CYTOSKELETON II: MICROFILAMENTS AND INTERMEDIATE FILAMENTS

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BRP, P. 659-, BKH 5th: p 754-766, 6th: 437-450, 7th:

MICROFILAMENTS 7nm (smallest), best known as **contractile filaments**

functions: structure: **cell cortex** (inside plasma membrane) & **microvilli core**
function: **cytoplasmic streaming**, **cleavage furrow**, also cause **locomotion**, **amoeboid movement**, **muscle contraction**

STRUCTURE: G actin, single-most abundant protein in cells (5% total) polymerizes into double stranded polymer of F **actin**, first seen in muscle, 7 nm diameter

ASSEMBLY: ATP bound to G actin monomers, cleaved to ADP on assembly.
Polar, added at one end (+), removed at other (-) like **treadmill** (p 438)
demonstrated by radioactive labeling. **Move toward nucleus.**

GENETICS: mostly **same for all species** (90% same AA for yeast & chicken)
(highly conserved sequence)

ACTIN-BINDING PROTEINS: many & varied, three classes of functions:

lengthening:	cap the + end, slow polymerization
depolymerizing:	prevents polymerization until needed (acrosomal reaction)
cross linking	stabilize structure as in membrane, cell shape

AFFECT ON CELL SHAPE:

cell cortex 3D mesh of actin and associated proteins supports cell membrane (stress fibers), movement

microvilli: increase cell surface area 20x, core of microfilaments, "+" ends at tip, extend to mesh at "-" end (terminal web), forms stable foundation for microvilli

MUSCLE CONTRACTION: p. 470 for actin, myosin, troponin, Ca^{++}, sarcomere, sarcoplasmic reticulum, nerve

INTERMEDIATE FILAMENTS: (8-12 nm diameter) First discovered in muscle cells. (p. 446)

Most stable, least soluble of cytoskeletal elements, only found in multicellular organisms
filamentous, remain after detergent removal of microtubules & microfilaments **globular subunits**.

Fibrous, **principal structural determinant**. Tension bearing, maintain nucleus position

TISSUE SPECIFICITY: composition varies tissue to tissue, can be used to identify tissue origin
Can be used to diagnose classes of secondary CA tumors by **immunofluorescence**

At least six classes of intermediate filaments based on AA sequence: (p. 447)

I	acidic cytokeratin	in epithelial tissues, forms terminal "web", form tonofilaments p. 760
II	basic cytokeratins	slightly heavier than acidic
III	vimentin	fibroblasts (connective tissues), lens, maintains cell shape
III	desmin	in muscles, supports contractile machinery
III	glial fibrillary acidic protein	maintains shep in astrocytes, glial cells
IV	neurofillament proteins	in nerves, axon strength, size
V	nuclear lamina	common to most animal cells, inside nuclear membrane scaffold, disassemble during mitosis
VI	nestin	neuronal stem cells. Unknown function

STRUCTURE & FUNCTION: products of related genes, classified by AA sequence (p. 448)
all are fibrous, have **conserved central domain flanked by variable terminal regions**
2 polypeptides = coil lengthwise to form a dimer with globular terminal domains
2 dimers wide, many long = protofilament (total of four, slightly displaced).
8 protofilaments = bound together to form intermediate filament

DISEASES: amyotrophic lateral sclerosis (ALS) and certain cardiomyopathies may be due to IF defect.