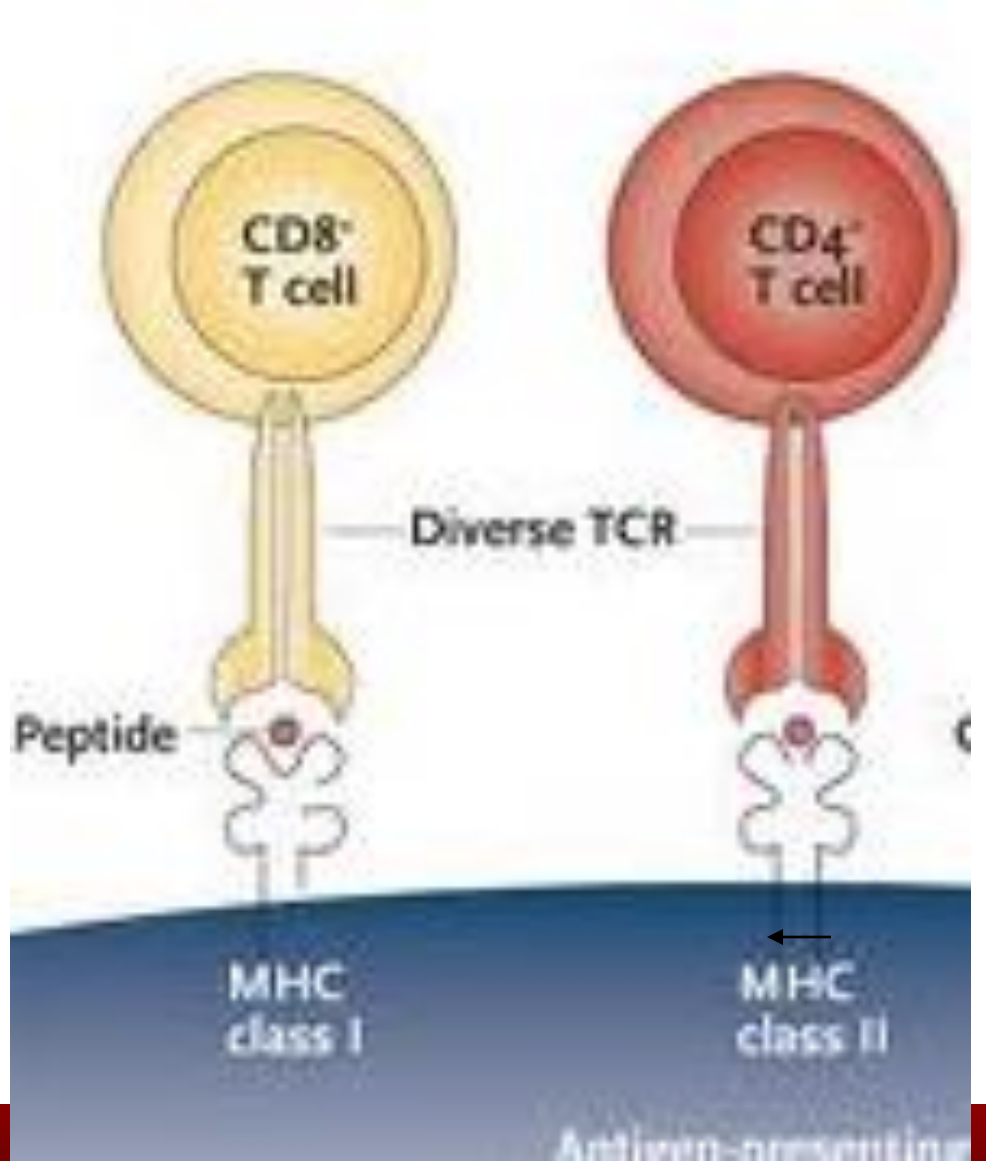
1) Macrophages
2) Dendritic cells
3) B cells

- Two important functions
  - Antigen presentation
  - provide 2nd signal for T cell activation - they provide co-stimulatory signals via B7 co-stimulators

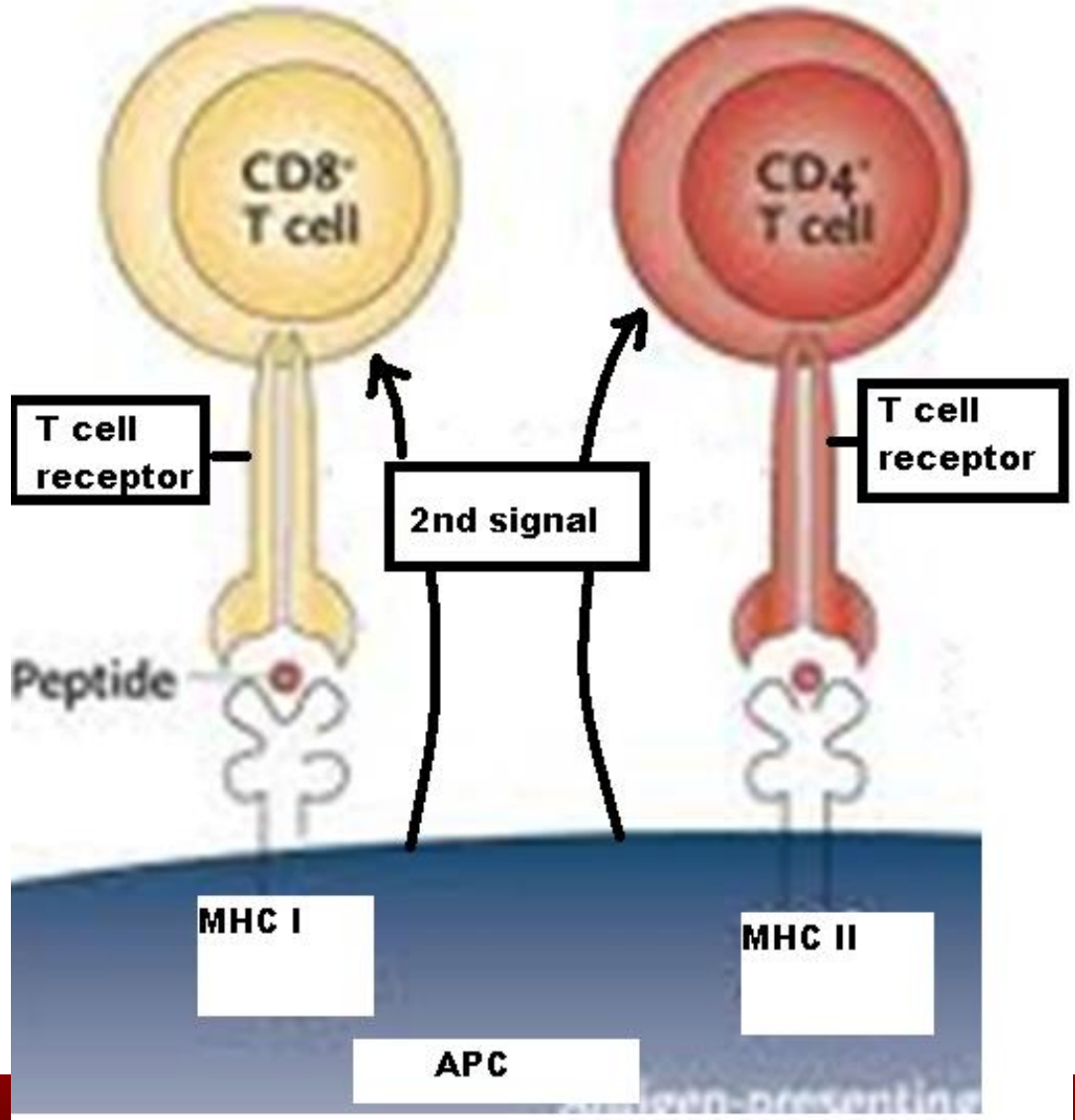
- They have both MHC class I and MHC class II molecules

- They identify PAMPs of microbes by pattern recognition molecules

# Recognition of processed antigens by T cells

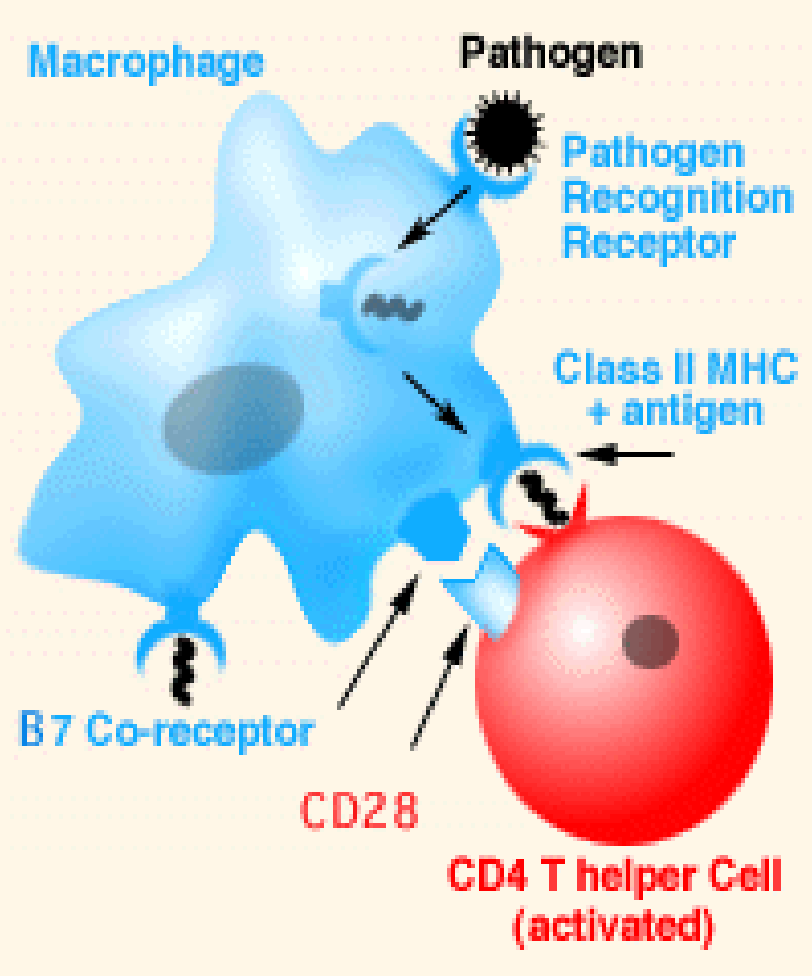


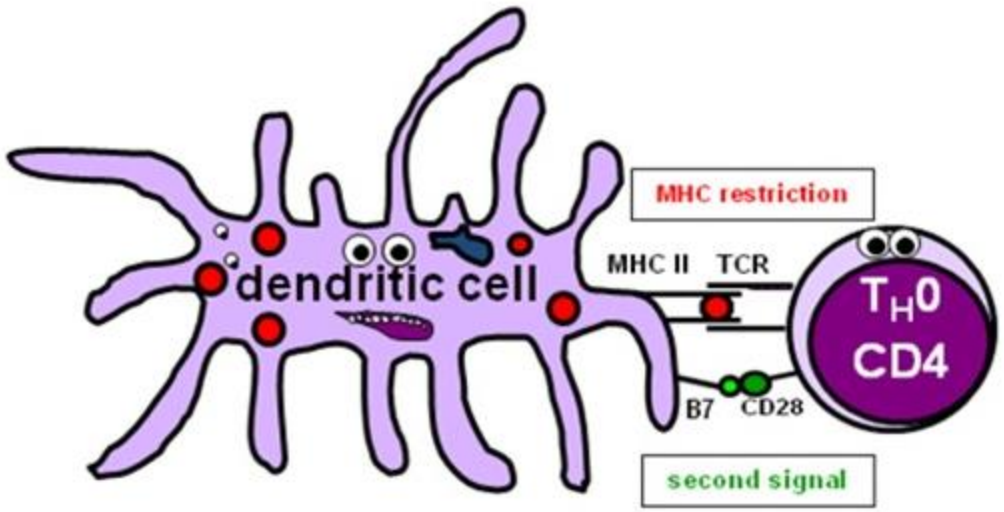
# T cell Activation



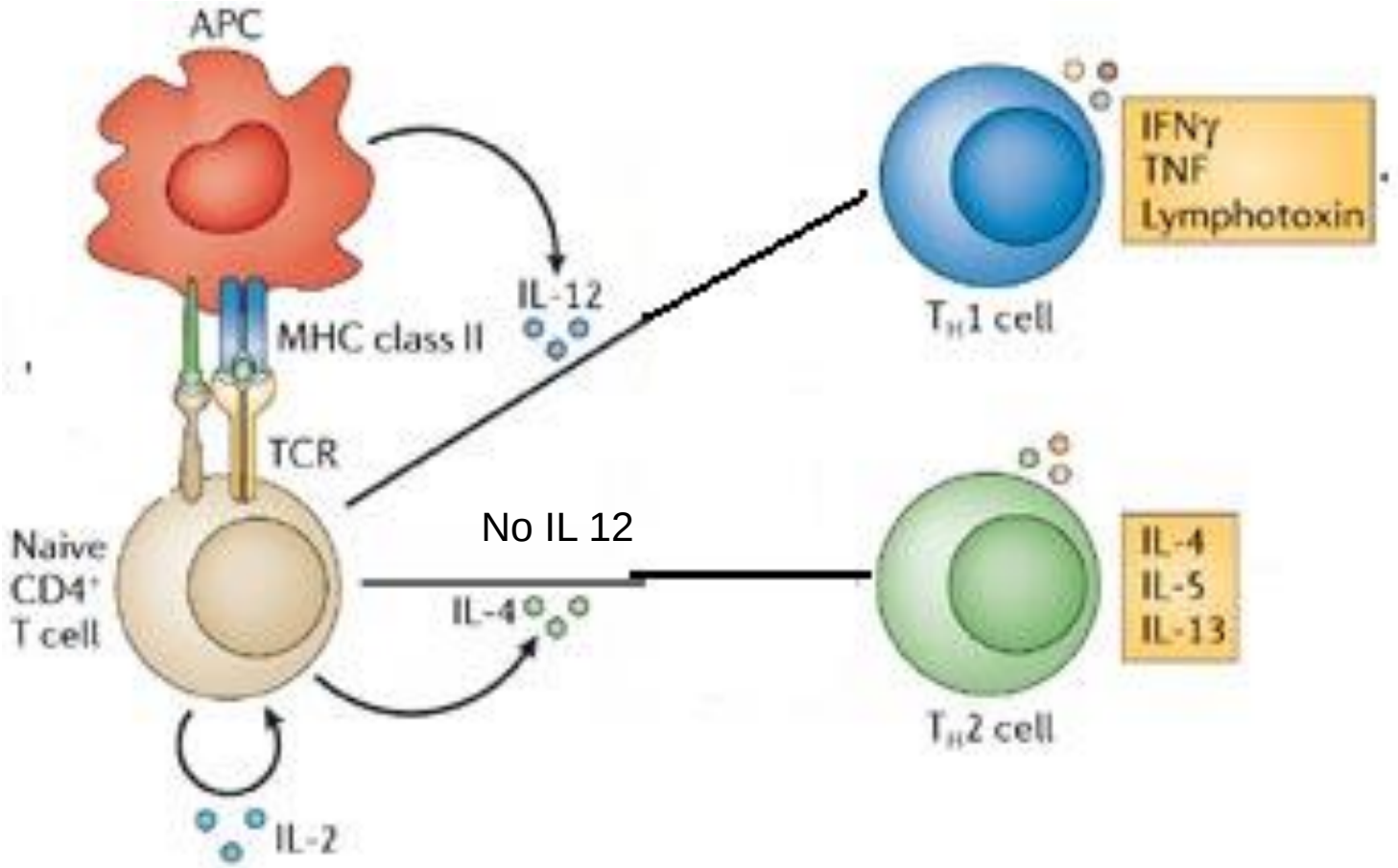
# T cell Activation

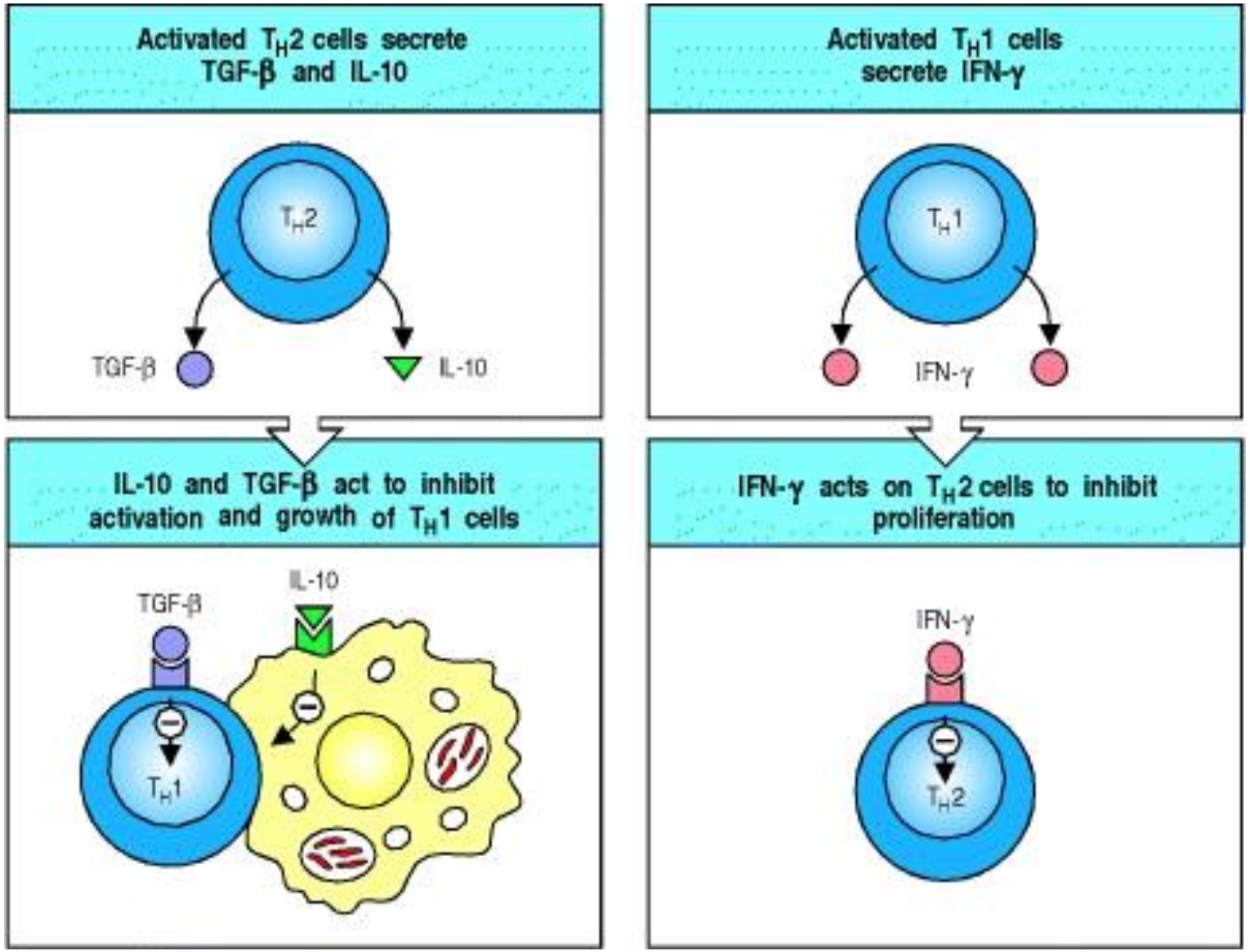
- In addition to Ag presentation, APC's provide 2nd signal to activate T cells via B7 co-stimulators + cytokines ---> activate T cells



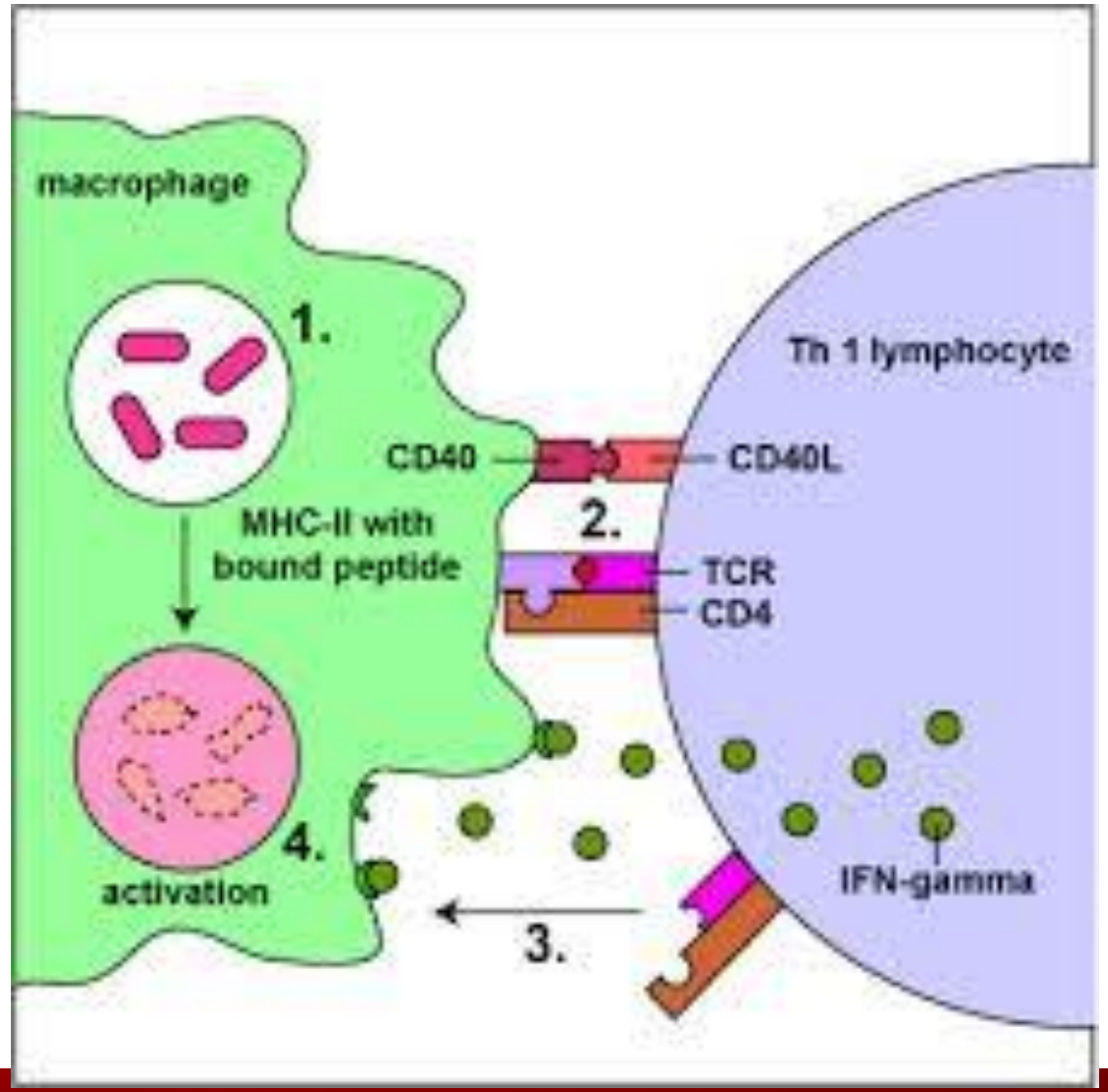
# $TH_1$ $TH_2$ Arm


APC
IL-12
MHC class II
TCR
Naive
CD4+
T cell
No IL 12
IL-4
IL-2
IFNγ
TNF
Lymphotoxin
TH1 cell
IL-4
IL-5
IL-13
TH2 cell


Activated $T_H2$ cells secrete TGF-β and IL-10
$T_H2$
TGF-β
IL-10
Activated $T_H1$ cells secrete IFN-γ
$T_H1$
IFN-γ
IL-10 and TGF-β act to inhibit activation and growth of $T_H1$ cells
TGF-β
IL-10
$T_H1$
IFN-γ acts on $T_H2$ cells to inhibit proliferation
IFN-γ
$T_H2$

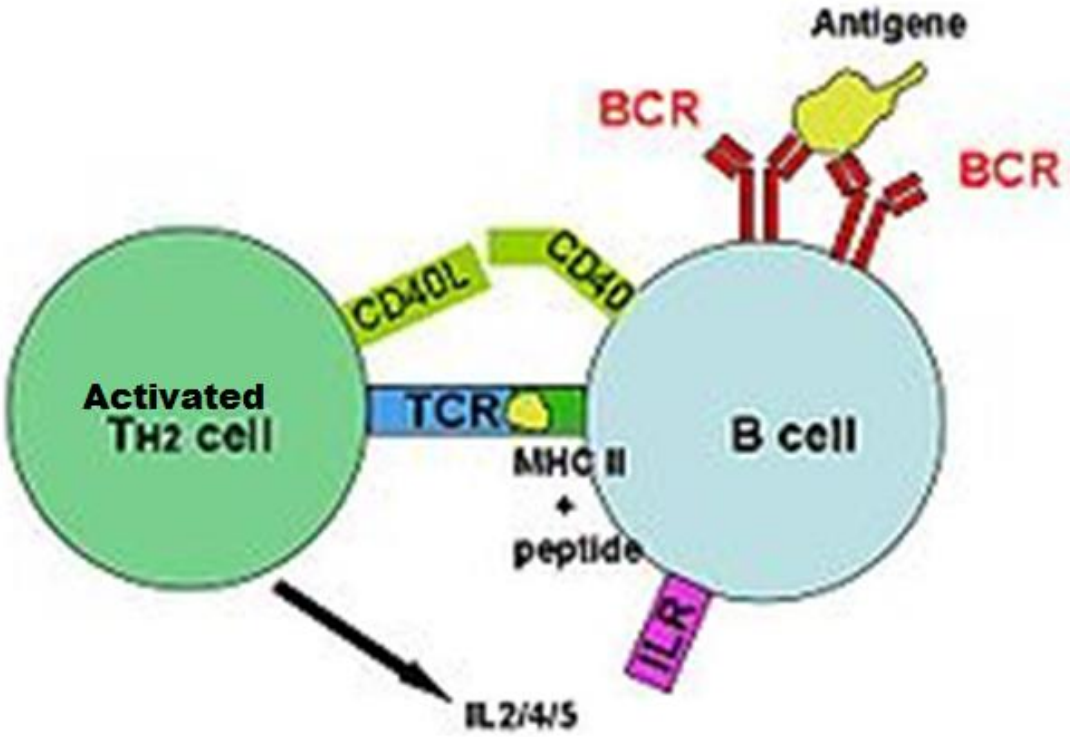
# Effector Mechanism of Th I

- Activation of Macrophage by $Th_1$ cells



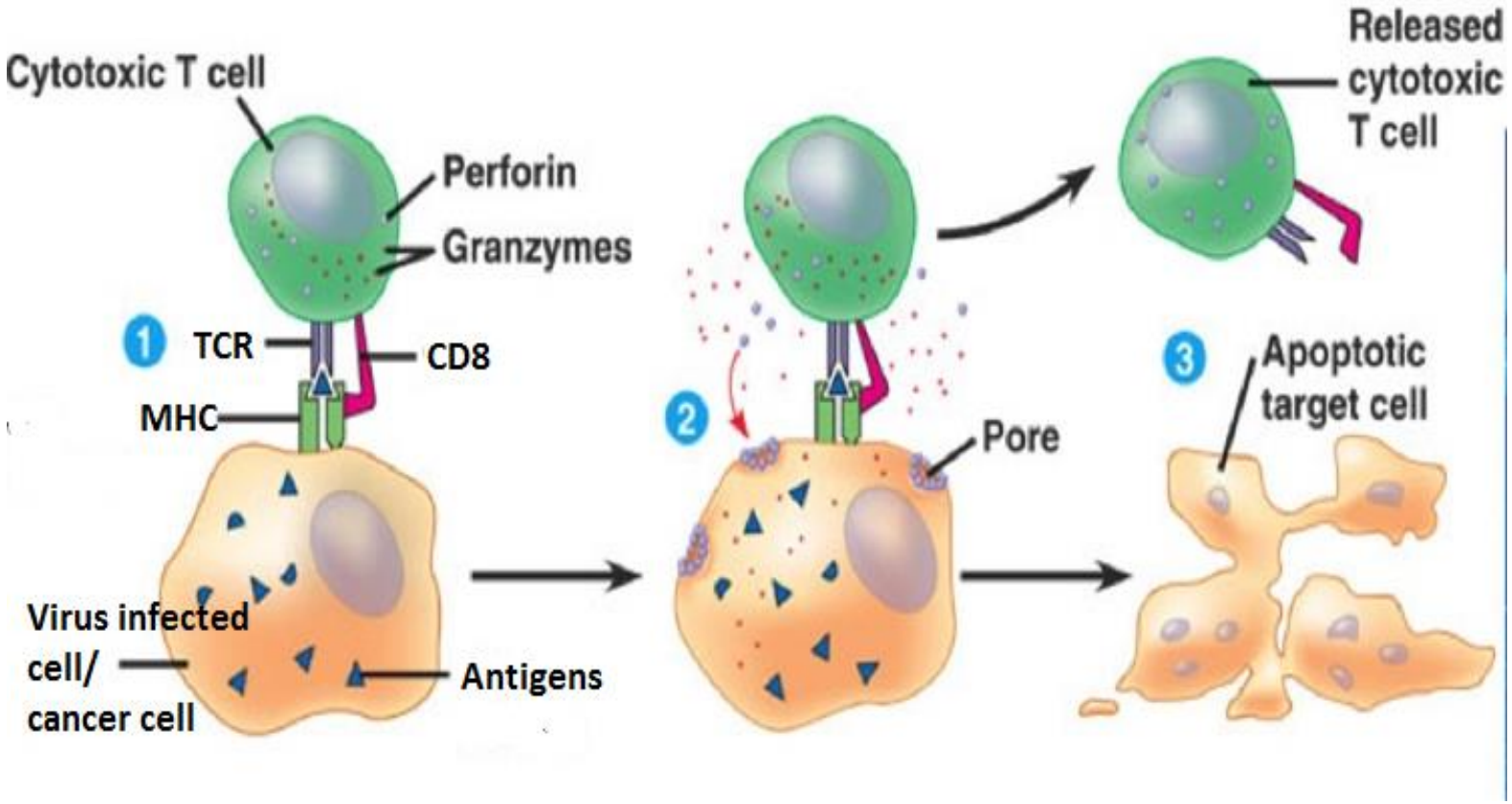
# Effector function of $Th_2$ cells

- Mainly help B cells
- Helps in
  - Class switching
  - Affinity maturation
  - Memory cells

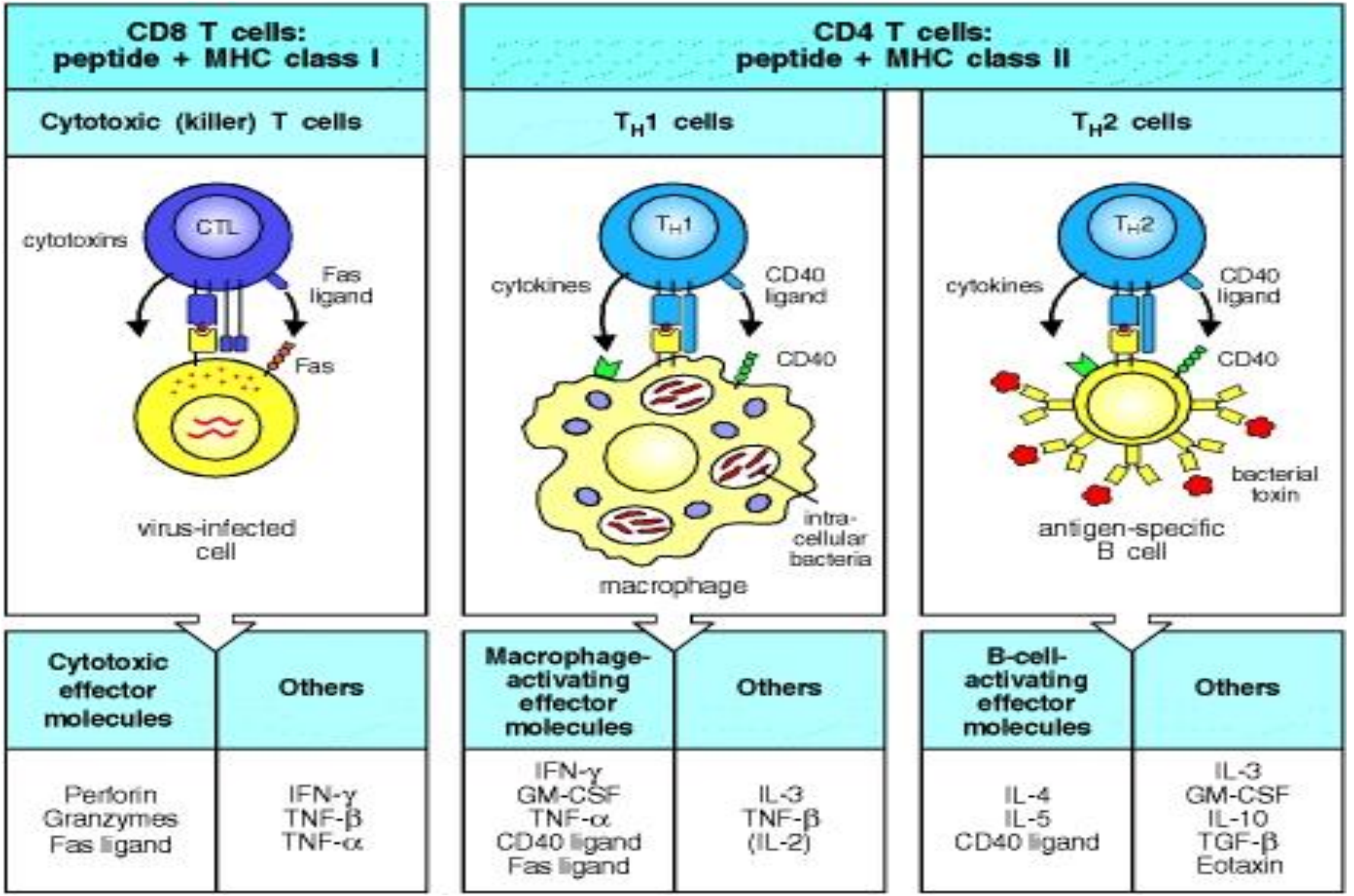


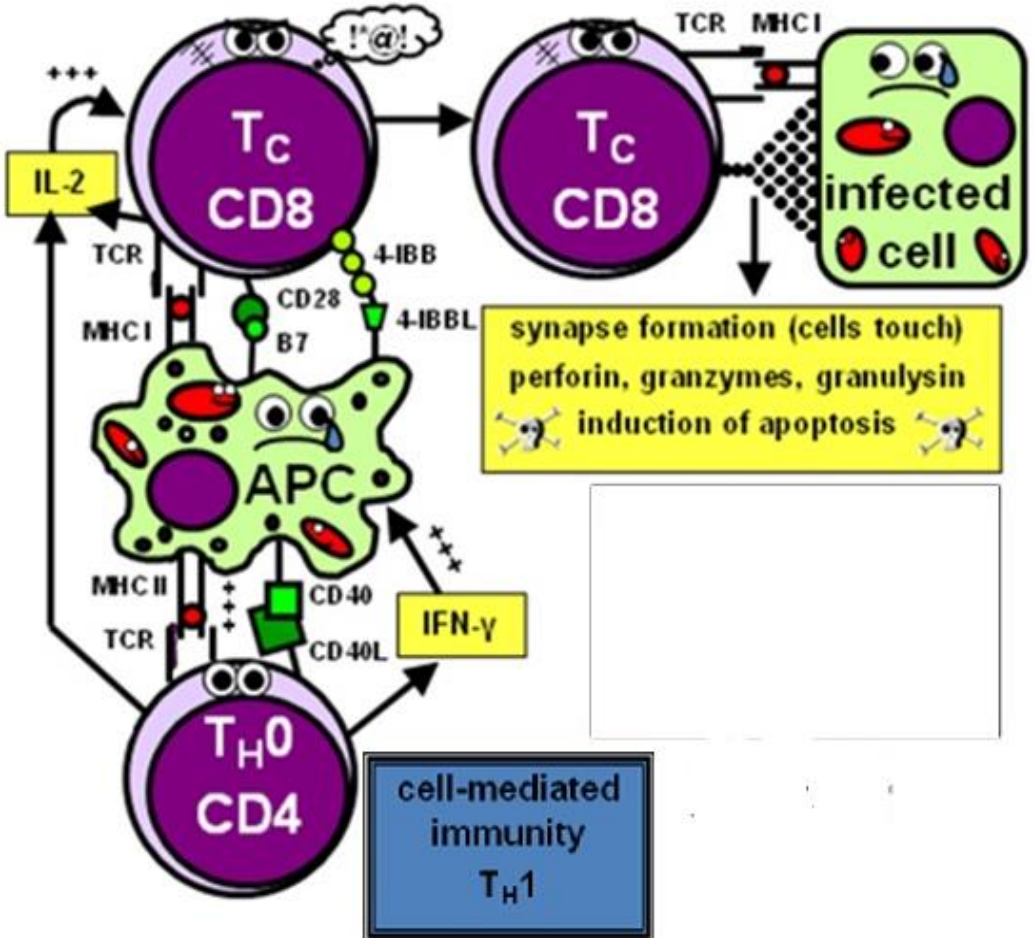
# Effector function of Tc Cells

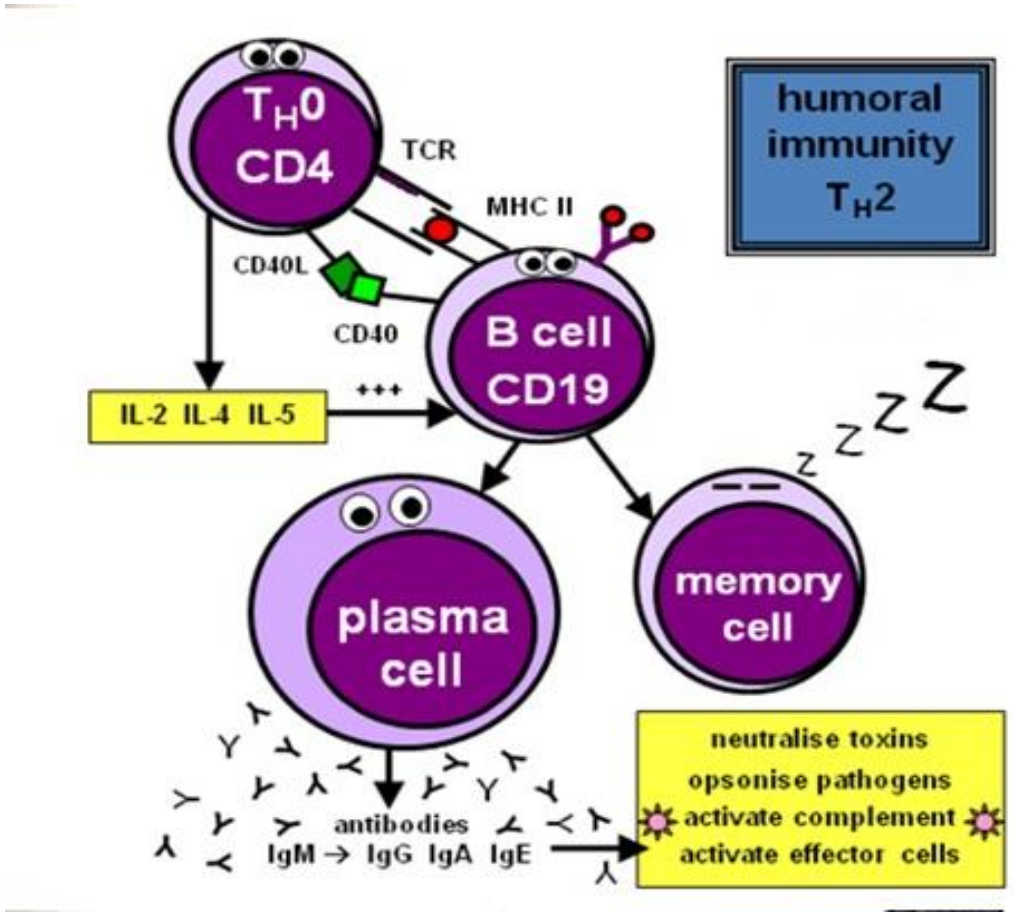
- Killing of virus infected cells and cancer cells by Cytotoxic T cells (Tc)



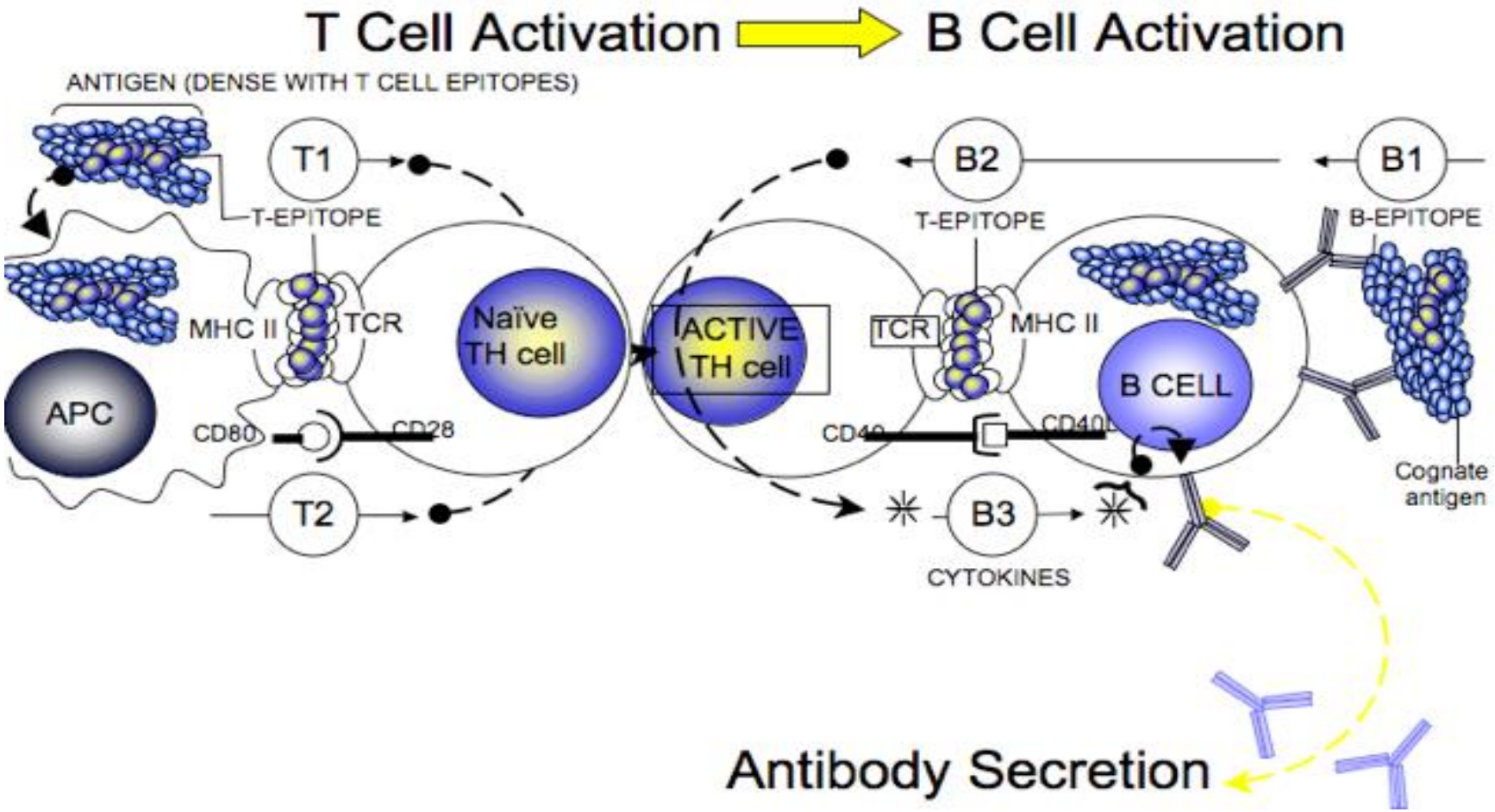
# Effector mechanisms of T cells

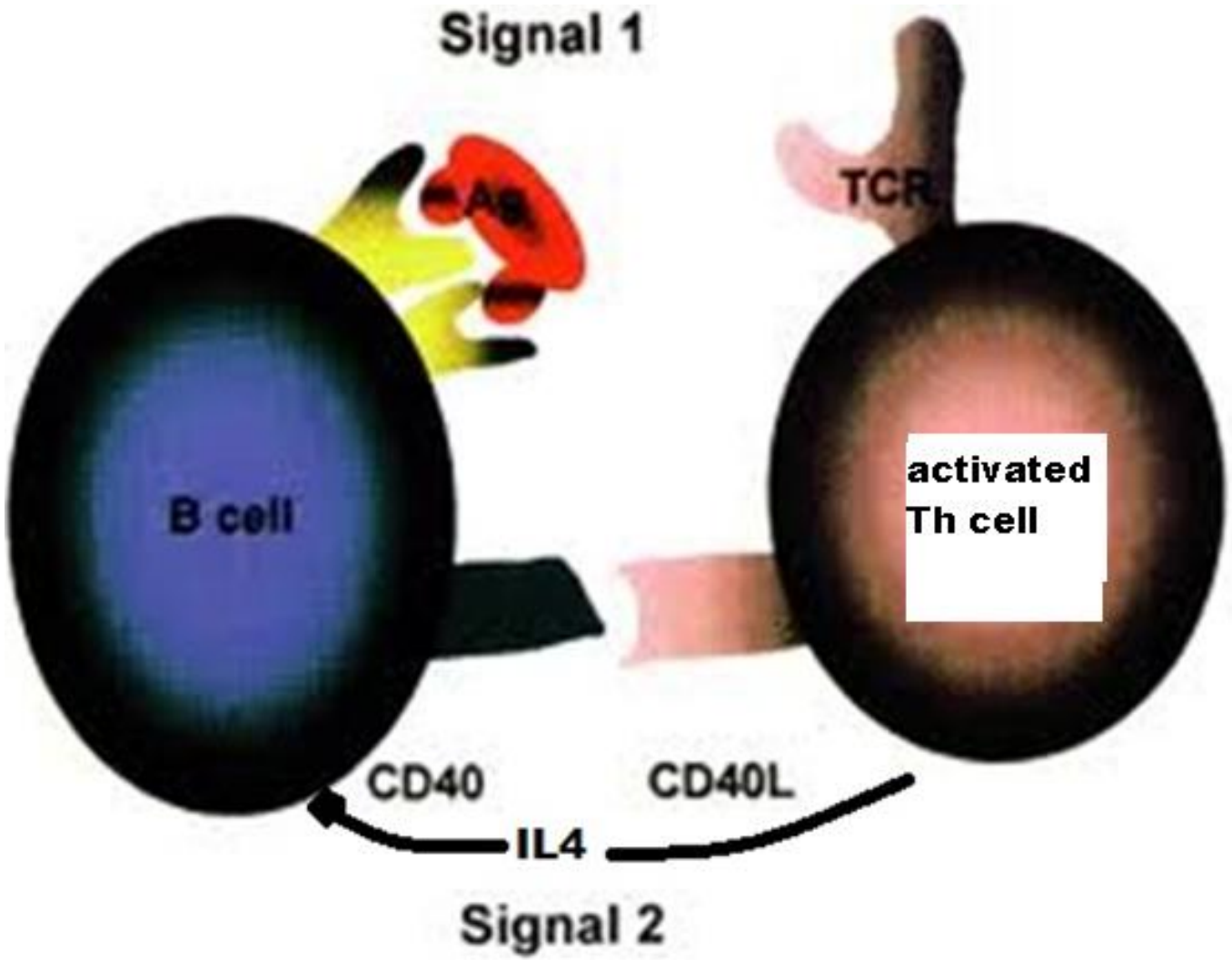


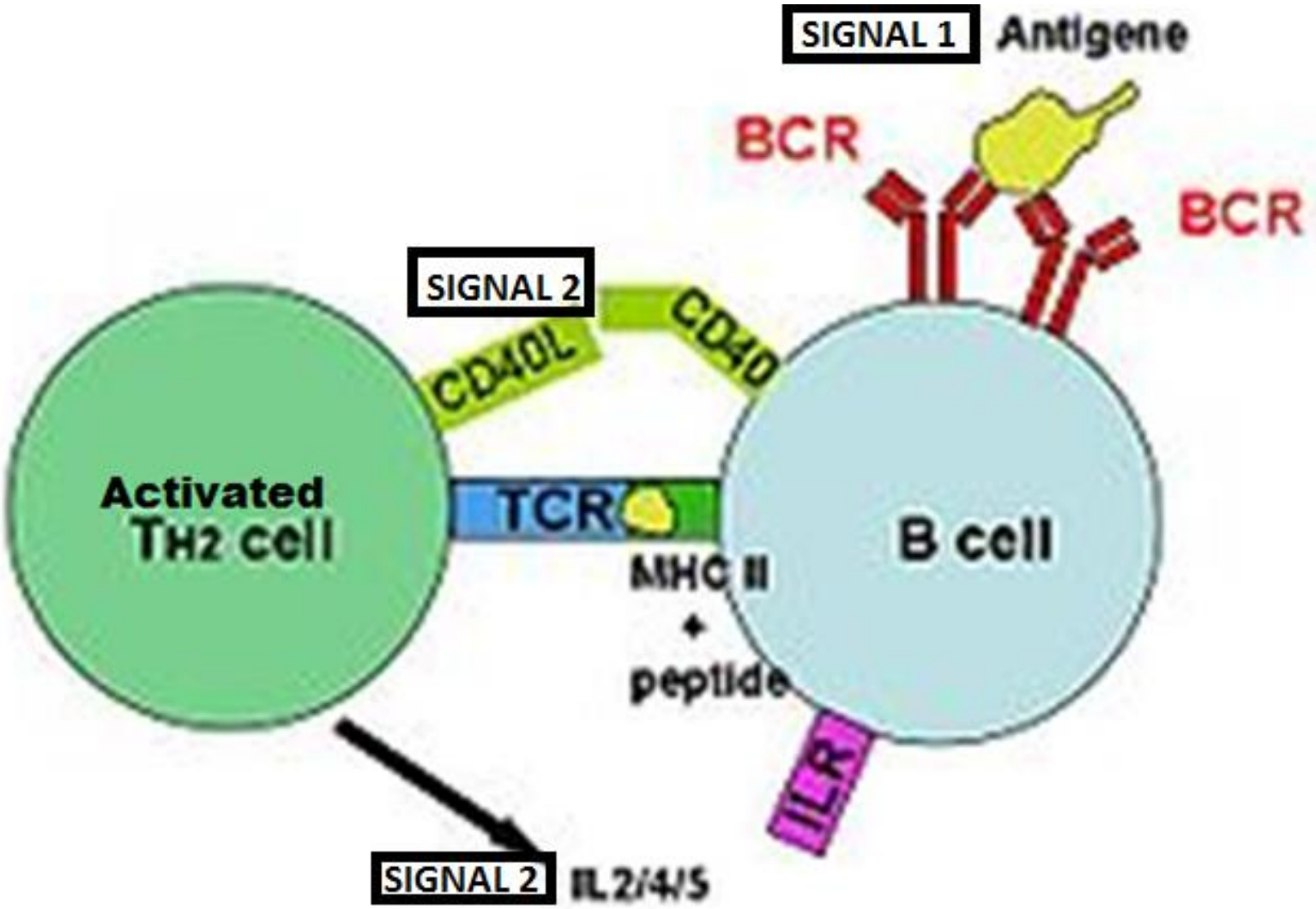

!@!
+++
TCR
MHC I
TC CD8
IL-2
TCR
4-IBB
CD28
4-IBBL
MHC I
B7
APC
MHC II
CD40
TCR
CD40L
IFN-γ
TH0 CD4
cell-mediated immunity TH1
TC CD8
infected cell
synapse formation (cells touch)
perforin, granzymes, granulysin
induction of apoptosis


TH0 CD4
TCR
MHC II
CD40L
CD40
B cell CD19
humoral immunity TH2
IL-2 IL-4 IL-5
+++
plasma cell
memory cell
antibodies
IgM → IgG IgA IgE
neutralise toxins
opsonise pathogens
activate complement
activate effector cells

# B cell activation



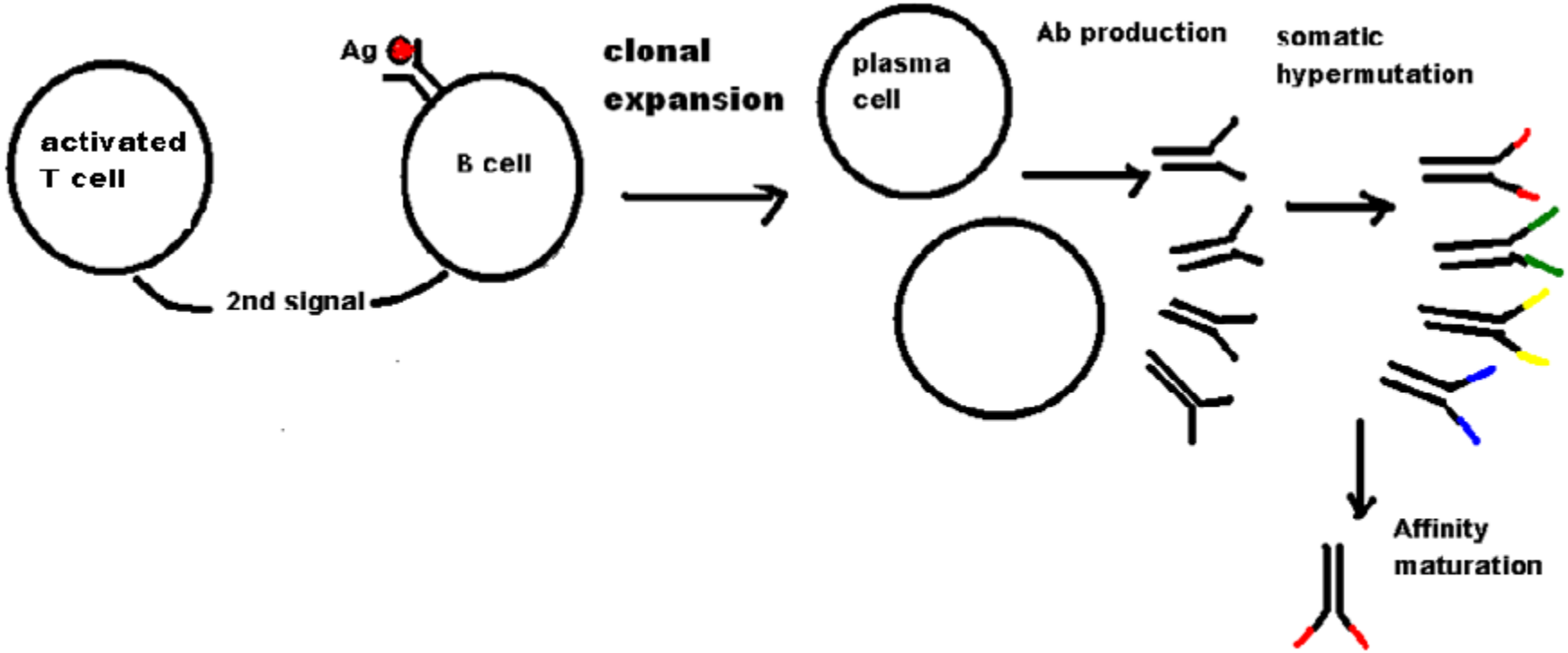

Signal 1
Ag
TCR
B cell
activated
Th cell
CD40
CD40L
IL4
Signal 2


SIGNAL 1
Antigene
BCR
BCR
SIGNAL 2
CD40L
CD40
Activated
TH2 cell
TCR
MHC II
+
peptide
B cell
ILR
SIGNAL 2
IL2/4/5

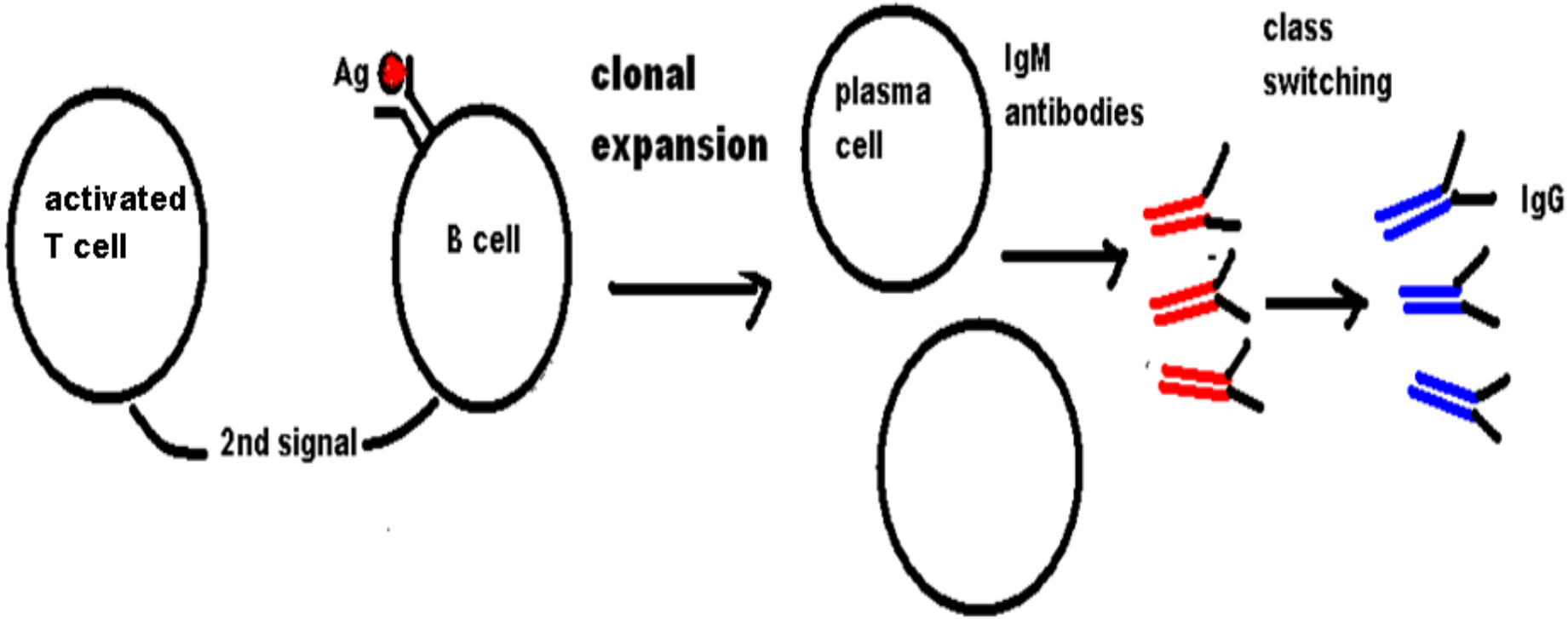
# T dependant Ags (Protein Ag)

- Somatic hypermutation
- Affinity maturation
- Isotope Switing (IgM ⟶ IgG)
- Memory cells

# Affinity maturation

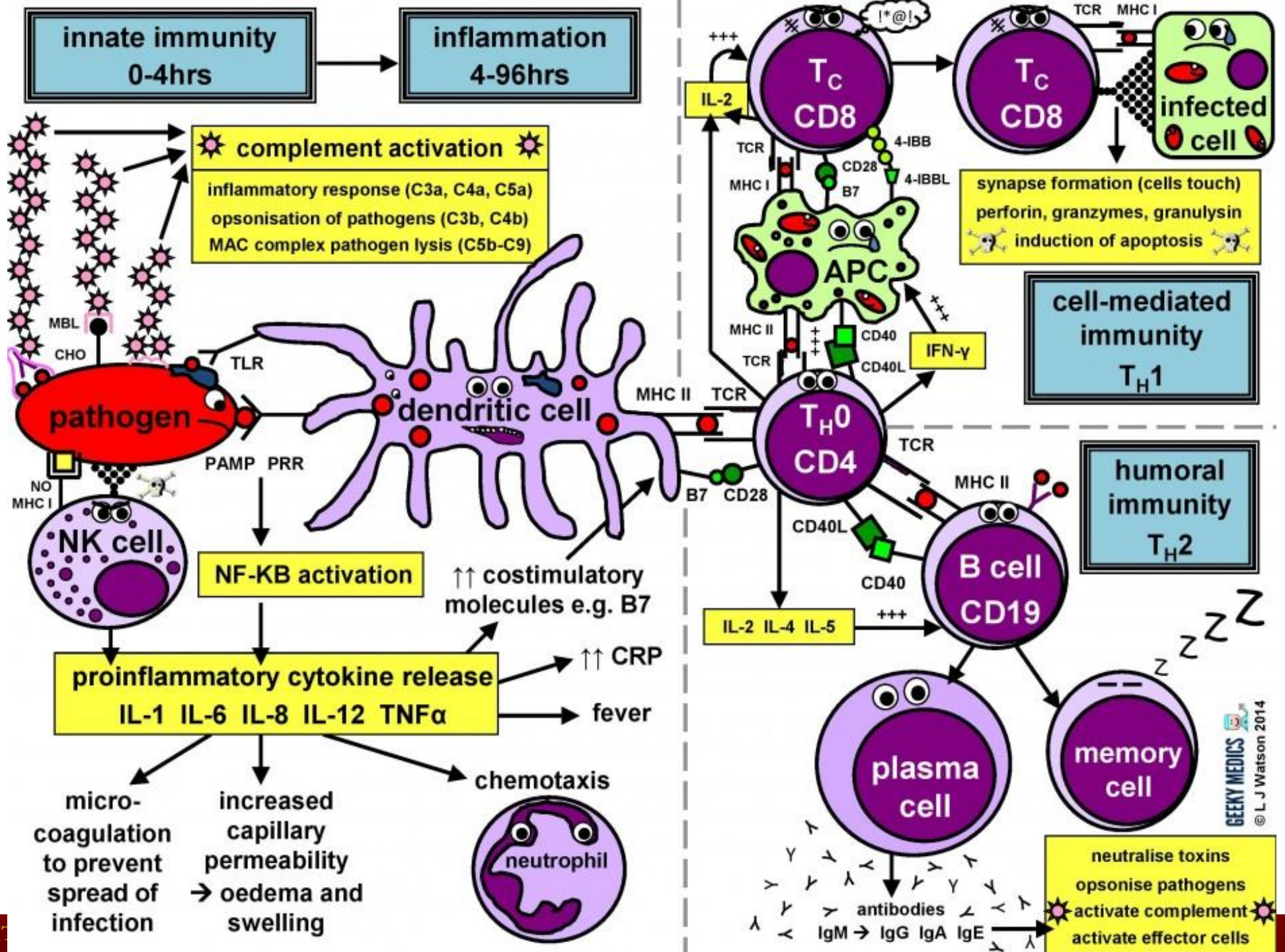


# Class switching



# T independent Ags (Non Protein Ags)

- Little/ No Somatic hypermutation
- Little/ No Affinity maturation
- Little/ No Isotope Switching (IgM is the main Ab))
- No Memory cells


innate immunity
0-4hrs
inflammation
4-96hrs
complement activation
inflammatory response (C3a, C4a, C5a)
opsonisation of pathogens (C3b, C4b)
MAC complex pathogen lysis (C5b-C9)
MBL
CHO
TLR
pathogen
PAMP PRR
dendritic cell
NO
MHC I
NK cell
NF-KB activation
↑↑ costimulatory molecules e.g. B7
proinflammatory cytokine release
IL-1 IL-6 IL-8 IL-12 TNFα
↑↑ CRP
fever
chemotaxis
neutrophil
micro-coagulation to prevent spread of infection
increased capillary permeability → oedema and swelling
+++
IL-2
$T_C$ CD8
!*@!
$T_C$ CD8
TCR
MHC I
infected cell
TCR
4-IBB
CD28
4-IBBL
MHC I
B7
synapse formation (cells touch)
perforin, granzymes, granulysin
induction of apoptosis
APC
cell-mediated immunity
$T_H1$
MHC II
CD40
TCR
CD40L
IFN-γ
MHC II
TCR
$T_H0$ CD4
TCR
B7
CD28
MHC II
humoral immunity
$T_H2$
CD40L
CD40
B cell CD19
IL-2 IL-4 IL-5
+++
plasma cell
memory cell
antibodies
IgM → IgG IgA IgE
neutralise toxins
opsonise pathogens
activate complement
activate effector cells
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# Adaptive immune response in specific infections

- Viral infections
  - Cytotoxic T cells
- Extracellular bacteria
  - Antibodies , TH2
- Intracellular bacteria
  - TH1

# Deregulation of adaptive immune response

- Autoimmune diseases
  - Autoantibodies
  - Auto-reactive T cells
  - Deregulated $T_{reg}$ cells

- Hypersensitivity responses
  - Type 1- IgE
  - Type 2 – IgG/IgM
  - Type 3 – IgG/IgM
  - Type 4 – T cells

# Dysfunction/ deficiencies in adaptive immune response

- Antibody deficiency
- T cell deficiency
- Combined immune deficiency

# Adaptive response modulation

- Vaccination
- Immunoglobulin therapy
- Monoclonal antibodies
- Desensitization
- Specific T cell transfusion

# Summary

- Activation of T lymphocytes
- Different effector functions of T cells
- Activation of B cells
- Effector functions of antibodies
- How immune cells communicate and work with each other to kill the pathogens
- Deregulations/ dysfunctions and deficiencies of adaptive immune response

# MCQ

- Adaptive response

1. Is limited to blood and circulatory system
2. Is activated by innate system
3. Is enhanced by repeated  exposure to same pathogen
4. Is artificially enhanced in the treatment of autoimmune diseases
5. Enhancement can be done by treatment with monoclonal antibodies
6. Antibodies are low in T cell deficiencies