**Connective Tissue:**

The different types of connective tissue are responsible for providing and maintaining the form of organs throughout the body. **Function of C.T:**  1- mechanical role, they provide a matrix that connects and binds other tissues and cells in organs 2- gives metabolic support to cells as the medium for diffusion of nutrients and waste products.

**Structural of C.T:** connective tissue is formed by three classes of components: **A**-cells, fibers, and ground substance. the major constituent of connective tissue is the **extracellular matrix .** **B**-Extracellular matrices consist of different combinations of **protein fibers** (collagen, reticular, and elastic fibers) and **ground substance.**

**I-Cells of Connective Tissue.**

|  |  |
| --- | --- |
| |  | | --- | | Functions of connective tissue cells. | |
| | **Cell Type** | **Activity** | **Representative Function** | | --- | --- | --- | | 1-Fibroblast, chondroblast, osteoblast, odontoblast | Production of fibers and ground substance | Structural | | 2-Plasma cell | Production of antibodies | Immunologic (defense) | | 3-Lymphocyte (several types) | Production of immunocompetent cells | Immunologic (defense) | | 4-Eosinophilic leukocyte | Participation in allergic and vasoactive reactions, modulation of mast cell activities and the inflammatory process | Immunologic (defense) | | 5-Neutrophilic leukocyte | Phagocytosis of foreign substances, bacteria | Defense | | 6-Macrophage | Secretion of cytokines and other molecules, phagocytosis of foreign substances and bacteria, antigen processing and presentation to other cells | Defense | | 7-Mast cell and basophilic leukocyte | Liberation of pharmacologically active molecules (eg, histamine) | Defense (participate in allergic reactions) | | 8-Adipocyte | Storage of neutral fats | Energy reservoir, heat production | |

**1**- **Fibroblasts**:

**A**-Fibroblasts synthesize collagen, elastin, glycosaminoglycans, proteoglycans and multiadhesive glycoproteins. **B**- Fibroblasts are the most common cells in connective tissue and are responsible for the synthesis of extracellular matrix components.

**2**-**Adipocytes**:

Adipocytes are connective tissue cells that have become specialized for storage of neutral fats or for the production of heat. Often called **fat cells,** they have considerable metabolic significance .

**3**- **Macrophages :**

**A**-Macrophages were discovered and initially characterized by their phagocytic ability. **B**-Macrophages derive from bone marrow precursor cells that divide, producing **monocytes** which circulate in the blood.

**4-Mast Cells**:

Mast cells are large, oval or round connective tissue cells,  whose cytoplasm is filled with basophilic secretory granules. The rather small, spherical nucleus is centrally situated .

**Function of mast cells:** Important molecules released from these cells includes:

**1**-        **Heparin**, that acts locally as an anticoagulant.

**2**-         **Histamine**, which promotes increased vascular permeability and smooth muscle contraction.

**3**-        **Serine proteases**, which activate various mediators of inflammation.

**4**-         **Eosinophil** and **neutrophil chemotactic factors** which attract those leukocytes

**5**-         **Leukotrienes** (or the slow-reacting substance of anaphylaxis, which also trigger smooth muscle contraction.

**5**- **Plasma Cells****:**

Plasma cells are large, ovoid cells that have a basophilic cytoplasm . **and** the nucleus of the plasma cell is generally spherical but eccentrically placed.

**6**-**Leukocytes**:

**A**-Connective tissue normally contains leukocytes that migrate from the blood vessels. Leukocytes  or white blood corpuscles, are the wandering cells of the connective tissue. **B**-They leave blood by migrating between the endothelial cells lining capillaries and postcapillary venules to enter connective tissue by a process called **diapedesis**. This process increases greatly during inflammation.

**II-Fibers:**

The connective tissue fibers are formed by proteins that polymerize into elongated structures. The three main types of connective tissue fibers are **collagen, reticular,** and **elastic fibers.** Collagen and reticular fibers are both formed by the protein **collagen,** and elastic fibers are composed mainly of the protein **elastin.** These fibers are distributed unequally among the types of connective tissue and the predominant fiber type is usually responsible for conferring specific properties on the tissue.

**1-Collagen** **Fibers:**

**i**-Its a family of structural proteins was selected by both environmental influences and the functional requirements of the animal organism and developed to acquire varying degrees of rigidity, elasticity, and strength. **ii**- The chief examples among its various types are present in the skin, bone, cartilage, smooth muscle, and basal lamina. **iii**-The collagens are produced by several cell types and are distinguishable by their molecular compositions, morphologic characteristics, distribution, functions, and pathologies. They are classified into the following four categories according to their structure and general functions.

**A**- **Collagens that Form Long Fibrils**:

**i**-The molecules of long fibril–forming collagens aggregate to form fibrils clearly visible in the electron or light microscope . Collagen type I is the most abundant and has a wide spread distribution. **ii**-It occurs in tissues as structures that are classically designated as **collagen fibers** forming structures such as tendons, organ capsules, and dermis.

**B-Fibril-Associated Collagens****:**

Fibril-associated collagens are short structures that bind the surfaces of collagen fibrils to one another and to other components. Molecules in this category are "fibril-associated collagens with interrupted triple helices."

**C-Collagens that Form Anchoring Fibrils**:

Anchoring collagen is type VII collagen, present in the anchoring fibrils that bind the basal lamina to reticular fibers in the underlying connective tissue .

**D-Collagens that Form Networks****:**

An important network-forming collagen is type IV collagen, whose molecules assemble in a meshwork that constitutes a major structural component of the basal lamina.

2- **Reticular Fibers**:

**i-reticular fibers** are now known to consist mainly of collagen type III, which forms extensive networks of extremely thin and heavily glycosylated fibers in certain organs. They are not visible in hematoxylin-and-eosin (H&E) preparations but can be easily stained black by impregnation with silver salts . **ii**-Reticular fibers constitute a network around the parenchymal cells of various organs (eg, liver, endocrine glands) and are particularly abundant in the framework of hematopoietic organs (eg, spleen, lymph nodes, red bone marrow). **iii**- In the latter sites the network is produced by fibroblast-like cells called **reticular cells**. The loose disposition of reticular fibers creates a flexible network in these organs and others that are subject to changes in form or volume, such as the arteries, uterus, and intestinal muscle layers.

**3**-**Elastic Fibers****:**

Elastic fibers are also thinner than the average collagen fiber and form sparse networks interspersed with collagen bundles in many organs subject to much bending or stretching, such as the wall of large arteries.

**Develop of Elastic fibers :** **(i)**-In the first stage, microfibrils forms from several different glycoproteins, notably the large glycoprotein called **fibrillin** . Fibrillin binds elastin and forms the scaffolding necessary for the deposition of elastin. Defective fibrillin results in the formation of fragmented elastic fibrils. **(ii)**- In the second stage of development, the protein **elastin** is deposited between the microfibrils, forming larger fibers. **(iii)**-During the third stage, elastin gradually accumulates until it comprises most of the fiber bundles, which are further surrounded by a thin sheath of microfibrils. **(iv)**-These are the mature **elastic fibers,** the most numerous component of the elastic fiber system. In the wall of large blood vessels, especially arteries, elastin also occurs as fenestrated sheets called **elastic lamellae**.

**III- Ground Substance**:

**i**-The ground substance is a highly hydrated, transparent, complex mixture of macromolecules, principally in three classes: **glycosaminoglycans**, **proteoglycans**, and **multiadhesive glycoproteins**. **ii**-The complex molecular mixture of the ground substance is transparent and rich in bound water. It fills the space between cells and fibers of connective tissue and, because it is viscous, acts as both a lubricant and a barrier to the penetration of invaders.

**Types of Connective Tissue**:

I- **Loose connective tissue** :

**i**-is a very common type of connective tissue that supports many structures which are normally under some pressure and low friction. It usually supports epithelial tissue, forms a layer around small blood and lymphatic vessels, and fills the spaces between muscle and nerve fibers. **ii**-Loose connective tissue is also found in the papillary layer of the dermis, in the hypodermis, in the linings of the peritoneal and pleural cavities, in glands, and in the mucous membranes supporting the epithelial cells.

**Areolar tissue:**

**i-Its** Loose connective tissue has all the main components of connective tissue (cells, fibers, and ground substance) in roughly equal parts. **ii**-The most numerous cells are fibroblasts and macrophages, but other types of connective tissue cells are also present. Collagen, elastic, and reticular fibers also appear in this tissue.

**II-Dense connective tissue**:

**i**- It has the same components found in loose connective tissue, but there are fewer cells and a clear predominance of collagen fibers over ground substance. **ii**-Dense connective tissue is less flexible and far more resistant to stress than is loose connective tissue.

**Types of** **Dense connective tissue:**

**A-Dense irregular connective tissue:**

**i-The** **dense irregular** connective tissue when the collagen fibers are arranged in bundles without a definite orientation. The collagen fibers form a 3-dimensional network in dense irregular tissue, providing resistance to stress from all directions. **ii-** Dense irregular connective tissue is often found closely associated with loose connective tissue.

**B-Dense regular connective tissue:**

**i**-The collagen bundles of **dense regular** connective tissue are arranged according to a definite pattern, with collagen fibers with the linear orientation of fibroblasts in response to prolonged stresses exerted in the same direction . This arrangement offers great resistance to traction forces. **ii**-Tendons and ligaments are the most common examples of dense regular connective tissue.

**III-Reticular Tissue**:

**1**-Individual reticular fibers form delicate three-dimensional networks that support cells in **reticular tissue**. This specialized connective tissue consists of reticular fibers of type III collagen produced by specialized fibroblasts called reticular cells . **2**- The reticular fibers provide the framework for hematopoietic organs and lymphoid organs (bone marrow, lymph nodes, and spleen). **3**-The reticular cells are dispersed along this framework and partially cover the reticular fibers and ground substance with cytoplasmic processes. The resulting cell-lined system creates a spongelike structure within which cells and fluids are freely mobile.

IV-**Mucous Tissue**:

**i-Muco****us tissue** is found mainly in the umbilical cord and fetal tissues. **ii**-Mucous tissue has an abundance of ground substance composed chiefly of hyaluronic acid, making it a jellylike tissue containing very few collagen fibers with scattered fibroblasts .