BHARATHIDASAN UNIVERSITY

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Programme: M.Sc., Biomedical Science

Course Code: BM35C6

Course Title: Immunology

Unit-III

Antigens

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Unit III:

Antigens – Factors influence immunogenicity, Epitopes, haptens – Effector molecules of innate system -Acute phase proteins, complements- classical & alternative pathways of complement system. Effector molecules of cell-mediated and humoral immune responses - cytokines - Properties, receptors and antibodies / Immunoglobulins – Structure, antigenic determinants, immunoglobulin classes and functional significances.

PRESENTATION: 2

Effector molecules of cell-mediated immune responses

1. **Cytokines- Ils, IFN-γ, TNF, GM-CSF**
2. **Cytotoxins- Perforin, Granzymes, Granulysin**
3. **Fas Ligand (FasL)**

Cell-mediated immunity primarily involves **T cells** (T lymphocytes) and their effector molecules to combat intracellular pathogens (like viruses and some bacteria), tumor cells, and to mediate graft rejection.

Effector Molecules in Cell-Mediated Immunity:

1.Cytokines:

1. **Interleukins (ILs):**
    1. **IL-2:** Produced by activated T cells, promotes T cell proliferation (autocrine and paracrine growth factor).
    2. **IL-12:** Promotes differentiation of CD4+ T cells into Th1 cells, which are crucial for activating macrophages and enhancing cell-mediated responses.
    3. **IL-4 and IL-5:** Produced by Th2 cells, involved in promoting B cell differentiation and isotype switching, as well as in regulating allergic responses.

2. Interferon-gamma (IFN-γ):

1. A key cytokine produced by Th1 cells, CD8+ cytotoxic T cells, and NK cells. It activates macrophages, enhancing their ability to kill intracellular pathogens, and promotes the development of further Th1 responses.

3. Tumor Necrosis Factor (TNF):

1. Produced by activated T cells and macrophages, it promotes inflammation, apoptosis of infected cells, and helps to recruit other immune cells to the site of infection.

4. Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF):

1. Stimulates the production of granulocytes and macrophages from hematopoietic progenitors, enhancing their numbers and function.

2. Cytotoxins:

•Perforin:

•A protein released by cytotoxic **T lymphocytes** (CTLs or CD8+ T cells) and natural killer **(NK) cells**.

•It forms **pores** in the membrane of target cells, leading to cell lysis.

•Granzymes:

•Serine proteases released by **CTLs and NK cells** that enter target cells through perforin-formed pores

and **induce apoptosis** by cleaving intracellular proteins.

•**Granulysin:**

•Released by **cytotoxic T cells and NK cells**, it has **antimicrobial and pro-apoptotic properties**,

directly killing bacteria and inducing apoptosis in infected or cancerous cells.

3. Fas Ligand (FasL):

•Expressed on the surface of **activated cytotoxic T cells**.

•It binds to the **Fas receptor on target cells, triggering apoptosis through the Fas-mediated death pathway.**

Effector Molecules of Humoral Immune Responses

- 1. Antibodies (Immunoglobulins)- IgG, IgA, IgM, IgE and IgD
- 2. Cytokines
- 3. Complement Components

Humoral immunity involves **B cells** (B lymphocytes) and the production of antibodies to neutralize extracellular pathogens, such as bacteria, viruses, and toxins, and facilitate their clearance by other immune components.

Key Effector Molecules in Humoral Immunity:

1.Antibodies (Immunoglobulins):

- Produced by plasma cells (differentiated B cells), antibodies are the primary effector molecules in humoral immunity.

They have several functions:

Neutralization:

Bind to pathogens or toxins, blocking their interaction with host cells.

Opsonization:

Coat pathogens to enhance phagocytosis by cells with Fc receptors (e.g., macrophages and neutrophils).

Complement Activation:

Trigger the classical pathway of the complement system, leading to pathogen lysis and enhanced phagocytosis.

Antibody-Dependent Cellular Cytotoxicity (ADCC):

Bind to infected cells or pathogens, allowing NK cells and other immune cells to recognize and kill them.

Different classes of antibodies include:

- **IgG:** Provides the majority of antibody-based immunity against pathogens and is the main antibody in circulation.

- **IgA:** Found in **mucosal areas** (e.g., gut, respiratory tract) and secretions like **saliva and breast milk**; important for mucosal immunity.

- **IgM:** The **first antibody produced during an initial immune response**; effective in complement activation and pathogen agglutination.

- **IgE:** Binds to allergens and triggers histamine release from mast cells and basophils; plays a key role in **allergic responses** and defense against **parasites**.

- **IgD:** Functions mainly as a receptor on B cells and has a role in B cell activation.

2.Cytokines:

- **Interleukins (ILs):**
  - **IL-4, IL-5, and IL-6:** Promote B cell proliferation, differentiation, and class-switching to produce different antibody types (e.g., switching from IgM to IgG or IgE).
  - **IL-10:** Produced by regulatory T cells and B cells; helps in suppressing immune responses and maintaining tolerance to prevent overactive immune reactions.

- **Transforming Growth Factor-beta (TGF-β):**
  - Involved in class-switching to IgA production and in the regulation of B cell responses.

3.Complement Components:

- As part of the humoral immune response, antibodies (particularly IgM and IgG) activate the complement cascade, resulting in opsonization, lysis of pathogens, and inflammation.
- **C3b:** A complement fragment that binds to the pathogen surface, marking it for phagocytosis.

Summary

•**Cell-mediated immunity** relies primarily on **T cells** and their effector molecules (cytokines, cytotoxins, and FasL) to eliminate infected or abnormal cells and activate other immune components.

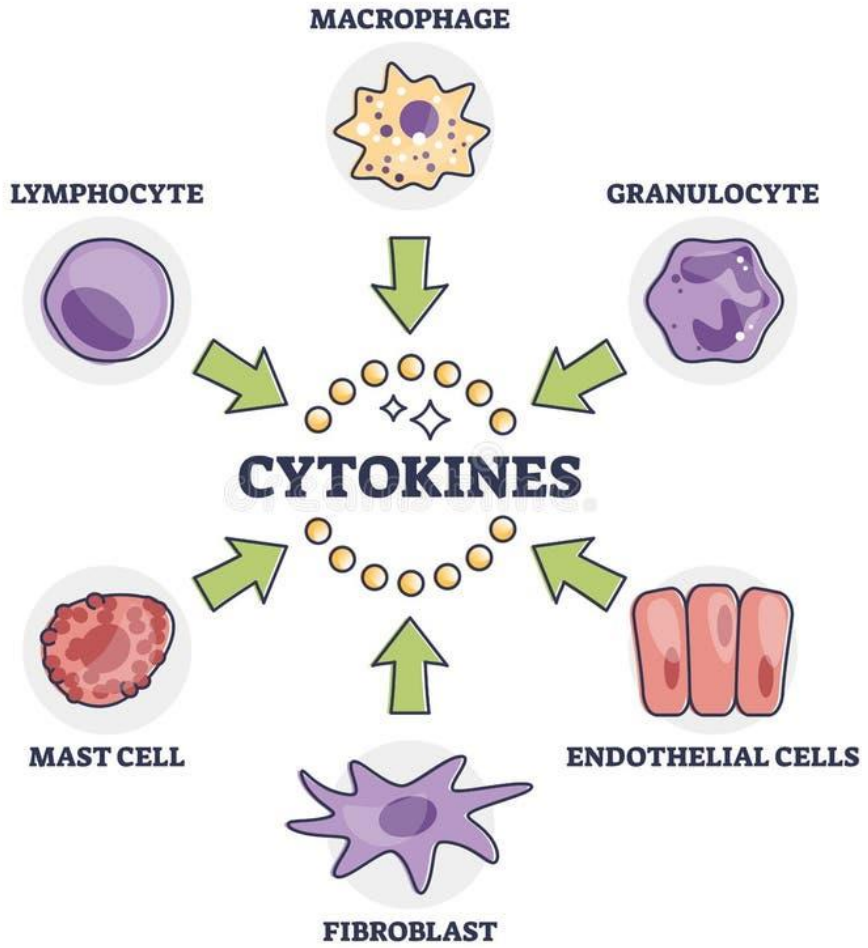
•**Humoral immunity** depends on **B cells** and their production of **antibodies**, which neutralize, opsonize, and activate the complement system to eliminate extracellular pathogens and toxins.

Both arms of the adaptive immune system collaborate to provide a comprehensive defense against a wide range of pathogens and maintain immune homeostasis.

CYTOKINES

- **Cytokines** are small proteins that play crucial roles in **cell signaling**, particularly in immune responses.
- They are produced by a variety of cells, primarily immune cells like macrophages, lymphocytes, and dendritic cells, but also non-immune cells such as endothelial cells and fibroblasts.
- Cytokines help mediate and regulate immunity, inflammation, and hematopoiesis.

Cytokines produced by different cells



Properties of Cytokines:

1. **Short half-life**: Most cytokines act locally rather than systemically due to their rapid degradation in the body.
2. **Low concentration**: They typically act in very low concentrations, but their effects are potent

1.Pleiotropy:

A single cytokine can act on different cell types and elicit various responses depending on the cell.

2. Redundancy:

Multiple cytokines can have the same effect on a target cell, compensating for one another in their function.

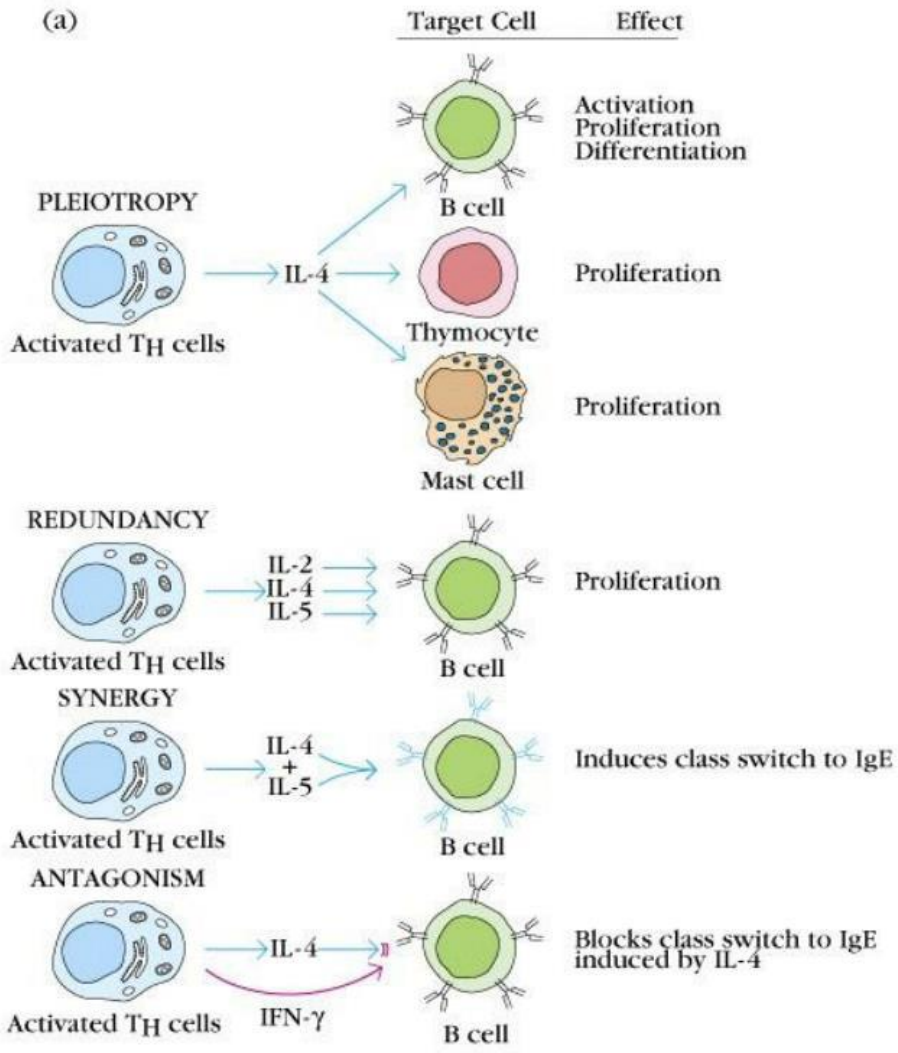
3. Synergy:

Cytokines can work together to amplify their effects.

4. Antagonism:

Some cytokines can inhibit the effects of others, creating a regulatory balance.

Properties of Cytokines



Cytokine Families

1	**Interleukins (IL**	Mostly produced by leukocytes, they **regulate immune responses and inflammation.**
2	**Interferons (IFN)**:	Primarily involved in **antiviral responses**, they also modulate immune activity.
3	**Tumor Necrosis Factors (TNF)**:	Promote inflammation and can induce **apoptosis** in target cells.
4	**Colony-Stimulating Factors (CSF)**:	Stimulate the **proliferation and differentiation of hematopoietic cells**.
5	**Chemokines**:	**Direct the migration of cells**, especially immune cells, during inflammation.
6	**Transforming Growth Factors (TGF)**:	**Regulate cell growth, differentiation, and immune suppression.**

Cytokine Receptors

Type I Cytokine Receptors (hematopoietin receptors):	Bind cytokines like **IL-2, IL-4, and erythropoietin (EPO)**.	Characterized by conserved motifs and subunits that interact with the **JAK-STAT signaling pathway**.
Type II Cytokine Receptors (interferon receptors):	Bind interferons (**IFNs) and IL-10** family members.	**Also activate the JAK-STAT pathway** but are structurally distinct from Type I receptors.
TNF Receptors:	Bind **TNF and related cytokines**	Can activate **pathways leading to inflammation (NF-κB activation) or apoptosis** (via death domains).
Immunoglobulin (Ig) Superfamily Receptors:	Bind cytokines like **IL-1**	can initiate a variety of **signaling cascades** that lead to inflammation.
Chemokine Receptors:	G protein-coupled receptors (**GPCRs**) that bind chemokines.	They **regulate cell migration** during immune responses.
TGF-β Receptors:	Serine/threonine kinase receptors that bind members of the **TGF-β family**.	They **regulate cell proliferation, differentiation, and immune suppression through the SMAD signaling pathway.**

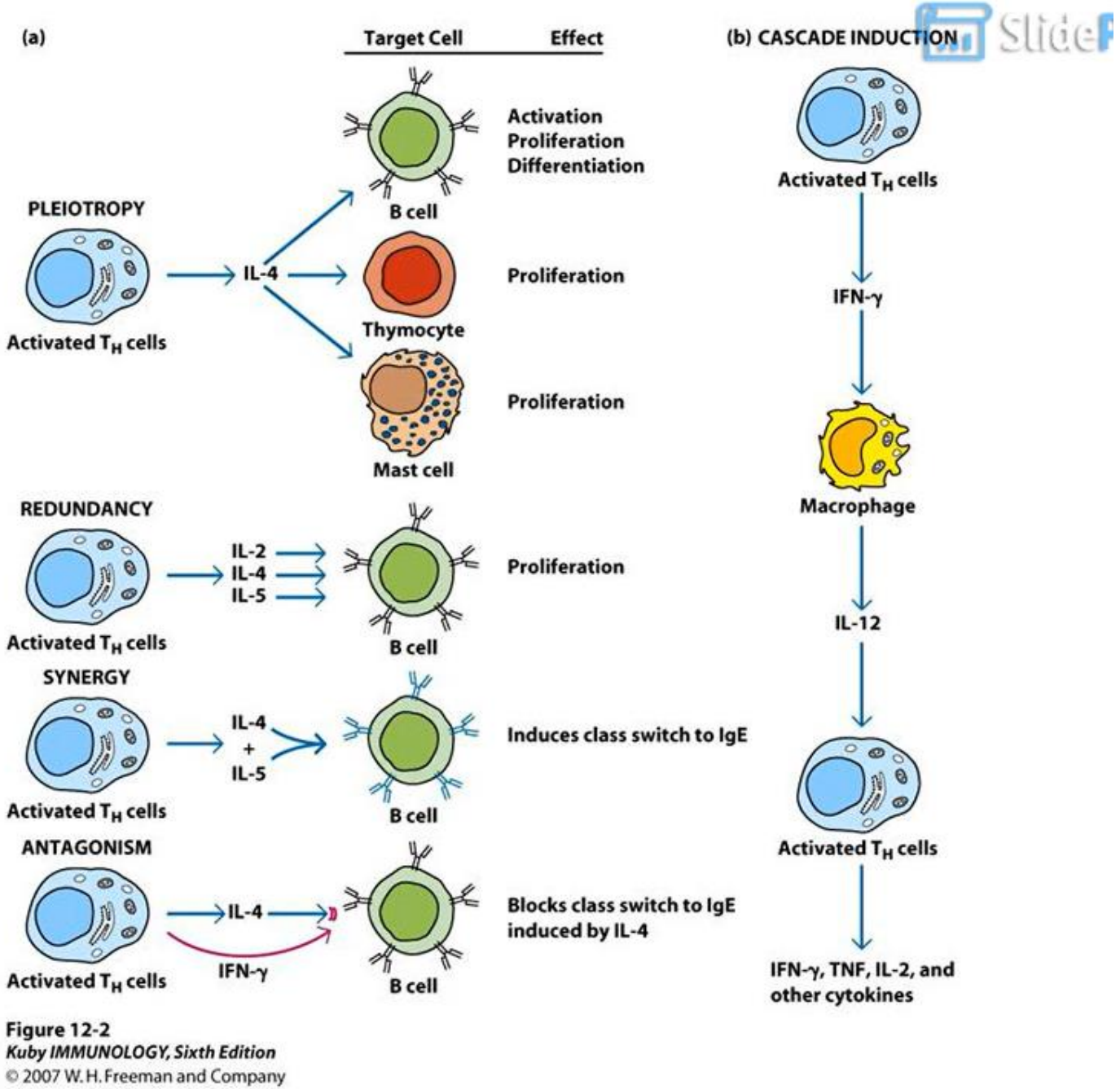


Figure 12-2
Kuby IMMUNOLOGY, Sixth Edition

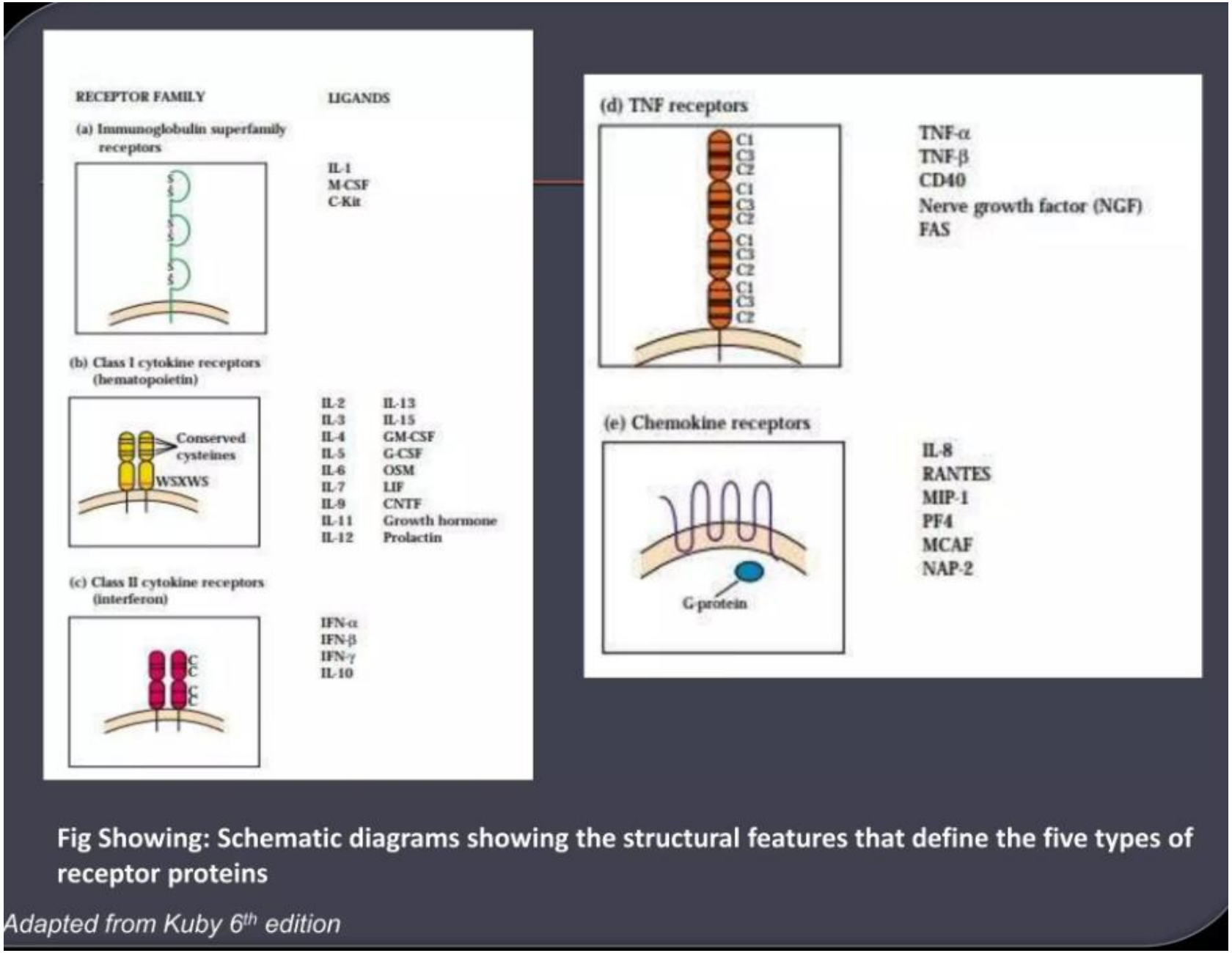


Fig Showing: Schematic diagrams showing the structural features that define the five types of receptor proteins

Adapted from Kuby 6th edition

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