Smooth Muscle Physiology

Special characteristics of smooth muscle
- NO CROSS-STRIATIONS!
- This is because actin and myosin are not arranged in orderly arrays. But they are still present
- Instead of Z-lines, there are DENSE BODIES in the cytoplasm
- TROPOinin IS ABSENT
- There are relatively few mitochondria
- There is no steady “resting membrane potential” – it fluctuates according to activity

Types of smooth muscle
- Unitary, or Visceral:
  - Large sheets
  - Many low-resistance gap junctions
  - Functions as a syncytium
  - Mainly found in hollow viscera
  - Nerve endings arrive at only a few of the cells; the action potential spreads to the others by gap junction conduction
- Multiunit smooth muscle:
  - Individual muscle units with few (or none) gap junctions
  - An example is the iris of the eye
  - Each cell has its own nerve ending

Blood vessels have both unitary and multi-unit smooth muscle in them.

UNITARY SMOOTH MUSCLE ELECTRICAL ACTIVITY
- UNITARY SMOOTH MUSCLE Characterized by
  - INSTABILITY OF THE MEMBRANE
  - CONTINUOUS, INVOLUNTARY, IRREGULAR CONTRACTIONS
  - This continuous state of partial contraction is called TONUS
  - Resting membrane potential varies – in periods of quiescence its between -20 to -65mV, but it all depends on how active the tissue is.
  - There are slow sine-wave fluctuations of membrane potentials, with random spikes which sometimes overshoot the 0-line
  - The spikes last about 50 ms
  - If you manage to catch a smooth muscle in a moment of inactivity, and stimulate it, the delay of the excitation-contraction coupling is about 0.5 seconds
MOLECULAR BASIS OF CONTRACTION

- **YES, THERE IS STILL CALCIUM INFLUX**
- **YES**, it still causes the contraction
- **HOWEVER**, the source of the calcium can be just about anywhere
  - Influx via the voltage-gated calcium channels in the sarcolemma
  - Influx from the intracellular sarcoplasmic reticulum stores via the ryanodine receptor
  - Influx from intracellular stores via the inositol triphosphate receptor (IP$_3$R)
  - Any combination of the above

- **Also, THERE IS NO TROPONIN TO BIND THE CALCIUM** – rather, myosin needs to be phosphorylated for the activation of the myosin ATPase
- **CALMODULIN** is the calcium-binding protein instead of troponin; the Ca$^{2+}$-calmodulin complex activates calmodulin light-chain kinase and this kinase phosphorylates the myosin light chain, which in turn increases the ATPase activity

- After doing its job, the myosin is dephosphorylated by myosin light chain phosphatase
- However this does not mean that the smooth muscle relaxes - there is a “latch” mechanism via which the actin and myocin remain cross-bridged even after the Ca$^{2+}$ concentration falls
- This produces SUSTAINED CONTRACTION WITH LITTLE ENERGY EXPENDITURE: which is great for vascular smooth muscle. Relaxation eventually occurs when the calcium-calmodulin complex eventually dissolves, or when some other mechanism intervenes.
- The sequence of events in multiunit smooth muscle is virtually identical to that in unitary smooth muscle
MECHANICAL AND CHEMICAL CHARACTERISTICS
- Unlike any other types of muscle, unitary smooth muscle will respond by contraction to being stretched.
- Stretch is followed by a decline in membrane potential, by an increased frequency of spikes, and by increased tone.

**ADRENALINE** and **NORADRENALINE** serve to relax intestinal smooth muscle.

**ACETYLCHOLINE** serves to cause contractions; this happens because the muscarinic receptors activate Phospholipase C, which in turn produces inositol triphosphate (IP3) and allows calcium release via inositol triphosphate receptors.

**MULTIUNIT SMOOTH MUSCLE** is the reverse: Noradrenaline tends to activate it, causing it to contract - even a small amount will result in something like an irregular tetanus, rather than a single twitch. A single twitch for multiunit smooth muscle is very similar to that of skeletal muscle, but it lasts about 10 times as long.

Relaxation

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Endothelial Cell

NO

Vascular smooth muscle cell

Activated guanylate cyclase

Guanylate cyclase

GMP

cGMP

cGMP-sensitive protein kinases and phosphatases

SMOOTH MUSCLE RELAXATION
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- “Endothelial-Derived Relaxation Factor”, EDRF, turned out to be nitric oxide (NO).
- It is a simple molecule which diffuses freely out of the endothelial cells into the smooth muscle of the blood vessels.
- Once inside, it activates soluble guanylate cyclase, which “cyclifies” guanosine monophosphate, turning it into cyclic GMP.
- The cGMP then goes on to activate a whole lot of cGMP-sensitive enzymes which have the net effect of relaxing this vascular smooth muscle.

Innervation of smooth muscle
- Unitary smooth muscle has dual innervations, from the sympathetic and the parasympathetic nervous systems, and it responds to both locally released synaptic mediators and to circulating autonomic hormones.
- THE FUNCTION OF THE NERVE SUPPLY IS NOT TO INITIATE MUSCLE ACTIVITY BUT TO MODIFY IT.

FORCE GENERATION AND PLASTICITY OF SMOOTH MUSCLE
- Smooth muscle is insanely efficient; in comparison with skeletal muscle, it contains 20% of the myosin, and has almost 100 times less ATPase activity- but the force it produces is approximately the same, per crosssectional area.
- The tradeoff is the velocity of contraction - the smooth muscle is much slower.
- THERE IS NO RESTING LENGTH: if you stretch a length of smooth muscle, it will increase its tension, and then gradually relax into the new length. So its impossible to correlate length and tension. In this sense, the smooth muscle behaves as a viscous mass, and so this feature is called PLASTICITY.

References: *Ganong Review of Medical physiology, 23rd ed, chapter 5*