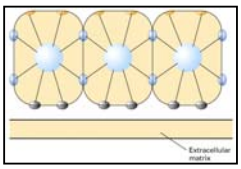
Intermediate filaments

Intermediate filaments

- Found in almost all eukaryotes (not in fungi)
- Intermediate in size between microfilaments and microtubules (10nm)
- Present only in cells that display multicellular organization

Intermediate filaments

- Strictly structural
- Most stable of all cytoskeletal structures
- Reinforce cells
- Distribute tensile forces across the cells in tissues
- Integrate cells into tissues
  - Stabilize desmosomes and hemidesmosomes

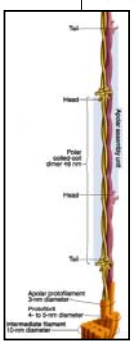


Intermediate filaments

- Heterogeneous structures (made out of many different proteins)
  - About 50 genes encoding 6 classes
- All intermediate filaments have common structure
  - Central α helical rods assembled into rope-like filaments
- Do not bind nucleotides

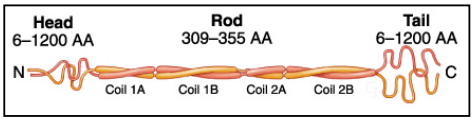
Intermediate filament structure

- Intermediate filament are polymers
- They have no polarity
- Constructed like a multistrand rope
- Structural unit is an apolar assembly made out of two antiparallel dimers



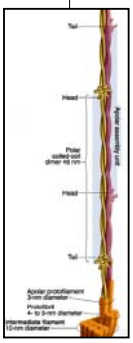
Intermediate filament dimer

- Two polypeptides form a dimer
  - They don't have to be identical
- N-terminal globular head domain
- Rod domain (coiled coil of 2 α - helices)
- C-terminal globular tail domain



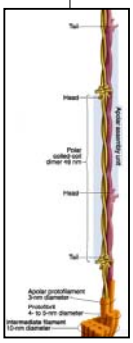
Intermediate filament structure

- Two dimers associate antiparallel to form an apolar assembly unit
- They polymerize in staggered fashion to form a protofilament



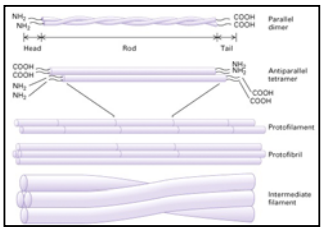
Intermediate filament structure

- Two protofilaments associate laterally to form a protofibril
- Four protofibrils form an intermediate filament



Intermediate filaments assembly

- Assembly - several intermediate structures
  - First assembly end to end
  - Later lateral interactions



Assembly and dynamics

- Spontaneously self assemble
  - Subunits added to both ends
- Very stable components but still with the fast turnover
- Phosphorylation of the head domain depolymerizes intermediate filaments
  - Exception neurofilaments

Intermediate filaments

- 6 classes based on sequence
- Classes greatly divergent in sequence
- Lamins expressed in nucleus of all cells
- Other only in specific tissues
- Major degenerative diseases of the skin, muscle and neurons are caused by disruption of the intermediate filament cytoskeleton

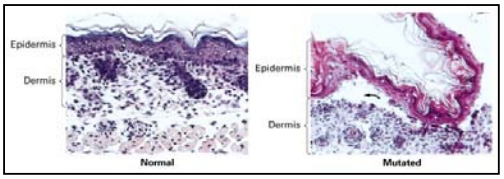
Acidic and basic keratins (type I and II)

- Expressed in epithelial cells
- Heterodimers that assemble into keratin filaments
- “Hard” and cytokeratins
- Loss leads to blistering, excess to hyperkeratosis

Epidermis

- Outer skin layer
- Keratin filaments cross-linked by fillagrin (IFAP)
- As the cells die filaments remain intact forming dead external layer of the skin

Disruption of keratin networks causes blistering

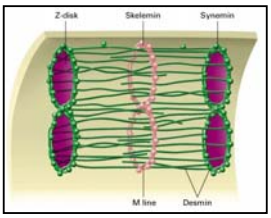


Type III

- Homo- and hetero- polymers
- Vimentin
  - Expressed in leukocytes, endothelial cells
  - Supports cellular membrane
- Glial fibrillary acidic protein – GFAP – in glial cells
- Peripherin in peripheral neurons

Type III

- Desmin
  - Stabilizes sarcomeres in muscle
  - Bound to Z disks

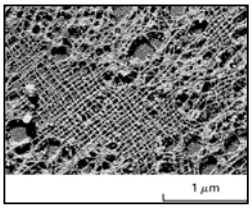


Type IV - neurofilaments

- Fill up axons
- Each heteropolymer composed of 3 polypeptides NF-L, NF-M, NF-H
- Determine axon diameter

Type V - lamins

- Found only in nuclei in both plant and animal cells
- Support nuclear membrane



Type VI

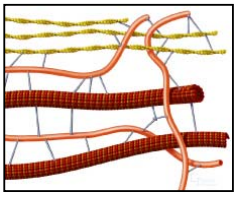
- Nestin expressed in embryonic neurons

Intermediate filament-associated proteins (IFAPs)

- Organize intermediate filaments in networks and bundles
- Cross-link intermediate filaments to plasma membrane, nuclear membranes, microtubules, microfilaments

Intermediate filament-associated proteins (IFAPs)

- Plectin
  - Plays a role in integrating the cytoskeleton with microfilaments and microtubules



Intermediate filament-associated proteins (IFAPs)

- Filaggrin
  - Cross links filaments in epidermal cells
  - Aggregates keratins
  - Structural core of dead skin

Diseases of the intermediate filaments

- Major degenerative diseases of the skin, muscle and neurons are caused by disruption of the intermediate filament cytoskeleton