SMOOTH MUSCLE CONTRACTION

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OBJECTIVES

• At the end of the lecture you should be able to:
  
• Explain the structure of smooth muscles.
• Identify multi unit and unitary smooth muscle.
• Discuss the mechanism of contraction of smooth muscle.
• Compare the structural and functional differences in skeletal and smooth muscles.
• Discuss the properties of smooth muscle.
Review of previous lecture
Review

- Energetics of skeletal muscle contraction
- Mechanics of skeletal muscle contraction
- Summation
- Tetanization
- Treppe/Staircase effect
- Length tension relationship
- Isometric and isotonic contractions
- Types of muscle fibers
- Remodeling of muscle
- Size principle
Summary of Mechanics of Skeletal Muscle

1. Muscles pull. The sarcomere shorten 30%
2. Muscle force can be graded by recruitment of motor units
3. Small motor units are activated first: the size principle
4. Muscle force can be increased by repetitive stimulation
5. Muscle velocity is inversely related to muscle force
6. Muscles fatigue: they drop force on continued use
7. Muscle are in certain amount of tautness even at rest
8. Muscle remolds to match the functions
TYPES OF MUSCLE
(a) Skeletal muscle

(b) Smooth muscle

(c) Cardiac muscle
SKELETAL MUSCLE

- Long cylindrical cells
- Many nuclei per cell
- Striated
- Voluntary
- Rapid contractions
CARDIAC MUSCLE

- Present in Heart.
- Branching cells
- One or two nuclei per cell
- Striated
- Involuntary
- Have medium speed of contractions
Smooth Muscle

- Present in visceral organs
- Fusiform cells
- One nucleus per cell
- Non-striated
- Involuntary
- Slow, wave-like contractions
Properties of Smooth Muscle

- One nucleus
- No troponin
- Dense bodies analogous to Z line
- Slow/Less myosin ATPase
- Little sarcoplasmic reticulum
- Caveoli
Types of Smooth Muscle
Single unit /unitary smooth muscle

Multi unit smooth muscle
• Diffuse junctions

• Contact Junctions
Receptors in smooth muscles

- For acetylcholine
  - Nicotinic : Ion channels
  - Muscarinic: Act via G protein

- For Epinephrine/Norepinephrine
  - Alpha and Beta adrenergic: Act via G protein
Smooth Muscle Contraction
Actin-myosin filaments

Uncontracted State

Contracted State

Dense Body

Attachment to cell Wall
Smooth Muscle Cell

Dense bodies → Contraction

Thick filament

Thin filament
Step-1 (a)

- The depolarization by ligand binding opens the voltage-gated channels and cause a Calcium influx.
Step-1 (b)

- This also causes a release of calcium from sarcoplasmic reticulum
SMOOTH MUSCLE CONTRACTION

Endoplasmic reticulum

Ca\(^{2+}\)

Unphosphorylated myosin light chain

No myosin ATPase activity

No crossbridge activity

Smooth muscle cell

Ca-calmodulin

MLCK

Phosphorylated myosin light chain

Myosin ATPase active

Crossbridge cycling

Contraction
Step-2

- Calcium binds with Calmodulin protein and makes Calcium Calmodulin Complex.
SMOOTH MUSCLE CONTRACTION

Ca^{2+} → Ca-calmodulin → MLCK → Phosphorylated myosin light chain → Myosin ATPase active → Crossbridge cycling → Contraction

Endoplasmic reticulum

Unphosphorylated myosin light chain

No myosin ATPase activity

No crossbridge activity
Step-3

- Joining of Calcium-calmodulin complex with Calmodulin dependent Myosin Light Chain Kinases (MLCK) and their activation.
SMOOTH MUSCLE CONTRACTION

Ca$^{2+}$

Endoplasmic reticulum

Ca$^{2+}$

Calmodulin

MLCK

Ca-calmodulin

Phosphorylated myosin light chain

No myosin ATPase activity

No crossbridge activity

Smooth muscle cell

Phosphorylated myosin light chain

Myosin ATPase active

Crossbridge cycling

Contraction

Unphosphorylated myosin light chain

No myosin ATPase activity

No crossbridge activity

Cycling

Contraction
Step-4

- Phosphorylation of Myosin Light Chains.
SMOOTH MUSCLE CONTRACTION

Ca$^{2+}$

Calmodulin

MLCK

Phosphorylated myosin light chain

MLCK

Ca-calmodulin

Smooth muscle cell

Endoplasmic reticulum

No myosin ATPase activity

No crossbridge activity

Unphosphorylated myosin light chain

Phosphorylated myosin light chain

Myosin ATPase active

Crossbridge cycling

Contraction
Step-5

- Increased ATPase activity and binding of phosphorylated Myosin to the Actin.
SMOOTH MUSCLE CONTRACTION

**Endoplasmic reticulum**
- Ca\(^{2+}\)
- Ca-calmodulin
- MLCK
- Ca-calmodulin complex
- Phosphorylated myosin light chain
- Myosin ATPase active
- Crossbridge cycling
- Contraction

**Smooth muscle cell**
- Unphosphorylated myosin light chain
- No myosin ATPase activity
- No crossbridge activity

**Ca\(^{2+}\) elevated**
- Increased Ca-calmodulin complex formation
- Phosphorylation of myosin light chain
- Activation of myosin ATPase
- Crossbridge cycling
- Contraction
Step-6

- Contraction by sliding of Myosin filament over the Actin filament by the help of the Myosin crossbridges.
Smooth Muscle Cell

Dense bodies

Contraction

Thick filament

Thin filament
Step-7

- Dephosphorylation of Myosin by Myosin phosphatase causing relaxation of the muscle.
Actin-myosin filaments
SMOOTH MUSCLE CONTRACTION

- **Ca$$^2+$$**
- **Calmodulin**
- **MLCK**
- **Ca-calmodulin**
- **Phosphorylated myosin light chain**
- **Myosin ATPase active**
- **Crossbridge cycling**
- **Contraction**
- **Endoplasmic reticulum**
- **Smooth muscle cell**

- **No myosin ATPase activity**
- **No crossbridge activity**
- **Unphosphorylated myosin light chain**
Summary

• Calcium ions increase in cell.
• Calcium ions bind to calmodulin.
• Calcium calmodulin complex binds with myosin light chain kinase.
• The enzyme complex helps myosin head to bind to actin.
• And also enhances myosin head ATPase which breaks up ATP into ADP and transfers the $P_i$ directly to myosin.
• This $P_i$ transfer leads to Contraction.
• When calcium is pumped out of the cell, the $P_i$ gets removed from myosin by another enzyme.
• The myosin becomes inactive, and the muscle relaxes.
<table>
<thead>
<tr>
<th><strong>Smooth Muscle</strong></th>
<th><strong>Skeletal Muscle</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow contraction</td>
<td>Rapid contraction</td>
</tr>
<tr>
<td>Slow cycling of Myosin cross bridges</td>
<td>Fast cycling of Myosin cross bridges</td>
</tr>
<tr>
<td>Low energy requirement</td>
<td>10-300 times more energy requirement</td>
</tr>
<tr>
<td>Latch mechanism</td>
<td>Nil</td>
</tr>
<tr>
<td>Stress-relaxation or reverse stress-relaxation</td>
<td>Nil</td>
</tr>
<tr>
<td>Calcium from ECF and sarcoplasmic reticulum</td>
<td>Calcium from sarcoplasmic reticulum</td>
</tr>
<tr>
<td>AP opens mostly calcium channels</td>
<td>AP opens sodium channels</td>
</tr>
<tr>
<td>Calcium binds to calmodulin and activates MLCK</td>
<td>Calcium binds to troponin C and causes the active sites to get attached to myosin</td>
</tr>
<tr>
<td>50 times longer latent period</td>
<td>Shorter latent period</td>
</tr>
<tr>
<td>Slower calcium pumps</td>
<td>Fast calcium pumps to pump back calcium into sarcoplasmic reticulum</td>
</tr>
<tr>
<td>Diffuse Junction/Contact Junction</td>
<td>NMJ</td>
</tr>
<tr>
<td>Maximum force of contraction is greater</td>
<td>Maximum force of contraction is lesser</td>
</tr>
<tr>
<td>Caveoli</td>
<td>T-Tubules</td>
</tr>
</tbody>
</table>
Latch Mechanism

**At rest**
- Myosin cannot bind to actin in the absence of light chain phosphorylation.

**Cycling bridges**
- Myosin rapidly dissociates from actin upon binding ATP during each cycle.
- Initial rise in muscle tension.

**Latch bridges**
- Dephosphorylated myosin dissociates from actin very slowly, producing slow bridge cycling.
- Maintained tension tonic contraction.
## Characteristics of skeletal, cardiac and smooth muscle cells.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Skeletal</th>
<th>Cardiac</th>
<th>Smooth muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (mm)</td>
<td>Up to 100</td>
<td>10</td>
<td>Up to 5</td>
</tr>
<tr>
<td>Length (mm)</td>
<td>200 000</td>
<td>50</td>
<td>Up to 200</td>
</tr>
<tr>
<td>T-tubules</td>
<td>Yes</td>
<td>Yes</td>
<td>No -Simple caveoli</td>
</tr>
<tr>
<td>Regular sarcomers</td>
<td>Distinct</td>
<td>Distinct</td>
<td>No -Look smooth</td>
</tr>
<tr>
<td>Regular Z-discs</td>
<td>Yes</td>
<td>Yes</td>
<td>No- but dense bodies</td>
</tr>
<tr>
<td>Regular myofibrils</td>
<td>Yes</td>
<td>Yes</td>
<td>Irregular myofibrils</td>
</tr>
<tr>
<td>Troponin</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Sarcoplasmic reticulum</td>
<td>Yes</td>
<td>Yes</td>
<td>Simple reticulum</td>
</tr>
<tr>
<td>Gap junctions</td>
<td>No</td>
<td>Yes</td>
<td>Yes (single-unit)</td>
</tr>
<tr>
<td>Extracellular Ca^{2+}</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Resting membrane pot. (mV)</td>
<td>-80</td>
<td>-90</td>
<td>-50</td>
</tr>
<tr>
<td>Force</td>
<td>High</td>
<td>High</td>
<td>Low maintained for longer period</td>
</tr>
<tr>
<td>Energy cost</td>
<td>300-fold</td>
<td>High</td>
<td>Low</td>
</tr>
</tbody>
</table>