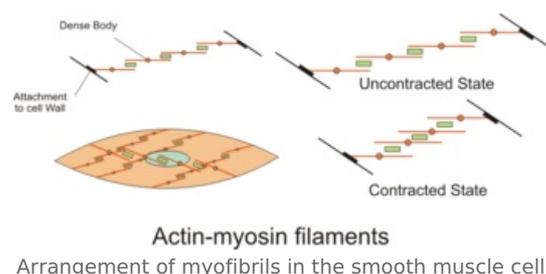


Contraction in smooth muscle

Structural differences between Striated and Smooth muscle

- Smooth muscle fibers do not have their myofibrils arranged in strict patterns as in striated muscle, thus no distinct striation is observed in smooth muscle cells under the microscopical examination.
- In smooth muscle, the sarcomeres are attached on structures called dense bodies playing the same role as Z disks in the striated muscle. They provide an anchoring site for the sarcomeres in order to induce mechanical work when the fibrils contract.
- Smooth muscle cells contain a single rod-like nucleus located in the center of the cell, whereas striated muscle cells are multinucleated and their nuclei are located on the periphery.
- Smooth muscle cells have a fusiform shape introducing a very distinct pattern of cell arrangement, whereas striated muscle cells have a rather rod-like shape.
- The resting membrane potential of a smooth muscle fiber is about -40 mV whereas in the striated muscle is about -90 mV.



Functional differences between Striated and Smooth muscle

- The smooth muscle contraction is much slower than in the striated muscle primarily due to the presence of G protein coupled ligand receptors instead of ion channel coupled ligand gated receptors present in striated muscle. Also, after activation of the receptors there is a long process in order to elicit an action potential, involving second messengers and activation of enzymes.
- Smooth muscle thin actin filaments lack troponin protein.
- In both striated and smooth muscle, contraction entirely depends on Ca^{2+} intracellular concentration but through different pathways. In striated muscle Ca^{2+} exposes actin binding sites promoting cross bridge formation between myosin and actin filaments, whereas in smooth muscle Ca^{2+} will activate kinases that will eventually induce conformational changes of the myosin heads in order to form cross bridges.
- Smooth muscle cell overall contraction squeezes the cell from every direction since the myofibrils are not arranged on the longitudinal axis of the cell. In striated muscle cell the overall contraction compresses mainly the two end towards the center of the cell minimizing the total length of the fiber.

Control of the smooth muscle contraction

Extrinsic control

- Neuronal control: smooth muscles are innervated by sympathetic fibers that cause both constriction and relaxation acting through different receptors. α adrenergic receptors primarily cause contraction and β adrenergic receptors relaxation. The parasympathetic effect is limited to absent.
- Humoral control: many different compounds induce either constriction or relaxation. Some of them are angiotensin II, ADH (vasopressin), epinephrine, ANP (atrial natriuretic peptide)

Intrinsic control

- Myogenic autoregulation: is not present in every smooth muscle of the human body. Found primarily in the blood vessels and especially in the afferent glomerular arterioles. This type of regulation is elicited due to stretching of the smooth muscle cells that will eventually induce spontaneous depolarization and contraction.
- Local humoral control: some compounds secreted by cells act in an autocrine or paracrine fashion contributing to the contraction and relaxation of smooth muscle cells. The most potent constrictor is the peptide endothelin whereas the most common vasodilator is adenosine. Others are bradykinin, prostaglandins, thromboxane A_2 , histamine, NO.

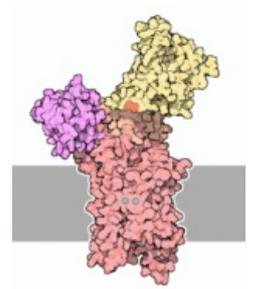
Smooth muscle contraction - step by step

- An action potential in the sympathetic motor neuron travels through the axon and reaches the synaptic terminal.
- The action potential causes activation of Ca^{2+} voltage gated channels on the presynaptic terminal inducing influx of Ca^{2+} ions inside the cytoplasm.
- The increase concentration of Ca^{2+} will eventually cause conformational changes of the microtubular component of the neuronal cytoskeleton that will promote exocytosis of synaptic vesicle promoting the expel of neurotransmitter norepinephrine in the interstitial space.
- Norepinephrine reaches the smooth muscle cell membrane where it bounds on a G protein coupled ligand gated channel receptor.

5. Once the transmitter-receptor complex is formed, an underlying protein undergoes conformational change that activates the G protein.
6. The inactive G protein consists of 3 heterogeneous α , β and γ subunits with GDP bound on the α subunit. Activation occurs when GDP is substituted with GTP which promotes dissociation of the G protein into α , β and γ -GTP individual components.
7. The α -GTP component binds on a specific enzyme called phospholipase C inducing its activation.
8. The activated phospholipase C cleaves phospholipids into DAGs (diacylglycerols) and IP_3 (inositol triphosphates).
9. The DAG and IP_3 act as second messengers that will activate Ca^{2+} channels. DAG binds on plasma membrane Ca^{2+} receptors opening a channel allowing Ca^{2+} influx. IP_3 binds on receptors on the sarcoplasmic reticulum and opens channels promoting Ca^{2+} outflux from the reticulum into the cytosol.
10. The Ca^{2+} accumulated inside the smooth muscle cell binds with calmodulin giving rise to the Ca^{2+} -calmodulin complex.
11. The Ca^{2+} -calmodulin complex binds and activates Myosin Light Chain Kinase (MLCK).
12. MLCK phosphorylates the myosin light chain enabling the myosin crossbridge to bind to the actin filament and allow contraction to begin.
13. Dephosphorylation of the myosin light chain with subsequent termination of muscle contraction occurs through activity of another enzyme called Myosin Light Chain Phosphatase (MLCP).
14. Contraction occurs as long as Ca^{2+} is present at high concentrations in the cytosol.

Removal of Ca from the smooth muscle cell

- **Na^+/Ca^{2+} antiporter:** located in the plasma membrane, through which 3 Na^+ ions are exchanged for a single Ca^{2+} ion. This type of Ca^{2+} transport occurs not directly through ATP cleavage but indirectly through a concentration gradient introduced by the Na^+/K^+ ATPase pump also located in the plasma membrane. This kind of transport is referred to as secondary active transport of Ca^{2+} ions.
- **Ca^{2+} ATPase pump:** located in the membrane of the sarcoplasmic reticulum that transports Ca^{2+} from the cytosol into the reticulum using ATP. This type of Ca^{2+} transport is referred to as the primary active transport of Ca^{2+} ions.



Ca^{2+} ATPase pump

Links

Bibliography

- HALL, John E. – GUYTON, Arthur C. *Guyton and Hall Textbook of Medical Physiology*. 12. edition. Saunders/Elsevier, 2010. ISBN 1416045740.
- Lecture Notes: Prof. MUDr. Jaroslav Pokorný DrSc.