CYTOSKELETON II: MICROFILAMENTS AND INTERMEDIATE FILAMENTS

12/4/91, rvsd 11/29/93, 11/30/94, 11/29/95, 12/4/96, 12/6/02, 5 Dec 03, 1 Dec 04, 19Nov07, 26Nov08, 30Nov09, 29N ov10
BRP, P. 659-, BKH 5th: p 754-766, 6th: 437-450, 7th: 437-476

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

functions: structural: **cell cortex** (inside plasma membrane) & **microvilli core**
functional: **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: move toward nucleus, one end add (+), removed at other (-): **treadmill** (p 438)
demonstrated by radioactive labeling.

GENETICS: mostly **same for all species** (90% same AA for yeast & chicken)
(I.e., 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

EFFECT 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: for actin, myosin, troponin, Ca^{++}, sarcomere, sarcoplasmic reticulum, nerve (p. 470) See videos :

a) nerve stimulation of contraction: http://www.youtube.com/watch?v=70DyJwwFnkU&feature=player_embedded
b) interaction of actin and myosin: http://www.youtube.com/watch?v=gJ309LfHQ3M
c) Nerve stimulation: http://www.youtube.com/watch?v=hzXVe4RS8-A

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

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

I	acidic cytokeratin	epithelial tissue tonofilament: forms terminal "web"
II	basic cytokeratin	epithelial tissue tonofilament, slightly heavier than acidic
III	vimentin	fibroblasts (connective tissues), lens, maintains cell shape
	desmin	in muscles, supports contractile machinery
	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, scaffold inside nuclear membrane, disassembles during mitosis
VI	nestin	neuronal stem cells. Unknown function

Can be used to diagnose classes of secondary CA tumors by **immunofluorescence**

STRUCTURE & FUNCTION: products of related genes, classified by AA sequence (p. 448)
have **highly 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.