02.12.10
Lecture 13 - Intermediate filaments
Intermediate filaments

- Present in nearly all animals, but absent from plants and fungi
- Rope-like network of filaments in the cell
- Principle function is maintenance of cell structure - provide tensile strength to the cell
Intermediate filaments share a common structure
Intermediate filaments differ from actin & microtubules:

- I.F.s do not have a defined polarity (i.e. no plus or minus ends)
- I.F.s have no associated motor proteins
- I.F.s do not bind to nucleotides (ATP or GTP)
- I.F.s are very stable compared to actin or microtubules
There are 4 classes of intermediate filament proteins:

- **Keratins**: in epithelia
- **Vimentin and vimentin-related proteins**: in connective tissue, muscle cells, and neuroglial cells
- **Neurofilaments**: in nerve cells
- **Nuclear lamins**: in all animal cells
Tissue-specific expression of I.F. proteins is useful for diagnostics

- Cancer cells - lose the characteristic shape of the parent tissue
- I.F. gene expression is often unaffected
- Identification of I.F. proteins in tumor biopsies using antibodies can pinpoint origin of tumors (I.e. neurofilaments in metastatic cells from brain cancers)
- Physicians tailor treatment to particular types of cancer
Keratin - the epithelial I.F.
Stratified squamous epithelium

- Stem cells in the interior
- Dead cells at outermost surface
- Keratin remains - hard, waterproof, resists abrasions
- Makes up hair, nails, skin, & feathers
Keratins form a strong network indirectly linked to neighboring cells

(A) 10 μm

(B) 5 μm

intermediate filaments
desmosome connecting two cells
Desmosomes mediate cell-cell adhesion between epithelial cells

Desmosomes are formed in specialized areas of cells - the cytoplasmic side contains tonofibrils that are anchored in a plaque of proteins.

Cadherin molecules provide the cell-cell interactions.
Hemidesmosomes mediate cell-matrix adhesion between epithelial cells and basal lamina.

Hemidesmosomes connect epithelial cells to the basal lamina. The integrin $\alpha_6\beta_4$ binds to proteins in the plaques and to laminin in the extracellular matrix.
Keratins allow sheets of cells to resist mechanical stresses

- Stretching a sheet of cells with intermediate filaments, cells remain intact and together.
- Stretching a sheet of cells without intermediate filaments, cells rupture.
Disruption of keratin networks causes blistering
Vimentin/desmin - the I.Fs present in connective tissue and muscles
Vimentin is required for trans-epithelial migration

• Endothelial transmigration - white blood cells leave the bloodstream to combat infection
• Process is impaired in vimentin mutant mice
Desmin filaments maintain muscle structural integrity

- Desmin filaments are tethered to the Z disk and envelope the sarcomere
- Don’t participate in contraction, but maintain structural integrity
- Mutant mice have misaligned muscle fibers
- Mutations in human desmin causes muscle disorders
Neurofilaments - I.F.s present in neurons
Neurofilaments are important for nervous system function

- Unlike other I.F.s, they have side arms that project from the core filament
- Fill and pack the cytoplasm of neurons
- Neurons in KO mice make axons with smaller diameters
- Charcot-Marie-Tooth disease: neuropathy where PNS degenerates
Neurofilaments are important for nervous system function
Nuclear lamins are I.F.s present in the nuclei of all cells

- Nuclear lamins form a basket-like structure on inner side of nuclear membrane
- Protects structure of nucleus
Nuclear lamins disassemble when cells enter mitosis
I.F.s are extensively cross-linked to actin and microtubules

- Microtubule (red), vimentin (orange), plectin cross-linker (blue)