Cytoskeleton

Bio-311
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Outline

• What is the cytoskeleton
• Self assembly and dynamic structure of the cytoskeleton
• Regulation of the cytoskeleton
• Motors and cytoskeleton
References

Alberts et al. Mol. Biol. Of the Cell
Boal D. Mechanics of the Cell
Structural Elements
Cellular “beams”? 

Immunostained actin
Dynamic Structure

Neuronal axon growth cone dynamics

Centrosomal microtubule dynamics
What is the Cytoskeleton

• Actin filaments (microfilaments)
• Microtubules
• Intermediate filaments

Janmey et al. (1991) JCB
f-actin (filamentous)

g-actin (globular)

α, β, γ isoforms

Monomer

375 a.a.

42 kDa
Intermediate Filament

Monomer
466 a.a. (vimentin)
57 kDa (usu. 40-70 kDa)

Keratin, Vimentin, Lamin, GFAP
Microtubule

8 nm \( \alpha \beta \) Tubulin dimer

Monomer: \( \alpha \) and \( \beta \) tubulin

451 a.a.
50 kDa
Other filaments

• Intracellular
  – Spectrin: RBCs
  – Fimbrin: microvilli, filopodia
  – Cellulose: plant cells

• Extracellular
  – Collagen
  – Fibronectin
Role in Cell Functions

- Cell migration - actin
- Sperm motility - microtubule
- Spindle assembly - microtubule
- Nuclear envelope breakdown - lamin
Protofilament structure and Dynamics

Bonds broken

Single protofilament  Multiple protofilaments

1

1

1

4
Critical concentration of polymerization $C_c = k_{off}/k_{on}$
Nucleation of Actin

A

Barbed Ends

Pointed ends

B

polymerization

Filament length (μm)

Time (sec)

C

De-polymerization

Filament length (μm)

Time (sec)

Fujiwara I et al. PNAS 2007;104:8827-8832
Free Nucleation of Microtubules

Oligomers
\[\text{Length} = 10, 18, 26 \text{ and } 34 \text{ nm}\]

Mozziconacci et al. (2008)
Polymerization 1

- **Plus** and **minus** ends: Conformational change-faster polymerization at one end
- NTP or NDP hydrolysis
  \[ \text{Growth}=0, \ C_c = k_{off}^D / k_{on}^T \]
- ATP/GTP caps
- Treadmilling
Polymerization 2

- **Treadmilling:**
  \( C_c(\text{minus}) > C_c(\text{plus}) \)

- **Dynamic instability**
  GTP-cap stable
Dynamics

Dynamic instability of microtubules

\[ <L> = \frac{v_g \cdot v_s}{v_s \cdot f_{cat} - v_g \cdot f_{res}} \]

Centrosome nucleated microtubules in cell free Xenopus egg extract

Verde et al. (1991)
Two State Polymer (TSP) vs. Single State Polymer (SSP)

\[ r_{on}, r_{off} \]

\[ v_g, v_s, f_c, f_r \]

\[ \delta = 8 \text{ nm} \]

\[ r_{on} = r_{off} = (v_g + v_s)/2\delta \approx 1890 \text{ min}^{-1} \]
Search and Capture

\[ 1 \, \mu m \]
Structure of polymer

Actin turn: 37 nm
4.7 subunits per turn
Structure of polymer

Avg. 13 protofilaments. But can range 9-16
## Role of drugs

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<th>Drug</th>
<th>Effect</th>
<th>Source</th>
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<tr>
<td>Actin</td>
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<tr>
<td>Latrunculin</td>
<td>Actin monomer stabilization</td>
<td>Latrunculia</td>
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<td>Phalloidin</td>
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<td>Cytochalasin</td>
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<td>Microtubule</td>
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<td>Taxol</td>
<td>Microtubule filament binding</td>
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<td>Colchicine, colcemid</td>
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<td>Autumn crocus</td>
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<td>Nocodazole</td>
<td>Tubulin sub-unit binding</td>
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