Ground substance

Ground substance is found in all cavities and clefts between the fibres and cells of connective tissues. Water, salts and other low molecular substances are contained within the ground substance, but its main structural constituent are proteoglycans.
Ground substance is soluble in most of the solvents used to prepare histological sections and therefore not visible in ordinary sections.

Proteoglycans are responsible for the *highly viscous character of the ground substance*. Proteoglycans consist of proteins (~5%) and polysaccharide chains (~95%), which are covalently linked to each other. The polysaccharide chains belong to one of the five types of *glycosaminoglycans*, which form the bulk of the polysaccharides in the ground substance.

Hyaluronan (or *hyaluronic acid*) is the dominant glycosaminoglycan in connective tissues. The molecular weight (MW) of hyaluronic acid is very high (~ MW 1,000,000). With a length of about 2.5 µm hyaluronan is **very large**. Hyaluronan serves as a "backbone" for the assembly of other glycosaminoglycans in connective and skeletal tissue, which results in even larger molecule complexes (MW 30,000,000 - 200,000,000).
Hyaluronan is also a major component of the synovial fluid, which fills joint cavities, and the vitreous body of the eye.

The remaining four major glycosaminoglycans are *chondroitin sulfate, dermatan sulfate, keratan sulfate* and *heparan sulfate*. These glycosaminoglycans attach via core- and link-proteins to a backbone formed by the hyaluronic acid. The coiled arrangement of the hyaluronan and other attached glucosaminoglycans fills a roughly spherical space with a diameter of ~0.5 µm. This space is called a *domain*. Neighbouring domains overlap and form a more or less continuous three-dimensional *molecular sieve* in the interstitial spaces of the connective tissues.

The large polyanionic carbohydrates of the glycosaminoglycans bind large amounts of water and cations. The bound water in the domains forms a medium for the diffusion of substances of low molecular weight such as gases, ions and small molecules, which can take the shortest route, for example, from capillaries to connective tissue cells. Large molecules are excluded from the domains and have to find their way through the spaces between domains.

The restricted motility of larger molecules in the extracellular space inhibits the spread of microorganisms through the extracellular space. A typical bacterium (0.5 x 1 µm) is essentially immobilised in the meshwork formed by the domains. The pathogenicity of a bacterium is indeed to some extent determined by its ability to find its way through the

mesh, and some of the more invasive types produce the enzyme *hyaluronidase*, which depolymerises hyaluronic acid.

The components of the ground substance, collagen, elastic and reticular fibres are synthesised by cells of the connective tissues, the fibrocytes.

Connective Tissue Cells

Connective tissue cells are usually divided into two groups based on their ability to move within the connective tissue. Fibrocytes (or fibroblasts) and fat cells are *fixed cells*. Macrophages, monocytes, lymphocytes, plasma cells, eosinophils and mast cells are *wandering cells*.

Fibrocytes

Fibrocytes are the most common cell type in connective tissues. They are the "true" connective tissue cells. Usually only their oval, sometimes flattened nuclei are visible in LM sections. The cytoplasm of a resting (i.e. inactive) fibrocyte does not contain many organelles. This situation changes if the fibrocytes are stimulated, for example, by damage to the surrounding tissue. In this case the fibrocyte is transformed into a fibroblast, which contains large amounts of the organelles which are necessary for the synthesis and excretion of proteins needed to repair the tissue damage (Which ones?). Fibrocytes do not usually leave the connective tissue. They are, however, able to perform amoeboid movement.

The terms fibrocyte and fibroblast refer here to the inactive and active cells respectively - at times you will see the two terms used as synonyms without regard for the state of activity of the cell.

Reticular cells

Reticular cells are usually larger than an average fibrocyte. They are the "fibrocytes" of reticular connective tissue and form a network of reticular fibres, for example, in the lymphoid organs. Their nuclei are typically large and lightly stained (H&E) and the cytoplasm may be visible amongst the cells which are housed within the network of reticular fibres.

Adipocytes

Fat cells or *adipocytes* are fixed cells in loose connective tissue. Their main function is (what surprise!) the storage of lipids. If "well fed" the cytoplasm only forms a very narrow rim around a large central lipid droplet. The flattened nucleus may be found in a slightly thickened part of this cytoplasmic rim - if it is present in the section, which may not be the case since the diameter of an adipocyte (up to 100 µm) is considerable larger than the thickness of typical histological sections. A "starving" adipocyte may contain multiple small lipid droplets and gradually comes to resemble a fibrocyte.

Lipid storage/mobilisation is under nervous (sympathetic) and hormonal (insulin) control. Adipocytes also have an endocrine function - they secrete the protein *leptin* which provides brain centers which regulate appetite with feedback about the bodies fat reserves.

Leptin deficiency in experimental animals results in obesity.

Adipocytes are very long-lived cells. Their number is determined by the number of preadipocytes (or lipoblast) generated during foetal and early postnatal development.

Macrophages

Macrophages arise from precursor cells called monocytes. Monocytes originate in the bone marrow from where they are released into the blood stream. They are actively mobile and leave the blood stream to enter connective tissues, where they differentiate into macrophages. Macrophages change their appearance depending on the demand for phagocytotic activity. Resting macrophages may be as numerous as fibrocytes.

Resting macrophages are difficult to distinguish from fibrocytes in H&E stained sections.

Connective tissue

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In the human body there are four types of tissue: (1) Epithelial, (2) **Connective**, (3) Muscle, and (4) Nervous Tissue.

- Blood functions in transport. Its extracellular matrix is blood plasma, which transports dissolved nutrients, hormones, and carbon dioxide in the form of bicarbonate. The main cellular component is red blood cells.

- Cartilage makes up virtually the entire skeleton in chondrichthyes. In most other vertebrates, it is found primarily in joints, where it provides cushioning. The extracellular matrix of cartilage is composed primarily of collagen.
- **Connective tissue**
    - Dense connective tissue or Fibrous connective tissue forms ligaments and tendons. Its densely packed collagen fibers have great tensile strength.
    - Loose connective tissue or Areolar connective tissue holds organs and epithelia in place, and has a variety of proteinaceous fibers, including collagen and elastin. It is also important in inflammation.
    - Reticular connective tissue is a network of reticular fibers (fine collagen) that form a soft skeleton to support the lymphoid organs (lymph nodes, bone marrow, and spleen.)
    - Adipose tissue contains adipocytes, used for cushioning, thermal insulation, lubrication (primarily in the pericardium) and energy storage.

Fiber types as follows: Collagenous fibers, elastic fibers, retucular fibers

[edit]

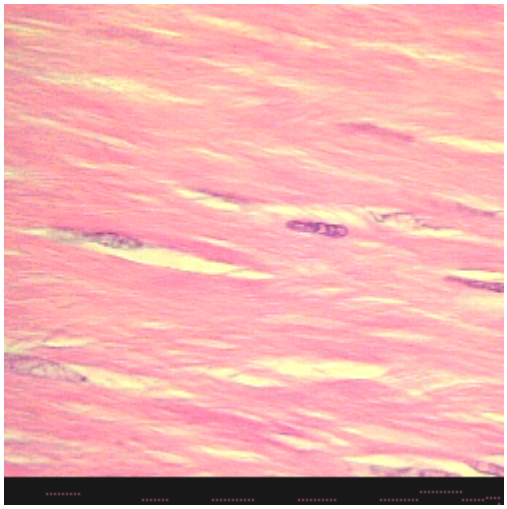
Disorders of connective tissue

Various connective tissue conditions have been identified; these can be both inherited and environmental.

- Marfan syndrome - a genetic disease causing abnormal fibrillin.
- Scurvy - caused by a dietary deficiency in vitamin C, leading to abnormal collagen.
- Ehlers-Danlos syndrome - a genetic disease causing progressive deterioration of collagens, with different EDS types affecting different sites in the body, such as joints, heart valves, organ walls, arterial walls, etc.
- Osteogenesis imperfecta (brittle bone disease) - caused by insufficient production of good quality collagen to produce healthy, strong bones.
- Spontaneous pneumothorax - collapsed lung, believed to be related to subtle abnormalities in connective tissue.
- Sarcoma - a neoplastic process originating in connective tissue

Connective Tissue

As the name implies, connective tissue serves a "connecting" function. It supports and binds other tissues. Unlike epithelial tissue, connective tissue typically has cells scattered throughout an extracellular matrix.



Irregular Dense Collagenous Connective Tissue -
Human Dura mater
Image courtesy of Richard Harris and BIODIAC.

Loose Connective Tissue

In vertebrates, the most common type of connective tissue is loose connective tissue. It holds organs in place and attaches epithelial tissue to other underlying tissues.

Loose connective tissue is named based on the "weave" and type of its constituent fibers. There are three main types:

Collagenous Fibers

Collagenous fibers are made of collagen and consist of bundles of fibrils that are coils of collagen molecules.

Elastic Fibers

Elastic fibers are made of elastin and are "stretchable."

Reticular Fibers

Reticular fibers join connective tissues to other tissues.

Fibrous Connective Tissue

Another type of connective tissue is fibrous connective tissue which is found in tendons and ligaments. Fibrous connective tissue is composed of large amounts of closely packed collagenous fibers.

Specialized Connective Tissues

Adipose

Adipose tissue is a form of loose connective tissue that stores fat.

Cartilage

Cartilage is a form of fibrous connective tissue that is composed of closely packed collagenous fibers in a rubbery gelatinous substance called chondrin. The skeletons of sharks and human embryos are composed of cartilage. Cartilage also provides flexible support for certain structures in adult humans including the nose, trachea and ears.

Bone

Bone is a type of mineralized connective tissue that contains collagen and calcium phosphate, a mineral crystal. Calcium phosphate gives bone its firmness.

Blood

Interestingly enough, blood is considered to be a type of connective tissue. Even though it has a different function in comparison to other connective tissues it does have an extracellular matrix. The matrix is the plasma and erythrocytes, leukocytes and platelets are suspended in the plasma.

Human Blood Cells

Share Your Opinions

What do you think? Have questions about connective tissue? Come on over to the Biology Forum and share your thoughts, opinions and feelings. Until next time...