

## 32: CONECTIVE TISSUE OVERVIEW, and COLLAGEN

The definition of a connective tissue isn't that it must connect something; some types of connective tissue do connect things. The definition of connective tissue comes from the microscopic view of these tissues. Connective tissues are made of three things: 1) specialized cells, 2) ground substance, and 3) protein fibers. In general, the **specialized cells** create the protein fibers and much of the ground substance. In other words, the specialized cells create the environment in which they live. The **ground substance** is the "background stuff" that everything is immersed in, and can be a solid, liquid or gel. **Protein fibers** can be **collagen**, **elastin**, or **reticular fibers**. Reticular fibers are basically very thin threads of collagen.

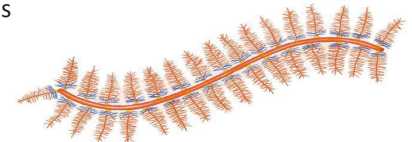
There are three types of connective tissue, with three subcategories under each. (The number three shows up a lot, as you will see!) **Fibrous** connective tissue is divided into **loose** (areolar), **dense**, and **adipose** (fat). **Cartilaginous** connective tissues are **hyaline**, **elastic** or **fibrocartilage**. The last category is a catch-all for everything else, and I have called it "other." These others include **bone**, **blood** and **lymph**. Don't worry that you don't know what all these tissues are. The important thing right now is to get this chart written so that you can come back to it later on, as we study each kind of connective tissue.

Let's start with a close-up look at **collagen**. The word collagen comes from the Greek word "kolla" which means "glue," and "gen," which means "to make." So collagen is...a glue-maker? Actually, this name makes sense if you know that for centuries, scrapings from animal hides were used to make glue, because skin has a lot of collagen in it. Collagen from animal hides is used today to make gelatin ("Jello") which is very gummy and sticky, like glue.

The smallest unit of collagen is a polypeptide (chain of amino acids) in an alpha helix shape. Three of these alpha helices are bound together to form the complete triple-helix collagen protein. (Every third amino acid in the chain is **glycine**, the smallest amino acid. Its small size helps the strands wind together very tightly.) The triple-helix proteins are assembled inside the endoplasmic reticulum of cells called fibroblasts. In order for the stapler enzyme inside the ER to be able to do its job and assemble these proteins, it needs a molecule of vitamin C (ascorbic acid) to attach to its active site. An extra molecule that is necessary for an enzyme to be able to do its job is called a **coenzyme** or **cofactor**. If there is a shortage of vitamin C, the body will not be able to produce good quality collagen, and a condition called **scurvy** will result. Many sailors died of scurvy in past centuries, before nutrition was recognized as a possible cause of disease.

The triple-helix collagen proteins exit the ER in vesicles and go over to a Golgi body where they are tagged with sugar tags that mean "put me outside the cell." The collagen proteins exit the Golgi and are taken (inside vesicles) to the plasma membrane where exocytosis occurs and they are put outside. Once outside the cell, collagen proteins begin to link up with each other and make larger strands. The first larger stand they make is called a **microfibril**. Then some microfibrils join together to make a **fibril**, and finally some fibrils are bound together to make a **fiber**. (Sometimes the fibers are bound into even bigger bundles.) This "bundles of bundles of bundles" organization is used in other tissue types, too, such as muscle. It is the ideal structure for achieving great strength.

**Fibroblasts** are cells that make collagen. Since they also secrete most of the things that form the ground substance, the fibroblasts really create their entire environment. The ground substance is made of 90 percent water 10 percent something called **proteoglycans**. The "proteo" part means "protein" and the "glycan" part means "sugar" (like "gluco"). A proteoglycan molecule looks a bit like a bottle brush. This picture shows many proteoglycans attached to a long "rope" molecule. The hairs of these brushes are long chains of sugars that are very hydrophilic. Thus, they attract lots of water molecules to the area. That is where the 90 percent water comes from. The proteoglycan molecules draw the water in and hold it there. The high water content of the dermal layer of skin (under the basement membrane) is partly what makes the skin so soft and resilient. (One of the first symptoms of serious dehydration is that the skin doesn't bounce back after you press it.) One of these brush molecules is called **chondroitin sulfate**, a very popular nutritional supplement that you can find in any pharmacy or grocery store.



The little brushy things are the proteoglycans. The orange stripe in the middle is hyaluronic acid.

The long rope molecule that all the bottle brush molecules are attached to is called **hyaluronic acid**. (*Hi-ah-lure-ON-ic*) The ends of the hyaluronic acid molecules are fastened to the collagen fibers. In many parts of the body, the space around the cells is filled with these ropes and bottle brushes. This space, all around the cells, is often called the **extracellular matrix**. "Extra" means "outside" in this case. Other things can float around in the extracellular matrix, too. White blood cells are often found here.

Hyaluronic acid is sometimes taken as a nutritional supplement by people who are wishing to avoid problems with connective tissue. The theory is that by supplying plenty of hyaluronic acid, the connective tissues will take these molecules in and use them to build extracellular matrix, and thus stay strong and healthy. Cosmetic companies have found a way to make hyaluronic acid into a facial cream. Claims are made that using these creams will slow down or reverse wrinkling. Does it work? One researcher in Japan believes it does. He moved to Yuzurihara, a small town north of Tokyo, in order to study its population of exceptionally healthy and long-living people. The elderly in this town look youthful, rarely get sick, and often live to be over 100. The researcher concluded that besides having an excellent diet and lifestyle, these people also happen to have available an ideal food source for longevity: a species of potato that is very high in hyaluronic acid. A lifetime of eating a diet high in hyaluronic acid (and also lots of green vegetables) has made diseases of aging very rare in this population. Many elderly people in this village reach their 90s without ever having been in a hospital.