

Session 22

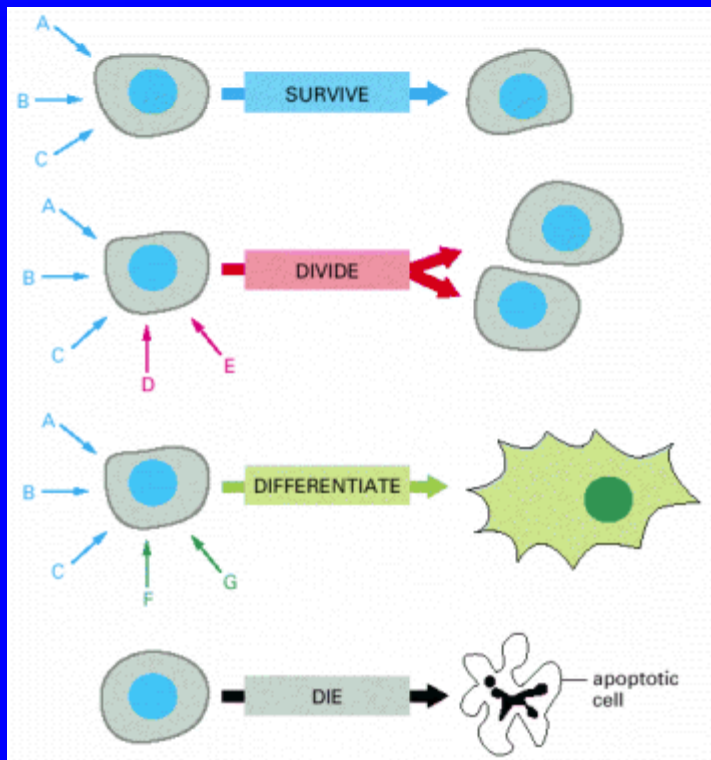
INTRO TO MECHANOTRANSDUCTION

Mechanotransduction

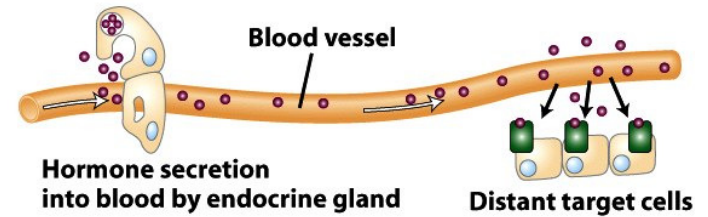
- ◆ “Conversion of mechanical stimulus into biochemical changes”
- ◆ External and internal forces affect biochemical activity in cells that leads to changes in cell function
- ◆ Response is also known as mechanobiology or mechanosensation

Extracellular Signals

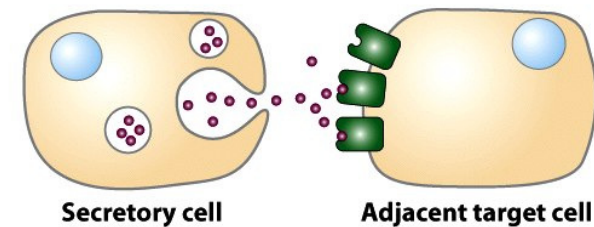
- Cells need signals to undergo appropriate response in function



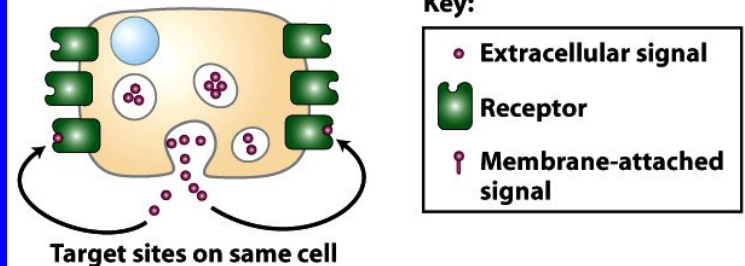
(a) Endocrine signaling



(b) Paracrine signaling



(c) Autocrine signaling



(d) Signaling by plasma membrane-attached proteins

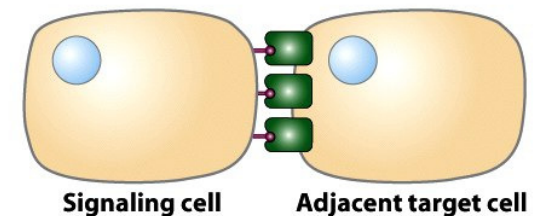
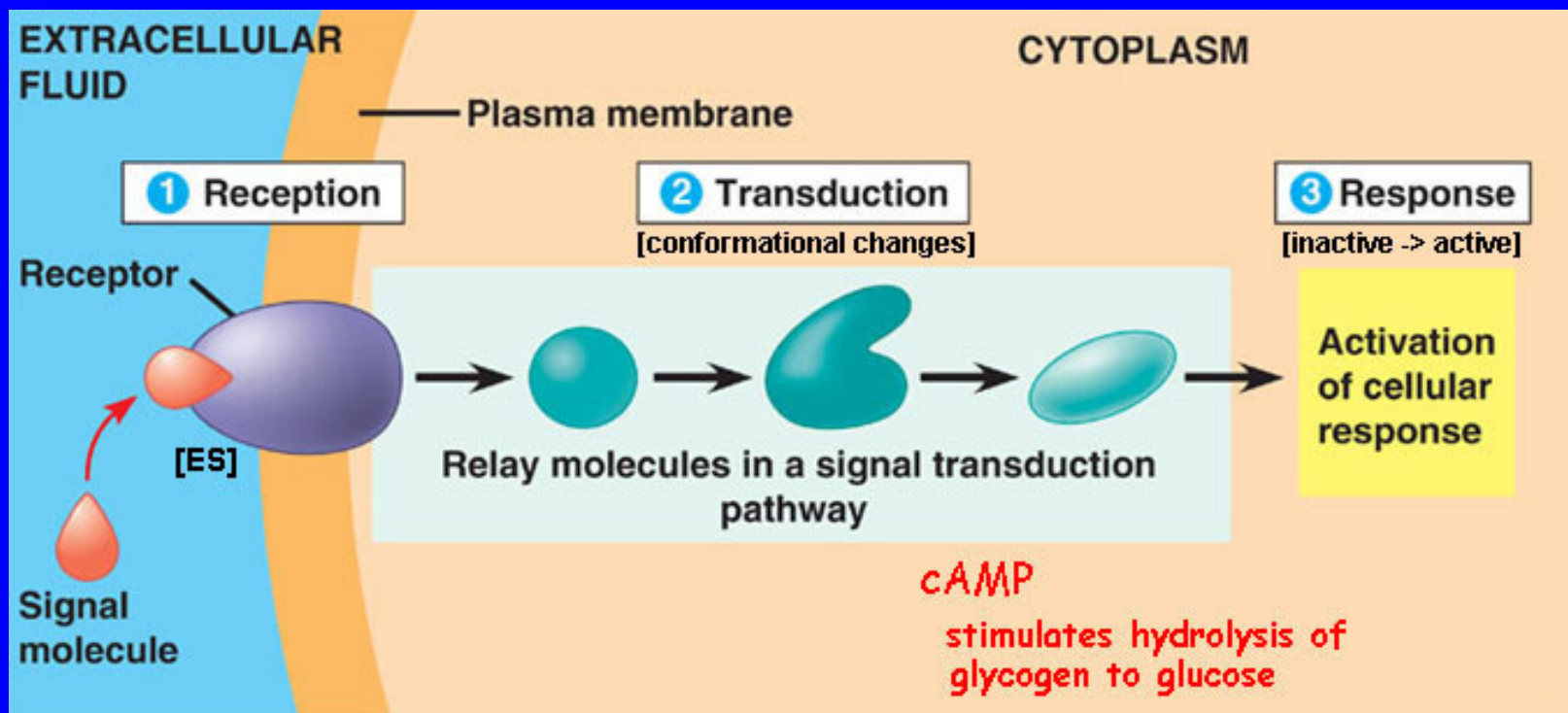


Figure 15-2
Molecular Cell Biology, Sixth Edition
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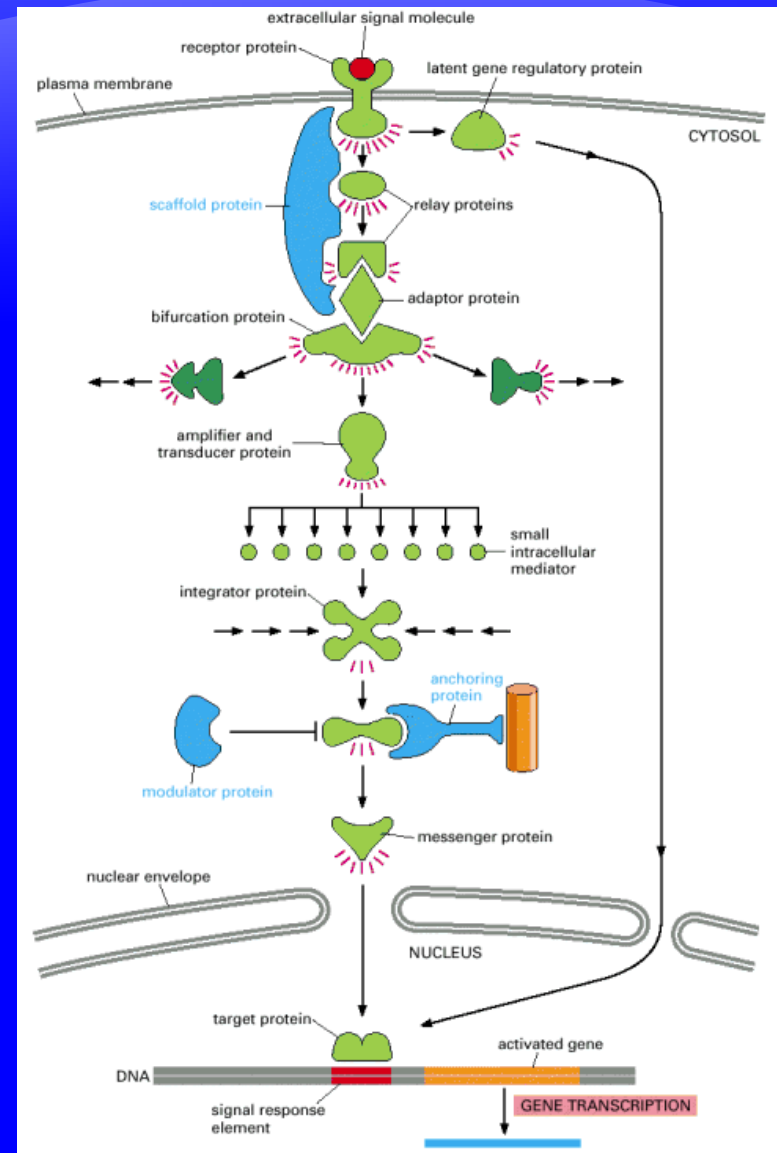
Signal Transduction

- ◆ Signal molecules: hormones, cytokines, chemo-attractants, growth factors, ECM ligands, cadherins



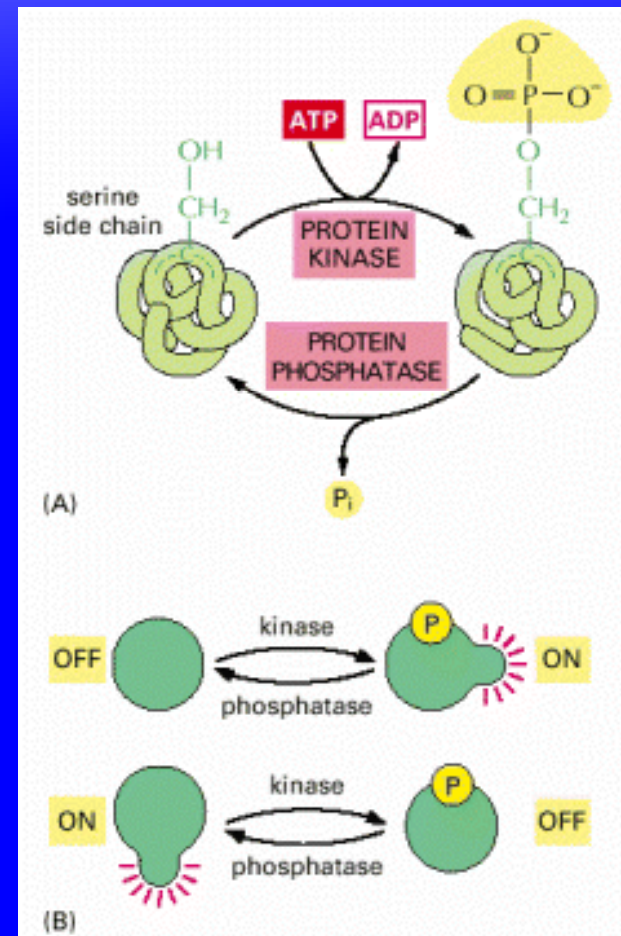
Intracellular Signaling Proteins

- ◆ Latent gene regulators activate at cell surface and initiate transcription
- ◆ Scaffolds cluster proteins together
- ◆ Relays simply pass along a signal
- ◆ Adaptors transmit signal between two others
- ◆ Bifurcators involve multiple pathways
- ◆ Amplifiers enhance a signal strength
- ◆ Transducers covert signal to other forms
- ◆ Small intracellular molecules promote rapid signal transport
- ◆ Integrators cross-reference different signaling pathways
- ◆ Modulators enhance signaling activity
- ◆ Anchors localize proteins at key sites
- ◆ Messengers carry signal into nucleus



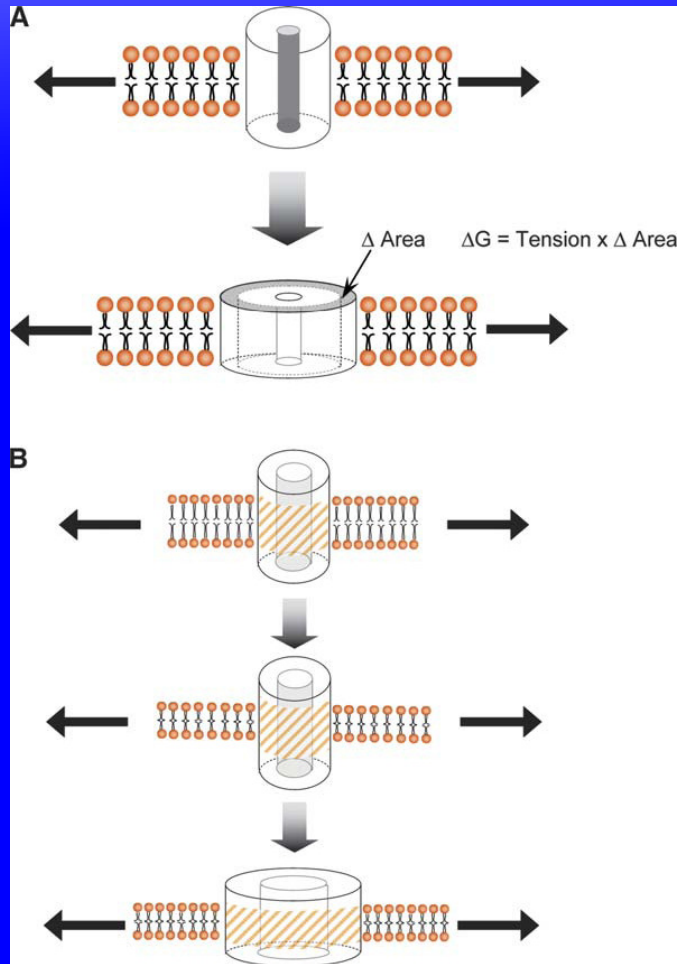
Phosphorylation

- ◆ Kinase:
 - ◆ e.g. Myosin Light Chain Kinase (MLCK)
 - ◆ Attachment of phosphate group from ATP
 - ◆ Binds to –OH amino acids (Serine S, Threonine T, Tyrosine Y)
- ◆ Phosphatase:
 - ◆ e.g. Myosin Light Chain Phosphatase (MLCP)
 - ◆ Removal of (P)
- ◆ Conformation Change
 - ◆ Off → On or On → Off

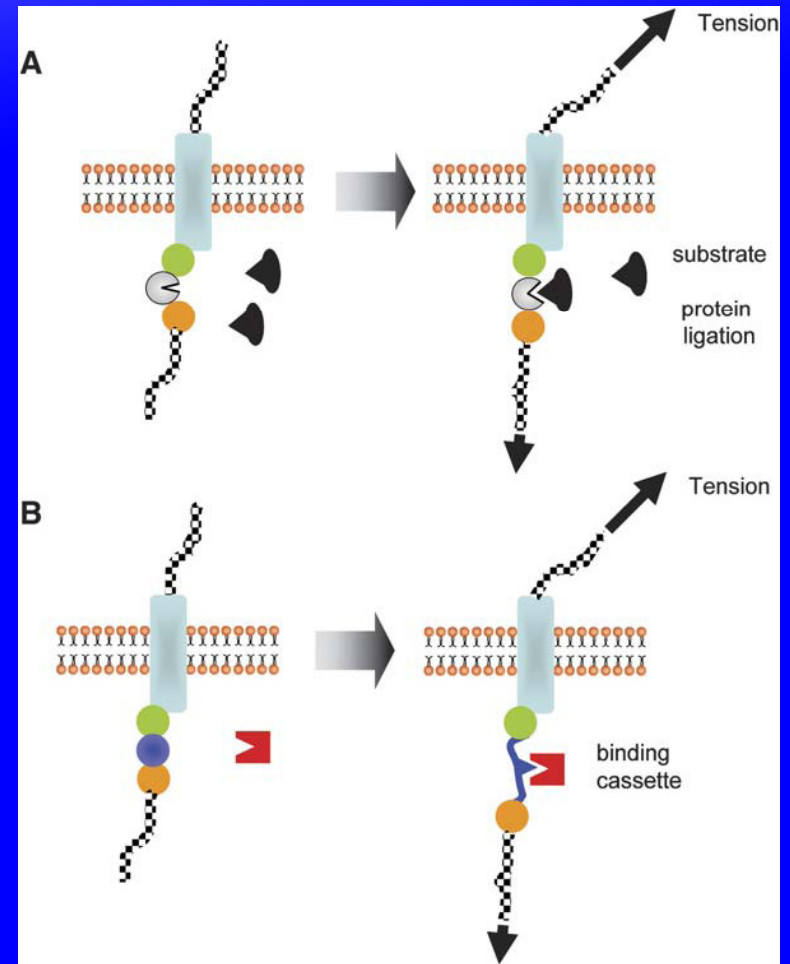


General Mechanisms

- ◆ Stretch Ion Channels

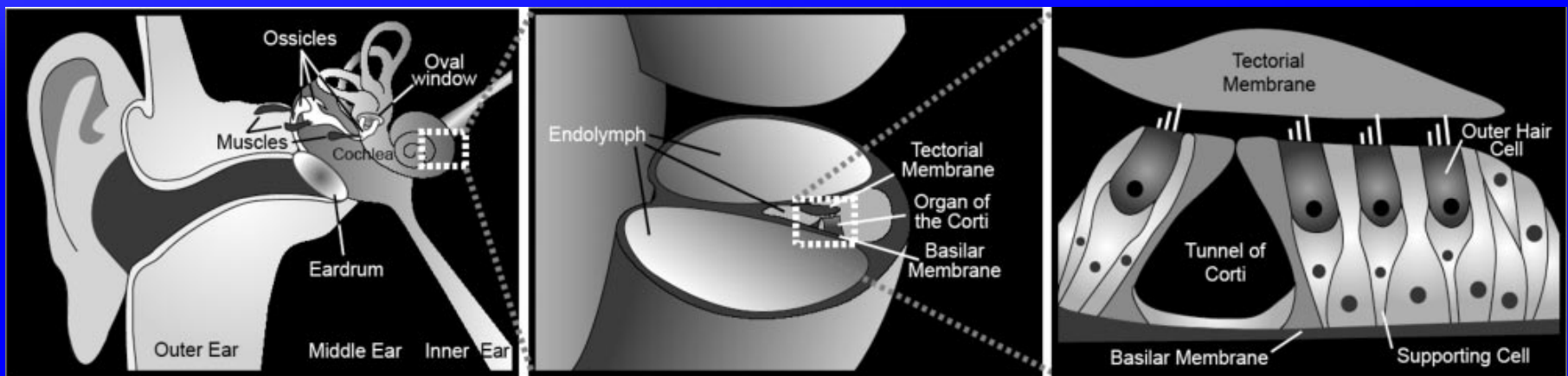


- ◆ Tension-altered Complexes



Hair Cell Mechanotransduction

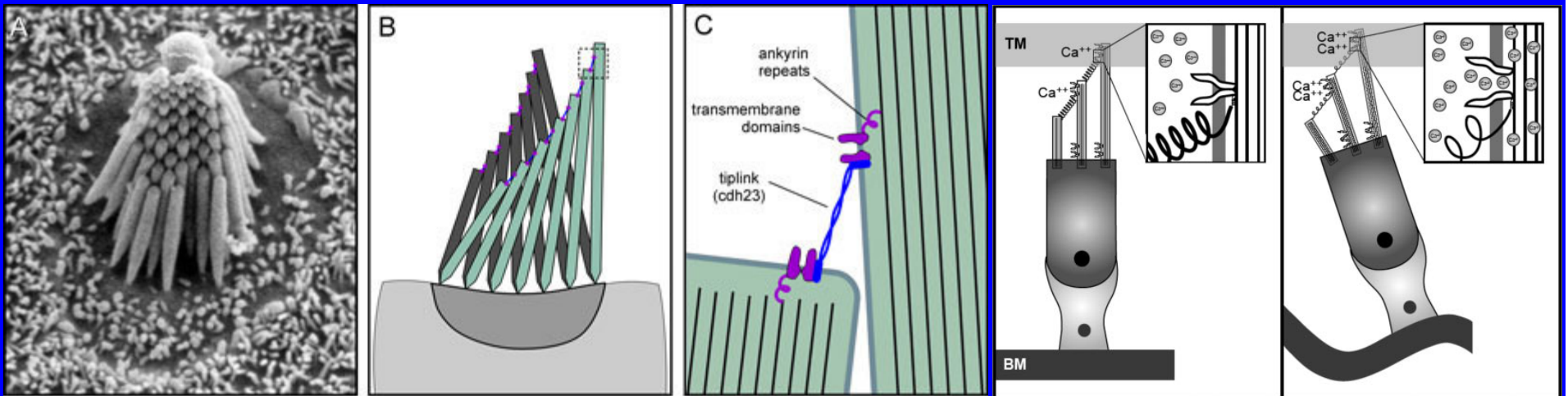
- ◆ Acoustic waves impact eardrum and amplify via ossicles & muscle pre-stress to oval window



- ◆ At oval window, pressure waves induce inner ear fluid (endolymph) to flow in cochlea
- ◆ Vibrations cause basilar membrane deflection that is detected by hair cells

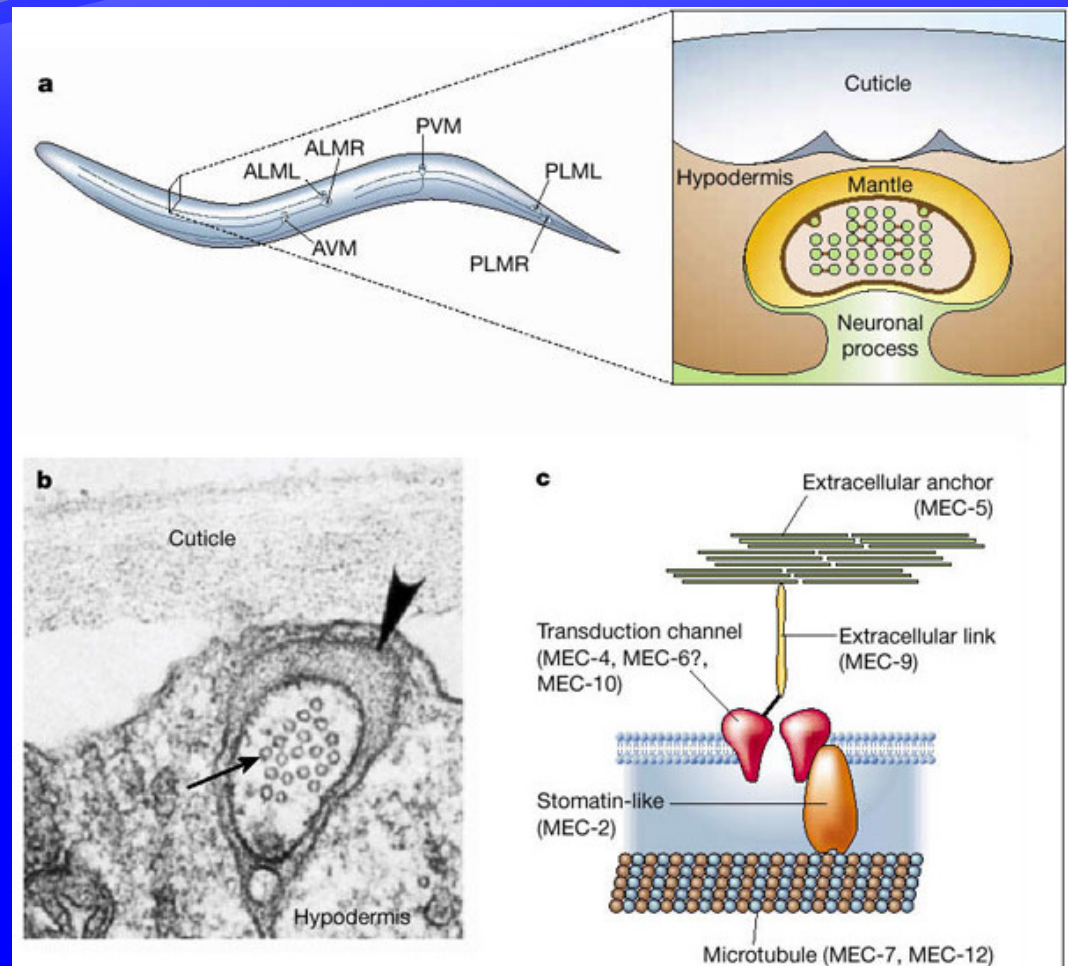
Mechanochemical Sound Conversion

- ◆ Sound induces basilar membrane to undulate
- ◆ Actin-rich stereocilia bend in response
- ◆ Tip-links open mechanically-gated ion channels
- ◆ Influx of Ca^{2+} causes membrane depolarization that activates auditory nerve



Mechanosensitivity to Touch

- ◆ *C. elegans* touch receptors found from mutations in *mec* gene
- ◆ Deflection in MTs relative to mantle opens mechanically gated ion channel and causes influx of Na^+ signal
- ◆ Homologue of *mec-2* in mammals is touch-sensitive



Common Transduction Themes

- ◆ Finely tuned
 - ◆ (Fast) amplification of small forces
- ◆ Linkages
 - ◆ Mechanotransduction requires intra- and extra-cellular connections
- ◆ Mechanosensitive proteins
 - ◆ Specific enzymatic activities or protein-protein interactions are force-dependent
- ◆ Adaptive
 - ◆ Readjustment of cell/tissue structure helps to diminish constant tension to mechanotransduction machinery
- ◆ Physiologically impacting
 - ◆ In addition to hearing and touch, force affects many tissue systems: cardiovascular, pulmonary, skeletal, and connective tissue