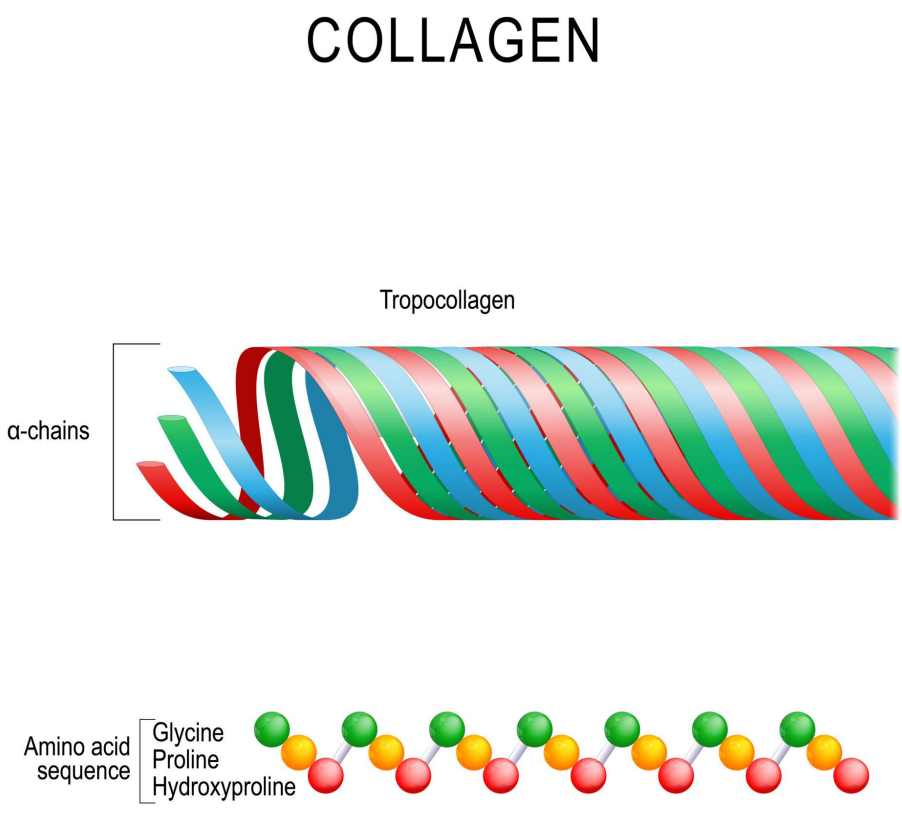
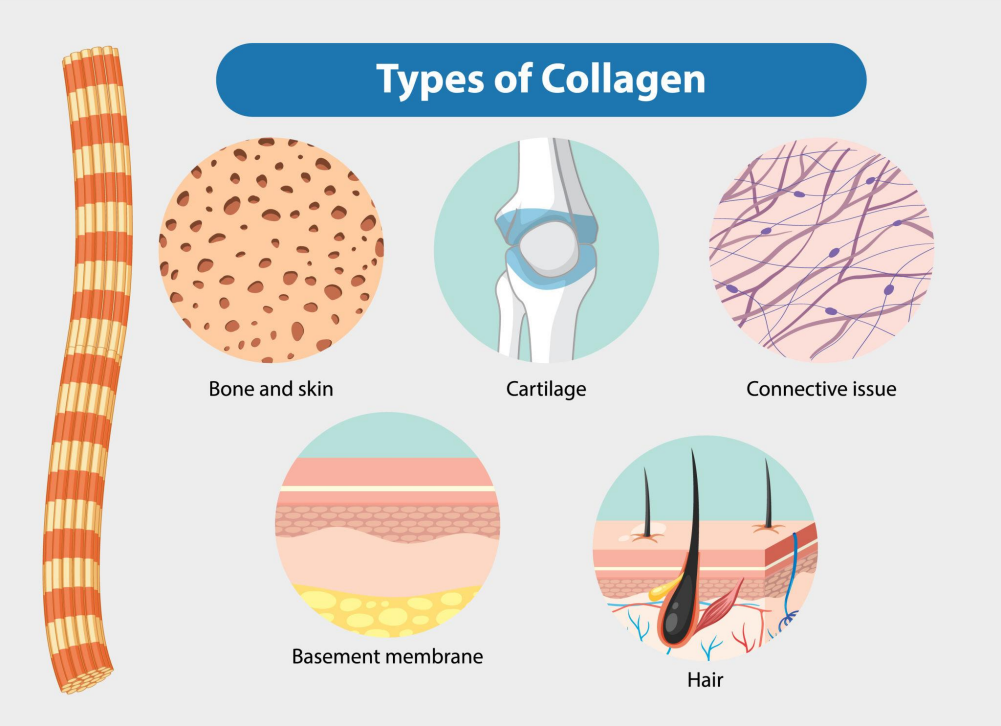
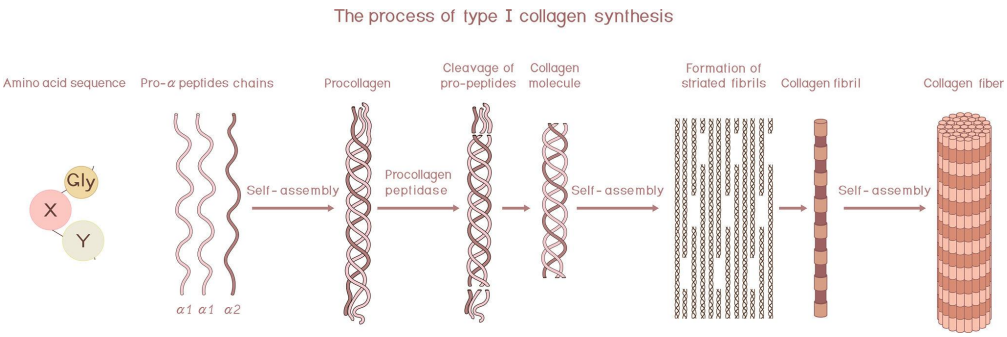
MEDICAL EDUCATION RESOURCE

Tissue Proteins in Health and Disease

Collagen



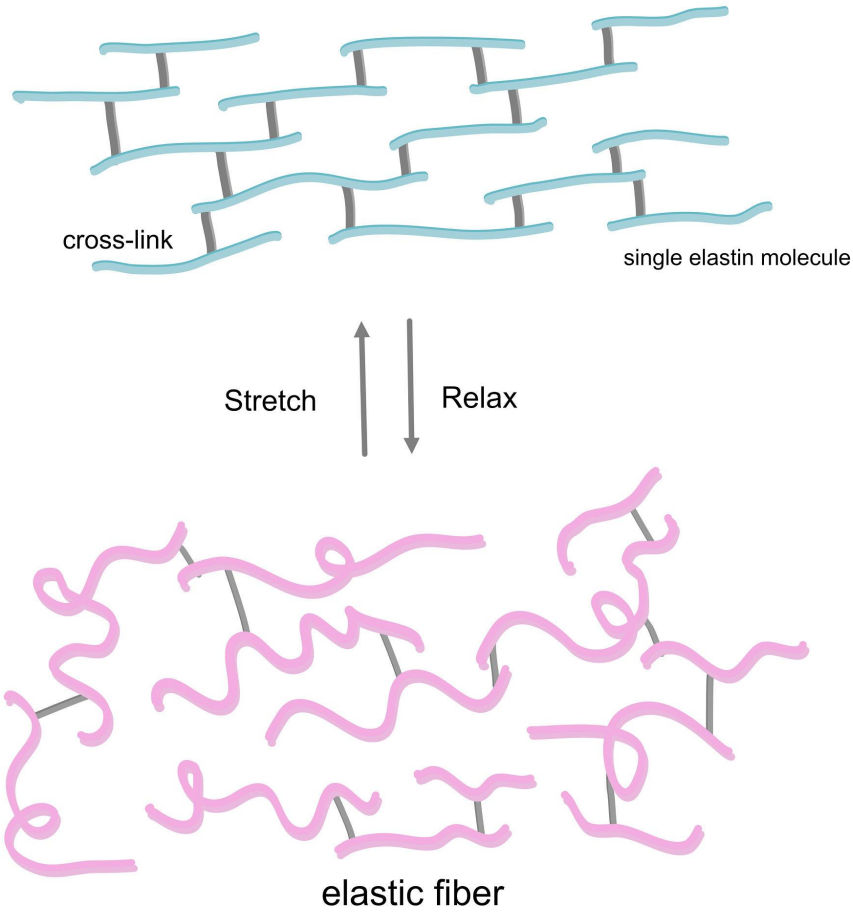


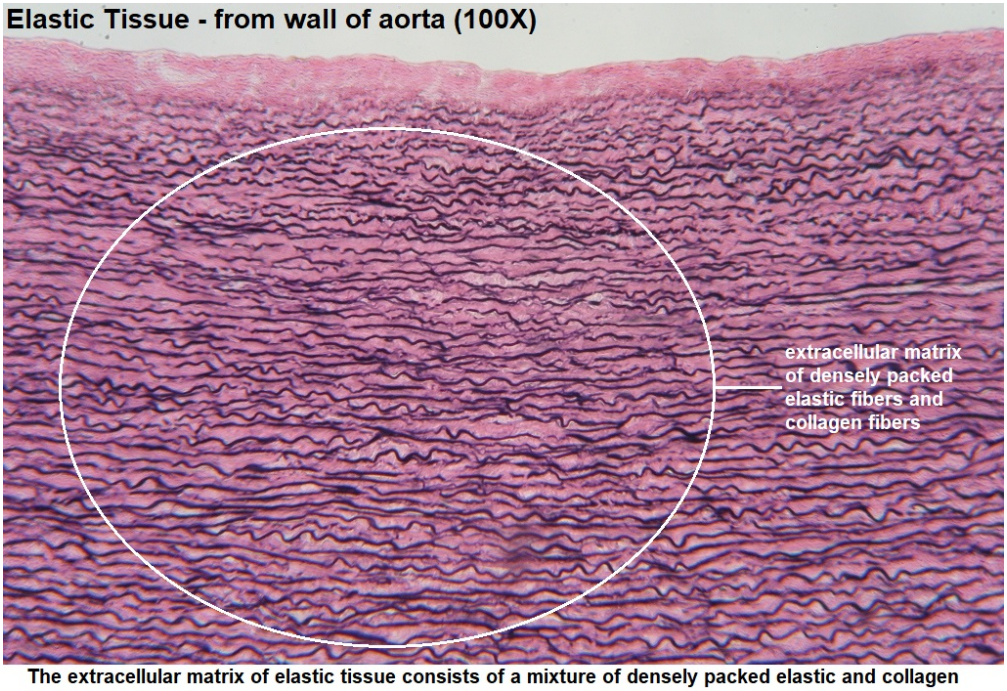


- **Definition**
  - Most abundant structural protein in the body.
- **Structure**
  - Triple helix composed of three ?-chains
  - Repeating sequence: Gly–X–Y (X = proline, Y = hydroxyproline)
- **Types**

    - Type I ? bone, skin, tendon
    - Type II ? cartilage
    - Type III ? blood vessels, skin
    - Type IV ? basement membrane
- **Synthesis**
    - Occurs in fibroblasts
    - Requires vitamin C for hydroxylation
- **Functions**
    - Tensile strength
    - Structural integrity
- **Diseases**
    - Scurvy ? defective collagen synthesis
    - Osteogenesis imperfecta
    - Ehlers–Danlos syndrome

Elastin


cross-link
single elastin molecule
Stretch
Relax
elastic fiber

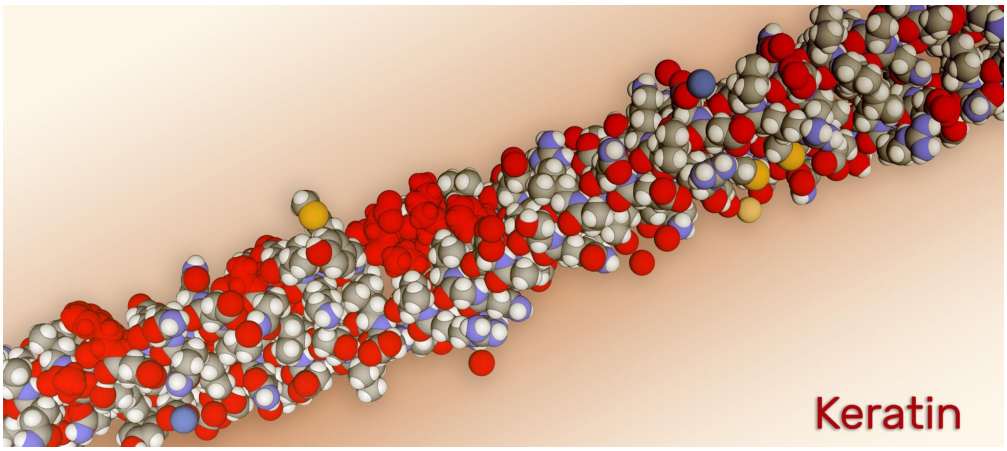


The extracellular matrix of elastic tissue consists of a mixture of densely packed elastic and collagen fibers and a small amount of viscous (thick) ground substance. Elastic tissue possesses a high ratio of elastic fibers compared to collagen fibers which gives it a strong yet stretchy property.

- **Definition**
  - Protein responsible for elasticity of tissues.
- **Structure**
  - Rich in glycine and proline
  - Cross-linked by desmosine and isodesmosine
- **Location**
  - Lungs
  - Skin
  - Blood vessels
- **Function**
  - Allows tissues to stretch and recoil

- **Disease association**
    - Cutis laxa
    - Emphysema (excess elastase activity)

Keratins

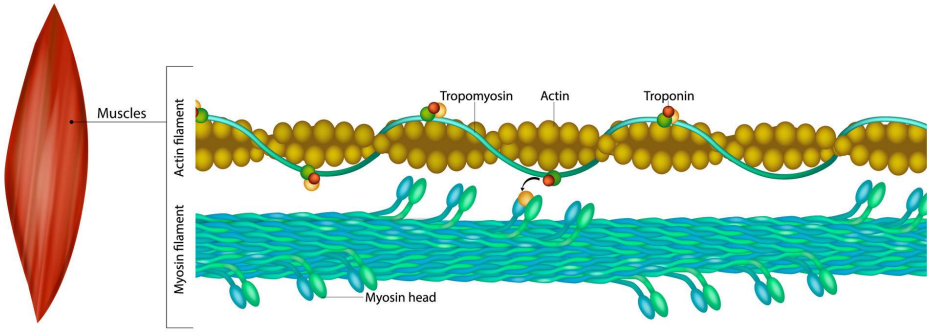


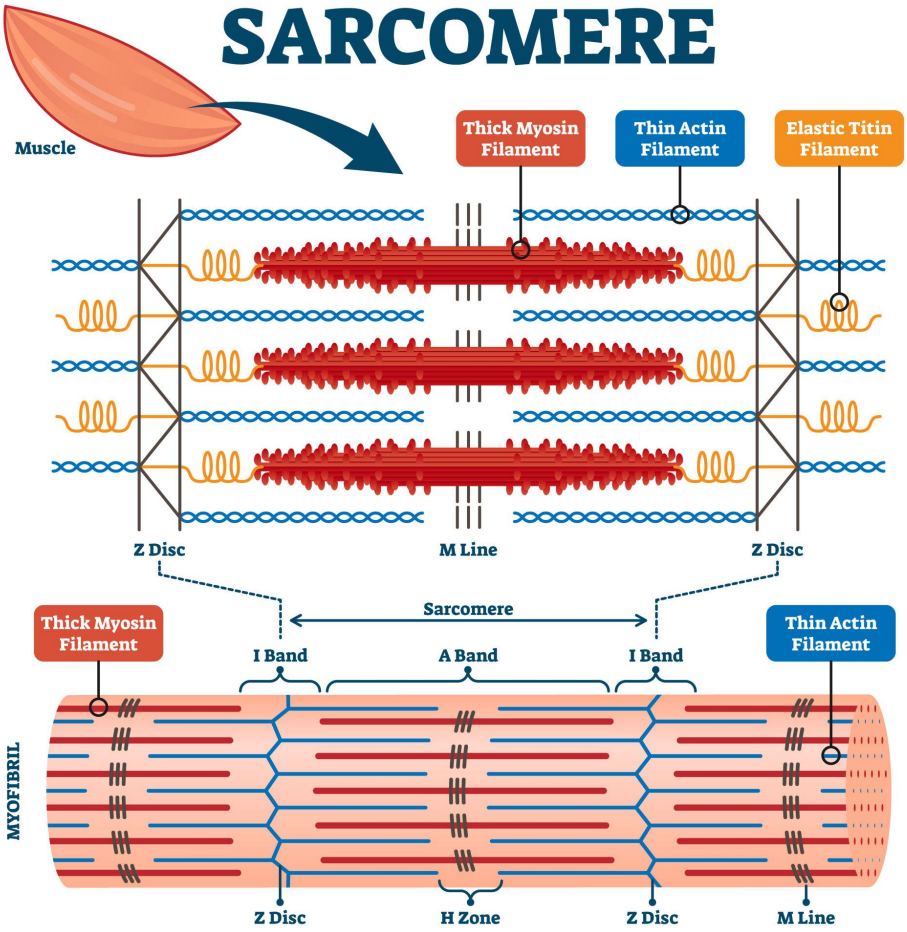
https://www.researchgate.net/publication/279967076/figure/fig4/AS%3A601804941320226%401520492887847/Keratin-in-epithelial-cells-

- **Definition**
    - Fibrous proteins forming intermediate filaments.
- **Types**
    - Hard keratin ? hair, nails
    - Soft keratin ? skin, epithelium
- **Structure**
    - ?-helical coiled-coil structure

- **Function**
    - Mechanical strength
    - Protection
- **Clinical relevance**
    - Epidermolysis bullosa
    - Hair and nail disorders

Contractile Proteins



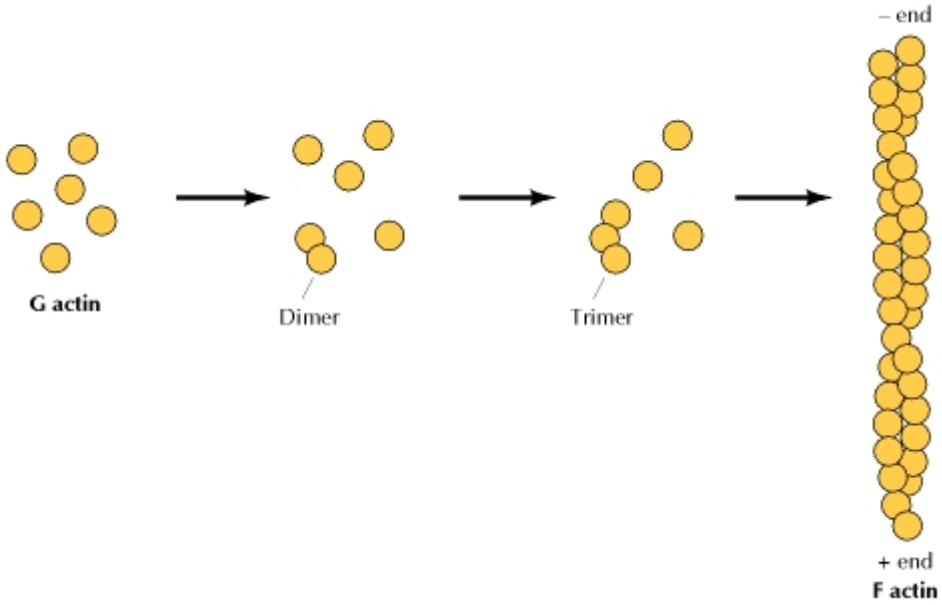


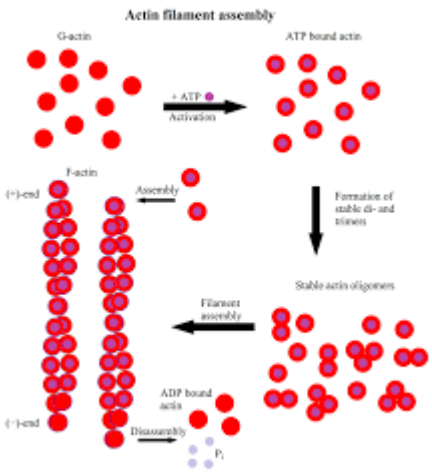
- **Definition**
  - Proteins responsible for muscle contraction.
- **Main proteins**
  - Actin
  - Myosin
  - Troponin
  - Tropomyosin
- **Location**

- Muscle fibers

- **Functional unit**
  - Sarcomere

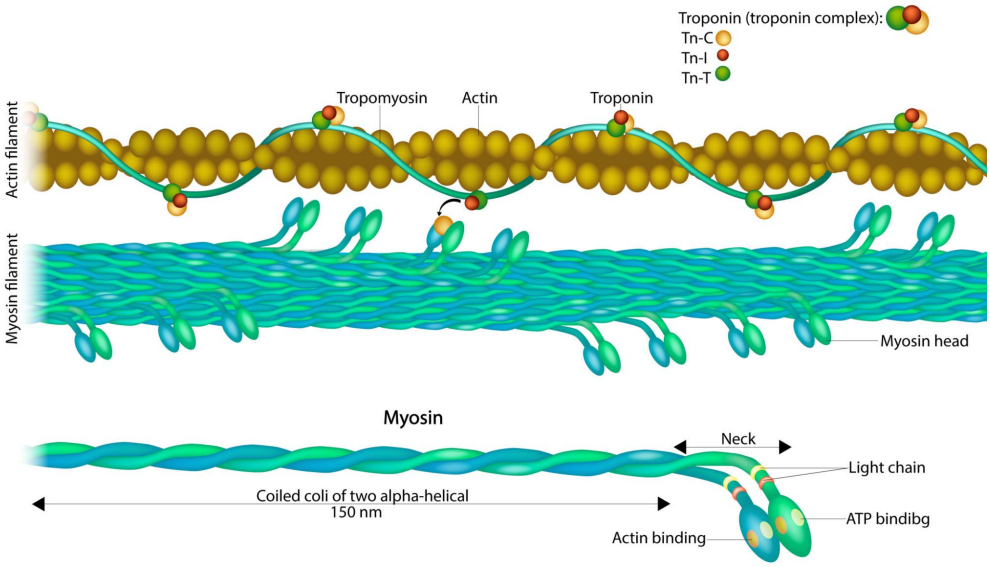
Actin

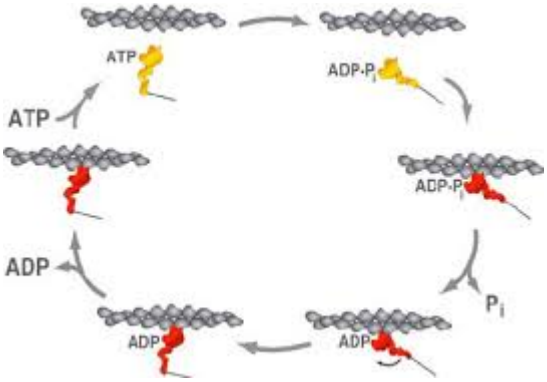




- **Definition**
    - Thin filament protein.
- **Forms**
    - G-actin (globular)
    - F-actin (filamentous)
- **Function**
    - Forms backbone of thin filament
    - Interacts with myosin during contraction

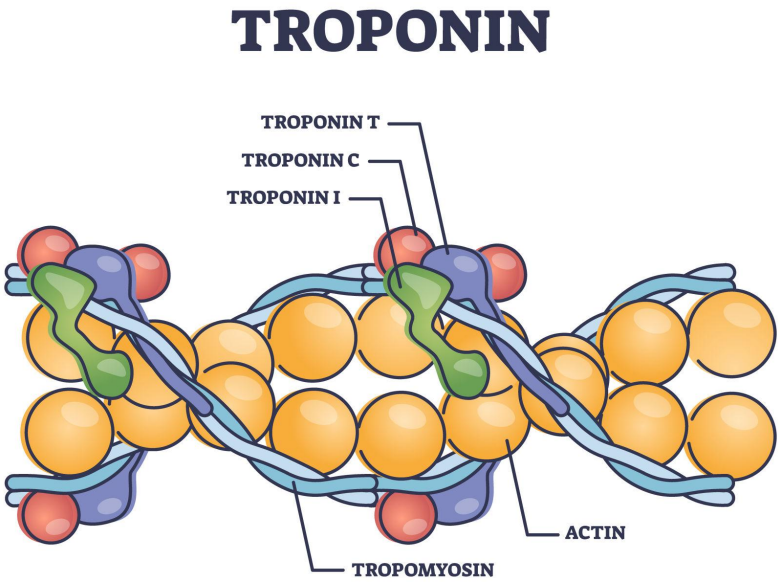
Myosin

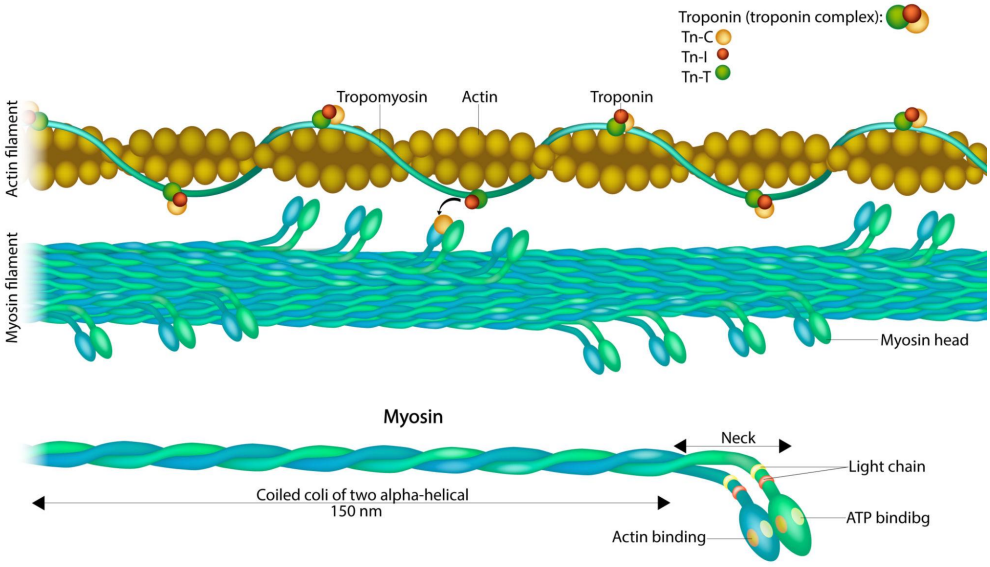




- **Definition**
    - Thick filament protein.
- **Structure**
    - Two heavy chains
    - Four light chains
- **Myosin head**
    - ATPase activity
    - Actin-binding site
- **Function**
    - Converts chemical energy into mechanical work

Troponin





- **Definition**
  - Regulatory protein complex on thin filament.

- **Components**
    - Troponin T ? binds tropomyosin
    - Troponin I ? inhibitory
    - Troponin C ? binds calcium
- **Clinical importance**
    - Cardiac troponins used as markers of myocardial infarction

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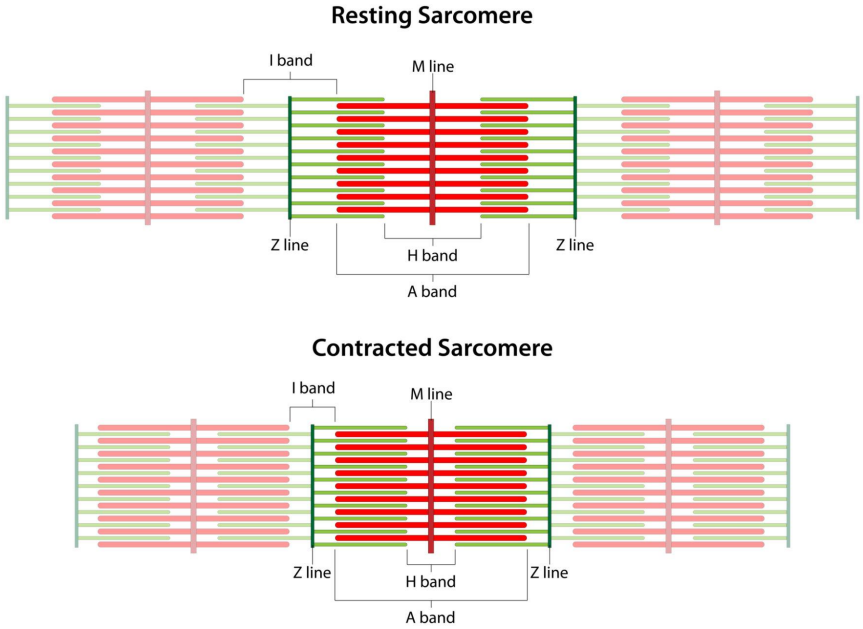
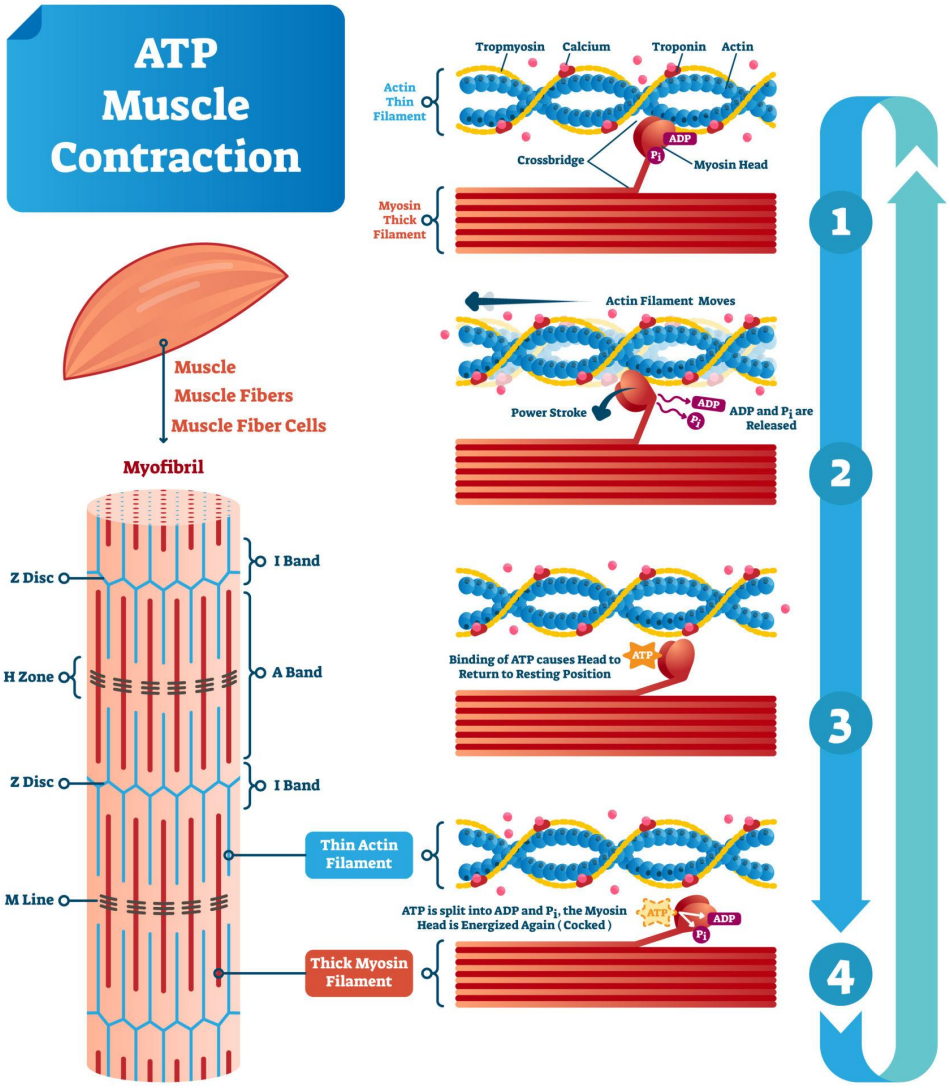
Muscle Contraction



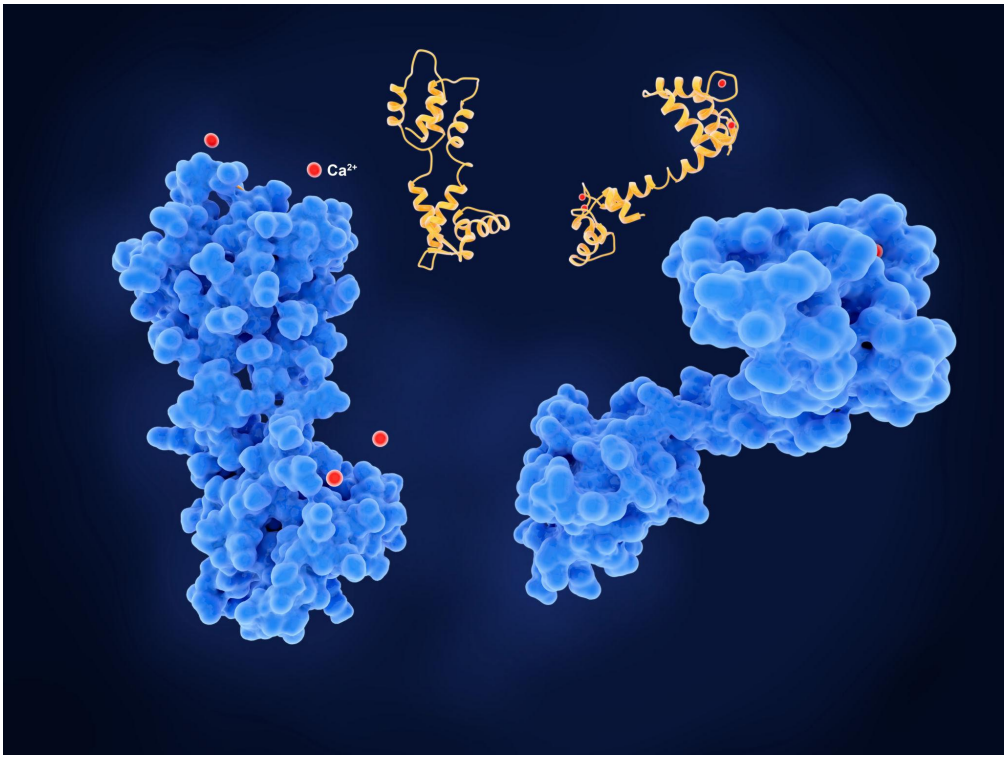


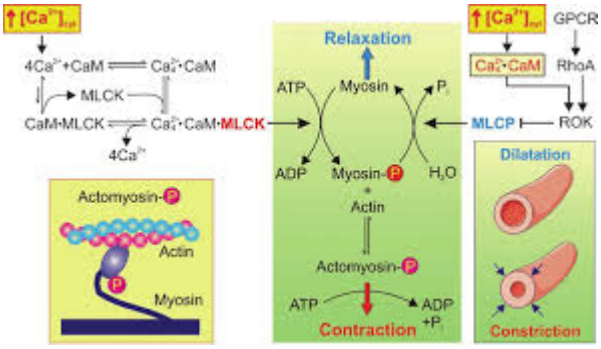
- **Theory**
    - Sliding filament theory
- **Steps**
    - Calcium release from sarcoplasmic reticulum
    - Calcium binds troponin C
    - Exposure of actin binding sites

- Cross-bridge formation
- ATP hydrolysis ? power stroke

- **Energy source**
  - ATP
- **Relaxation**
  - Calcium pumped back into sarcoplasmic reticulum

Calmodulin





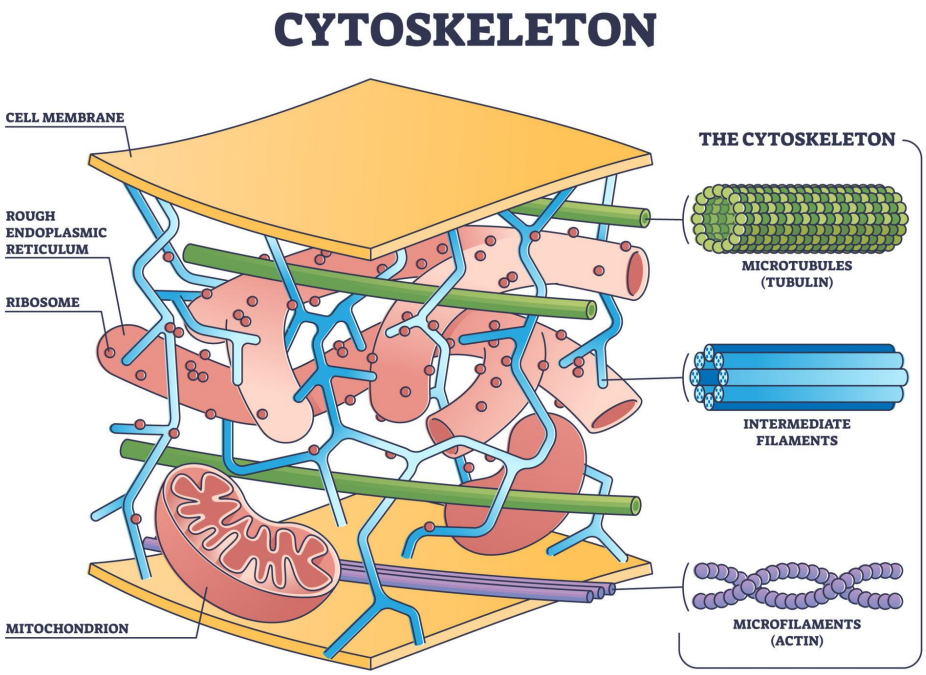
- **Definition**
  - Calcium-binding regulatory protein.
- **Structure**
  - Binds four Ca²? ions
- **Functions**
  - Activates enzymes
  - Regulates smooth muscle contraction
- **Mechanism**
  - Ca²?–calmodulin complex activates myosin light chain kinase
- **Difference from troponin**
  - Present in smooth muscle and non-muscle cells
  - Troponin is absent in smooth muscle

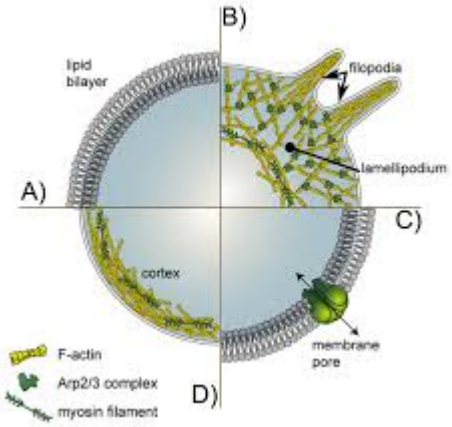
Rapid exam memory hooks

- **Collagen** ? strength

- **Elastin** ? elasticity
- **Keratin** ? protection
- **Actin + myosin** ? movement
- **Troponin** ? $Ca^{2?}$ control (cardiac marker)
- **Calmodulin** ? $Ca^{2?}$ regulator in smooth muscle

Microfilaments

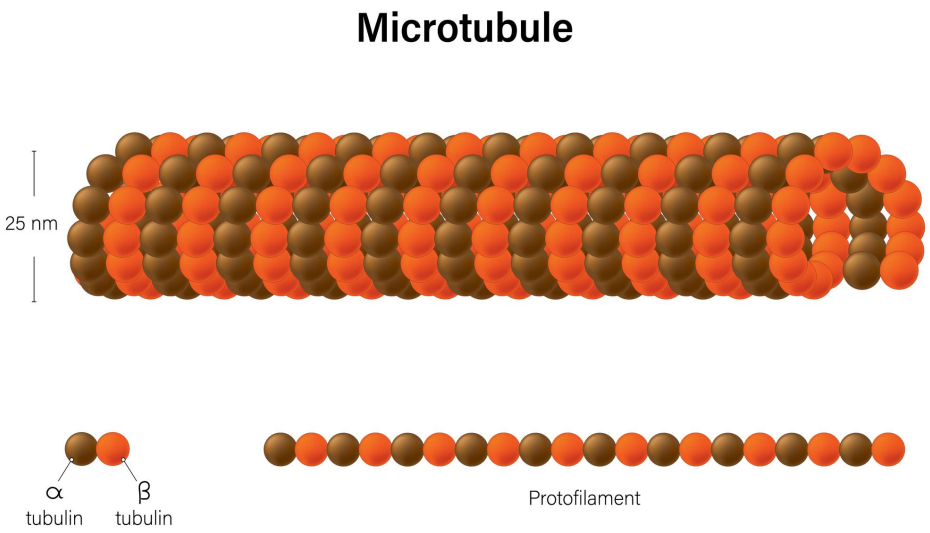




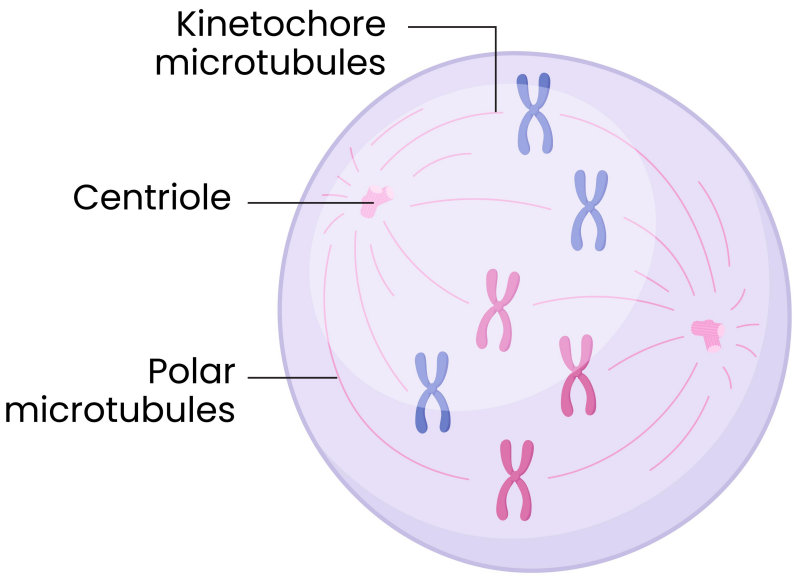
- **Definition**
  - Thin cytoskeletal filaments composed mainly of actin.
- **Diameter**
  - ~7 nm
- **Structure**
  - Polymerized F-actin from G-actin subunits
- **Functions**
  - Maintenance of cell shape
  - Cell motility
  - Muscle contraction
  - Cytokinesis
- **Associated proteins**
  - Myosin
  - Tropomyosin

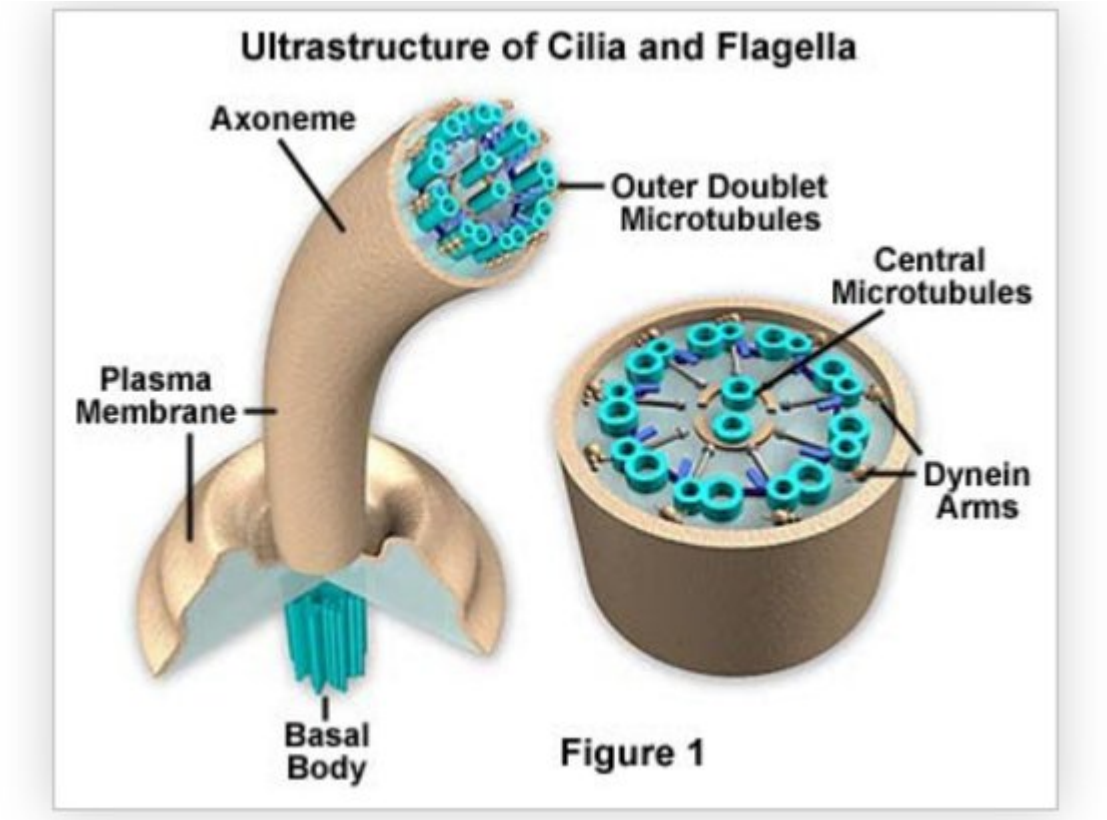
- **Clinical relevance**
    - Defects affect cell movement and muscle function

Microtubules



Prometaphase

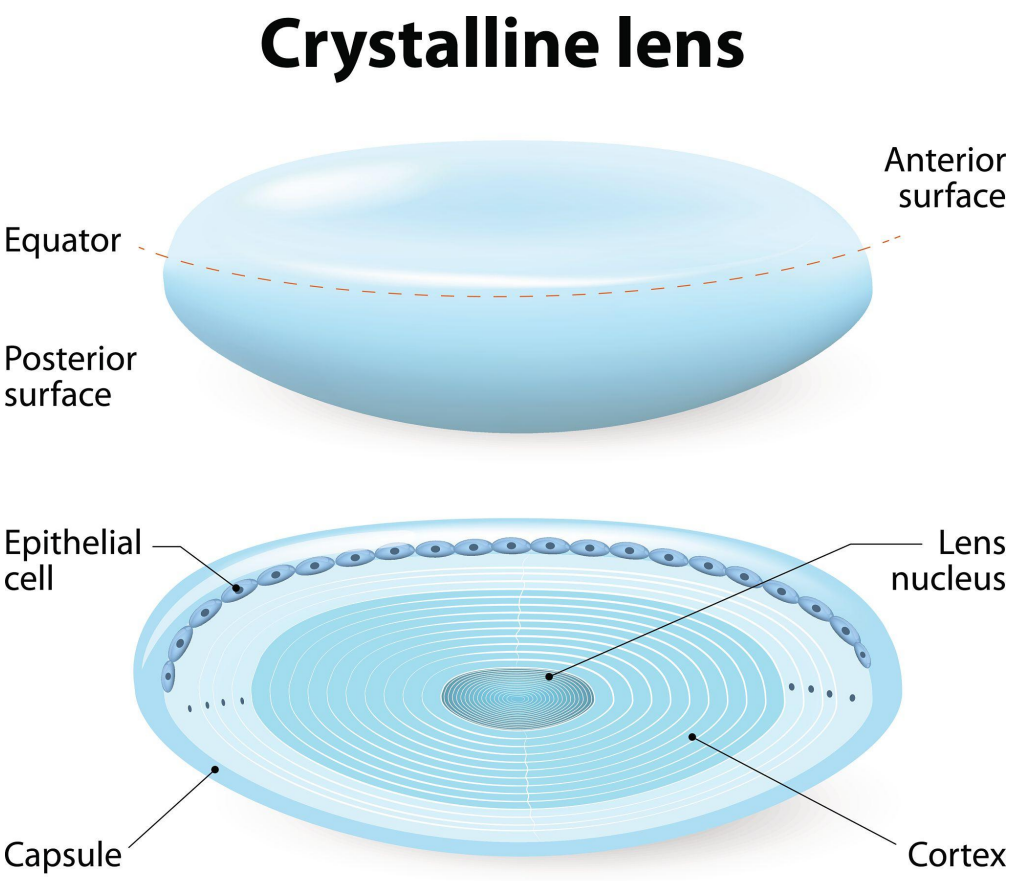


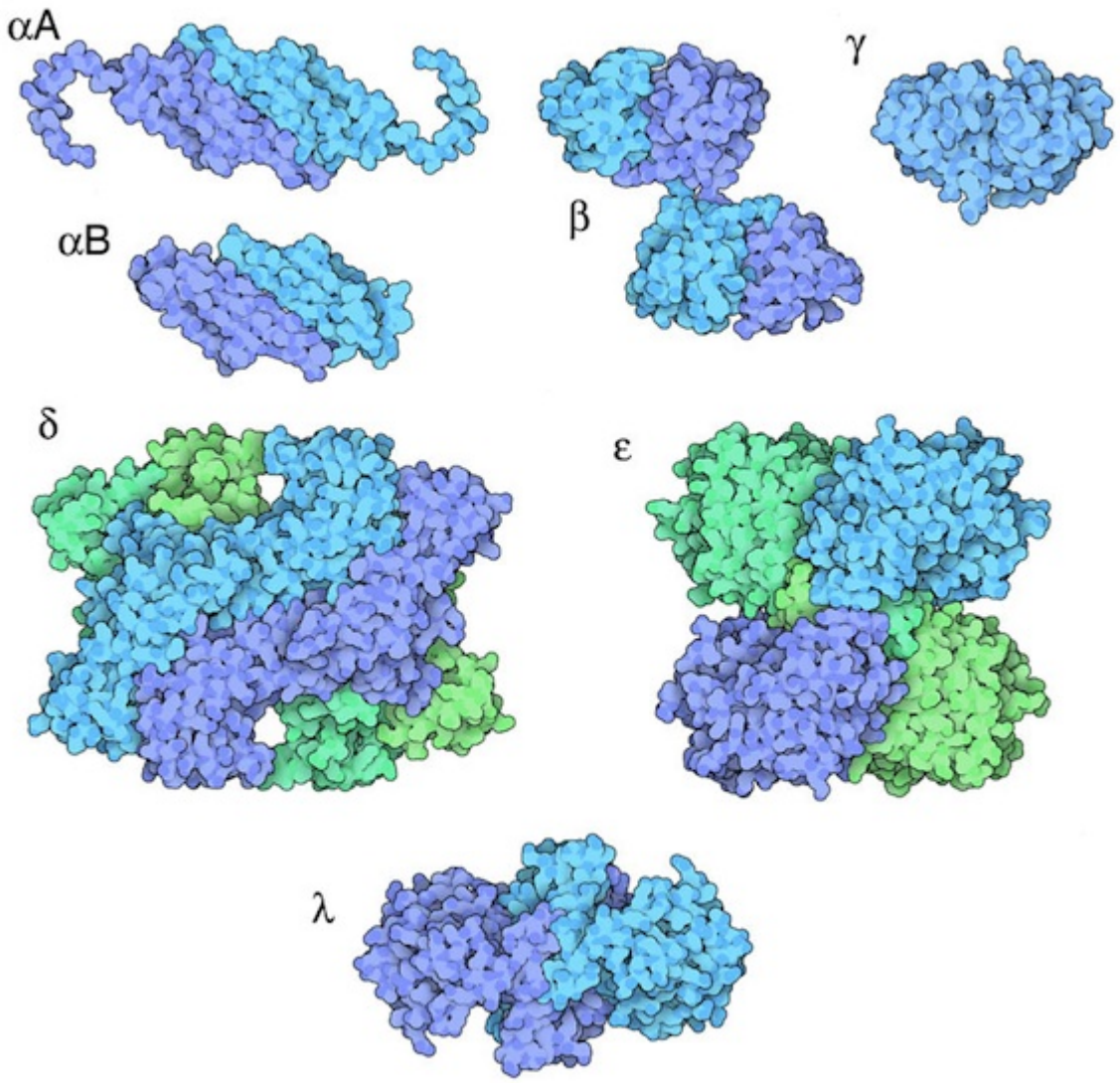


- **Definition**
  - Hollow cylindrical cytoskeletal structures.
- **Diameter**
  - ~25 nm
- **Composition**
  - ?-tubulin and ?-tubulin dimers
- **Functions**
  - Mitotic spindle formation
  - Intracellular transport
  - Cilia and flagella movement

- **Arrangement**
    - 9+2 structure in cilia and flagella
- **Drug relevance**
    - Target of anticancer drugs (vincristine, paclitaxel)

Lens Proteins





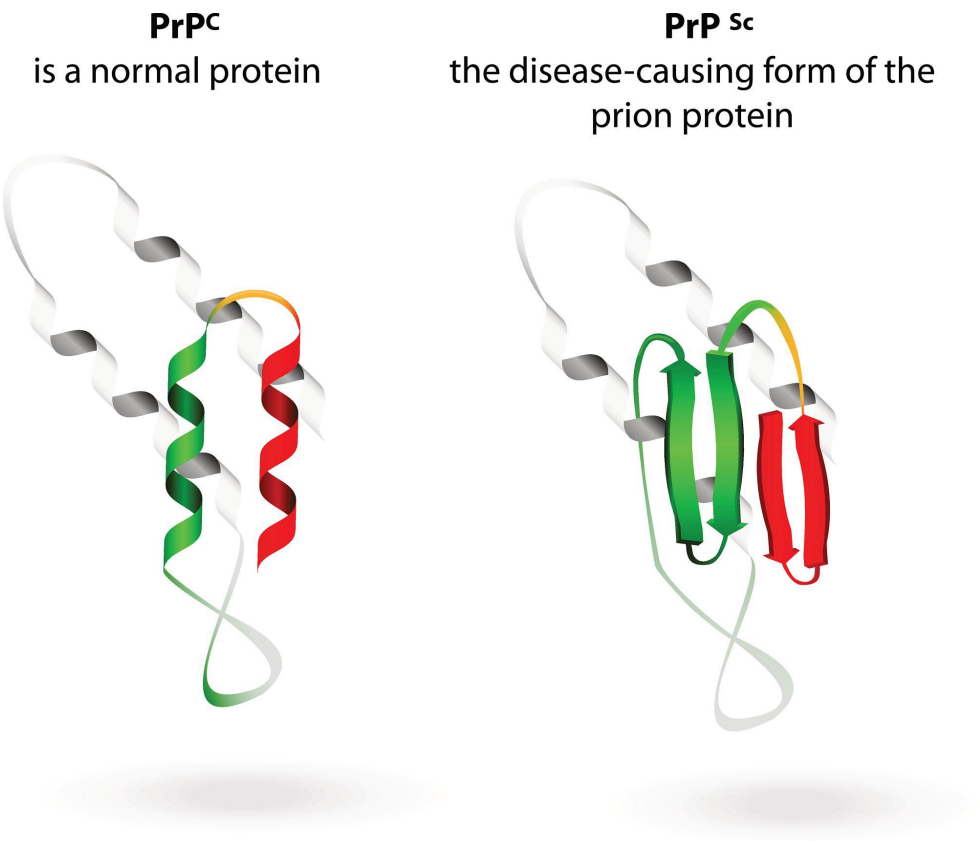
- **Definition**
    - Structural proteins maintaining lens transparency.
- **Major proteins**
    - ?-crystallins
    - ?-crystallins
    - ?-crystallins
- **Functions**

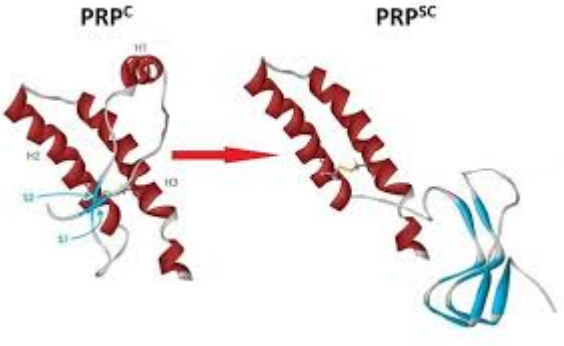
- Transparency of lens
- Refractive properties

- **Special feature**
  - Extremely long half-life

- **Disease association**
  - Cataract due to protein aggregation and oxidation

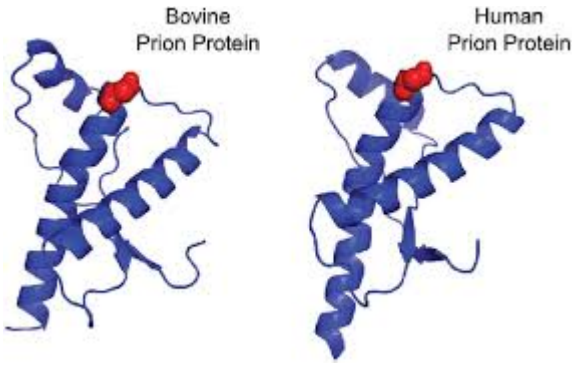
Prions

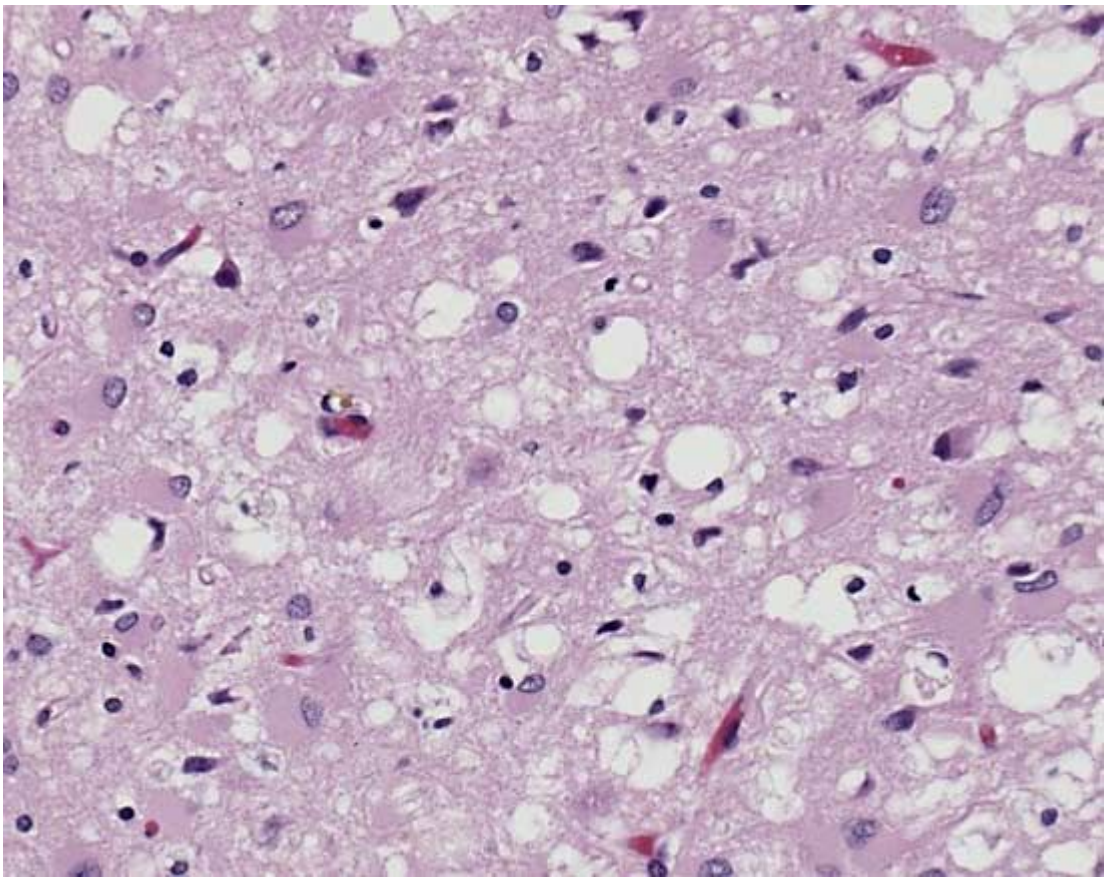




- **Definition**
  - Infectious protein particles without nucleic acid.
- **Normal protein**
  - PrP? (cellular prion protein)
- **Pathogenic form**
  - PrP?? (scrapie form)
- **Biochemical change**
  - ?-helix ? ?-sheet conversion
- **Properties**
  - Resistant to heat and proteases
  - Induce misfolding of normal proteins

Human Prion Diseases



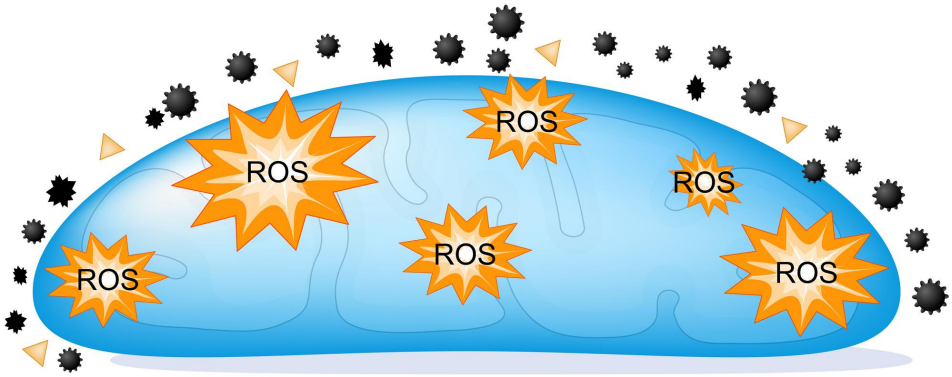


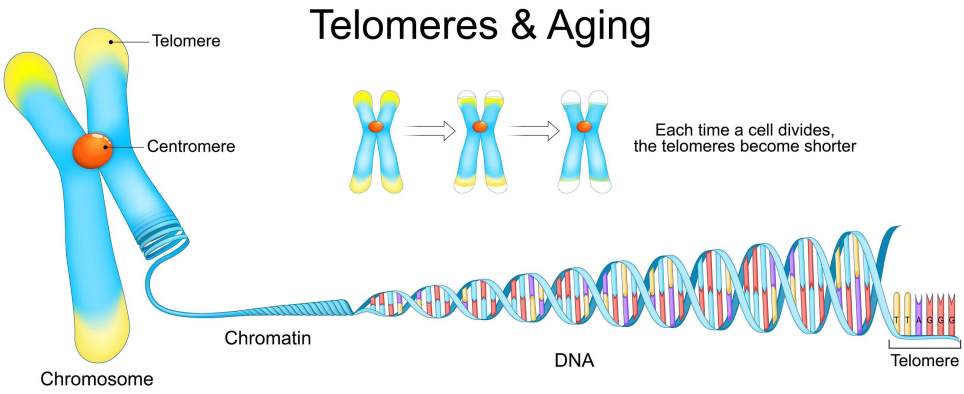
- **Group**
    - Transmissible spongiform encephalopathies
- **Examples**
    - Creutzfeldt–Jakob disease

    - Variant CJD
    - Kuru
    - Fatal familial insomnia
- **Pathology**
    - Spongiform degeneration of brain
    - Neuronal loss
- **Clinical features**
    - Rapidly progressive dementia
    - Ataxia
    - Myoclonus
- **Outcome**
    - Always fatal

Biochemistry of Aging

OXIDATIVE STRESS



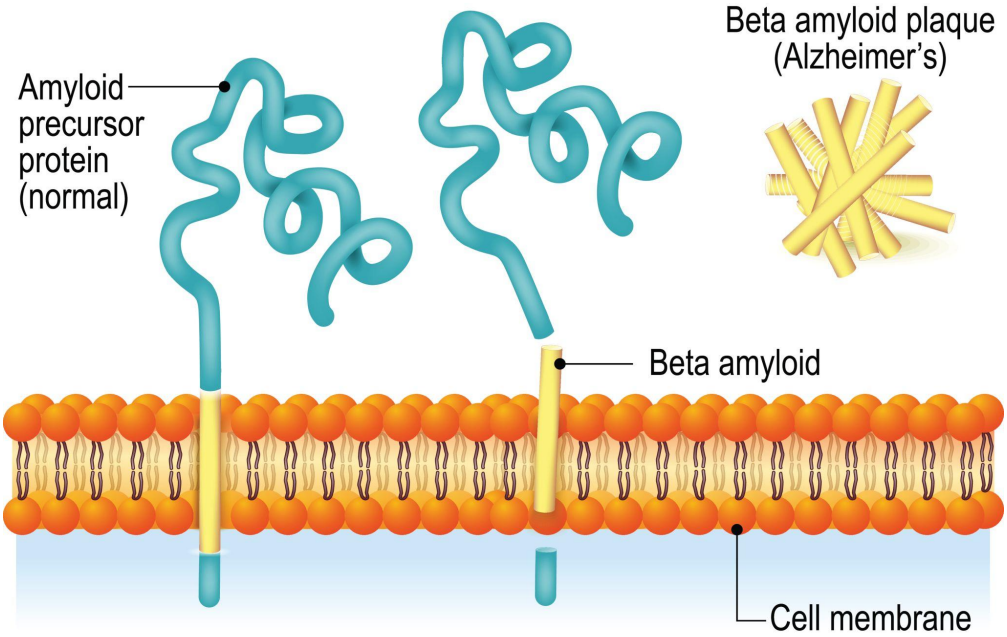


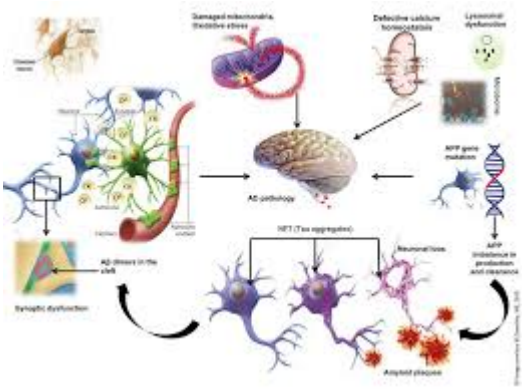
- **Definition**
  - Progressive decline in physiological function with age.
- **Major theories**
  - Free radical theory
  - Telomere shortening
  - Protein glycation

- **Biochemical changes**
    - Increased oxidative stress
    - Decreased DNA repair
    - Accumulation of damaged proteins
- **Role of antioxidants**
    - Reduce oxidative damage
- **Clinical relevance**
    - Increased risk of degenerative diseases

Alzheimer’s Disease

Amyloid-plaque formation





- **Definition**
  - Progressive neurodegenerative disorder causing dementia.
- **Key biochemical abnormalities**
  - Amyloid-? plaque deposition
  - Neurofibrillary tangles (hyperphosphorylated tau)

- **Pathogenesis**
    - Abnormal processing of amyloid precursor protein
    - Synaptic dysfunction
- **Neurotransmitter deficit**
    - Acetylcholine deficiency
- **Clinical features**
    - Memory loss
    - Cognitive decline
- **Biochemical hallmark**
    - Protein misfolding and aggregation

Rapid exam memory hooks

- **Microfilaments** ? actin ? movement
- **Microtubules** ? tubulin ? mitosis & transport
- **Lens proteins** ? crystallins ? transparency
- **Prions** ? infectious proteins
- **Aging** ? oxidative damage + telomeres
- **Alzheimer’s** ? amyloid ? + tau

FAQs – Tissue Proteins, Prions, Aging & Neurodegeneration

Microfilaments

What are microfilaments?
Thin cytoskeletal filaments composed mainly of actin.

What is the diameter of microfilaments?
Approximately 7 nm.

What is the basic structural unit of microfilaments?
G-actin polymerized to form F-actin.

Functions of microfilaments?
Maintenance of cell shape, cell motility, muscle contraction, and cytokinesis.

Microtubules

What are microtubules?
Hollow cylindrical cytoskeletal structures composed of tubulin.

Which proteins form microtubules?
?-tubulin and ?-tubulin dimers.

What is the diameter of microtubules?
Approximately 25 nm.

Functions of microtubules?
Mitotic spindle formation, intracellular transport, and cilia/flagella movement.

What is the structural arrangement in cilia and flagella?
9 + 2 microtubule arrangement.

Name drugs acting on microtubules.
Vincristine, vinblastine, paclitaxel.

Lens Proteins

What are the major proteins of the lens?
Crystallins.

Types of crystallins?
?-, ?-, and ?-crystallins.

Why are lens proteins unique?
They have an extremely long half-life.

Function of lens proteins?
Maintain lens transparency and refractive power.

Biochemical basis of cataract formation?
Protein aggregation and oxidative modification of crystallins.

Prions

What are prions?
Infectious protein particles lacking nucleic acids.

What is the normal prion protein?
PrP? (cellular prion protein).

What is the pathogenic prion protein?
PrP?? (scrapie form).

What structural change occurs in prion disease?
Conversion of ?-helix to ?-sheet structure.

Why are prions resistant to heat and proteases?
Due to high ?-sheet content.

Human Prion Diseases

What are prion diseases collectively called?
Transmissible spongiform encephalopathies.

Examples of human prion diseases?
Creutzfeldt–Jakob disease, variant CJD, Kuru, fatal familial insomnia.

Characteristic pathological feature of prion diseases?
Spongiform degeneration of the brain.

Outcome of prion diseases?
Always fatal.

Biochemistry of Aging

What is aging?
Progressive decline in physiological function with advancing age.

Major biochemical theories of aging?
Free radical theory, telomere shortening, protein glycation.

Role of free radicals in aging?
Cause oxidative damage to DNA, proteins, and lipids.

What happens to DNA repair with aging?
It decreases.

Role of antioxidants in aging?
Reduce oxidative stress and cellular damage.

Alzheimer’s Disease

What is Alzheimer’s disease?
A progressive neurodegenerative disorder causing dementia.

Key biochemical hallmarks of Alzheimer’s disease?
Amyloid-? plaques and neurofibrillary tangles.

What forms amyloid plaques?
Amyloid-? peptide derived from amyloid precursor protein.

What are neurofibrillary tangles composed of?
Hyperphosphorylated tau protein.

Which neurotransmitter is deficient in Alzheimer’s disease?
Acetylcholine.

Why is Alzheimer’s considered a protein misfolding disorder?
Due to abnormal aggregation of amyloid-? and tau proteins.

One-Line Exam Memory Hooks

- **Microfilaments** ? actin ? movement
- **Microtubules** ? tubulin ? mitosis & transport
- **Lens proteins** ? crystallins ? transparency
- **Prions** ? infectious proteins without nucleic acid
- **Aging** ? oxidative damage + telomere loss

- **Alzheimer's** ? amyloid ? + tau tangles

MCQs – Cytoskeleton, Prions, Aging & Alzheimer's

Microfilaments

1. Microfilaments are primarily composed of:
A. Tubulin
B. Keratin
C. Actin
D. Myosin
Answer: C

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2. Diameter of microfilaments is approximately:
A. 3 nm
B. 7 nm
C. 10 nm
D. 25 nm
Answer: B

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3. G-actin polymerizes to form:
A. Myosin
B. Tropomyosin
C. F-actin
D. Tubulin
Answer: C

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4. Microfilaments are NOT involved in:
A. Cell motility
B. Cytokinesis
C. Muscle contraction
D. Mitotic spindle formation
Answer: D

Microtubules

5. Microtubules are composed of:
A. Actin monomers

B. ?- and ?-tubulin
C. Intermediate filaments
D. Myosin heavy chains
Answer: B

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6. Diameter of microtubules is:
A. 7 nm
B. 10 nm
C. 15 nm
D. 25 nm
Answer: D

---

7. Which structure has a 9 + 2 microtubule arrangement?
A. Centriole
B. Mitotic spindle
C. Cilia and flagella
D. Basal body
Answer: C

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8. Microtubules play a major role in:
A. Apoptosis
B. Intracellular transport
C. DNA replication
D. Protein synthesis
Answer: B

---

9. Which anticancer drug acts by inhibiting microtubule polymerization?
A. Methotrexate
B. Vincristine
C. Cyclophosphamide
D. Doxorubicin
Answer: B

Lens Proteins

10. Major structural proteins of the lens are:
A. Collagens
B. Elastins
C. Crystallins
D. Keratins
Answer: C

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11. Which crystallin acts as a molecular chaperone?

A. ?-crystallin

B. ?-crystallin

C. ?-crystallin

D. ?-crystallin

Answer: A

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12. Lens proteins are unique because they:

A. Are rapidly degraded

B. Have very short half-life

C. Have extremely long half-life

D. Are replaced daily

Answer: C

---

13. Cataract formation is mainly due to:

A. Increased protein synthesis

B. Protein aggregation and oxidation

C. Increased glucose uptake

D. DNA damage

Answer: B

Prions

14. Prions are composed of:

A. DNA and protein

B. RNA and protein

C. Protein only

D. Lipoprotein

Answer: C

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15. Normal cellular prion protein is designated as:

A. PrP??

B. PrP?

C. PrP?

D. PrP?

Answer: B

---

16. Pathogenic prion protein differs by having increased:

A. ?-helical content

B. ?-sheet structure

C. Random coil

D. Disulfide bonds

Answer: B

---

17. Prions are resistant to:
A. Heat
B. Proteases
C. UV radiation
D. Both A and B
Answer: D

Human Prion Diseases

18. Human prion diseases are also known as:
A. Amyloidoses
B. Lysosomal storage disorders
C. Transmissible spongiform encephalopathies
D. Demyelinating disorders
Answer: C

---

19. Which is NOT a prion disease?
A. Creutzfeldt–Jakob disease
B. Kuru
C. Alzheimer’s disease
D. Fatal familial insomnia
Answer: C

---

20. The hallmark pathology of prion disease is:
A. Demyelination
B. Spongiform degeneration of brain
C. Plaque formation
D. Neuronal calcification
Answer: B

Biochemistry of Aging

21. Free radical theory of aging proposes damage mainly to:
A. RNA only
B. DNA, proteins, and lipids
C. Carbohydrates only
D. Cell membrane receptors
Answer: B

---

22. Telomere shortening primarily affects:

A. Mitochondrial DNA

B. Ribosomal RNA

C. Chromosomal stability

D. Protein synthesis

Answer: C

---

23. Advanced glycation end products (AGEs) accumulate due to:

A. Lipid peroxidation

B. Non-enzymatic glycation

C. Protein phosphorylation

D. DNA methylation

Answer: B

---

24. With aging, DNA repair capacity:

A. Increases

B. Remains unchanged

C. Decreases

D. Is absent

Answer: C

---

25. Antioxidants delay aging by:

A. Increasing mutations

B. Reducing oxidative stress

C. Enhancing apoptosis

D. Inhibiting telomerase

Answer: B

Alzheimer’s Disease

26. Alzheimer’s disease is characterized by:

A. Demyelination

B. Protein misfolding

C. Glycogen accumulation

D. Lipid storage

Answer: B

---

27. Major component of amyloid plaques is:

A. Tau protein

B. Amyloid-? peptide

C. ?-synuclein

D. Prion protein

Answer: B

---

28. Neurofibrillary tangles are composed of:

A. Amyloid-?

B. ?-synuclein

C. Hyperphosphorylated tau

D. Actin

Answer: C

---

29. Amyloid-? is derived from:

A. Tau protein

B. Prion protein

C. Amyloid precursor protein

D. ?-crystallin

Answer: C

---

30. Neurotransmitter deficiency in Alzheimer's disease is mainly:

A. Dopamine

B. Serotonin

C. Acetylcholine

D. GABA

Answer: C

Integrated / Conceptual

31. Microfilaments and microtubules together form part of:

A. Nuclear matrix

B. Cytoskeleton

C. Extracellular matrix

D. Basement membrane

Answer: B

---

32. Loss of microtubule function most directly affects:

A. Cell shape only

B. Protein synthesis

C. Mitosis

D. Glycolysis

Answer: C

---

33. Which protein misfolding disorder is infectious?

A. Alzheimer's disease

B. Parkinson’s disease
C. Prion disease
D. Huntington disease
Answer: C

---

34. Cataract formation is accelerated by:
A. Reduced oxidation
B. Increased antioxidant activity
C. Oxidative stress
D. Increased DNA repair
Answer: C

---

35. Aging is associated with:
A. Increased telomerase activity
B. Reduced oxidative damage
C. Accumulation of damaged proteins
D. Enhanced DNA repair
Answer: C

---

36. Which cytoskeletal element is thickest?
A. Microfilaments
B. Intermediate filaments
C. Microtubules
D. Actin filaments
Answer: C

---

37. Alzheimer’s disease primarily affects:
A. Motor neurons
B. Sensory neurons
C. Cortical neurons
D. Spinal neurons
Answer: C

---

38. Which protein acts as chaperone in the lens?
A. ?-crystallin
B. ?-crystallin
C. ?-crystallin
D. Keratin
Answer: C

---

39. Prion diseases progress because:

A. Immune response destroys neurons

B. Protein induces misfolding of normal proteins

C. Viral replication occurs

D. DNA mutations accumulate

Answer: B

---

40. Alzheimer's disease is NOT characterized by:

A. Memory loss

B. Cognitive decline

C. Rapid spongiform change

D. Amyloid deposition

Answer: C

High-Yield Exam Traps

41. Microtubules are absent in:

A. Cilia

B. Flagella

C. Centrioles

D. RBCs

Answer: D

---

42. Protein aggregation is central to:

A. Cataract

B. Alzheimer's disease

C. Prion diseases

D. All of the above

Answer: D

---

43. Aging increases susceptibility to:

A. DNA damage

B. Protein oxidation

C. Degenerative diseases

D. All of the above

Answer: D

---

44. Tau protein normally stabilizes:

A. Microfilaments

B. Intermediate filaments

C. Microtubules

D. Actomyosin complex

Answer: C

---

45. Loss of tau function leads to:

A. Increased microtubule stability

B. Microtubule disassembly

C. Increased actin polymerization

D. Reduced amyloid formation

Answer: B

---

46. Which disease is always fatal?

A. Alzheimer’s disease

B. Cataract

C. Prion disease

D. Parkinson’s disease

Answer: C

---

47. Crystallin aggregation causes loss of:

A. Lens elasticity

B. Lens transparency

C. Retina function

D. Corneal curvature

Answer: B

---

48. Free radicals primarily damage cells by:

A. Enzyme activation

B. Oxidative stress

C. Increased ATP production

D. Gene amplification

Answer: B

---

49. Cytoskeletal drugs are useful in cancer because they:

A. Kill non-dividing cells

B. Inhibit mitosis

C. Increase apoptosis only

D. Reduce angiogenesis

Answer: B

---

50. Alzheimer’s disease belongs to which group?

A. Infectious diseases

B. Autoimmune diseases

C. Neurodegenerative diseases

D. Metabolic disorders
Answer: C

A. Clinical Problem-Based MCQs

(Single best answer)

1. A patient receiving vincristine develops mitotic arrest in tumor cells. The drug acts by disrupting:
A. Microfilaments
B. Intermediate filaments
C. Microtubules
D. Actomyosin complex
Answer: C

---

2. A 65-year-old patient presents with progressive memory loss. Brain biopsy shows extracellular plaques composed of amyloid-?. The peptide is derived from:
A. Tau protein
B. Prion protein
C. Amyloid precursor protein
D. ?-synuclein
Answer: C

---

3. A middle-aged individual develops rapidly progressive dementia with myoclonus. EEG shows periodic sharp waves. Most likely biochemical abnormality is:
A. Neurofibrillary tangles
B. ?-helix ? ?-sheet protein conversion
C. Dopamine deficiency
D. Lysosomal enzyme deficiency
Answer: B

---

4. A newborn has normal vision at birth but develops cataract later in life due to aggregation of lens proteins. The most likely biochemical cause is:
A. Increased protein synthesis
B. Oxidative modification of crystallins
C. DNA mutation
D. Reduced ATP production
Answer: B

---

5. A cultured malignant cell line grows in suspension without attachment. This property depends on alteration of:
A. Contact inhibition
B. Apoptosis
C. Anchorage dependence
D. Telomerase activity
Answer: C

---

6. A patient with Alzheimer's disease has deficiency of a neurotransmitter synthesized from choline. Which enzyme is targeted therapeutically?
A. Monoamine oxidase
B. Acetylcholinesterase
C. Dopamine ?-hydroxylase
D. Glutamate decarboxylase
Answer: B

---

7. A laboratory experiment shows disruption of cytokinesis after actin depolymerization. The affected cytoskeletal element is:
A. Microtubules
B. Intermediate filaments
C. Microfilaments
D. Neurofilaments
Answer: C

---

8. An elderly patient shows increased oxidative stress markers and shortened telomeres. This best supports which theory of aging?
A. Genetic theory
B. Free radical theory
C. Immunological theory
D. Hormonal theory
Answer: B

---

9. A patient with prion disease shows resistance of the infectious agent to protease digestion. This is due to:
A. Presence of nucleic acid
B. High ?-helical content
C. Increased ?-sheet structure
D. Lipid coating
Answer: C

---

10. Loss of tau protein function in neurons primarily causes instability of:
A. Actin filaments
B. Intermediate filaments
C. Microtubules
D. Myelin sheath

Answer: C

B. Assertion–Reason Questions

(Choose the correct option)

A. Both A and R are true and R explains A

B. Both A and R are true but R does not explain A

C. A is true but R is false

D. A is false but R is true

1.

Assertion: Microtubules are essential for mitosis.

Reason: They form the mitotic spindle required for chromosome separation.

Answer: A

2.

Assertion: Lens proteins are susceptible to aggregation.

Reason: Lens crystallins have an extremely long half-life.

Answer: A

3.

Assertion: Prion diseases do not elicit an immune response.

Reason: Prions lack nucleic acids.

Answer: B

4.

Assertion: Alzheimer’s disease is a protein misfolding disorder.

Reason: Amyloid-? and tau proteins aggregate abnormally.

Answer: A

5.

Assertion: Aging is associated with increased oxidative damage.

Reason: Antioxidant defense mechanisms decline with age.

Answer: A

6.

Assertion: Microfilaments are thicker than microtubules.

Reason: Microfilaments have a diameter of about 7 nm.

Answer: C

7.
Assertion: Prion diseases are always fatal.
Reason: Prion proteins cause progressive neuronal degeneration.
Answer: A

C. Viva Voce

Rapid-Fire Viva (One-liners)

What are microfilaments composed of?
Actin.

Diameter of microfilaments?
~7 nm.

Main protein of microtubules?
?- and ?-tubulin.

Arrangement of microtubules in cilia?
9 + 2 pattern.

Major proteins of the lens?
Crystallins.

Which crystallin acts as molecular chaperone?
?-crystallin.

Define prions.
Infectious protein particles without nucleic acid.

Normal prion protein is called?
PrP?.

Pathogenic prion form?
PrP??.

Main biochemical change in prions?
?-helix to ?-sheet conversion.

Clinical Viva

Why are prion diseases not detected by routine sterilization?
Prions are resistant to heat and proteases.

Why do cataracts increase with age?
Accumulation and oxidation of lens proteins.

Why are microtubules important targets in cancer therapy?
They are essential for mitosis.

Why is Alzheimer's disease progressive?
Continuous accumulation of misfolded proteins.

Why is acetylcholine deficient in Alzheimer's disease?
Loss of cholinergic neurons.

Examiner's One-Line Killers

- **Cytoskeleton failure = loss of order**
- **Prions prove proteins alone can be infectious**
- **Aging is oxidative damage plus repair failure**
- **Alzheimer's is memory loss written in protein aggregates**