



Lectures of Histology

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Connective Tissue

Connective tissue serves as a connecting link for binding, supporting, and strengthening all other body tissues together, as well as serve as frameworks, fill spaces, store fat, produce blood cells, protect against infection, and repair tissue damage.

* Components of Connective Tissue

- 1. Cells
- **2.** Protein fibers
- 3. Ground substance

Protein fibers and **ground substance** are collectively called extracellular matrix (ECM) that consist of different combinations of protein fibers (collagen, elastic fibers). The composition and structure of extracellular matrix determines function and characteristic of connective tissue (Fig.1).

Connective tissue originates from mesenchyme, a tissue developing mainly from the middle layer of the embryo, the **Mesoderm**. Mesenchyme consists largely of viscous ground substance with few collagen fibers.



Fig. 1: Connective tissue.

* Functions of Connective Tissues

- Enclosing and separating organs.
- Connecting tissues to one another (ligaments and tendons).
- Supporting and moving (Joints, cartilage, and bones).
- Storing, insulating, and cushioning (adipose tissue).
- Transport and protection (blood).

* Cells of Connective Tissue

- <u>- Fixed cells/</u> appear in tissue in somewhat stable numbers (e.g., fibroblast, mesenchymal cells, adipocyte).
- <u>- Wandering cells/</u> found in tissue as response to infection/injury (migrate from blood stream to perform their function in other regions of C.T.), (e.g., macrophage, mast cell, plasma cells, leukocytes).

1. Fibroblast

The most common cell in connective tissue proper (Fig.2), produce and maintain most of the extracellular components (matrix). The term "**fibroblast**" denotes to <u>active cell</u> while "**fibrocyte**" denote to <u>quiescent cell</u>.

Fibroblast larger than **fibrocyte** and has more abundant irregularly processes cytoplasm, containing much RER and a well-developed Golgi apparatus, with a large, ovoid, euchromatic nucleus and a prominent nucleolus (fibrocyte has much less RER and darker more heterochromatic nucleus).

Fibroblasts involved in wound healing, sometimes called <u>myofibroblasts</u>, have a well-developed contractile function and are enriched with a form of actin.



Fig. 2: Fibrocyte and Fibroblast.

2. Mesenchymal cell

It is undifferentiated and have large nuclei, with prominent nucleoli and fine chromatin, in addition to thin cytoplasmic processes. These cells producing all types of connective tissue (Fig.3).



Fig. 3: Mesenchymal cell.

3. Adipocyte (fat cell)

Found in C.T. of many organs, specialized for cytoplasmic storage of lipid as neutral fats, or less commonly to produce heat (Fig.4).



Fig. 4: Adipocyte.

4. Plasma cell

It is lymphocyte–derived, antibody-producing cell, relatively large, ovoid has basophilic cytoplasm rich in RER and a large Golgi apparatus near the nucleus that may appear pale in routine histologic preparations (Fig.5). Nucleus of plasma cell is generally spherical and contain compact, peripheral regions of heterochromatin alternating with lighter areas of euchromatin. A few plasma cells are present in most C.T.



Fig. 5: Plasma cell.

5. Macrophage

Has highly developed phagocytic ability and removal of dead cells, tissue debris, or other particulate material, being especially abundant at sites of inflammation. Size and shape vary corresponding to their state of functional activity. Has an eccentrically located, oval or kidney-shaped nucleus. In TEM, macrophages are shown to have a characteristic irregular surface with folds and indentations (related to their pinocytotic and phagocytic activities) (Fig.6). They generally have well-developed Golgi complexes and many lysosomes. Macrophages derive from monocytes that circulate in the blood. They are distributed throughout the body and are normally present in the stroma of most organs, but have different names in various organs (e.g., <u>Kupffer cells</u> in liver, <u>microglial cells</u> in CNS, <u>Langerhans cells</u> in skin, <u>osteoclasts</u> in bone, and <u>dust cells</u> in lung).



Fig. 6: Macrophage.

6. Mast cell

It is oval shaped cell, filled with basophilic secretory granules which often obscure the central nucleus (Fig.7). These granules are electron-dense and of variable size. Mast cell function in the localized release of many bioactive substances important in the local inflammatory response, innate immunity, and tissue repair. The molecules released from these cells' secretory granules includes: heparin, histamine, eosinophil and neutrophil chemotactic factors, cytokines. Release of certain chemical mediators stored in mast cells promotes the allergic reactions known as immediate hypersensitivity reactions because they occur within a few minutes after the appearance of an antigen in an individual previously sensitized to that antigen.



Fig. 7: Mast cell.

7. Leukocytes

Other white blood cells or leukocytes (Fig.8) normally comprise a population of wandering cells in connective tissue, derived from circulating blood cells, they leave blood by migrating between the endothelial cells of vessels to enter connective tissue. This process increases greatly during inflammation, which is a vascular and cellular defensive response to injury or foreign substances. Most leukocytes function in connective tissue only for a few hours or days and then undergo apoptosis.



Fig. 8: Leukocyte.

* Fibers

These are elongated structures formed from proteins that polymerize after secretion from fibroblasts. Three main types include collagen, elastic, and reticular fibers (Fig.9). Collagen and reticular fibers are both formed by proteins of collagen, while elastic fibers are composed mainly of protein elastin. These fibers are distributed unequally among the different types of connective tissue, with the predominant fiber type conferring most specific tissue properties.



Fig. 9: Types of fibers.

- Collagen fibers

White colored when fresh, un-branched, present in bundle, extremely strong, flexible, inelastic (resistant to normal tearing forces) (Fig.10). Form from collagen protein, which are composed of fibril formed by microfibrillar subunits. There are 28 collagen types in vertebrates, can be categorized according to their structure: (fibrillar collagens, sheet-forming collagens). Collagen is a key element of all connective tissues (found in abundance in bone, cartilage, tendon, and ligament).



Fig. 10: Collagen fibers.

- Elastic fibers

Thinner than collagen fibers, but branched, elastic, and strong (Fig.11) or found as elastic lamellae, made up of elastin protein. Form sparse networks of microfibrils interspersed with collagen bundles in many organs, particularly those subject to regular stretching or bending. Elastic fibers have rubberlike properties that allow tissue containing these fibers, such as the stroma of lungs, to be stretched or distended and return to their original shape, they found also in the walls of large blood vessels.



Fig. 11: Elastic fibers.

- Reticular fibers

Found in connective tissue of many organs, notably in spleen, lymphnodes, reticular lamina of basement membranes, typically also surround adipocytes, smooth muscle, and small blood vessels (delicate networks of reticular fibers serve as the supportive stroma for the parenchymal secretory cells and rich microvasculature of liver and endocrine glands). Reticular fibers consist mainly of collagen type III (Fig.12).



Fig. 12: Reticular fibers.

* Ground substance

Is a highly hydrated (with much bound water), transparent, complex mixture of three major kinds of macromolecules: glycosaminoglycans (GAGs), proteoglycans, and multi-adhesive glycoproteins. Ground substance is filling the space between cells and fibers in connective tissue, allows diffusion of small molecules and, because it is viscous, acts as both a lubricant and a barrier to the penetration of invaders. Physical properties of ground substance also influence various cellular activities.

The largest and most ubiquitous GAG is hyaluronan (also called hyaluronic acid). Hyaluronan forms a viscous, pericellular network which binds a considerable amount of water, giving it an important role in allowing molecular diffusion through connective tissue and in lubricating various organs and joints.