Manipulation of host cell biology
By bacterial pathogens:
with particular interest on intracellular vesicular trafficking

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April 26, 2005

A variety of bacterial pathogens

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Pathogenic bacteria have virulence genes
at different locations

Extracellular bacteria utilize Type III secretion for colonization

Enteropathogenic E. coli use Type III secretion to induce pedestal formation

Intracellular bacteria utilize Type III secretion for cell invasion

Salmonella use Type III secretion to induce trigger mechanism of phagocytosis

Yersinia adhesins bind to cell integrins for zipper mechanism of phagocytosis
Intracellular bacteria enter host cell by phagocytosis

Listeria escape from phagocytic vacuole into cytosol

Other intracellular bacteria survive in the vacuole

Listeria in the cytosol polymerize actin for spreading

Mycobacterium marinum escape into cytosol and polymerize actin
Mycobacterium marinum spread from cell to cell via actin-based motility.

Pathogens intercept different cellular components for the same function.

Mycobacteria utilize mechanism similar to Shigella.

Intracellular vesicular trafficking network.

Intracellular vesicular fusion requires SNAREs.

v-SNAREs pair with particular t-SNAREs for fusion.

Syntaxins are t-SNAREs that bind to other t-SNARE and v-SNARE.

Rab GTPases guide vesicular membrane transport.

Rabs work together with Rab effectors to regulate the initial docking and tethering of the vesicle to the target membrane.

<table>
<thead>
<tr>
<th>Proteins</th>
<th>Organelle</th>
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<tbody>
<tr>
<td>Rab1</td>
<td>ER and Golgi complex</td>
</tr>
<tr>
<td>Rab2</td>
<td>cis-Golgi network</td>
</tr>
<tr>
<td>Rab3A</td>
<td>synaptic vesicles, secretory granules</td>
</tr>
<tr>
<td>Rab4</td>
<td>early endosomes</td>
</tr>
<tr>
<td>Rab5A</td>
<td>plasma membrane, clathrin-coated vesicles</td>
</tr>
<tr>
<td>Rab5C</td>
<td>early endosomes</td>
</tr>
<tr>
<td>Rab6</td>
<td>medial and trans-Golgi cisternae</td>
</tr>
<tr>
<td>Rab7</td>
<td>late endosomes</td>
</tr>
<tr>
<td>Rab8</td>
<td>secretory vesicles (basolateral)</td>
</tr>
<tr>
<td>Rab9</td>
<td>late endosomes, trans-Golgi network</td>
</tr>
</tbody>
</table>
**Rab GTPases cycling and Rab effector tethering**

**Mycobacteria phagosome maturation is arrested at steps between Rab5 and Rab7**

**Mycobacteria phagosome retains Rab5 but excludes EEA1**

**Recruitment of EEA1 on phagosome of latex beads is dependent on PI3-kinase**

**Mycobacteria ManLAM or inhibition of PI-3K activity abrogates phagosomal acidification**

**Mycobacteria ManLAM inhibits delivery of syntaxin6 and lysosome hydrolase to the latex bead phagosome**
Mycobacteria inhibition of phagosome maturation

Intracellular Ca++ signaling and phago-lysosomal fusion

Ca++ signaling enhances phagosome-lysosome fusion

Ca++/Calmodulin complex regulates signaling molecules

Activation of Ca++/Calmodulin kinase II

Phagosomes containing live M. tuberculosis exhibit decreased levels of CaM compared with phagosomes of killed mycobacteria
Phosphorylation of CaMKII on *M. tuberculosis* phagosomes is dependent on cytosolic Ca\(^{2+}\) and CaM.

Inhibition of CaMKII blocks the Ca\(^{2+}\)-dependent maturation of *M. tuberculosis* phagosomes to phagolysosomes.

Mycobacteria inhibition of phagosome maturation.

PI3-kinase activity and phosphorylation of inositols.

Recruitment of PH-domain molecules to the membrane by PIP3.

Vesicular transport from ER to Golgi.
Vesicular transport from ER to Golgi

Transport of a phagosome-containing Legionella to the ER