# Molecular structure of skeletal muscle and function of nerve-muscle junction

Dr. Simge Aykan

Department of Physiology

# Skeletal Muscle

- Muscle fiber
  - Fusion of undifferentiated myoblasts into a single multinucleated cell during development
    - Each nucleus participates in regulation of gene expression and protein synthesis within its local domain
  - Differentiation completed around birth
    - Increase in size from infancy to adulthood

- Satellite cells
  - Undifferentiated stem cells
  - Between the plasma membrane and surrounding basement membrane
  - Differentiation to myoblast

# Skeletal Muscle

- Muscle
  - a number of  skeletal muscle fibers bound together by connective tissue
- Tendon
  - Bundles of connective tissue consisting of collagen fibers

# Thick filament

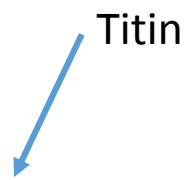
- Myosin
- Two globular heads and a long tail
- Cross-bridge: contact with thin filament and exert force during contraction
- Actin binding site: attachment to actin
- ATP binding site : myosin-ATPase

# Thin filaments

- Actin, nebulin, troponin, tropomyosin
  - Actin: two interwined, helical chains. Core of the thin filament. Binding site for myosin
  - Nebulin: thin filament assembly
  - Troponin & Tropomyosin: regulation of contraction

# Sarcomere

- One unit of repeating pattern of thick and thin filaments
  - *A band*: thick filaments
  - *Z line*: network of interconnecting proteins
  - *I band*: thin filaments only
  - *H zone*: space between opposing ends of the thin filaments
  - *M line*: proteins that link the central region of thick filaments



- Sarcoplasmic retikulum
- Terminal cisternae (lateral sacs)
  - Calsequestrin :$Ca^{2+}$ binding element
  - Storage of large quantitiy of $Ca^{2+}$
- Transverse tubules (T-tubules)
  - Associated with terminal cisternae
  - Continous with the plasma membrane
  - Action potential propogation to interior of the muscle
  - Continous with extracellular fluid

# Contraction

- Activation of the force-generating sites within muscle fiber (the cross-bridges)

# Neuromuscular junction

- Alpha motor neurons
  - Cell bodies in brainstem and spinal cord
  - Myelinated, largest diameter axons
  - High velocity action potential propagation (minimal delay)

# Motor Unit

- A motor neuron and innervated muscle fibers
  - Located in one muscle
  - Distributed throughout the muscle
  - All fibers stimulated at once
- The number of fibers innervated by a single motor neuron varies (from a few to thousand)
  - The fewer the number of fibers per neuron
    - the finer the movement

# Neuromuscular junction

- Acetylcholine (ACh)
- Motor end plate

# Neuromuscular junction

- Action potential
- $Ca^{2+}$ entry
- Acetylcholine release

- Nicotinic Ach receptors open (Na and K Channel)
- $Na^{+}$ entry
- *End-plate potential (EPP)*

# End plate potential

- Transmission is fast and reliable
  - An action potential in the motor axon always causes an action potential in the muscle cell it innervates
    - One of the largest synapses in the body
    - The postsynaptic membrane of the folds is packed with neurotransmitter receptor
  - Single action potential in the presynaptic terminal triggers the exocytosis of about 200 synaptic vesicles, causing an EPSP of 40 mV or more

# End plate potential

- Local currents
  - Similar to unmiyelinated axons
  - Propogation in both directions

- Muscle fiber action potential initiation
- Voltage gated $Na^+$ channels open

# Termination of signal

- ACh $\xrightarrow{\text{Acetylcholineesterase}}$ Acetate + Choline

- Less ACh
- Less binding to receptor
- End of EPP

# Organophosphates

- Inhibits AChE
- Channels stay open
  - maintained depolarization of the end plate
- Can not produce action potentials
  - the voltage-gated Na+ channels in the membrane become inactivated, which requires repolarization to reverse
- Desensitization of ACh receptors
  - Current stops entering
  - Na+ channels rectivated
  - Loss of receptor responsiveness to ACh causes skeletal muscle paralysis and death from asphyxiation