Histology

faculty of medicine - JU2017

◉ Sheet ○ Slides

Number

13

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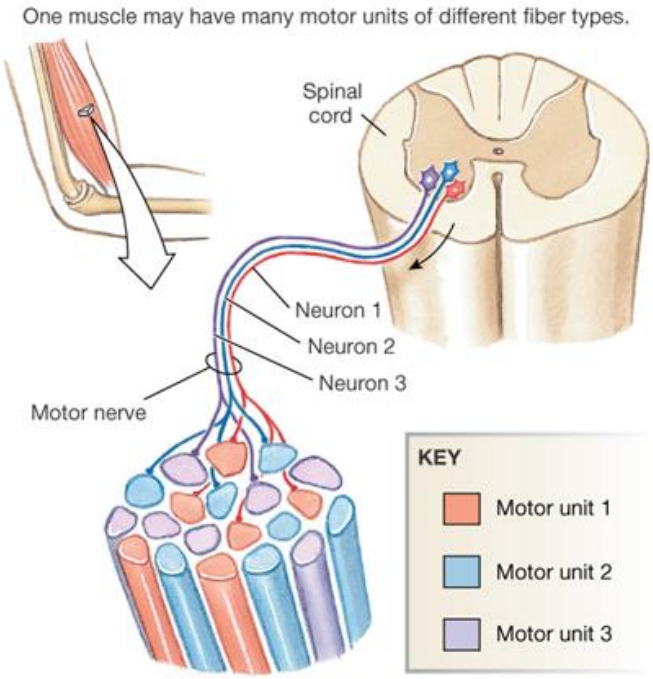
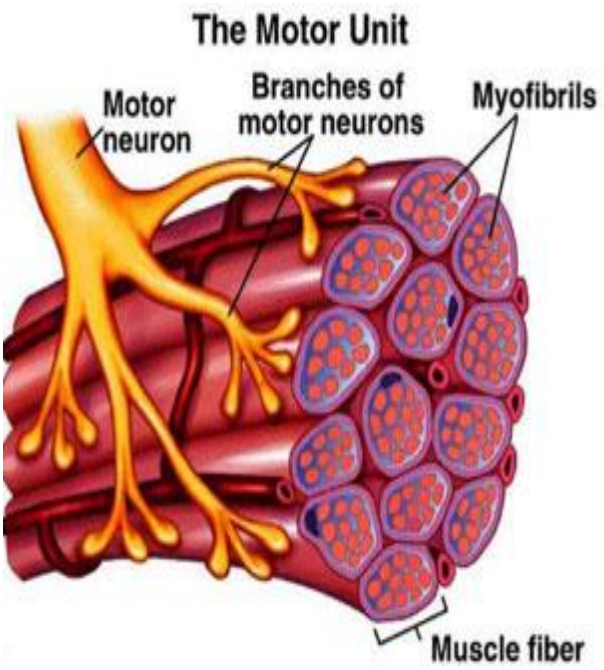




- **Motor unit:** it's the muscle cells that are supplied by a single neuron/axon, it's size is variable according to the muscle action. **EX:** quadriceps muscle is a large muscle and its contraction is gross, a single axon supplies thousands of muscle fibers. **Another example** is hand muscles they might have ten muscle cells supplied by a single axon (fine movement, small motor unit), **muscles of the eye:** one axon supplies one or two muscle fibers in order to produce a fine movement. The finer the movement, the fewer muscle fibers per motor unit

Muscle spindle:

- **Acts as proprioceptors (proprioception: muscle sense).**
- **Acts as stretch detectors.**
- **Provides the central nervous system (CNS) with data from musculoskeletal system.**
- **A muscle spindle is encapsulated by modified perimysium.**
- **Contains few thin modified muscle fibers filled with nuclei.**
- **Called also intrafusal muscle fibers.**
- **Sensory axons wrap around individual muscle fibers.**
- **Detects any changes in length and tension of the muscle caused by body. movement, and send this information to CNS to detect the position of body parts.**
- **Most of this proprioceptive information is processed at a subconscious level.**

Types of Muscles:

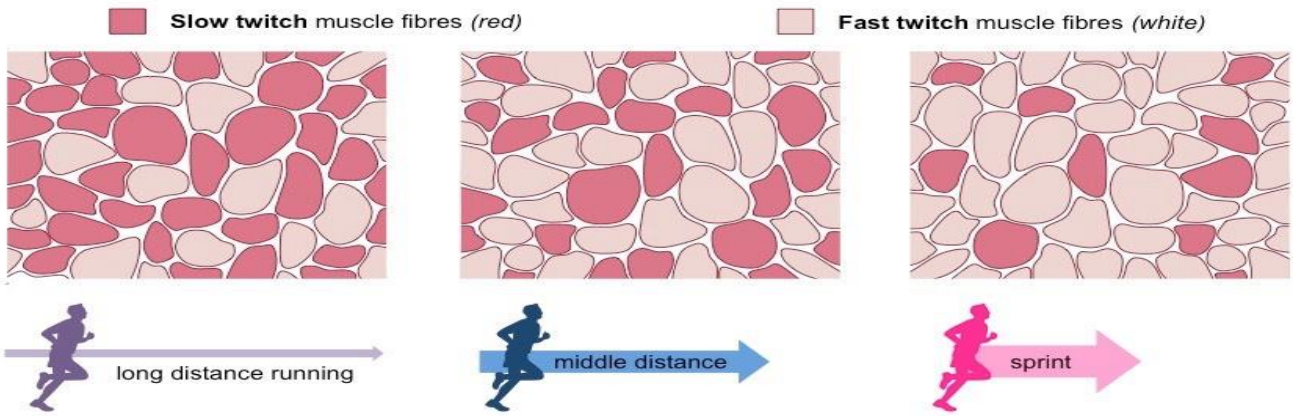
-We have 3 different types of skeletal muscle fibers in our body:

1. Slow fibers (Red Muscles)

2. Fast fibers (White Muscles)

3. Intermediate fibers.

The main difference between types is how they produce ATP. The color of the muscle is different (Grossly not histologically)



Slow Fibers (Red Muscles):

1. They produce their ATP's by Oxidative phosphorylation in Mitochondria, which produces high amounts of ATP in a long time (slow) (Aerobic reactions inside the mitochondria = Oxygen is used)

2. The fuel for the production of ATP is Fatty acids (mainly), fatty acids are produced by metabolism of fats, so in order to burn fat in the body, you need to work aerobically

> **(Aerobic exercises are called so because people are activating their red muscles to burn fats, so they are usually preceded with warm up exercises, to supply the muscles with high amount of oxygen)**
>
> **(Thin people usually have higher amount of red muscles fibers than white muscle fibers).**

3. They look red because:

a. They have high amount of mitochondria

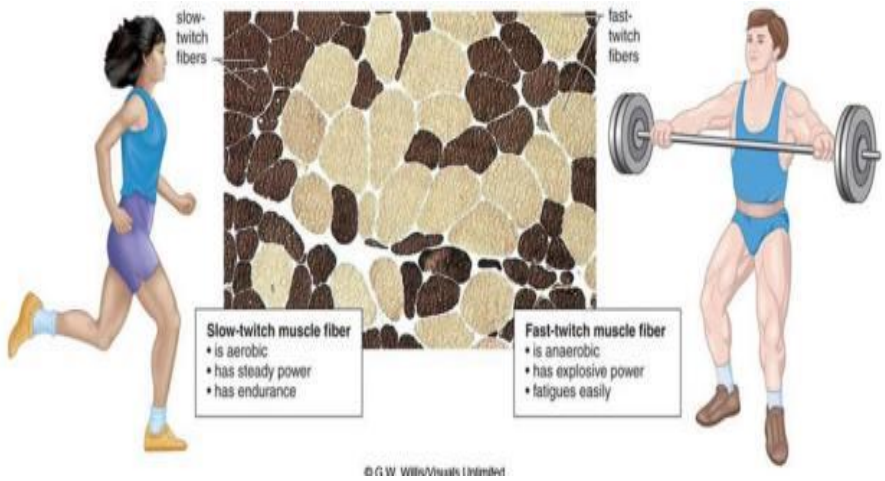
b. They are highly vascularized because they need high amounts of O2 to produce contraction

c. They contain high amounts of Myoglobin (Hemoglobin like protein, has heme (iron), and is an oxygen binding protein)

4. The ATPase activity of their myosin's heads is low, so the contraction is slow.

5. This slow contraction is prolonged (for a long time but slow).
6. They don't get Fatigue easily.

Examples: Spinal muscles, muscles of the back, hip flexors (postural muscles are mainly red fibers)



Fast Fibers (White Muscles)

1. They are white in color, because they don't have high amounts of myoglobin and mitochondria.
2. They don't need Oxygen to produce ATP (Anaerobic reactions in the cytoplasm instead of the mitochondria).
3. Glycolysis: production of ATP without the need of oxygen, it occurs in the cytoplasm directly and quickly.
4. They are called Fast fibers because:
→ They produce ATP quickly within the cytoplasm by glycolysis, they produce fast contractions.
5. The ATPase activity of their myosin's heads is high
6. They are larger than red fibers.
7. They produce fast and strong contraction but for short time.
8. Activated in weight lifting activities, for example if you are carrying a heavy object, you give maximum force but this contraction will not last for a long time

For Example: people who sprint (run at maximum speed for short distance) produce very strong contractions for a short period of time (white fibers), while Marathon runners have higher amount of red fibers, they run long distance for a long period of time without getting fatigue (their speed is moderate).

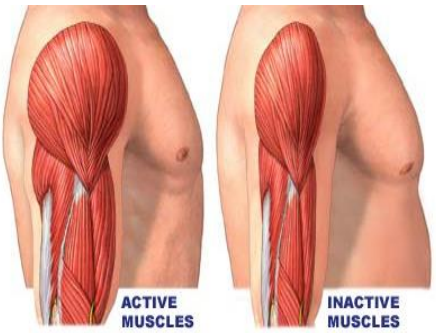
9. Why do they look white?
a. they have few mitochondria, few capillaries
b. they store high amount of glycogen
10. They get fatigue easily because one of the byproducts of Glycolysis is Lactic acid (it causes burning sensation but it will soon be absorbed).
11. The fuel for these muscles is: Glucose.

Third: Intermediate Fibers:

1. They have characteristics between both the white and the red

2. They are more resistant to fatigue than the white fibers but less than the red.
3. They are faster than red muscle fibers.

***MOTOR UNIT: number of muscle cells supplied by single Axon**



- Each motor unit is composed of certain types of muscle fibers, red or white. *So All muscle fibers of a motor unit are of the same type.*

-If I cut the nerve supply of one motor unit that supplies red fibers and connect it to white fibers, after stimulation these white fibers will be converted to red fibers, which means that the nervous input has a role in determining the type of fibers.

-By exercises, we can change the fiber's type.
-note red fibers are usually less in diameter .
*** Skeletal Muscles contract when they are stimulated, if you cut the nerve supply, paralysis will occur.**

- Muscle atrophy: loss of tone and mass from lack of stimulation. Muscle becomes smaller and weaker. This is could be a result of not using the muscle.

-Muscle Hypertrophy:

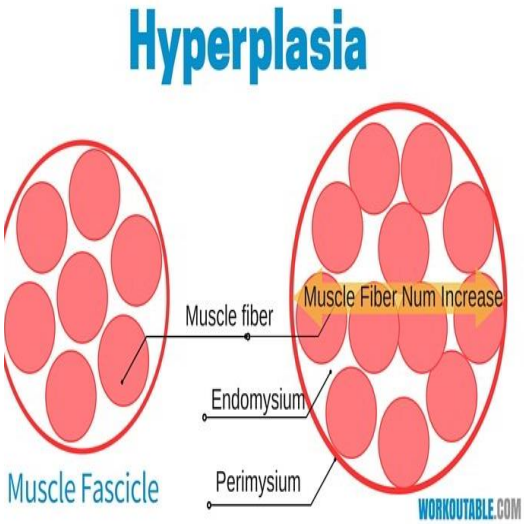
Hypertrophy: is an increase in the size of the muscle.

By increasing the synthesis of their proteins (more amount of both actin and myosin), so the myofibril itself gets thicker and so on, and the size of the muscle will increase.

-Hyperplasia:

Hyperplasia: increase in the number of the cells.

- we said earlier that skeletal muscle cell can undergo hypertrophy (highly muscular people), and it can rarely undergo hyperplasia because the amount of the satellite cells is very minimal.



ALL OR NONE principle: each muscle fiber either contracts completely or not at all, why? due to the presence of T-tubules (invagination from the sarcolemma and it

reaches each myofibril within the muscle cell) so when the action potential reaches the muscle cell, all the myofibrils within the muscle cell will contract leading to the all or none principle. This applies also to the motor unit, either there is contraction in all the muscle cells that belong to one motor unit or there is no contraction at all

Cardiac muscle

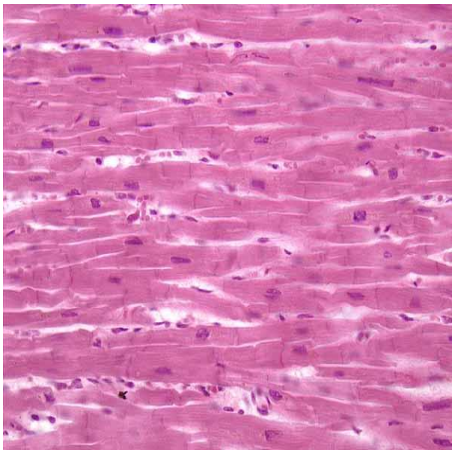
- ✓ **Cardiac muscle is striated (composed of repeated units of sarcomeres inside the myofibril as in skeletal muscle)**
- ✓ **Self excitatory and electrically coupled:** this means that these cardiac muscle cells are able to initiate contraction **without nerve input (no motor end plate).** this is called **Myogenic activity of the cardiac cells.**

  ****Myogenic activity: they generate their own electrical impulses (pacemaker).**
- ✓ **Force of contraction is modulated by autonomic nervous system (sympathetic and parasympathetic)(only to control the force of contraction not to initiate it).**

  Sympathetic: increase the force of contraction.

  Para sympathetic: decrease the force of contraction.

The main similarities between cardiac and skeletal muscle are:

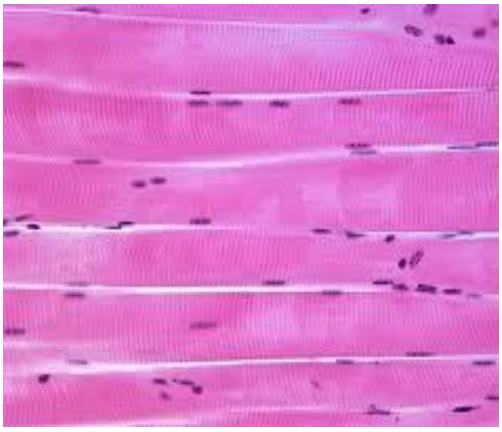


1. Both are striated.

2. Both are composed of myofibrils, each myofibril is surrounded by a network of sarcoplasmic reticulum

3. Almost the same contraction mechanism.

The main differences between cardiac and skeletal muscle are:

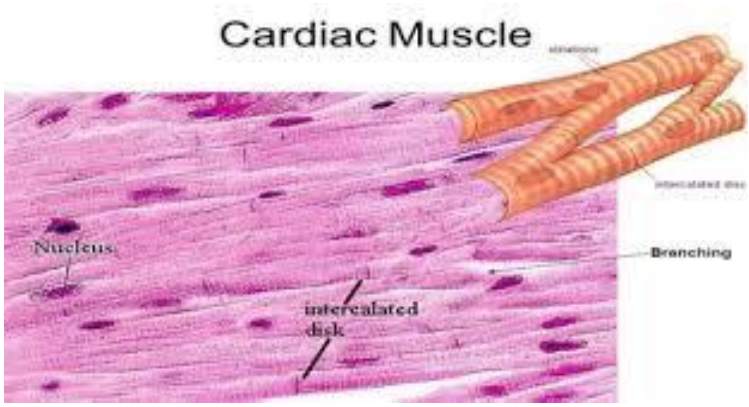


1. The cardiac muscle is also called muscle fiber, but compared with the skeletal fibers, cardiac muscle cells are shorter and interconnected (branched, to provide wave of contraction).

2. Cardiac muscle cell is single nucleated but sometime it is binucleated while skeletal muscle cell is multi-nucleated.

3. The one nucleus in the cardiac muscle cell is located in the center, while the multi-nuclei of skeletal muscle are found under the sarcolemma (in the periphery).

4. the striations of cardiac muscle are less distinct (obvious), while it's more obvious in skeletal muscle. *Why?*



Because cardiac muscle cells have higher amount of mitochondria than skeletal muscle, these mitochondria are located between the myofibrils. In addition, heart muscle cells store glycogen so the higher amount of mitochondria ,glycogen, lipid inside the cytoplasm results in less obvious striations, while in the skeletal muscle, the sarcomeres are arranged above each others, so it appears uniformly striated, more obvious than the cardiac muscle. (But both skeletal and cardiac muscle are striated).

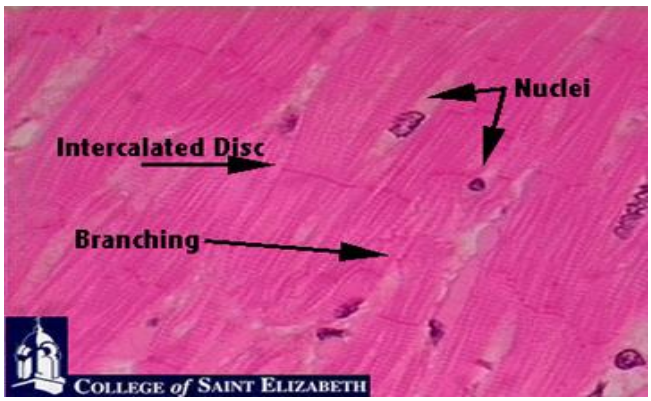
**** (the stored lipids and glycogen are used as a fuel for the cardiac muscle cells).**

****The heart muscle contracts all time so it needs large amount of mitochondria (up to 40% of cell volume) in order to produce ATP for muscle contraction.**

5. The sarcolemma of the cardiac muscle cell also has invaginations. T-tubules also surround each myofibril, but instead of having triads (as in case of skeletal muscle) we have diads. Diad: is one T-tubule with one tubular end of SR. The sarcoplasmic reticulum in the case of cardiac muscle is less extensive and less-well organized (smaller in size and less branched) than in skeletal muscle.

****In general T tubules in cardiac muscle are larger and occur near to the Z line of sarcomere.**

6. Diads are found near the Z line but triads are found in the skeletal muscle at the junction between the A and I bands.

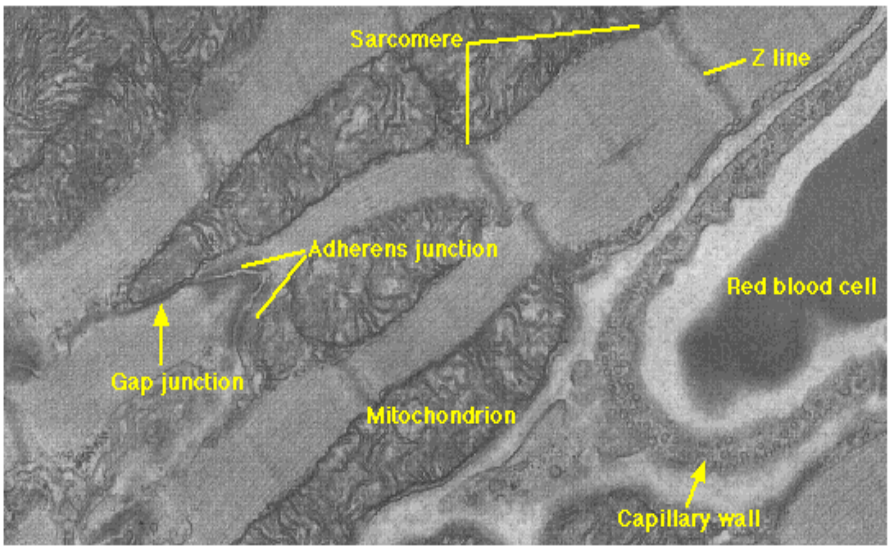


The cardiac muscle cells are branched, short and connected to each other by step-like lines called intercalated discs.

**** Intercalated discs:**

Zigzag- like structure, Step-Like structure connecting two cardiac muscle cells together, it has two parts:

- **Horizontal Part.**
- **Vertical Part.**



Muscle tissue

It contains 3 types of junctions:

A. Gap junctions (not exclusive to epithelial cells, we have them also between cardiac muscle cells). Gap junctions are located in the horizontal part of intercalated disk. Gap junctions allow movement of ions between cardiac muscle cells; this allows contraction of the whole muscle uniformly as one unit (although it's composed of many cells) .

B. It also contains desmosomes and fascia adherens (Located in the vertical part of intercalated disk), to anchor cardiac cells together mechanically and prevent detachment and pulling apart of cells when the heart is contracting.

NOTE: 1. The fascia adherens has the same concept as Zonula adherens which is found between epithelial cells.

In epithelium it is called zonula because it forms a belt like structure around epithelial cells. But between the heart muscle cells, it forms spot-like areas like the desmosomes)

2. The difference between desmosomes and fascia adherence: (desmosomes are associated with → intermediate filaments

while fascia adherens are→ associated with actin filaments).

- Cardiac muscle cells don't contain satellite cells therefore these cells are not able to regenerate in case of injury.

- Hyperplasia doesn't happen in cardiac muscles, cardiac muscle cells don't regenerate, they have No satellite cells (skeletal muscles have limited ability to regenerate because they contain few satellite cells).

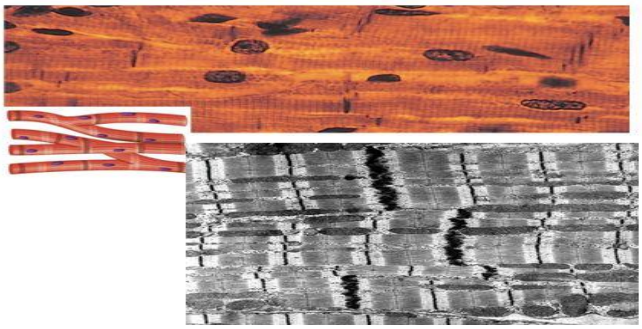
- Note that satellite cells are undifferentiated stem cells (myoblasts) and they remain in the skeletal muscle tissue after differentiation, can be found within the external lamina of muscle cell.

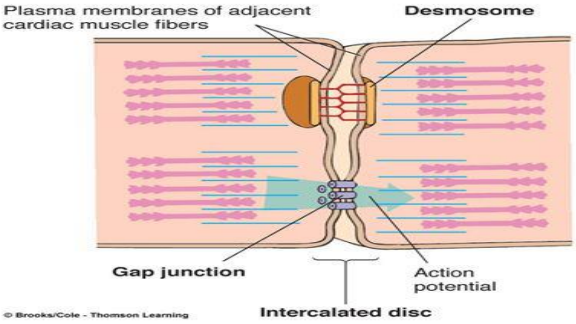
- They are trying to use stem cells inside the heart in order to regenerate cardiac cells to replace the damaged area of the heart, instead of heart implant (stem cell technology).

- The cardiac muscle cells can undergo hypertrophy (increase in the cell size).

Cardiac Muscle Fibers

- Interconnected by intercalated discs and form functional syncytia
- Within intercalated discs – two kinds of membrane junctions
  - Desmosomes
  - Gap junctions
    - Ap's

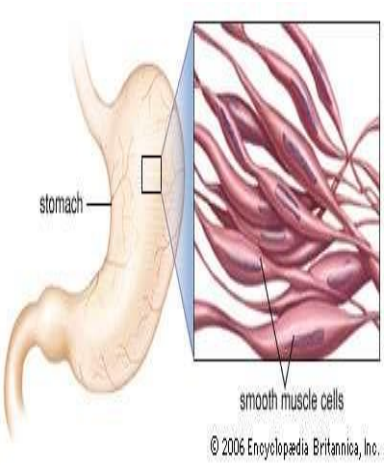


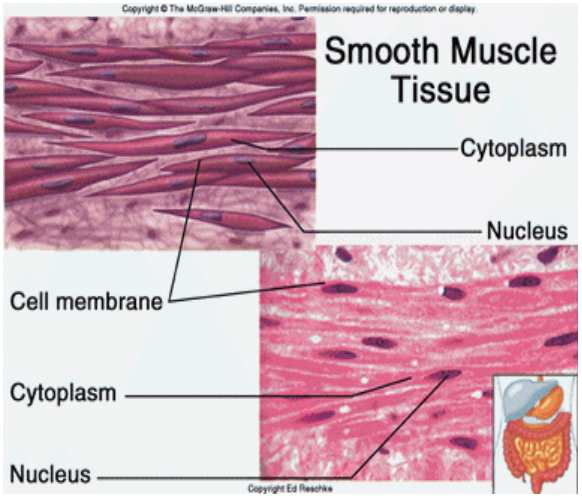


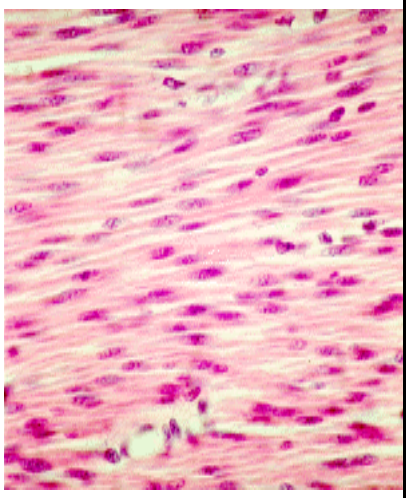
Smooth muscle:

- ✓ Smooth muscles are called smooth because they don't have any striations, but this doesn't mean they don't have actin and myosin, they do have, but they are not arranged into sarcomeres. Therefore they don't appear striated

- ✓ **Cardiac and skeletal muscle cells contain actin and myosin arranged into sarcomeres – striations.**







- ✓ **FOUND INSIDE THE WALLS OF HOLLOW ORGANS AND TUBES IN THE BODY**

**** It has 6 major locations:**

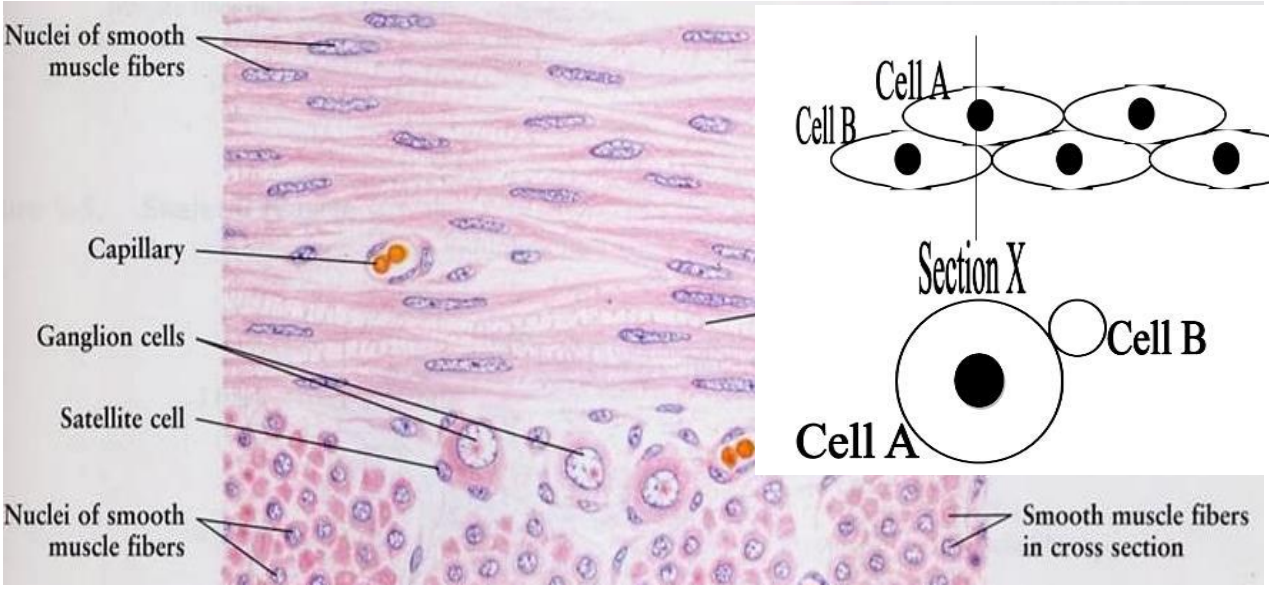
Inside the eye, wall of vessels, respiratory tubes, urinary organs, digestive tubes, reproductive organs.

- ✓ **smooth muscles contraction is involuntary (not under our conscious control).**
- ✓ **They are spindle (fusiform) in shape, broad in the center and narrow at the periphery.**
- ✓ **Smooth muscle cells called also fibers (although they don't look like fibers, but in general all muscle cells are called muscle fibers).**
- ✓ **smooth muscles are single-nucleated (one nucleus in the middle of the cell).**
- ✓ **the smooth muscle cells are arranged into sheets (above each other), the narrow area of one smooth muscle is above the broad area of another smooth muscle cell (to have minimal spaces between the cells)**
- ✓ **they are tightly packed with small amount of loose connective tissue (endomysium) to support individual cells and has high amount of reticular fibers.**

  reticular fibers : they give support to certain organs and they support individual cells)

  ****endomysium: loose connective tissue rich in reticular fibers.**
- ✓ **Usually, the sheets are perpendicular to each other (at right angles to each other).**
- ✓ **Smooth muscles don't get fatigue (the contractions are slow, sustained, and resistant to fatigue)**

✓ **These cells are surrounded by basal lamina, we call it external lamina.**



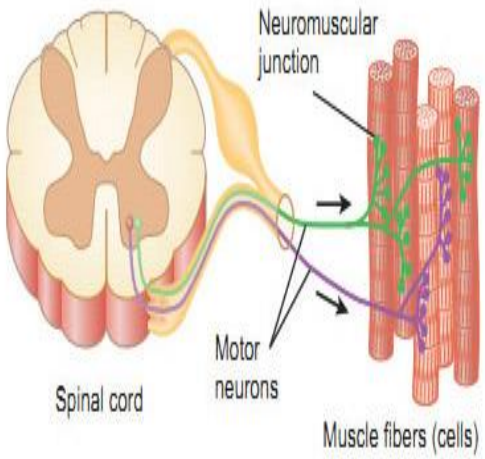
****if we look at a longitudinal section along the long axis of the smooth muscles, the previous features (spindle-shaped, tapering, singly –nucleated,…) would be visible.**

***If we take a cross section through smooth muscles, we'll see different rounded profiles with different diameters, some containing the nucleus and some do not (each cell contains a nucleus, but it depends on the plane of the cut, if it's in the middle of the cell, the nucleus would be visible, if it's in the periphery, we wouldn't see the nucleus). In addition, if the section is in the middle of the cell, the circle would be big, but if it's on the periphery, the circle would be small.**

****Smooth muscles produce peristalsis movement (الحركة المَعَوية) which is a continuous movement.**

- Smooth muscle cells are connected by gap junctions, which allow small ions and molecules to pass from one cell to the next allowing the spread of depolarization.

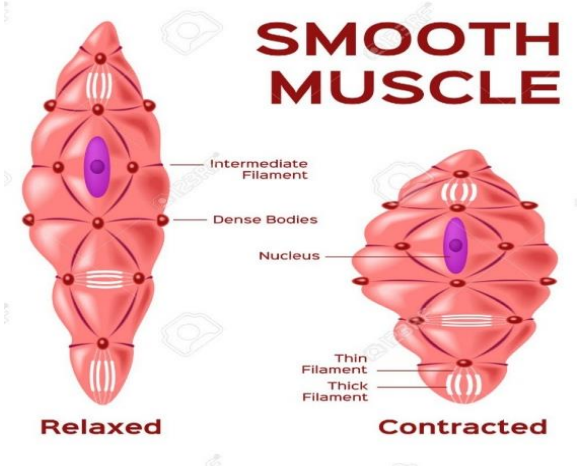
- Smooth muscle cells in certain location have high synthetic activity, like in the wall of blood vessels; they synthesize the components of ECM



**** Do they need nerve supply in order to contract?**

In general, we say that smooth muscles are controlled by neuro-endocrine impulses (neuro: receives nerve supply, endocrine: affected by local hormones that increase or decrease the contraction) and they are sensitive to stretch.

Examples:

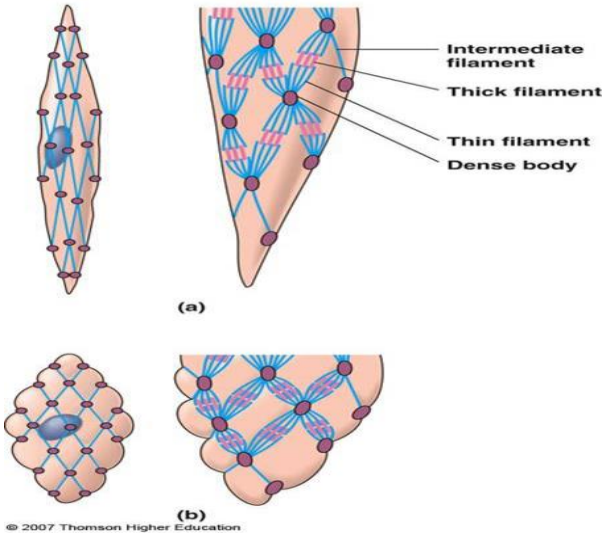


1) **They can be activated by stretch, When stretch happens in the urinary bladder for example (because of the accumulation of urine), the reflex of the muscles is to contract, Which means that smooth muscles don't always require a nervous signal (have Myogenic activity), they may be stimulated by stretching or hormones.**

Note: that gap junctions also present between smooth muscle cells and allow the multicellular tissue to contract as a single unit, providing better efficiency and force.

2) Smooth muscles in the walls of blood vessels for example receive nerve supply to contract to cause constriction or dilatation.

From this figure:



*** We find actin, myosin and intermediate filaments inside smooth muscle cells.**

*** We find what's called "dense bodies", which are equivalent to Z-lines in the skeletal muscle.**

*** Dense bodies are composed of α- actinin, the actin filaments are attached to the dense bodies.**

* * Dense bodies have two types:

1) Dense bodies close to the plasma membrane (submembranous dense bodies)

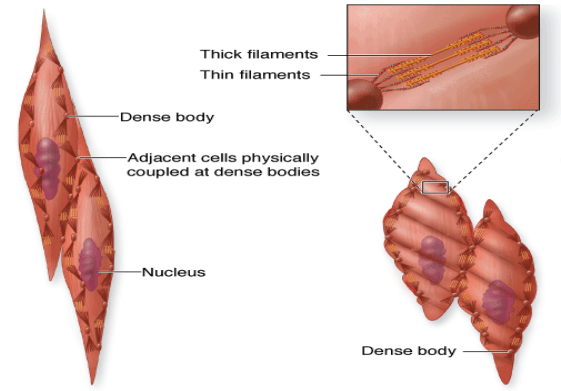
2) Dense bodies within the cytoplasm, called " intra-cytoplasmic dense bodies"

*** Instead of having Z-lines, we have dense bodies, actin filaments are attached to dense bodies and in between we find myosin filaments.**

* When the cell contracts, the **dense bodies get closer to each other**, the overlap between actin and myosin increases.

* Refer to the figure to notice the difference in shape between the contracted muscle (scalloped) and the flattened (relaxed) muscle.

* When the cell contracts, it becomes rounded with scalloped surface.



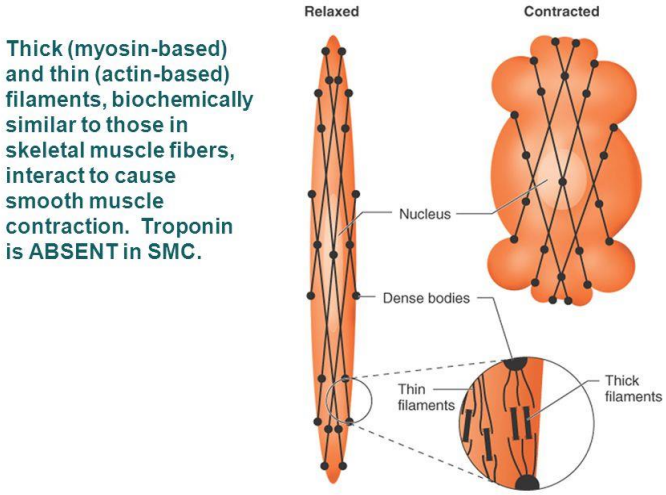
Source: Mescher AL: *Junqueira's Basic Histology: Text and Atlas, 12th Edition*: http://www.accessmedicine.com

**Myofilaments inside the smooth muscle consist of 3 types:

1) Actin.

2) Myosin.

3) Intermediate filaments (like desmin and vimentin) which connect dense bodies together.



** Intermediate filaments are the cytoskeleton of the smooth muscle cell; the intermediate filaments are connected to other intermediate filaments via dense bodies. The dense bodies (near the plasma membrane) are attached by adherens junctions to other smooth muscle cells

** No troponin in thin filaments of smooth muscle (instead they have calmodulin-Calcium binding protein)

- Has scattered smooth endoplasmic reticulum (SR)

** On the plasma membrane of smooth muscle cells, we find certain structures called caveolae, short depressions of the sarcolemma (short and shallow invaginations of the plasma membrane) of the smooth muscle.

** The importance of these caveolae: They have high concentration of receptors (proteins and lipids) because these cells can be controlled by hormones, so we find this high concentration of receptors that have several functions in signal transduction and act as stretch sensors that can sense the stretching of the organ itself (these cells are easily activated).

** Smooth muscles can undergo Hypertrophy and Hyperplasia.

Example: **the wall of the uterus –which is composed of smooth muscle cells-, gets larger in size during pregnancy because these cells *can* undergo mitosis and increase in number (hyperplasia) in addition to increasing in size (hypertrophy).**

**** Smooth muscles are the only type that has high regeneration power. Why? The reason is because these cells are less differentiated cells and can undergo mitosis ** When the cells are less differentiated, they are able to divide. Skeletal muscle cells are highly differentiated (can't undergo division) and if regeneration of skeletal muscles occurs, it would be because of the satellite cells (myoblasts that remain inside the muscle tissue).**

Ultrastructure of Smooth Muscle cell:

*** actin and myosin filaments .**

*** Intermediate filaments associated dense bodies.**

**** Which type of muscles can undergo Hypertrophy? All types of muscle**

****Which type of muscles can undergo Hyperplasia? Smooth muscles and rarely skeletal muscle**

Note : **in extreme cases like in highly-muscular bodies, Hyperplasia might happen in skeletal muscles. But normally it's hypertrophy that occurs.**

> All muscle cells in the 3 types are surrounded by thin basal lamina (external lamina) and loose type of connective tissue that contains high amount of reticular fibers (endomysium) > Remember that reticular fibers support individual cell.