# Cells of cellular response

## There are three main types of cells of cellular response:

- **Dendritic cells**
- **T Helper cells**
- **Cytotoxic T cells**

# Dendritic cells

- **Dendritic cells** (DCs) are **immune cells** and form part of the mammalian immune system.

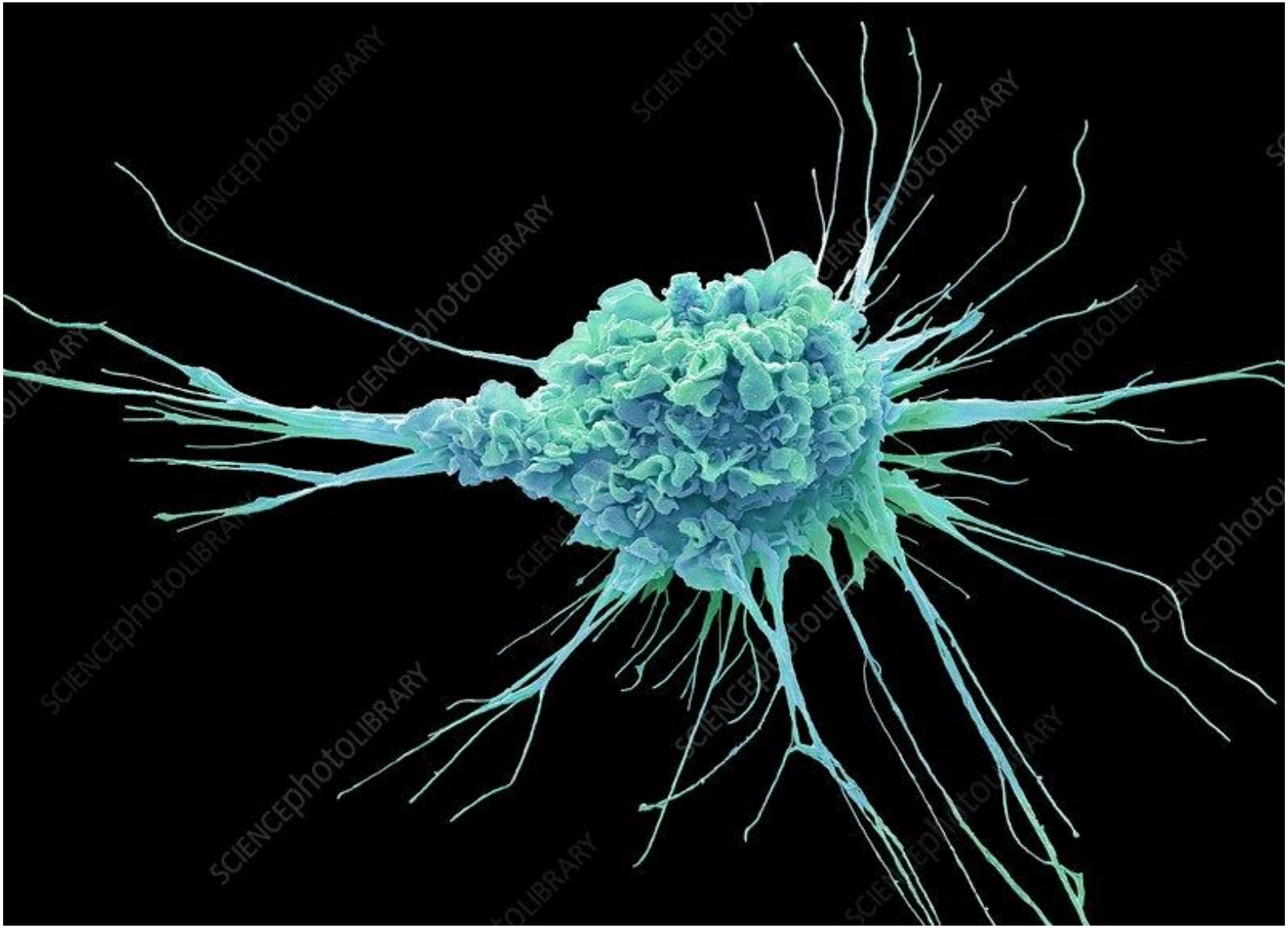
- These are **derived** from **hemopoietic bone marrow progenitor cells** (descendants of stem cells).

- Their main function is to **process antigenic material** and **present it on the surface** to other cells of the immune system, thus functioning as **antigen-presenting cells.**

- **Dendritic cells** are present in small quantities in **tissues** that are in contact with the **external environment**.

- These include mainly the **skin (Langerhans cells)** and the inner lining of the **nose, lungs, stomach** and **intestines**.

- They can also be found in an **immature state** in the **blood**.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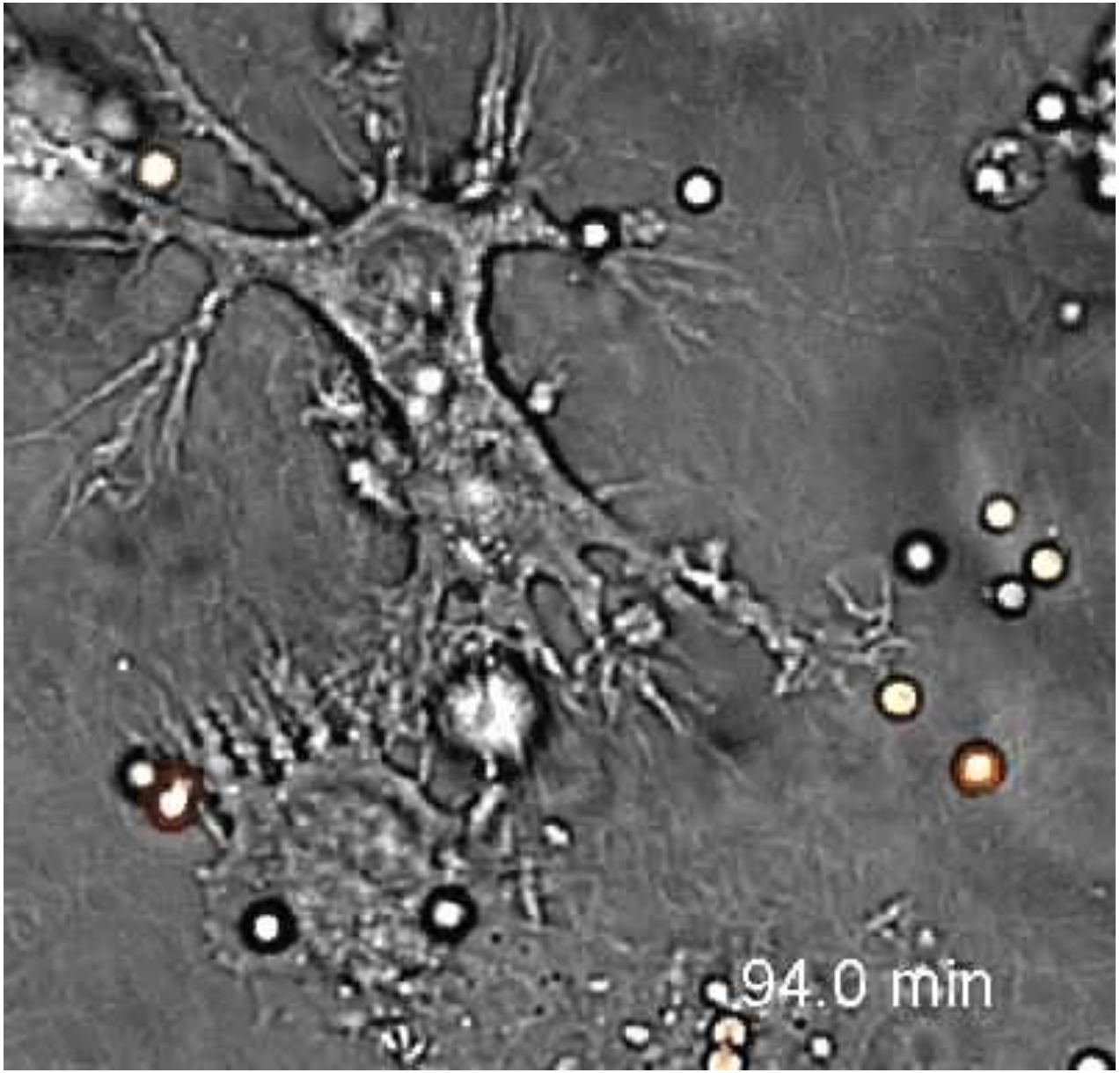
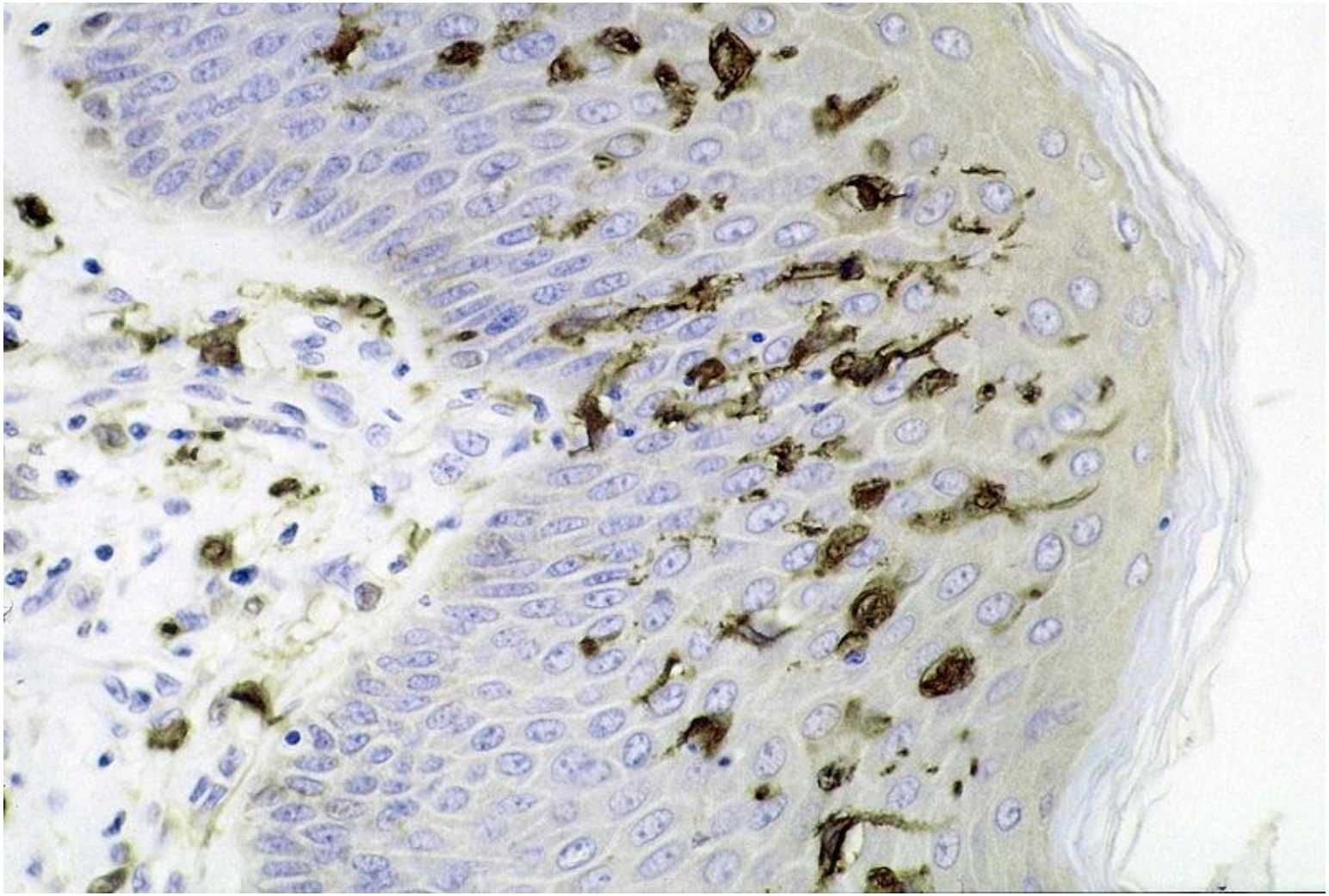



**Dendritic cells capturing conidia (fungal spores)**



**Dendritic(Langerhans cells) cells in skin**

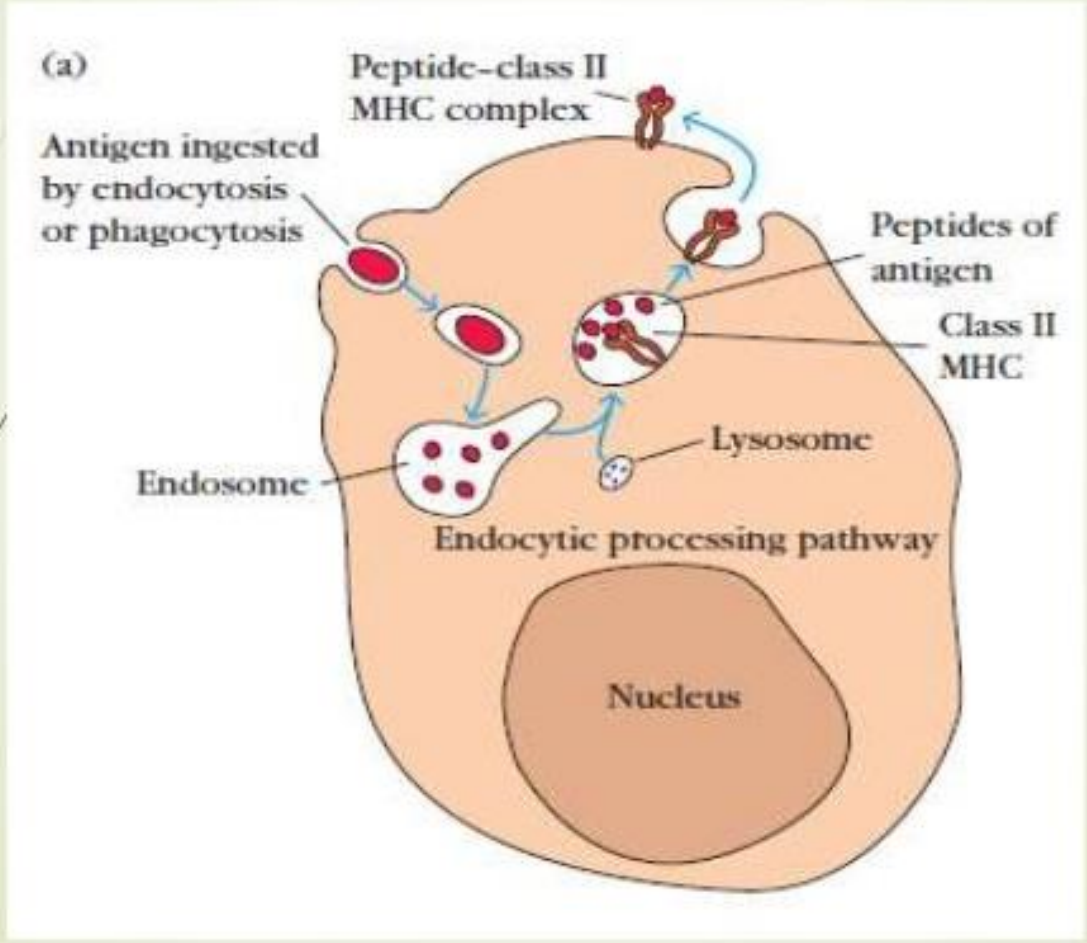
## Maturation

- Once **immature dendritic cells** come into contact with a presentable antigen, they **phagocytose** it and are converted from **immature to mature dendritic cells.**

- **Mature dendritic cells** degrade the **antigen into small pieces** and present those fragments at their **cell surface** using **MHC II molecules**.

- Now they are ready to act as **APC** (antigen presenting cells).

# Processing of Exogenous Antigen



## Types of dendritic cells

- Dendritic cells can be **"myeloid"** or **"plasmacytoid" ("lymphoid")** depending on haematopoietic precursor.

- **Myeloid dendritic cells (mDC)** secrete **IL-2** and have **TLR 2, TLR 4.**

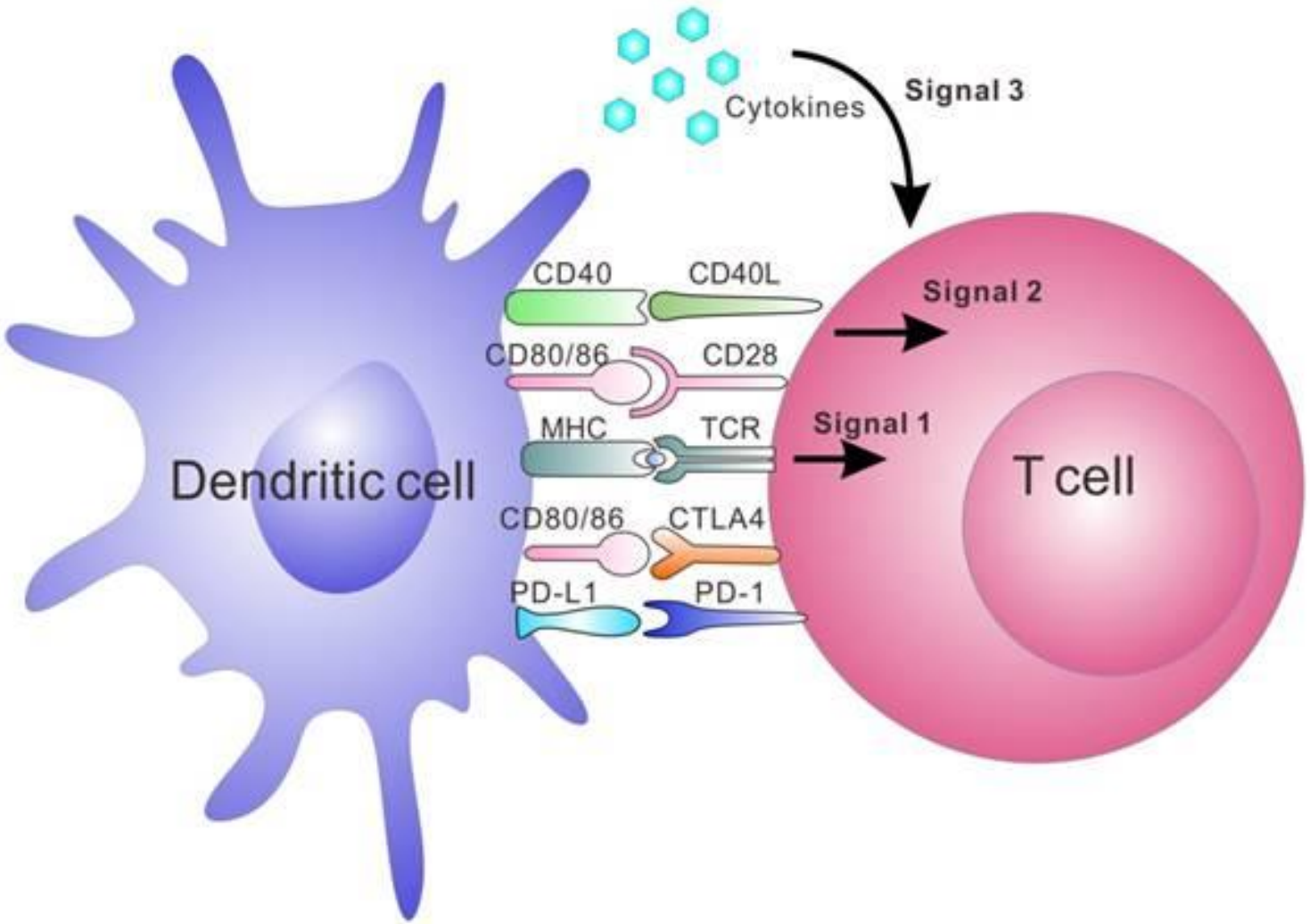
- **Plasmacytoid dendritic cells (pDC)** produce **interferon-α** and have **TLR 7** and **TLR9**.

## Interaction with T cells

- As **APC**, they upregulate **CCR7**, a **chemotactic receptor** that induces the dendritic cell to **travel** through the **blood stream** to the **spleen** or through the **lymphatic system** to a **lymph node**.
- In the **lymphoid tissues,** they **interact** with **helper T-cells.**
- They can also interact directly with **killer T-cells** by presenting antigen bound to **MHC I molecules.**
- In this way they initiate the **adaptive** immune response.

- Simultaneously, they **upregulate** cell-surface receptors that act as co-receptors in T-cell activation such as **CD80, CD86,** and **CD40.**

- This process greatly enhance their ability to **activate T-cells**.


Cytokines
Signal 3
CD40
CD40L
Signal 2
CD80/86
CD28
MHC
TCR
Signal 1
Dendritic cell
T cell
CD80/86
CTLA4
PD-L1
PD-1

## Interaction with B cells

- They also activate **B-cells** by presenting them with antigens **derived from the pathogen**, alongside non-antigen specific **costimulatory signals.**

- This interaction involves **MHC II** molecules**.**

## Unique character of dendritic cells

- **Macrophages** and **B cells** (the other professional antigen-presenting cells) can **only** activate **memory T-cells.**

- **Dendritic cells** can activate **both memory** and **naive T cells.**

## Communication with other cells

- The dendritic cells are constantly in **communication** with other cells in the body.

- This communication can take the form of **direct cell-to-cell contact** based on the interaction of cell-surface proteins.

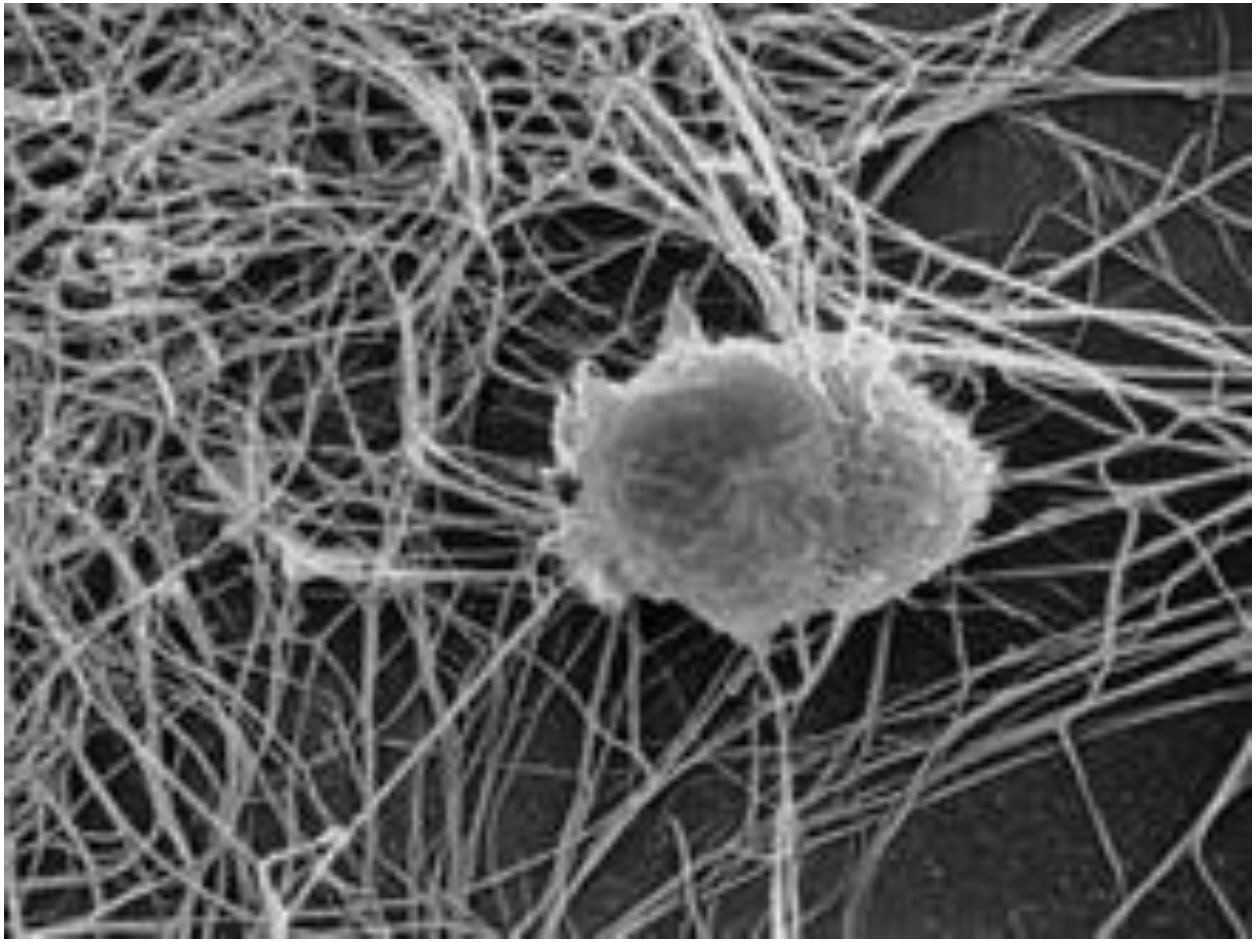
  An example of this includes the interaction of the receptor **CD40** of the dendritic cell with **CD40L** present on the lymphocyte.

- However, the cell-cell interaction can also take place at a distance via **cytokines.**

## Follicular dendritic cells (FDC)

- FDC are cells of the immune system found in **lymph follicles.**
- They are probably not of hematopoieic origin, but simply **look similar** to true dendritic cells.
- They share their **appearance** and **some aspects of their function** with the other types of dendritic cells.
- They assist in **B cell maturation** by the presentation of **intact antigen** to the B cells.
- They **do not have the capacity** to process the antigen and chop it down to pieces.

# Follicular dendritic cells (FDC)



# T helper cells

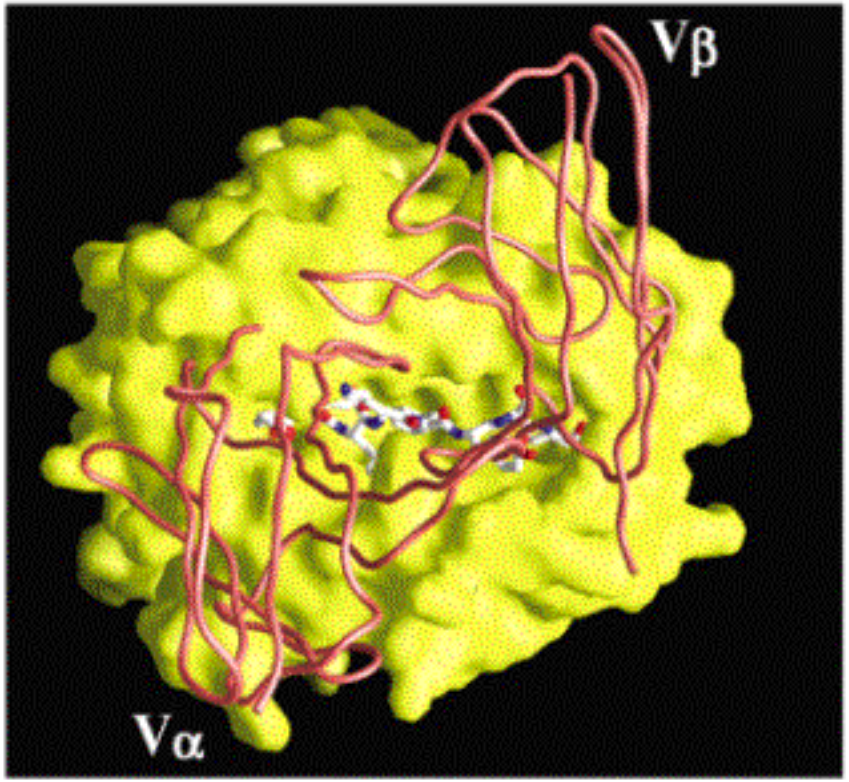
- **T helper cells** (also known as **effector T cells** or **Th cells**) are a **sub-group** of lymphocytes.
- These cells are **unusual** in that they have **no cytotoxic or phagocytic activity.**
- They **cannot kill** infected host cells or pathogens.

But **Th cells** are **particularly important** in the immune system:

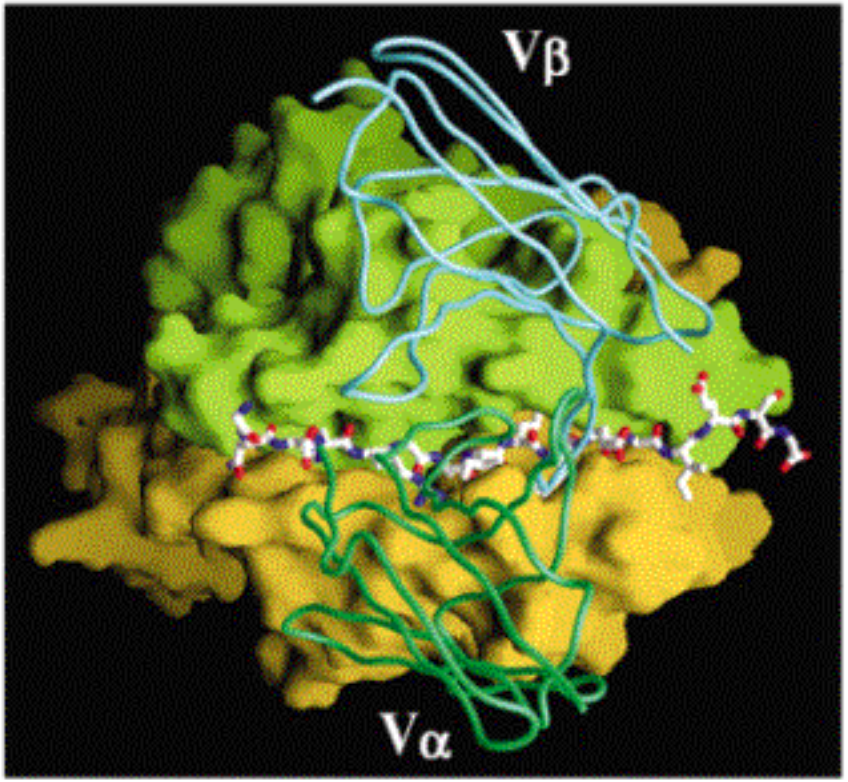
- They are **essential** in determining **B cell antibody class switching** and **affinity maturation.**
- They are also required for the **activation** and **growth** of **cytotoxic T cells.**
- And in maximizing **bactericidal** activity of **phagocytes** such as **macrophages.**

- Mature **Th cells** are believed to always express the **surface protein CD4.**
- T cells expressing **CD4** are also known as **CD4+** T cells.
- **CD4+** T cells have **TCRs** with an affinity for **Class II MHC.**
- **Class II MHC** proteins are generally only found on the surface of professional **antigen-presenting cells (APCs).**
- **Class I MHC** proteins are present on the surface of all nucleated cells.

- The antigens that bind to MHC proteins are always **short peptides**, 8-10 amino acids long for **MHC Class I**, and up to 25 or so for **MHC Class II.**




(a) TCR–peptide–class I MHC




(b) TCR–peptide–class II MHC

## Subclasses of Th cells

After many cell generations, the **Th cell's progenitors** differentiate into **effector Th cells, memory Th cells**, and **suppressor Th cells:**

- **Effector Th cells** secrete **cytokines**, proteins or peptides that stimulate or interact with other leukocytes, including **Th cells.**
- **Memory Th cells** are used to act as later effector cells during a **second** immune response.
- **Suppressor T cells** are believed to play an important role in the **self-limitation** of the immune system. They have been shown to **prevent** the development of various **auto-immune diseases**.

There are **two** major subtypes of **Th effector** cells, **Th1** and **Th2** cells:

## Th1 cells

- **Th1 cells** have macrophage as main partner and produce **IFN-γ** and **tumor necrosis factor-β.**
- They **stimulate** cellular immune system by **maximizing the killing efficacy** of the macrophages and the **proliferation** of **cytotoxic CD8+ T cells.**
- They also secrete **IL-12** that stimulates the production of **IFN-γ** in helper T cells, thereby promoting the **Th1 profile**.

## Th2 cells

- **Th2 cells** are activated by **IL4** and produce **IL4, IL5, IL6, IL10**, and **IL13.**

- They activate **humoral** immune system by stimulating B-cells into **proliferation**, by inducing **B-cell antibody class switching**, and increasing **antibody production**.

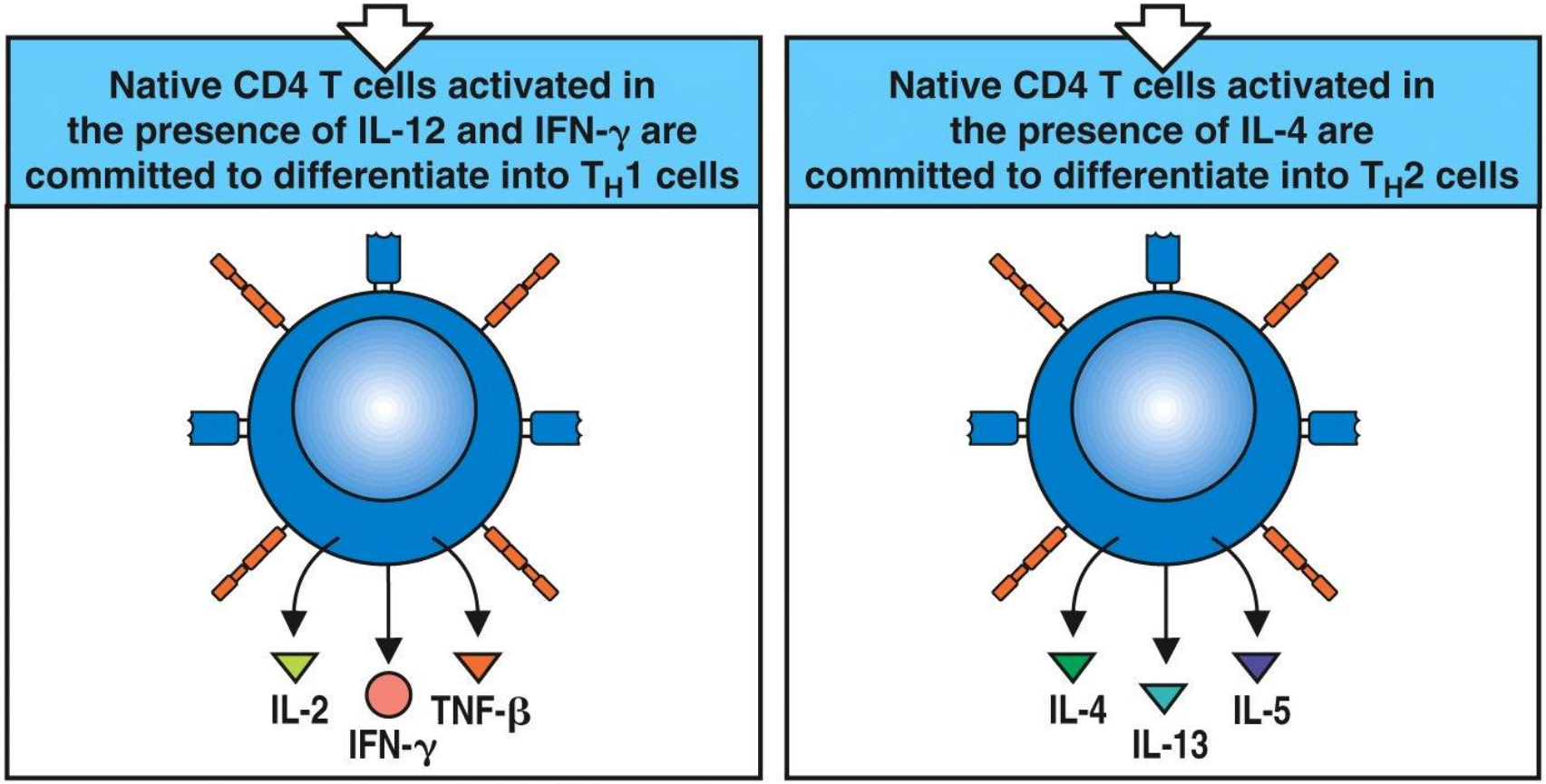



Figure 10-9 part 2 of 2 Immunobiology, 6/e. (© Garland Science 2005)

# Cytotoxic T cells

- A **cytotoxic T cell** (also known as **CTL, T-Killer cell, CD8+ T-cells** or **killer T cell**) belongs to a **sub-group** of T lymphocytes which are **capable of inducing the death** of infected somatic or tumor cells.

- Most **cytotoxic T cells** express **T-cell receptors (TcRs)** that can recognize a specific antigenic peptide bound to **Class I MHC molecules**, present in all nucleated cells.

- They also have a **glycoprotein** called **CD8**, which is attracted to non-variable portions of the **Class I MHC molecule.**

- **CD8+ T cells** are recognized as **CTL cells** once they become activated.

- The activation of **cytotoxic T cells** is dependent on several **simultaneous interactions** between molecules expressed on the surface of the T cell and molecules on the surface of the APC.

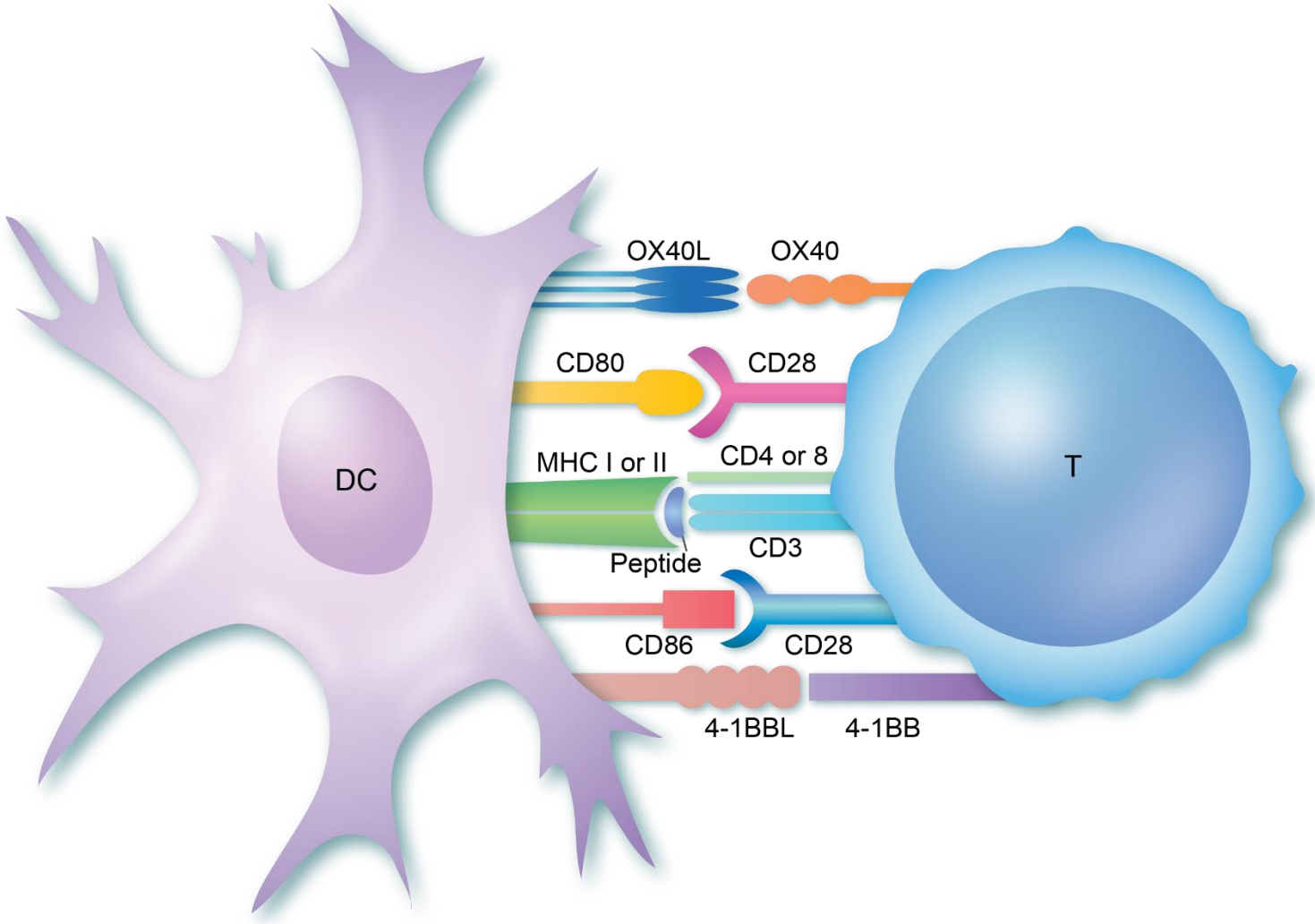
## Activation of CTL cells

- The **first signal** is generated by interaction between **TCR on T cell** and **peptide bound MHC class I molecule** on APC.

  This signal is stabilized by interaction between the **CD8** and the **class I MHC molecule**.

- The **second signal** is generated by interaction between **CD28 molecule** on the T cell and **CD80** or **CD86** on APC.

  **CD80** and **CD86** are known as ***co-stimulators*** for T cell activation.


OX40L
OX40
CD80
CD28
MHC I or II
CD4 or 8
DC
T
Peptide
CD3
CD86
CD28
4-1BBL
4-1BB

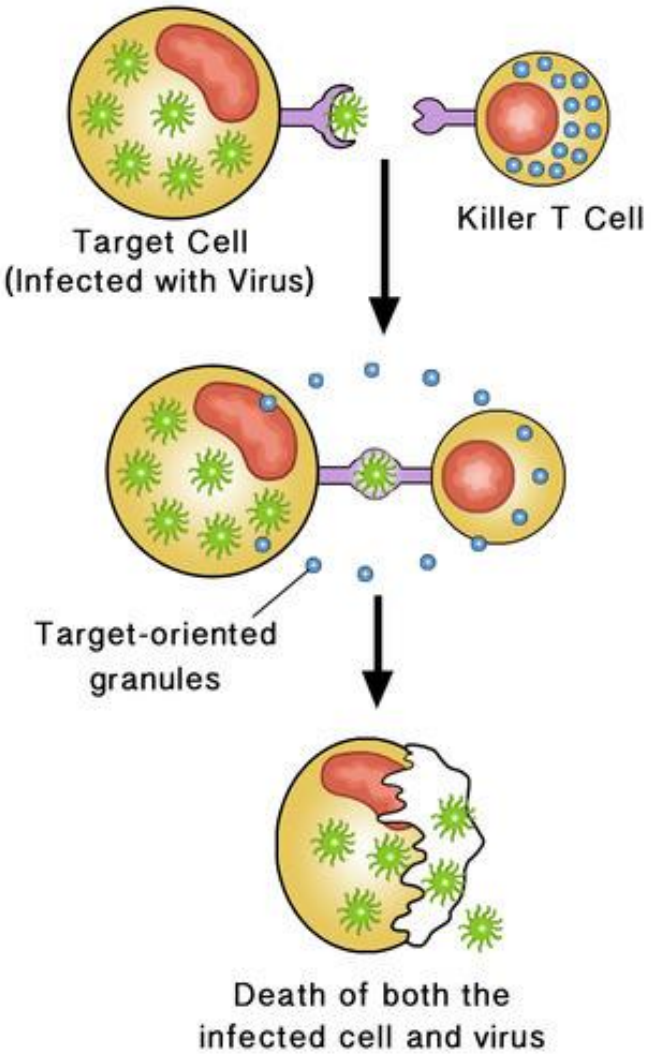
- Once activated, the **Cytotoxic T cells** undergoes **clonal expansion** with the help of **IL-2** that is a growth and differentiation factor for **T cells**.

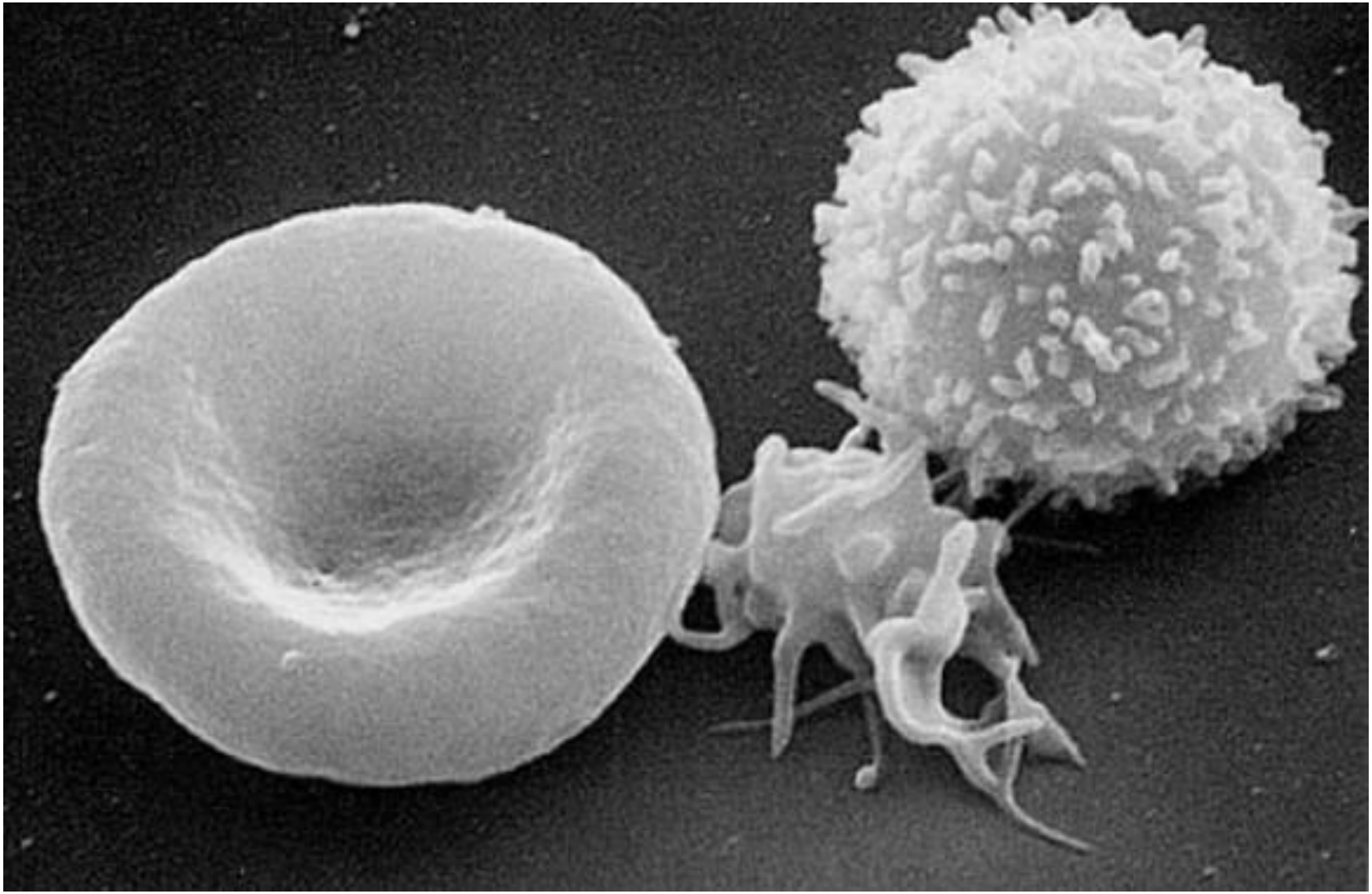
- This **increases** the number of **cells specific for the target antigen** that can then travel throughout the body in search of **antigen-positive** somatic cells.

- When they encounter **infected/dysfunctional** somatic cells, TC cells release the cytotoxins **perforin** and **granulysin**.

- Both form **pores** in the target cell's plasma membrane.

- It allows **granzyme**, a serine protease, to enter the target cell which then activate a series of enzymes, the **caspase cascade**, that eventually lead to **apoptosis (programmed cell death).**


Target Cell
(Infected with Virus)
Killer T Cell
Target-oriented
granules
Death of both the
infected cell and virus



اگر آپ کو علم مغرور کر رہا ہے

تو یہ جہالتِ اکبر ہے

**Cats win a battle** Battle of Pelusium 525 BC


Thank You!