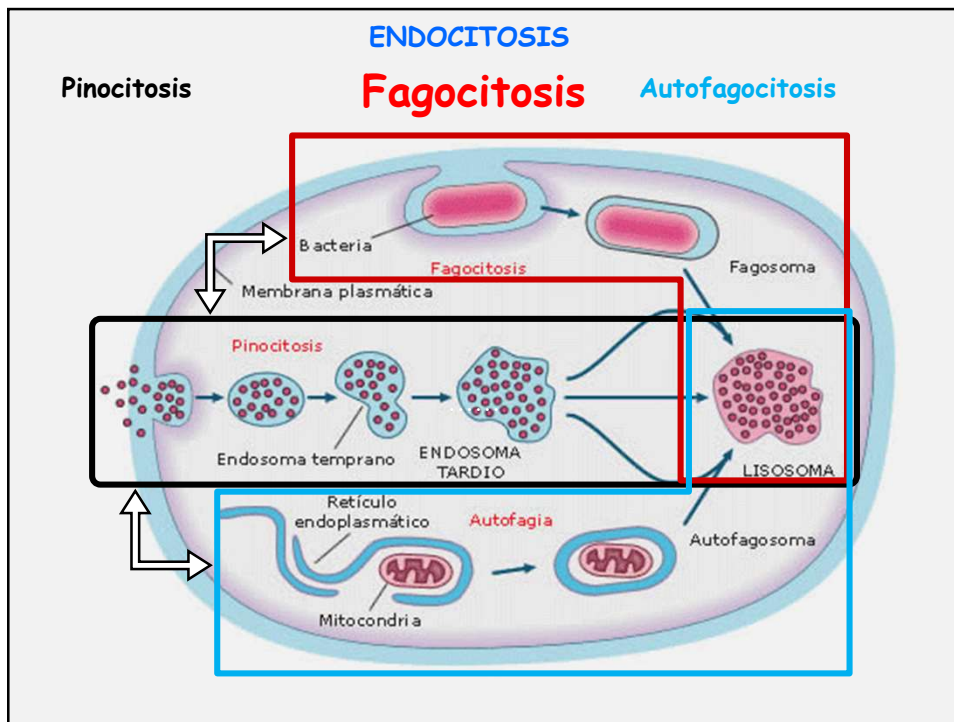


1

Mecanismos de defensa de la célula hospedadora

- Fagocitosis: lisosomas
- Estallido respiratorio (NADPH oxidasa)
- Defensinas
- Presentación de antígenos

2



3

ENDOCITOSIS

Pinocitosis (endocitosis)

- fase fluida
- mediada por receptores (absortiva)

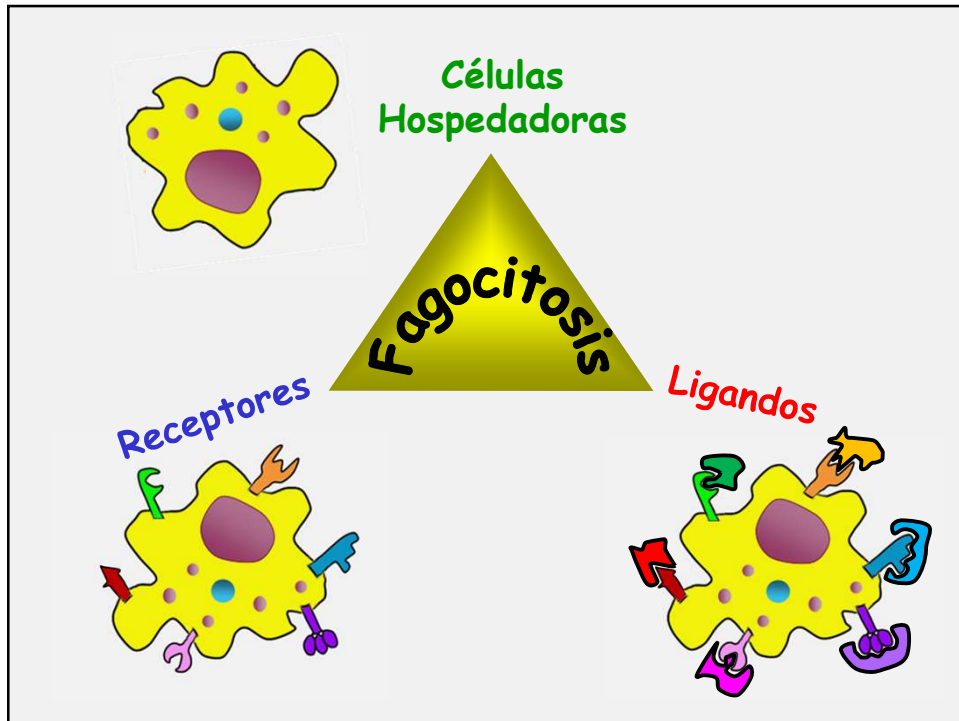
➤ tráfico intracelular: compartimientos endosomales

Fagocitosis

- heterofagocitosis (fagocitosis)
- autofagocitosis (autofagia)

➤ tráfico intracelular: compartimientos fagosomales

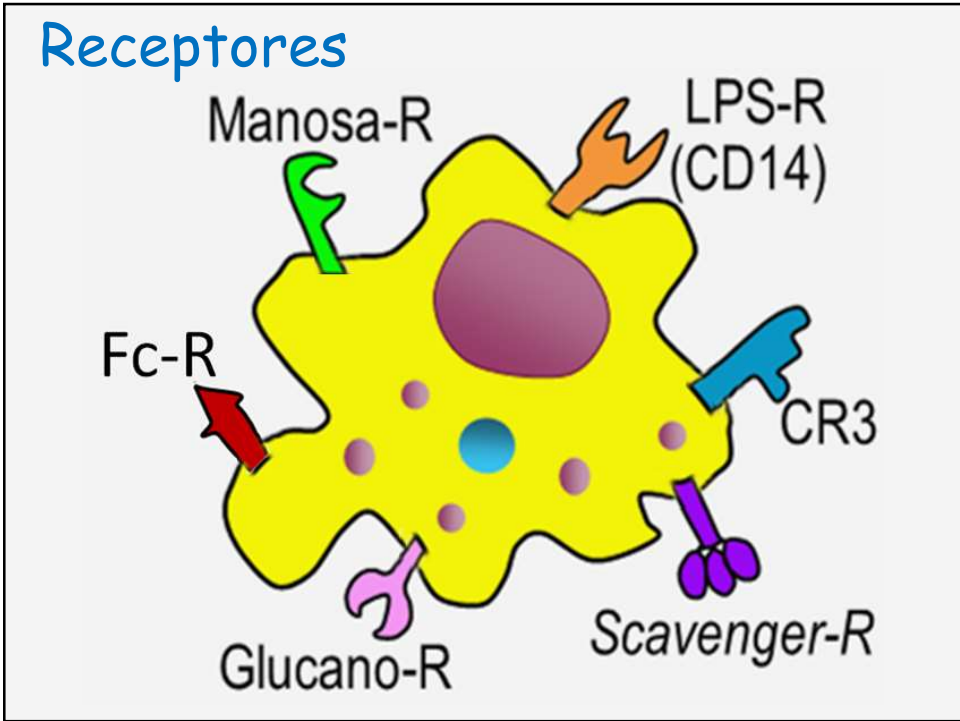
4



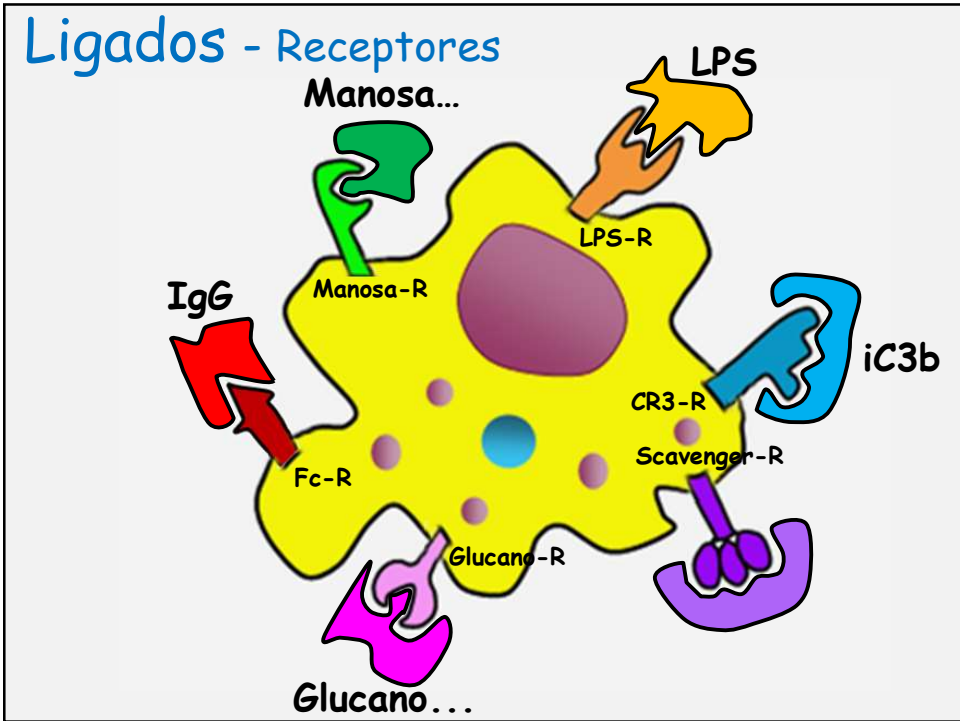
5



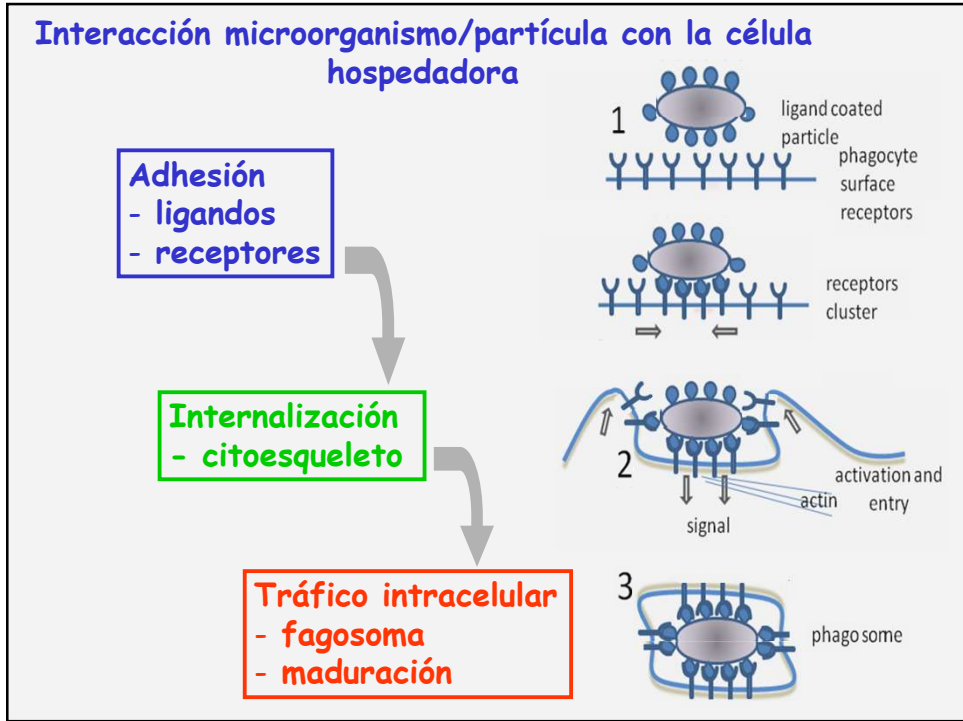
6



7



8

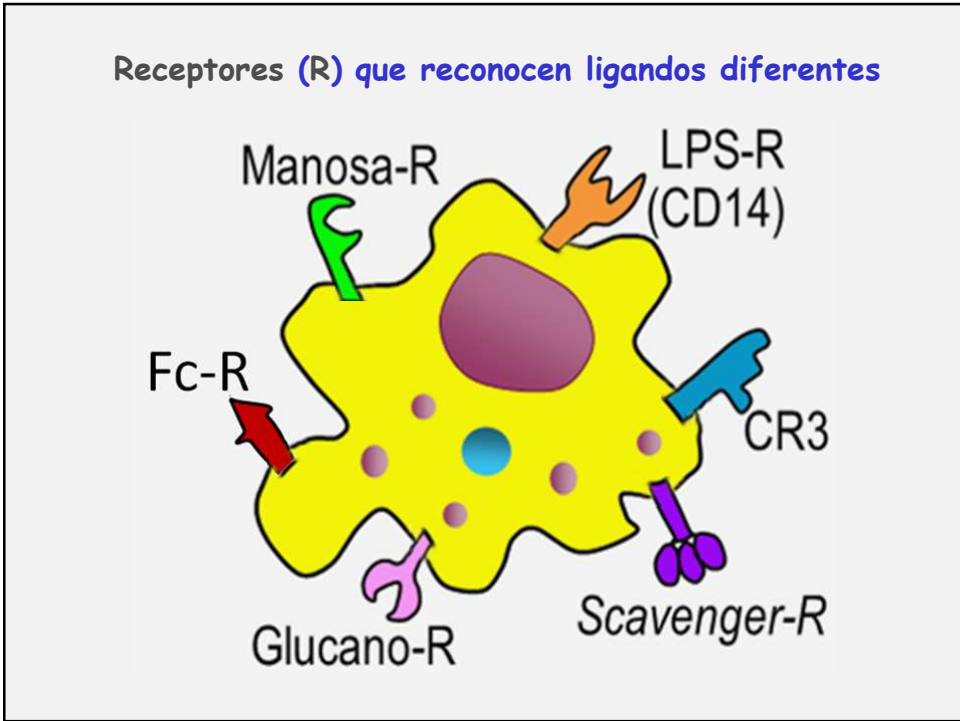


9

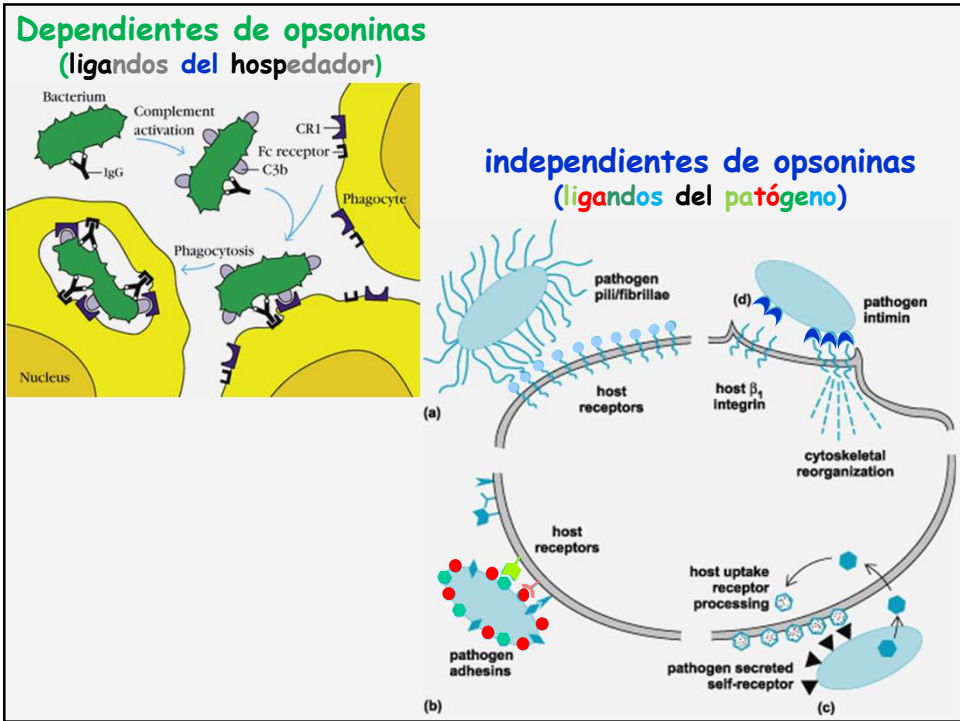
Receptores involucrados en fagocitosis

Receptor		Superfamilia de genes	Ligando
Dependientes de opsoninas <div style="border: 1px solid green; padding: 2px; width: fit-content;"> Ligandos del hospedador (Opsoninas) </div>	<ul style="list-style-type: none"> - FcγRI - FcγRIIA/C - FcγRIII 	<ul style="list-style-type: none"> - Inmunoglobulina - Inmunoglobulina - Inmunoglobulina 	<ul style="list-style-type: none"> - IgG monomérica - IgG inmunocomplejos - IgG inmunocomplejos
Independientes de opsoninas	<ul style="list-style-type: none"> - CR3 - α₅β₁ - α₅β₃ 	<ul style="list-style-type: none"> - Integrina - Integrina - Integrina 	<ul style="list-style-type: none"> - fragmento del complemento iC3b - fibronectina - fibronectina, vitronectina, células apoptóticas
<div style="border: 1px solid blue; padding: 2px; width: fit-content;"> Ligandos del patógeno </div>	<ul style="list-style-type: none"> - a Manosa - a β-glucano - "Scavenger" de Mφ - CD14^c 	<ul style="list-style-type: none"> - lectina 	<ul style="list-style-type: none"> - residuos terminales de manosa y fucosa - β-glucano - complejos polianiónicos (LPS y ácido lipoteicoico en la superficie de bacterias), células apoptóticas, lipoproteínas, proteoglicanos. - células apoptóticas

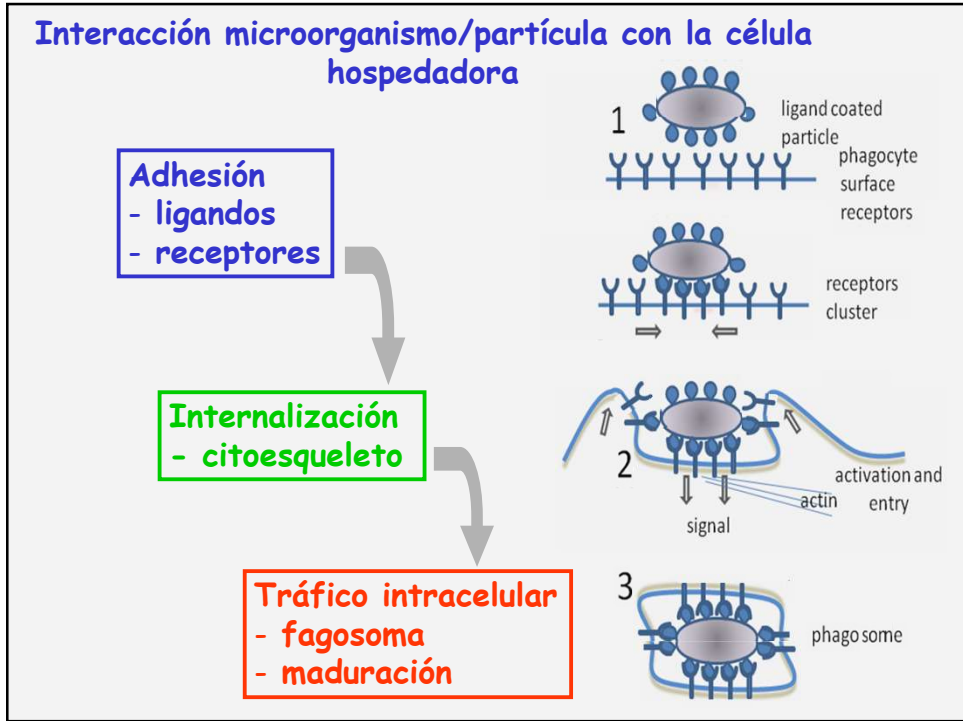
10



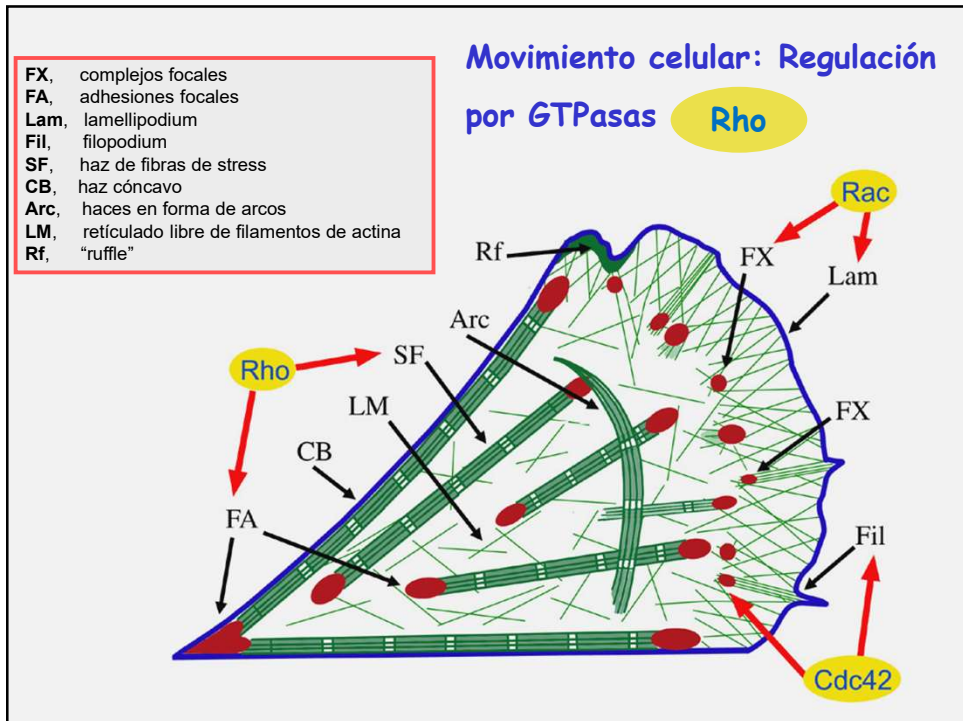
11



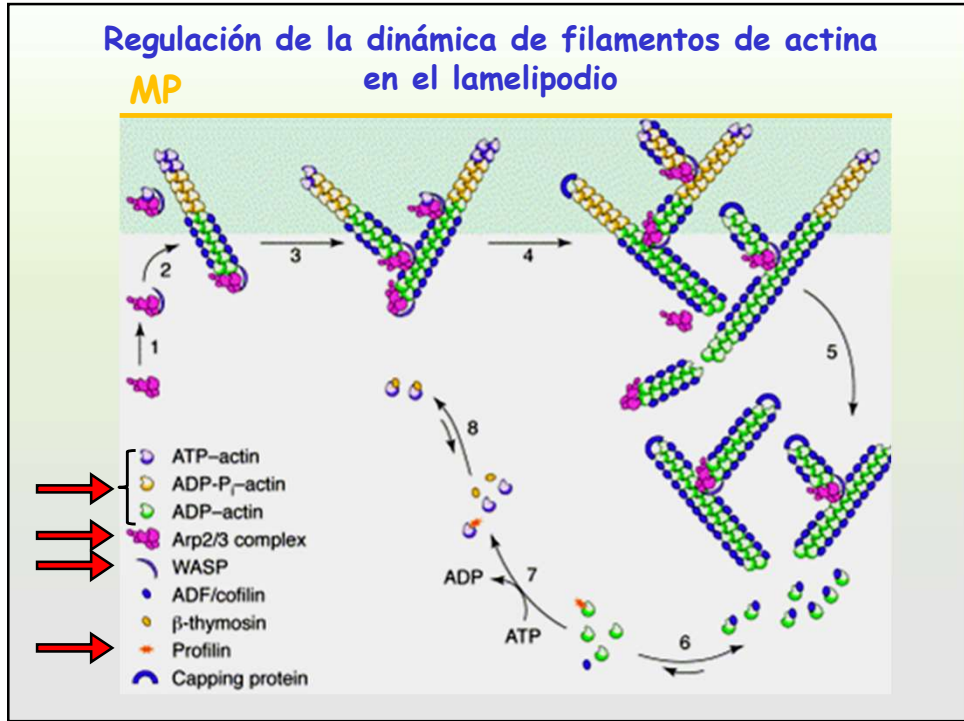
12



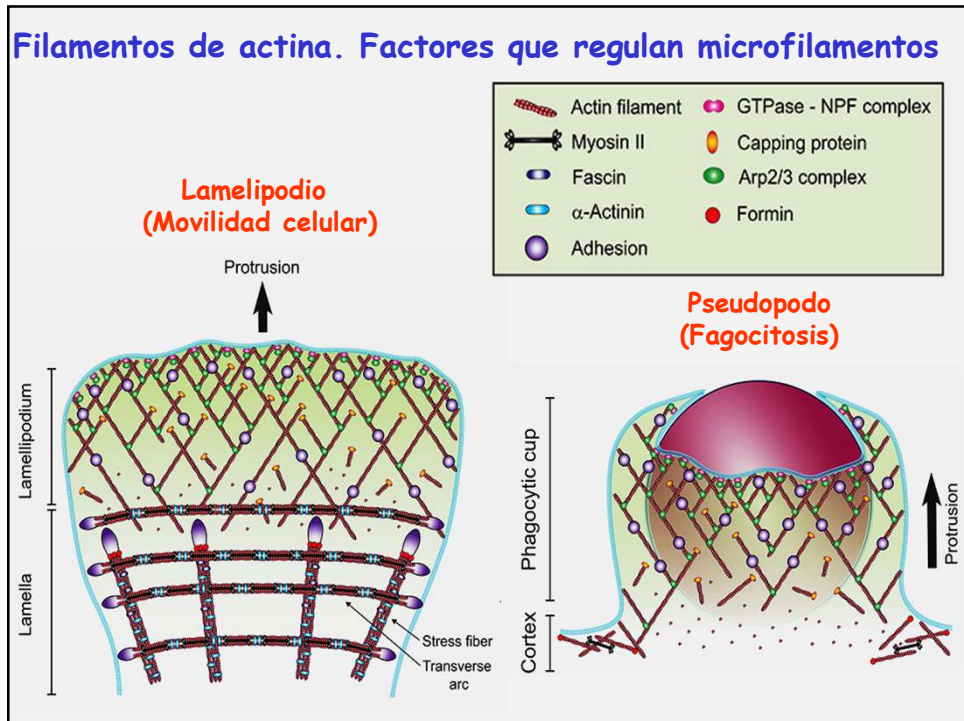
13



14

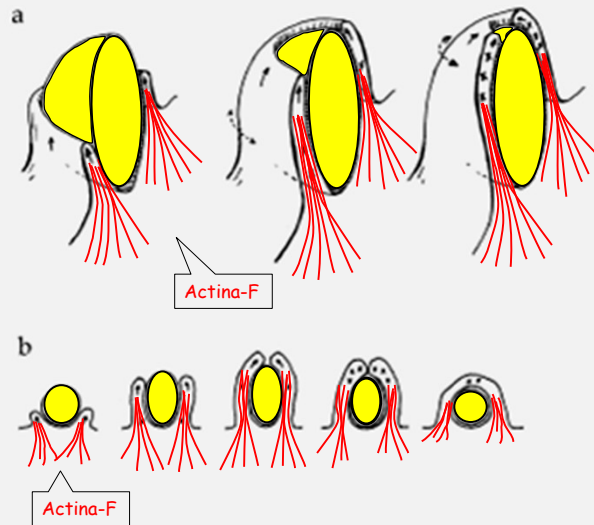


15



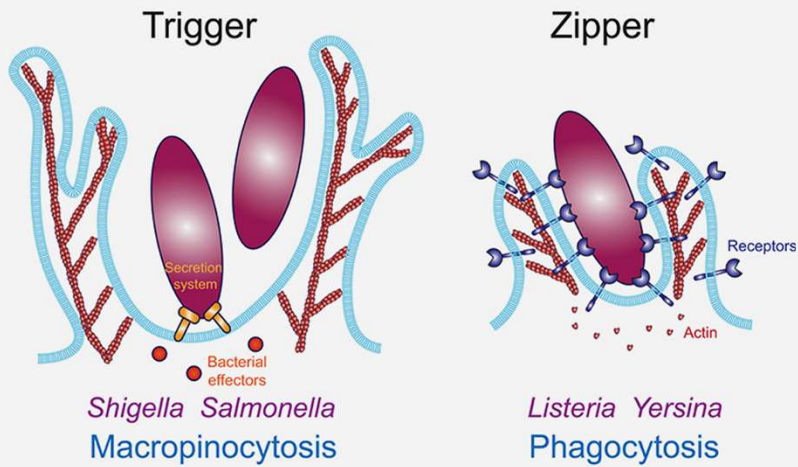
16

Extensión del pseudópodo y cierre del fagosoma durante el proceso de fagocitosis

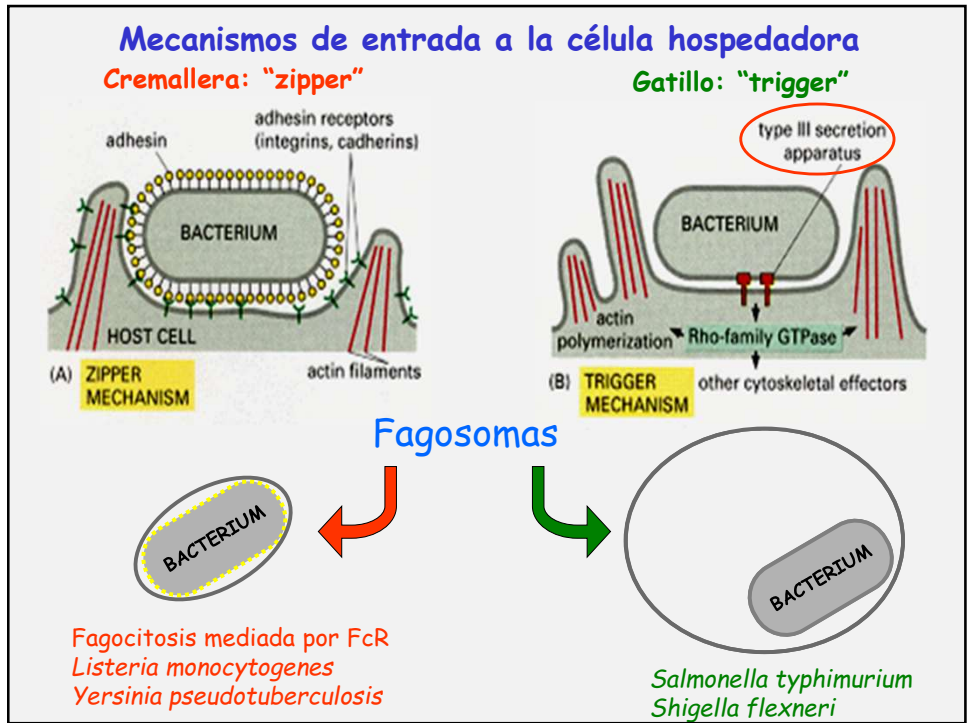


17

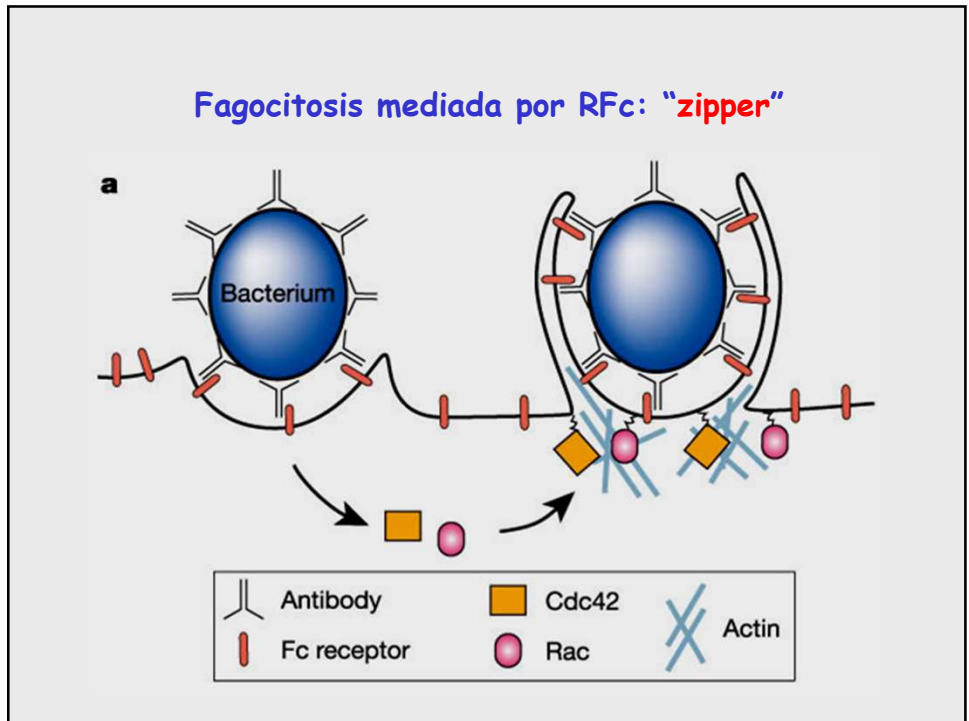
Mecanismos de entrada a la célula hospedadora



18

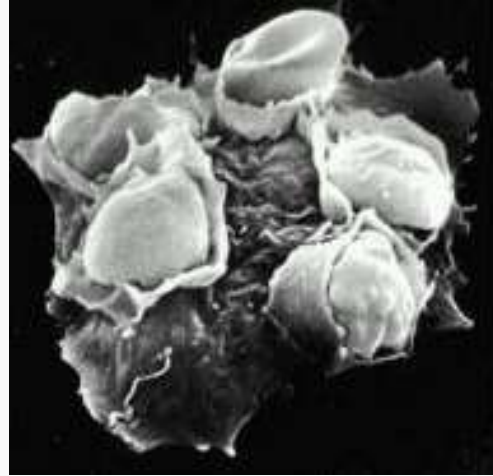
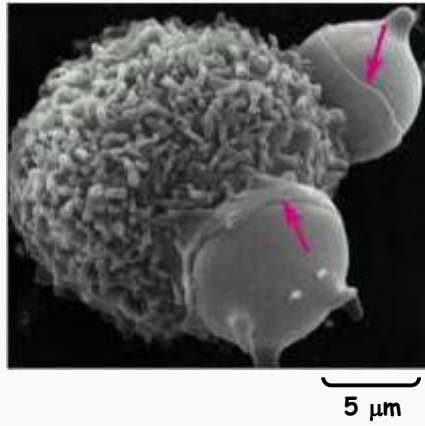


19



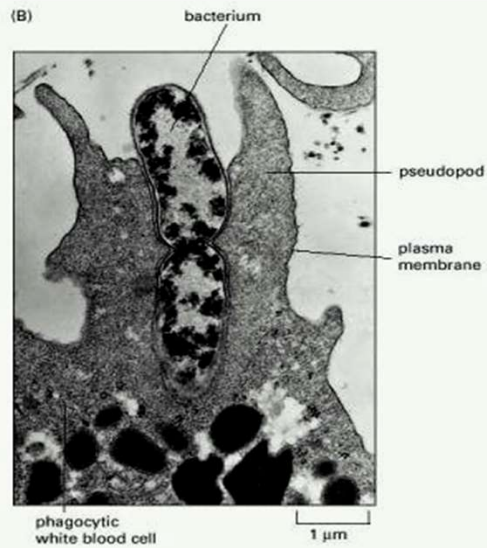
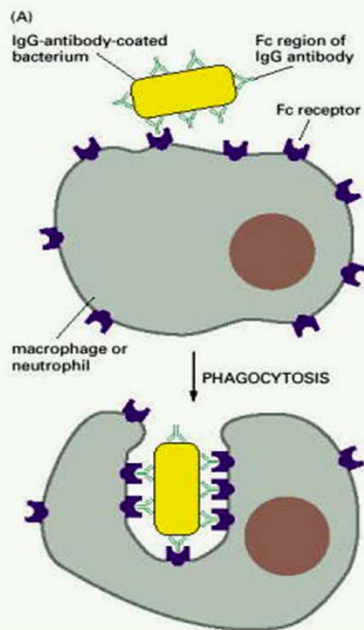
20

Fagocitosis de GR opsonizados con IgG (opsonina)

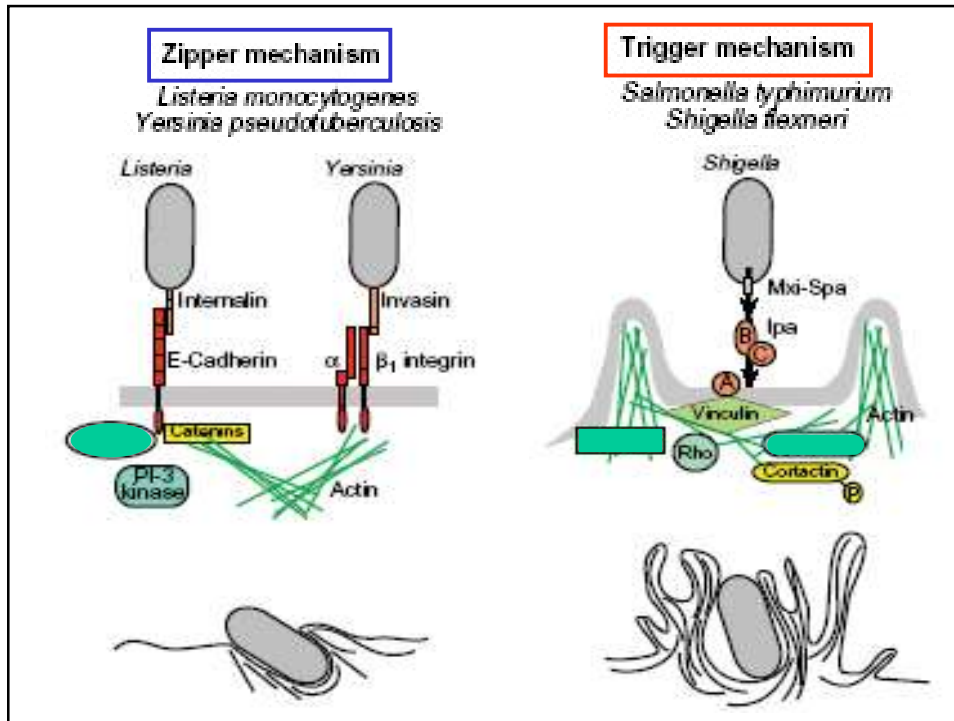


21

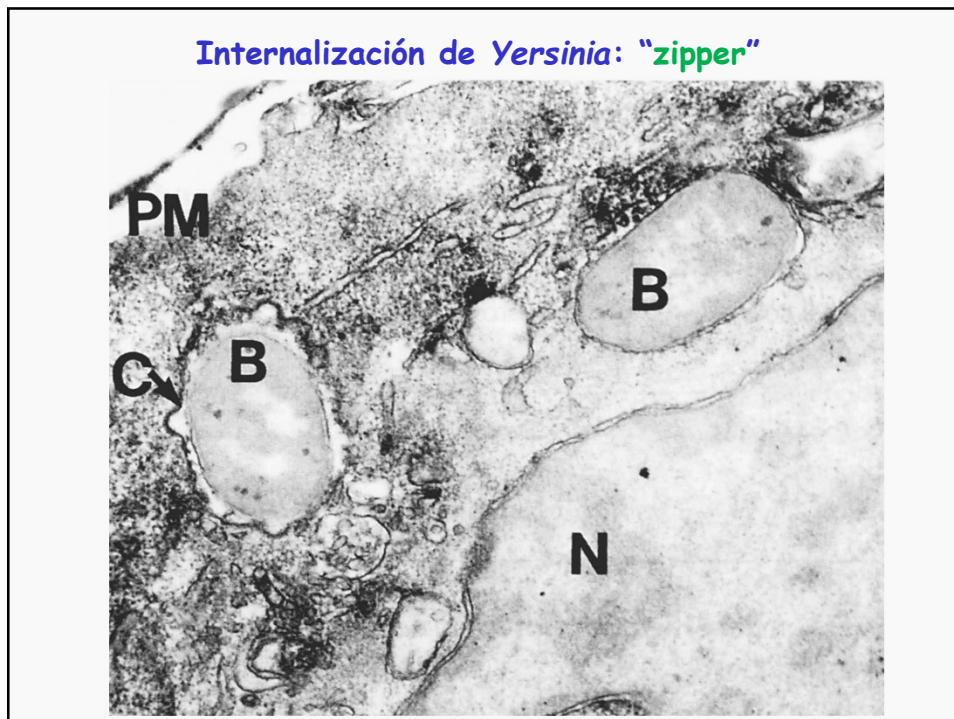
Fagocitosis de bacterias opsonizadas con IgG



22

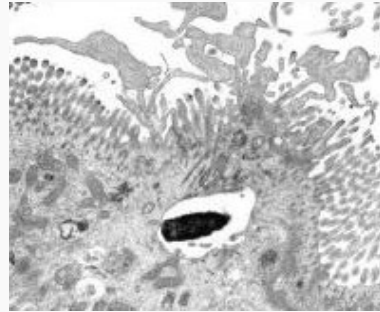
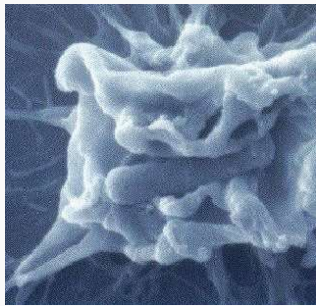
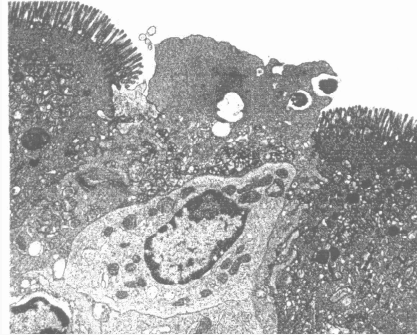
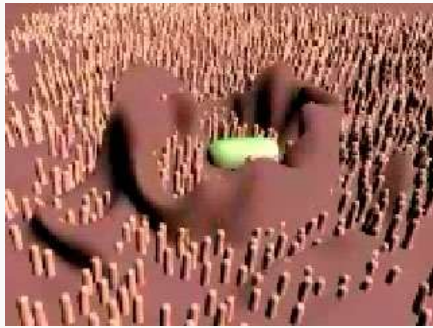


23



24

Internalización de *Salmonella*: "trigger"



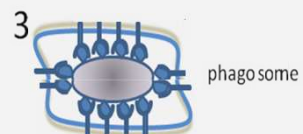
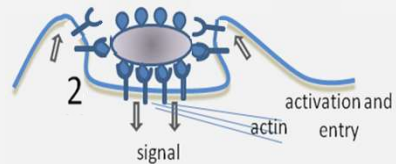
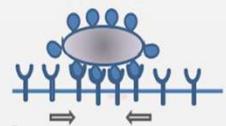
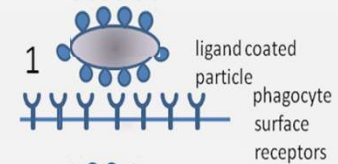
25

Interacción microorganismo/partícula con la célula hospedadora

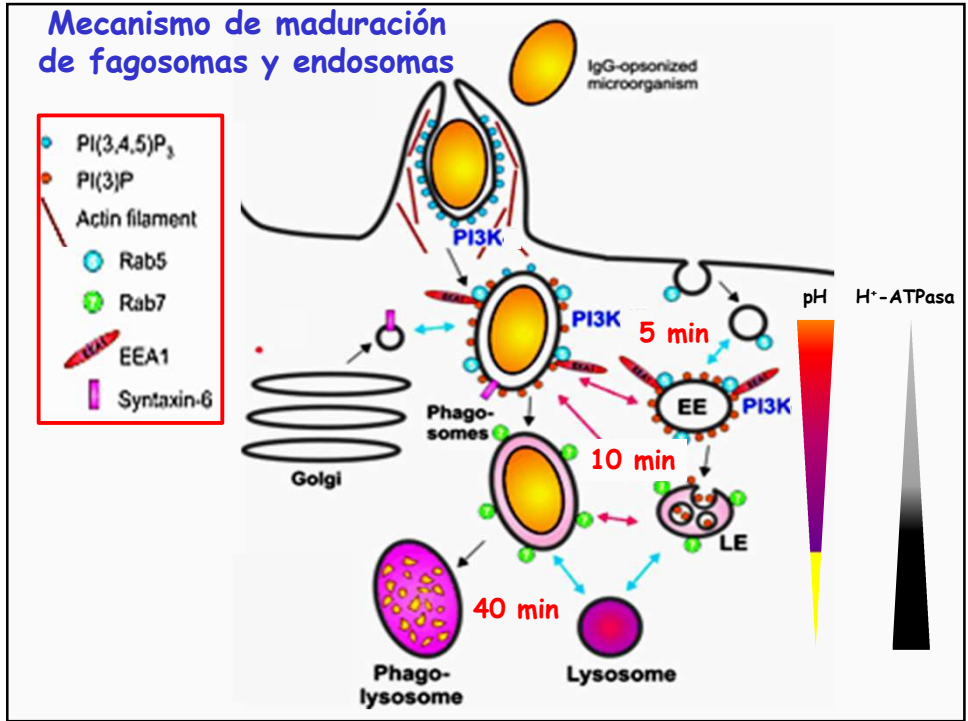
Adhesión
- ligandos
- receptores

Internalización
- citoesqueleto

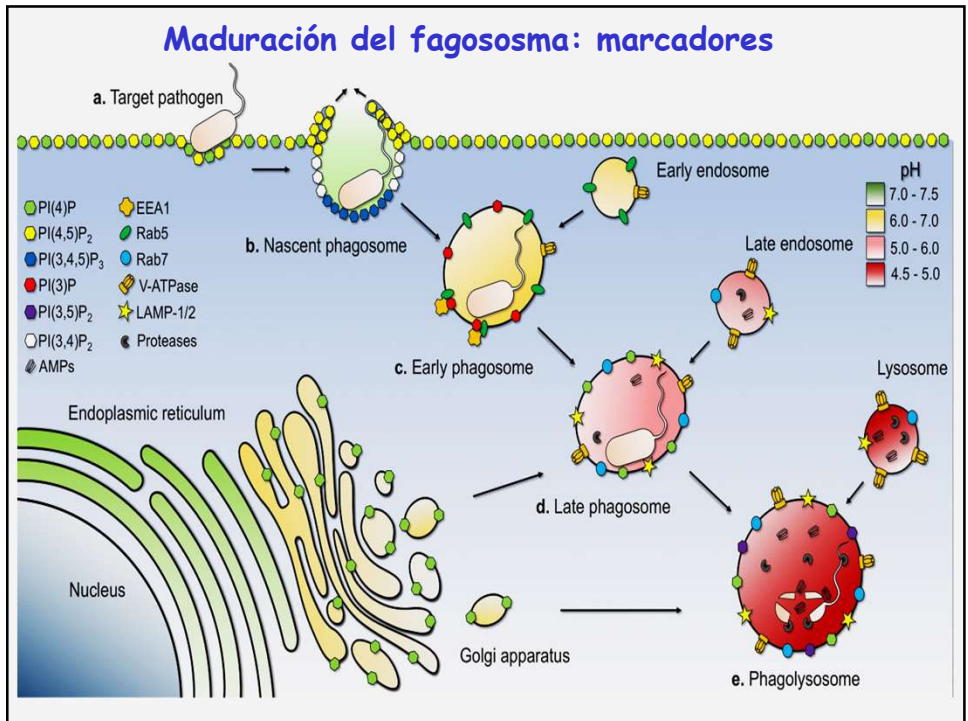
Tráfico intracelular
- fagosoma
- maduración



26

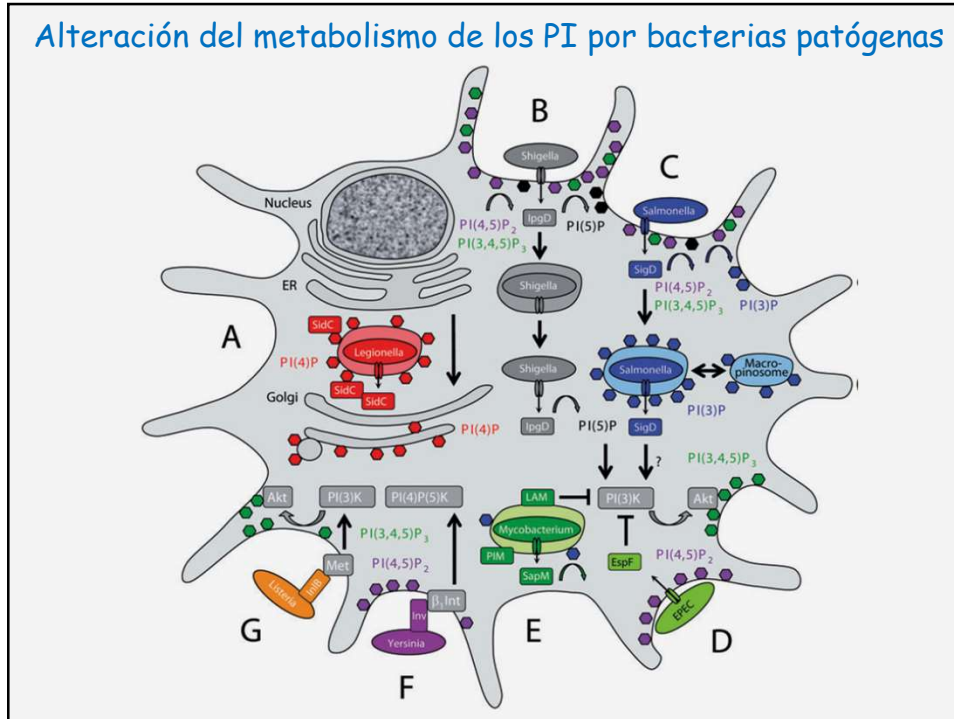


27



28

Alteración del metabolismo de los PI por bacterias patógenas



29

Fig. 1. Subversion of host cell phosphoinositide metabolism by pathogenic bacteria.

A. *Legionella pneumophila* replicates in an ER-derived vacuole, which is modulated by class I PI(3)Ks. The protein SidC is secreted by the Icm/Dot T4SS and specifically binds to PI(4)P on the vacuole.

B. *Shigella flexneri* invades host cells and escapes the phagosome by secreting the phosphatidylinositol phosphatase lpgD and other effectors via the Mxi-Spa T3SS. Production of PI(5)P from PI(4,5)P₂ by lpgD facilitates bacterial entry and activates class I PI(3)Ks, which contributes to host cell survival by activating the serine/threonine kinase Akt.

C. *Salmonella enterica* triggers uptake by secreting the phosphatidylinositol phosphatase SigD/SopB and GEFs (guanine nucleotide Exchange factors) via a T3SS. SigD/SopB dephosphorylates PI(4,5)P₂, thus facilitating entry of the bacteria. After uptake, SigD/SopB (i) maintains high levels of PI(3)P on the vacuole to promote fusion with PI(3)P-containing macrophagosomes, (ii) activates Akt-dependent cell survival pathways, and (iii) triggers host cell fluid secretion by producing inositol(1,4,5,6)P₄.

D. Enteropathogenic *E. coli* (EPEC) replicate extracellularly on 'pedestals' and prevent phagocytosis by injecting the type III-secreted effector EspF. By an unknown mechanism class I PI(3)Ks are inhibited, leading to an accumulation of PI(4,5)P₂.

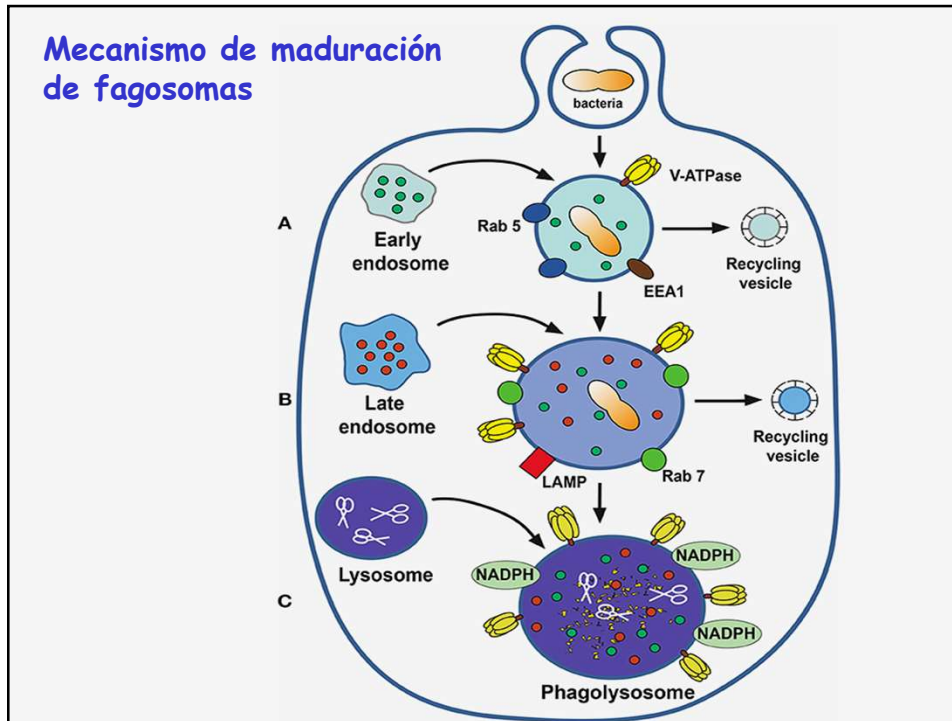
E. *Mycobacterium tuberculosis* interferes with the endosomal pathway by depleting the phagosome from PI(3)P. The phosphatidylinositol analogue LAM (lipoarabinomannan) blocks activation of class III PI(3)Ks by interfering with Ca²⁺/calmodulin/calmodulin kinase II-dependent signalling, and SapM dephosphorylates PI(3)P on the vacuole. PIM (phosphatidylinositol mannoside) promotes fusion between phagosomes and early endosomes.

F. *Yersinia spp.* are phagocytosed upon the interaction between invasin and host cell b1 integrin receptors. This interaction leads to an Arf6-dependent recruitment and activation of PI(4)P(5)Ka, producing PI(4,5)P₂ at the entry site.

G. *Listeria monocytogenes* invades host cells by receptor-mediated phagocytosis, including binding of InlB to the host cell Met receptor, which leads to activation of PI(3)Ks and Akt.

30

Mecanismo de maduración de fagosomas



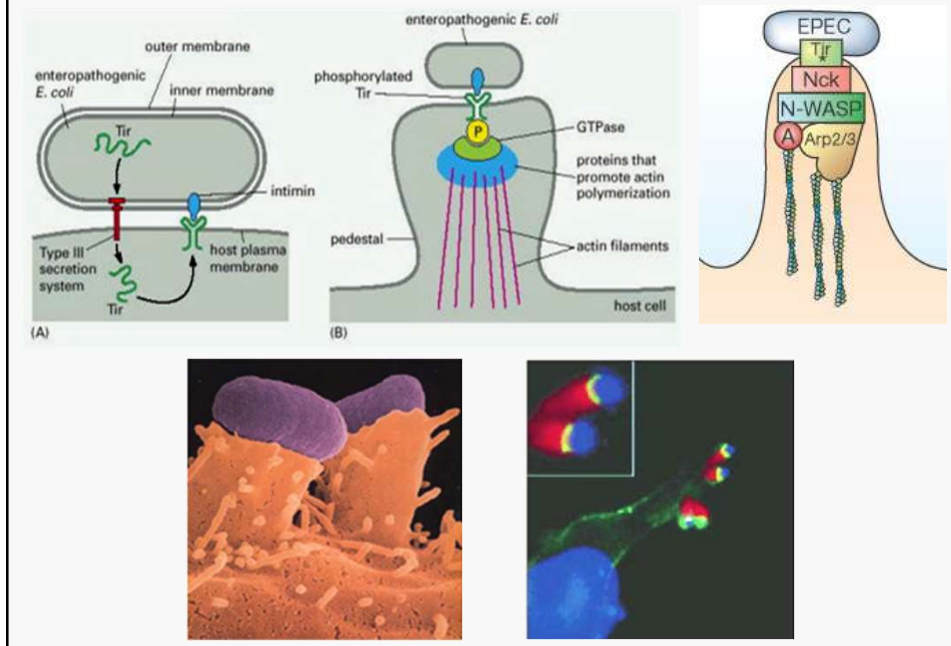
31

Marcadores moleculares en la vía endo/fagocítica

Compartimiento	Marcador	pH
Endosoma Temprano ("sorting endosome") Fagosoma Temprano	<ul style="list-style-type: none"> ➤ EEA1 ➤ Rab5 ➤ PI3P ➤ Sintaxina 13 ➤ Transferrina ➤ VAMP-3 	≈ 6.5
Endosoma Tardío Fagosoma Tardío	<ul style="list-style-type: none"> ➤ Rab 7 ➤ Rab 9 ➤ Receptor a Manosa 6-fosfato (M6PR) ➤ Sintaxina 7 ➤ LAMPs ➤ Ácido lisobisfosfatídico (LBPA) 	5.5-6.0
Lisosoma Fagolisosoma	<ul style="list-style-type: none"> ➤ LAMPs ➤ Catapsina D madura ➤ Marcador endocitado por fase fluida por ≥ de 2h 	4.5-5.5

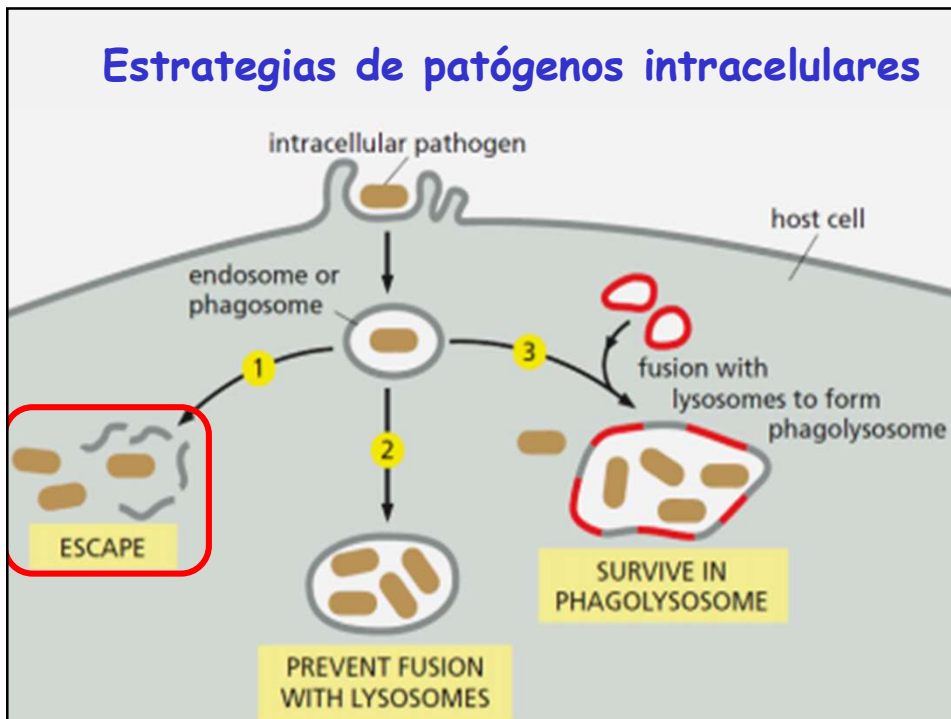
32

Interacción de *E. coli* (EPEC) con la célula hospedadora

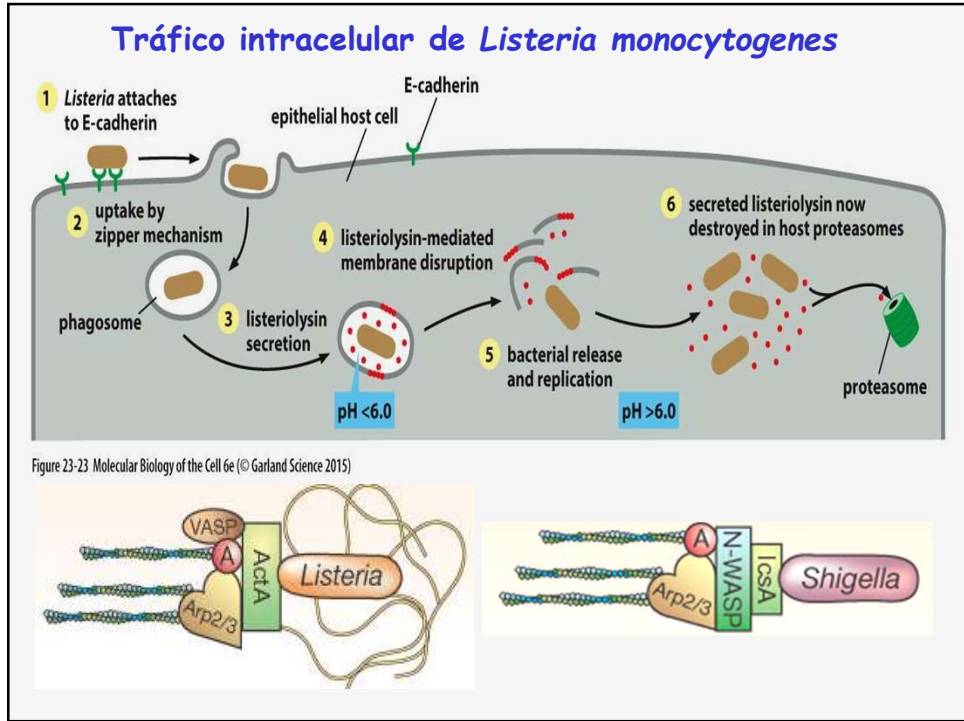


35

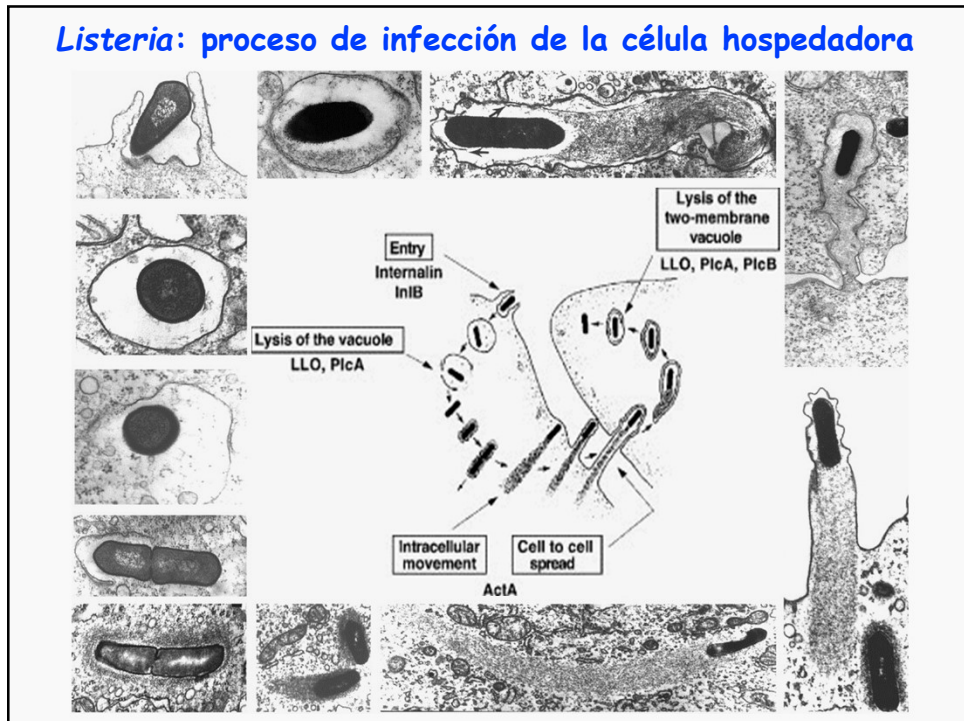
Estrategias de patógenos intracelulares



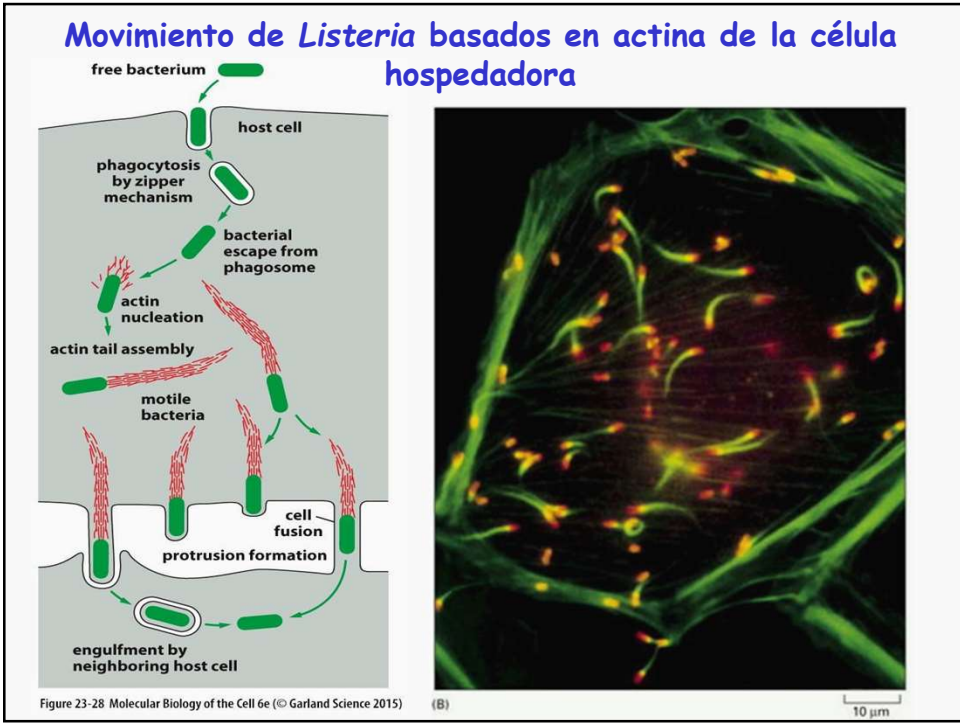
36



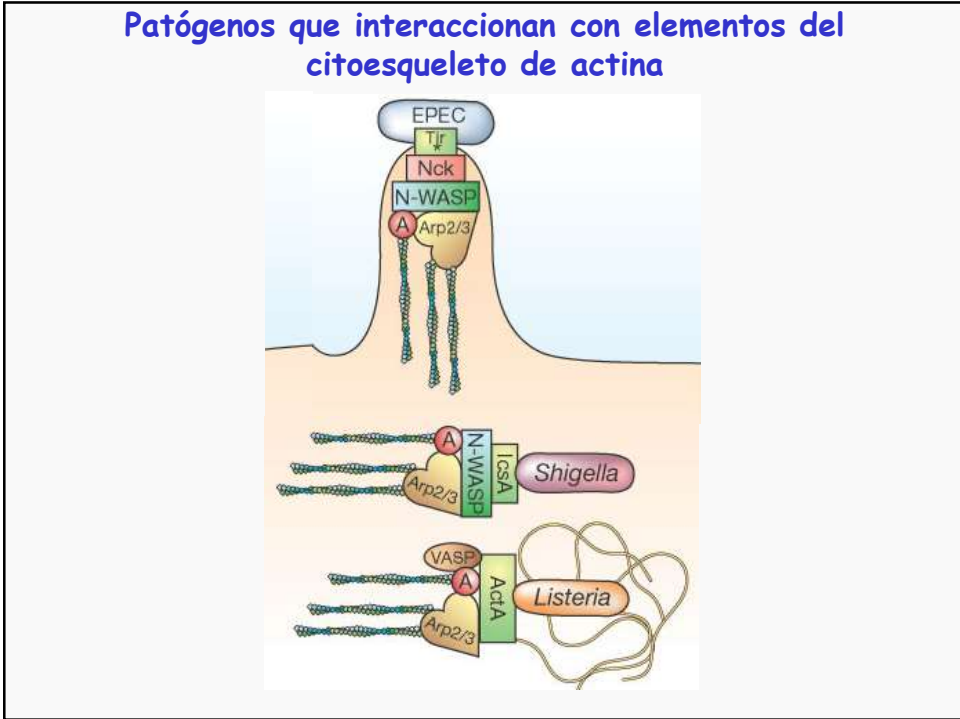
37



38

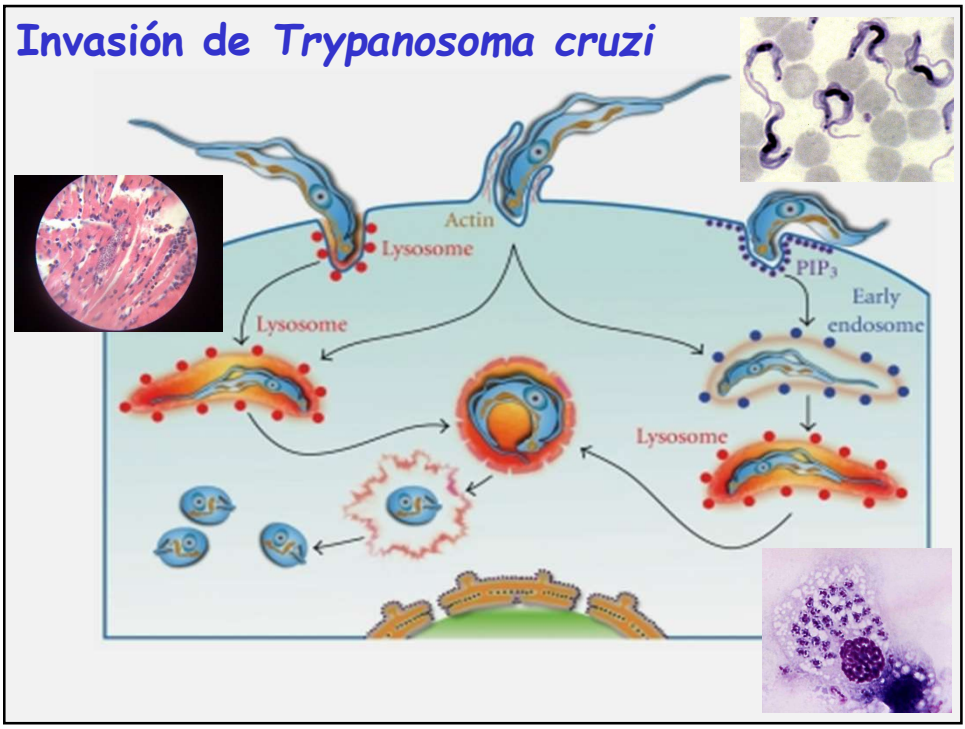


39

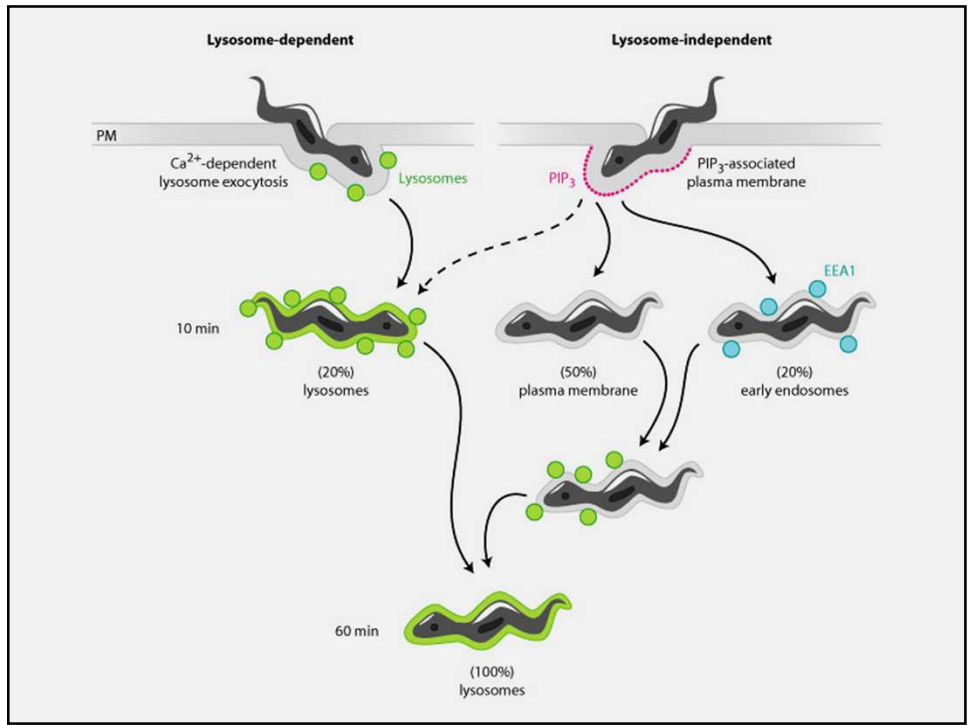


40

Invasión de *Trypanosoma cruzi*

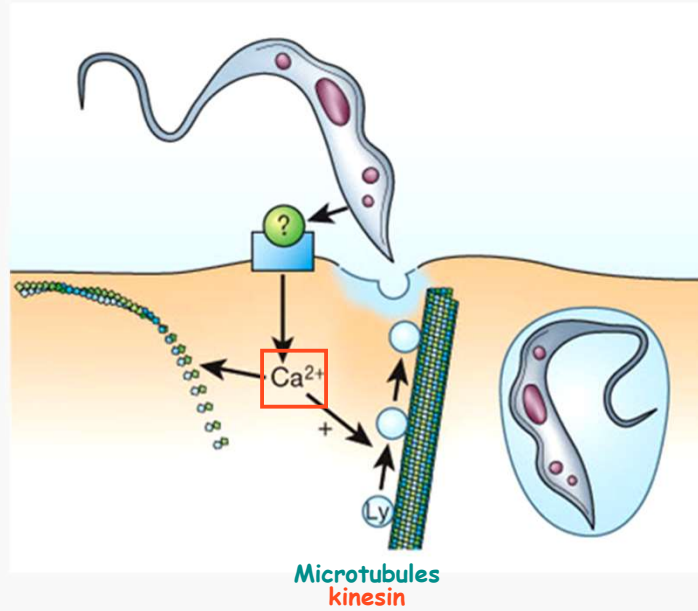


41

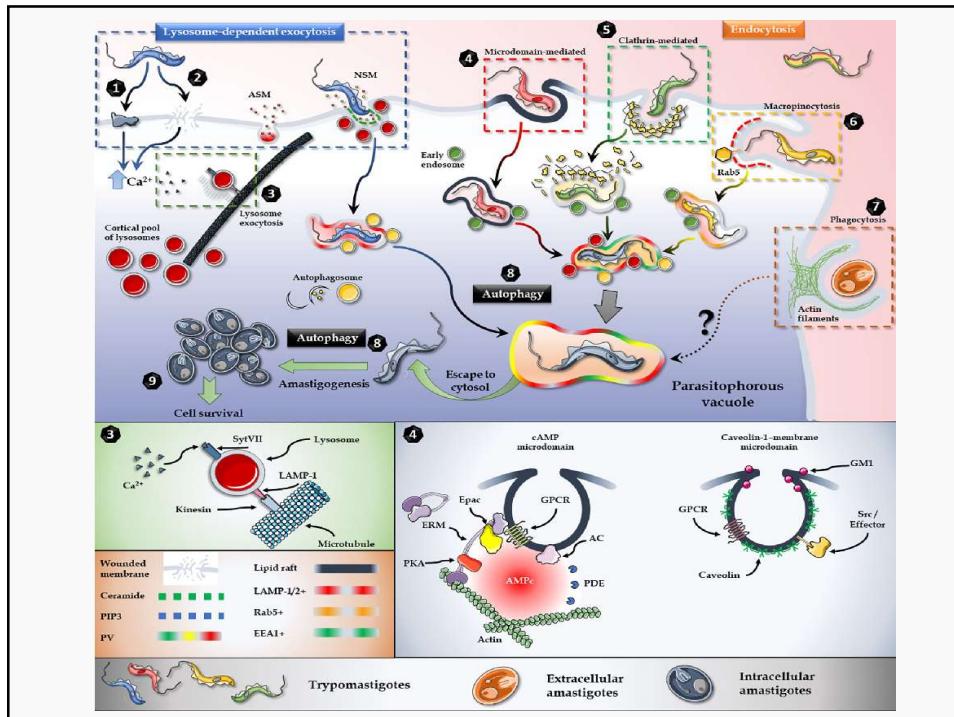


42

Invasión de *Trypanosoma cruzi* a la célula hospedadora

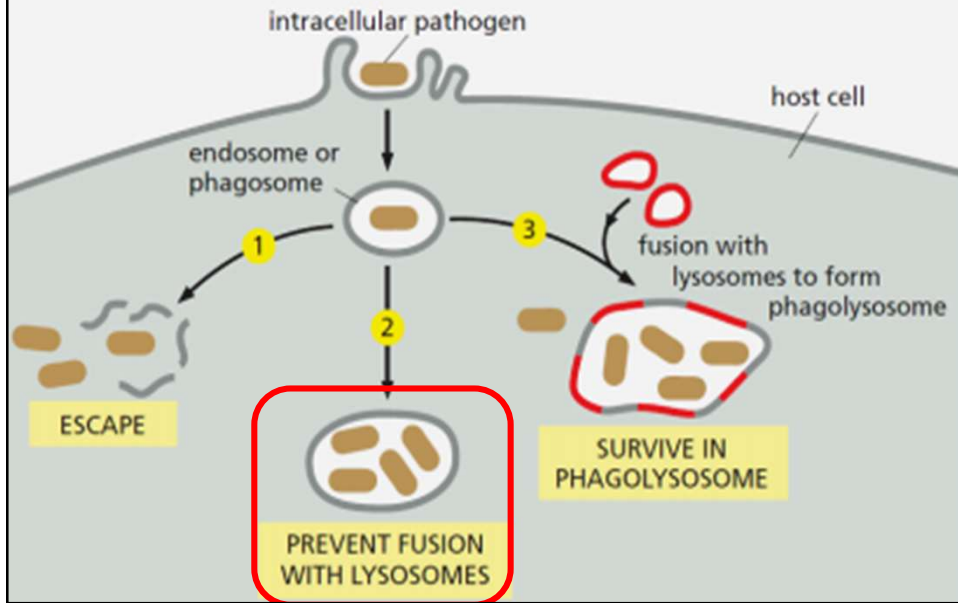


43

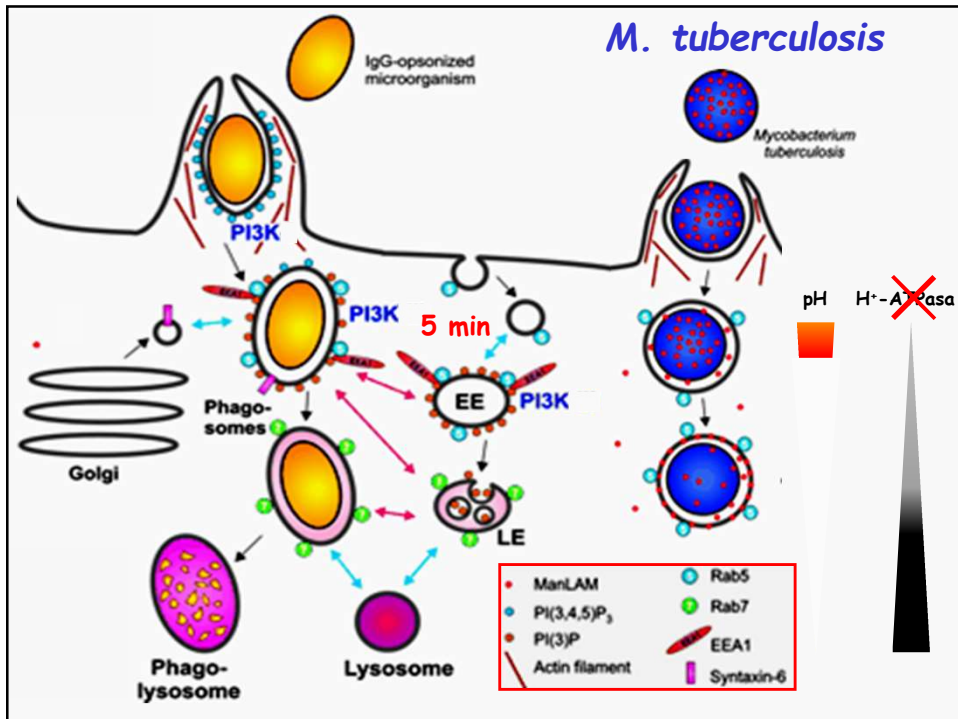


44

Estrategias de patógenos intracelulares

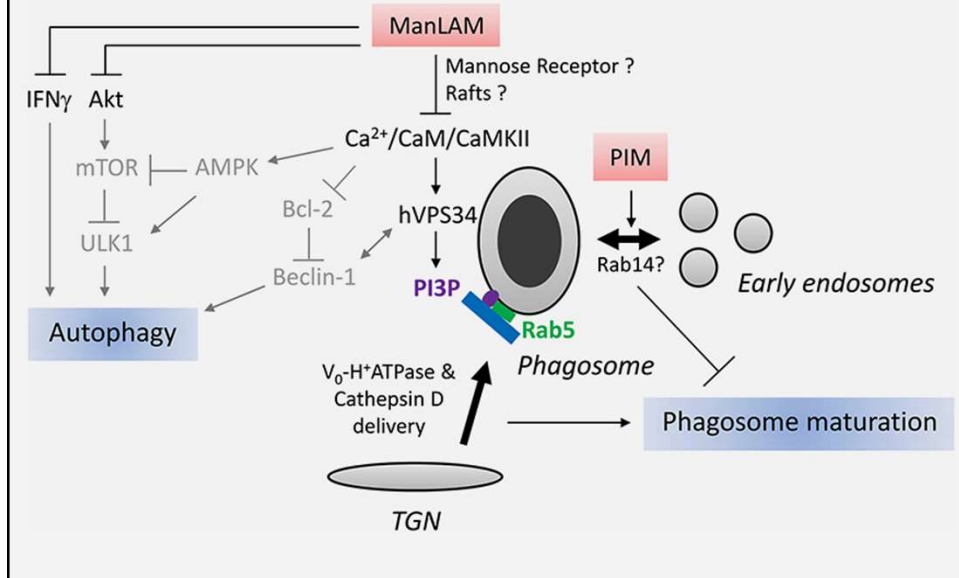


45



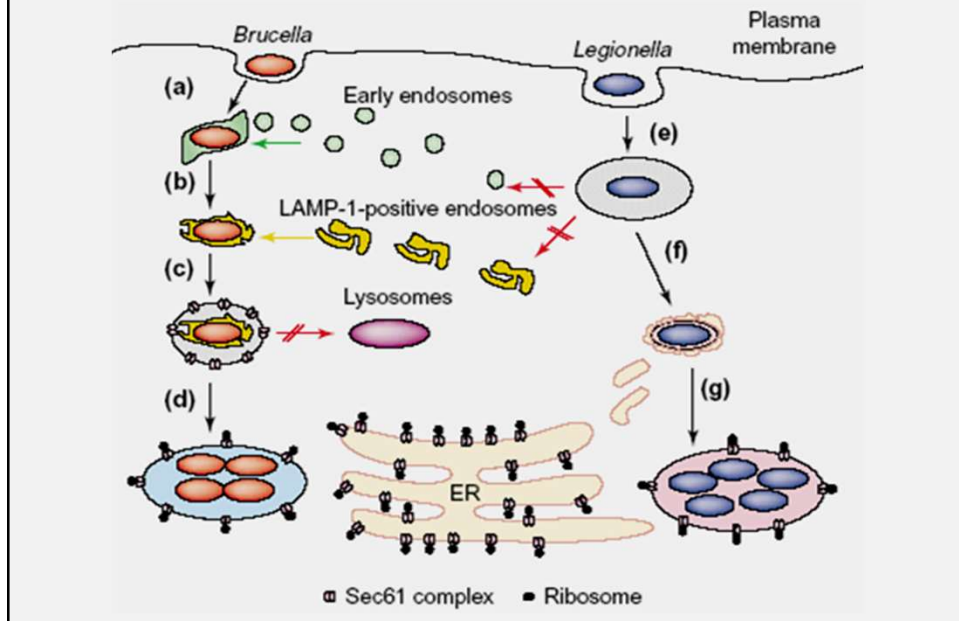
46

Estrategia de *M. tuberculosis*

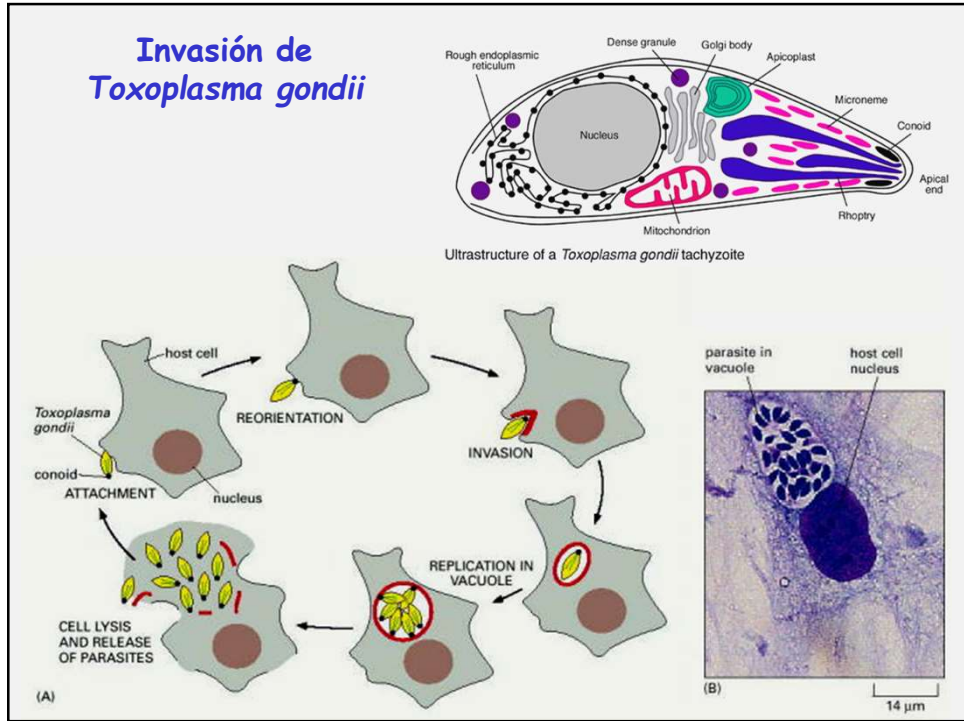


47

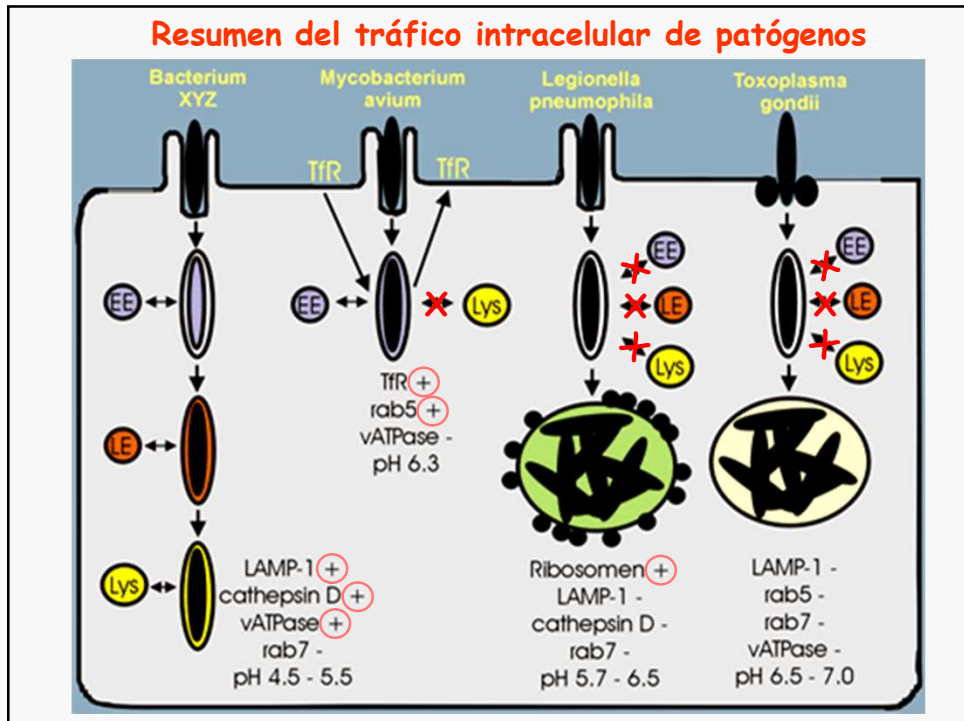
Tráfico intracelular de *Brucella* y *Legionella*



48



49



50

Resumen del tráfico intracelular de patógenos

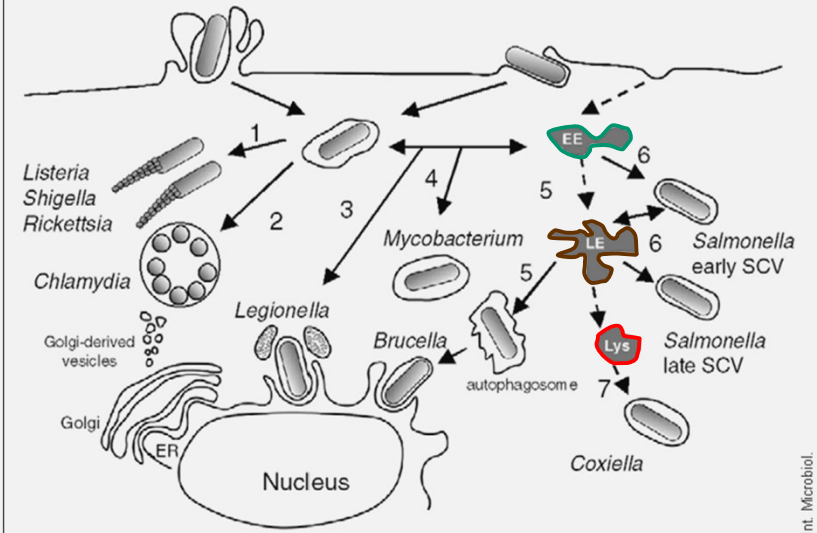
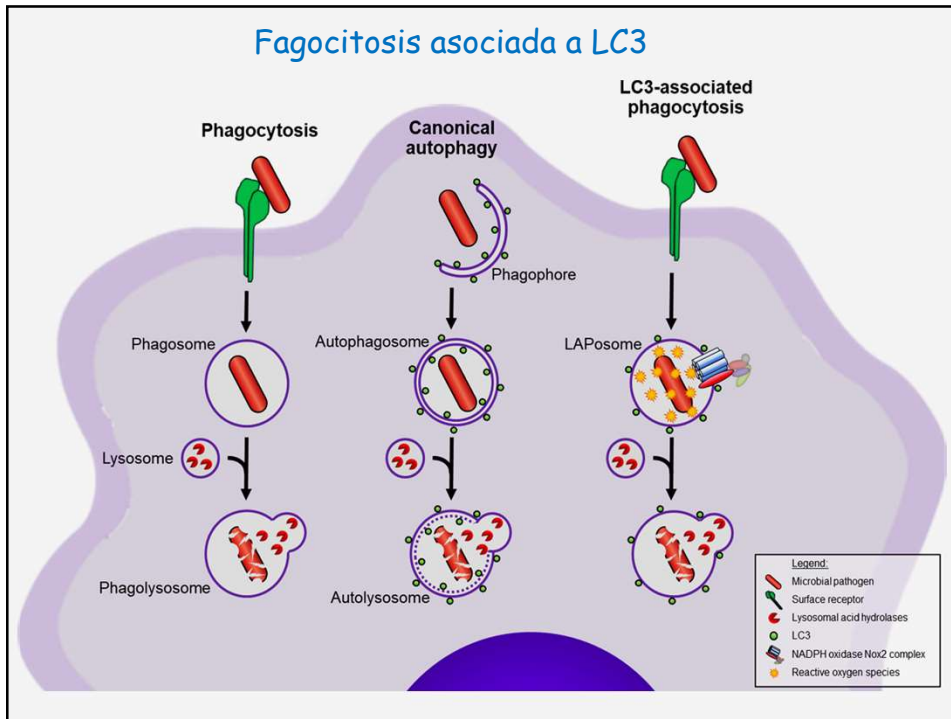


Fig. 2. Lifestyles of intracellular bacterial pathogens. (1) Bacterial escape into the cytosol and intracellular movement directed by actin tails. (2) Segregation from the endocytic route and formation of a unique inclusion vacuole by interaction with Golgi-derived vesicles. (3) Segregation from the endocytic route at the early endosome (EE) stage and formation of an endoplasmic reticulum (ER)-like phagosomal compartment. (4) Arrest of phagosome maturation at the EE stage. (5) Segregation from the endocytic route at the late endosome (LE) stage into an ER-like phagosome. (6) Transient arrest of phagosome maturation at EE and LE stages. (7) Phagosome maturation completed up to fusion with lysosomes. Lys, lysosome, SCV, *Salmonella*-containing vacuole. See text for details.

51

Fagocitosis asociada a LC3

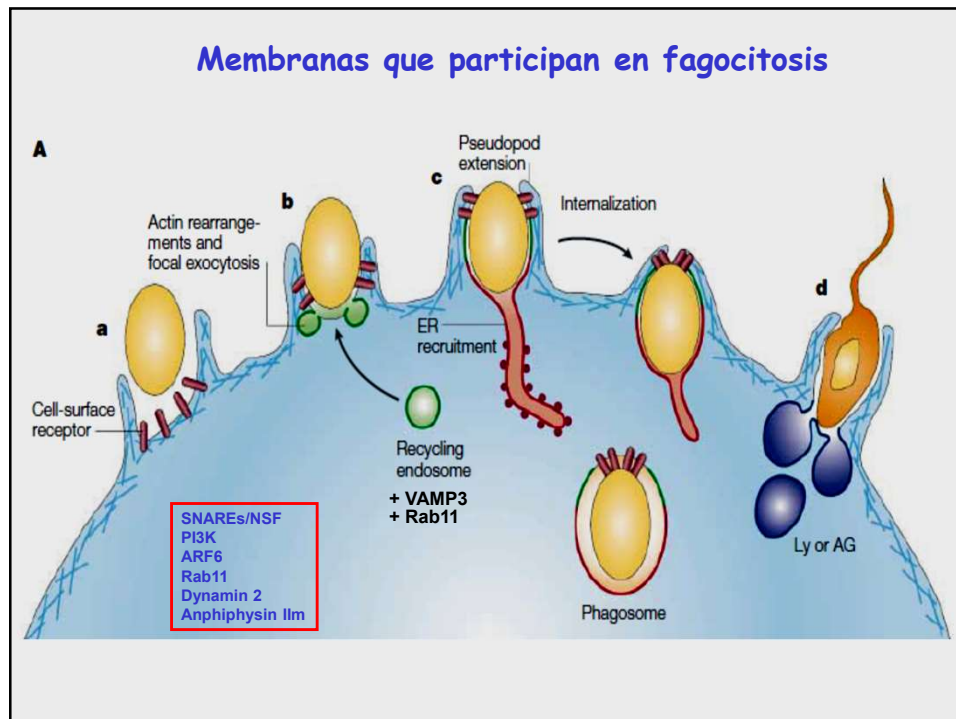


52

La formación del fagosoma requiere un gran aporte de membrana de la célula hospedadora

¿Cuál es el origen de esa membrana?

53

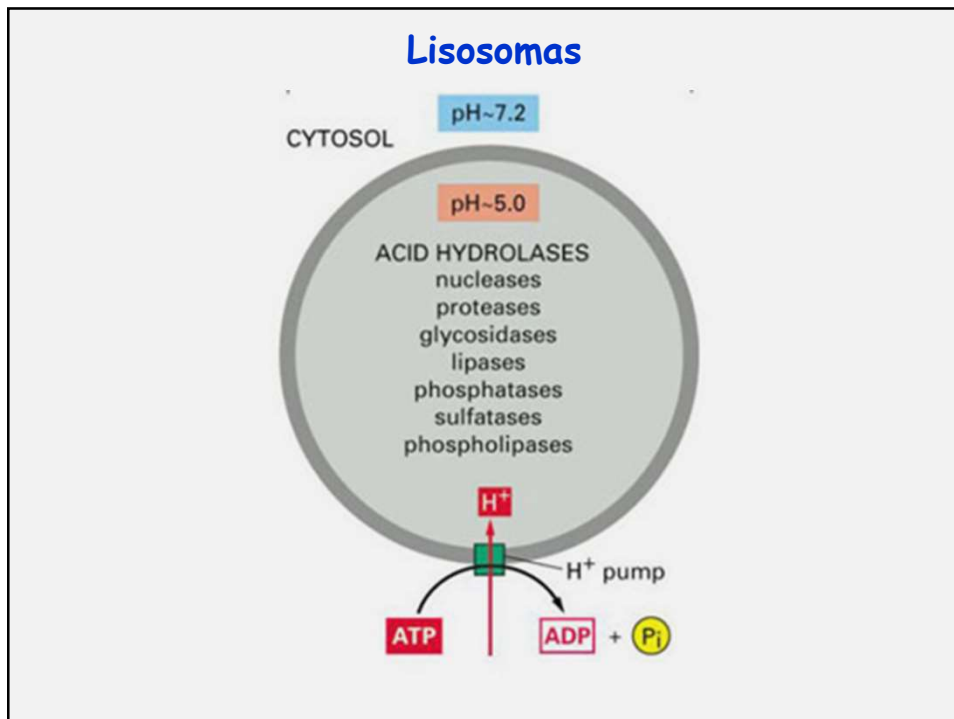


54

Mecanismos de defensa de la célula hospedadora

- Fagocitosis: lisosomas
- Estallido respiratorio (NADPH oxidasa)
- Defensinas
- Presentación de antígenos

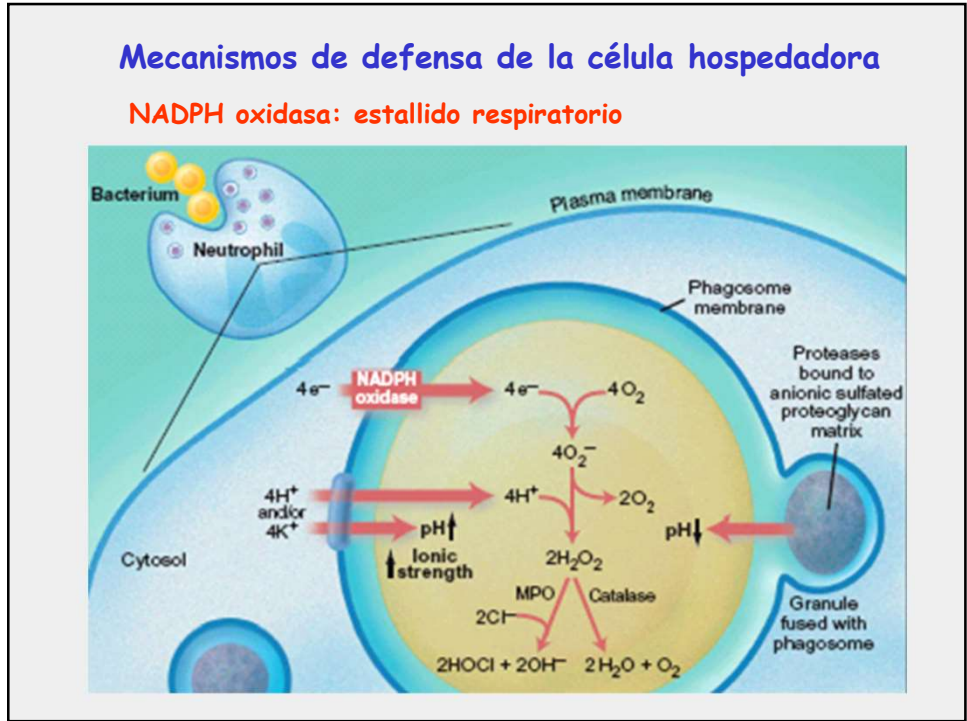
55



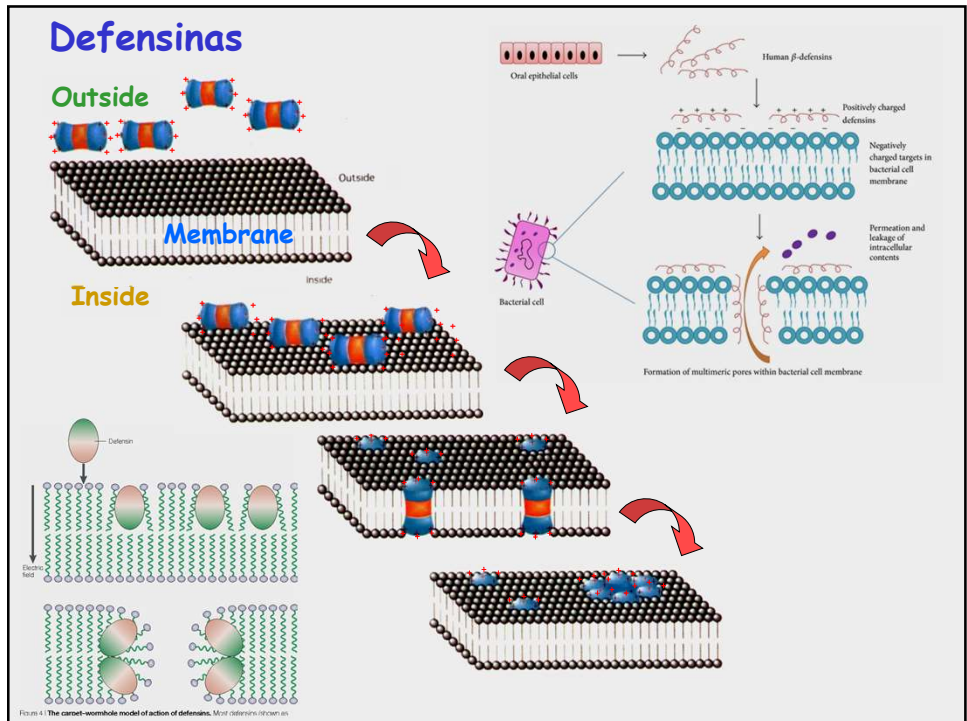
56

Mecanismos de defensa de la célula hospedadora

NADPH oxidasa: estallido respiratorio

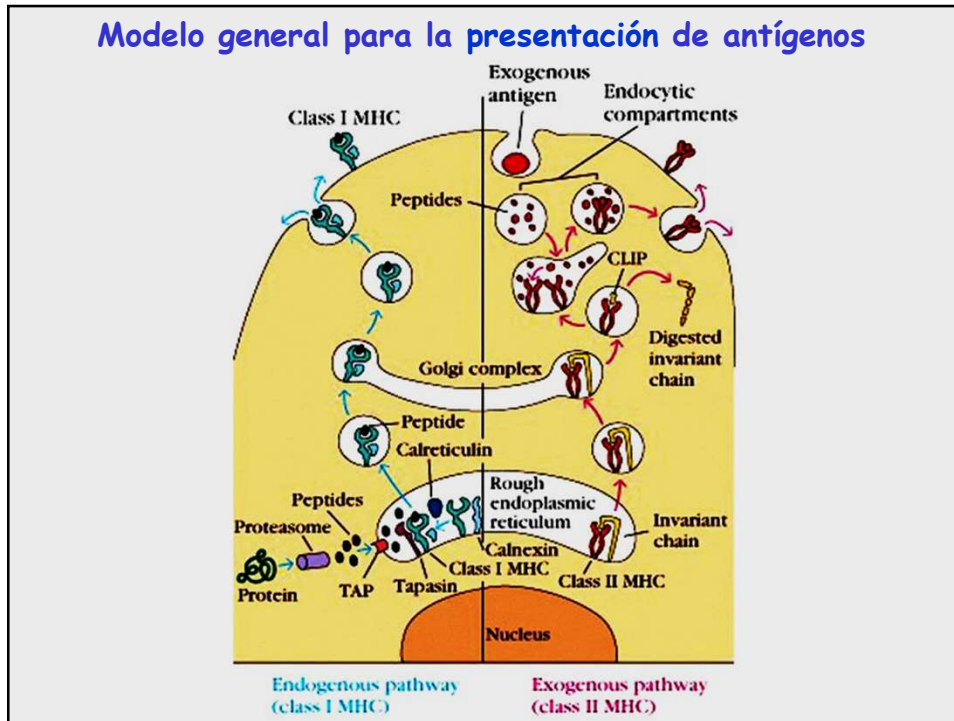


57



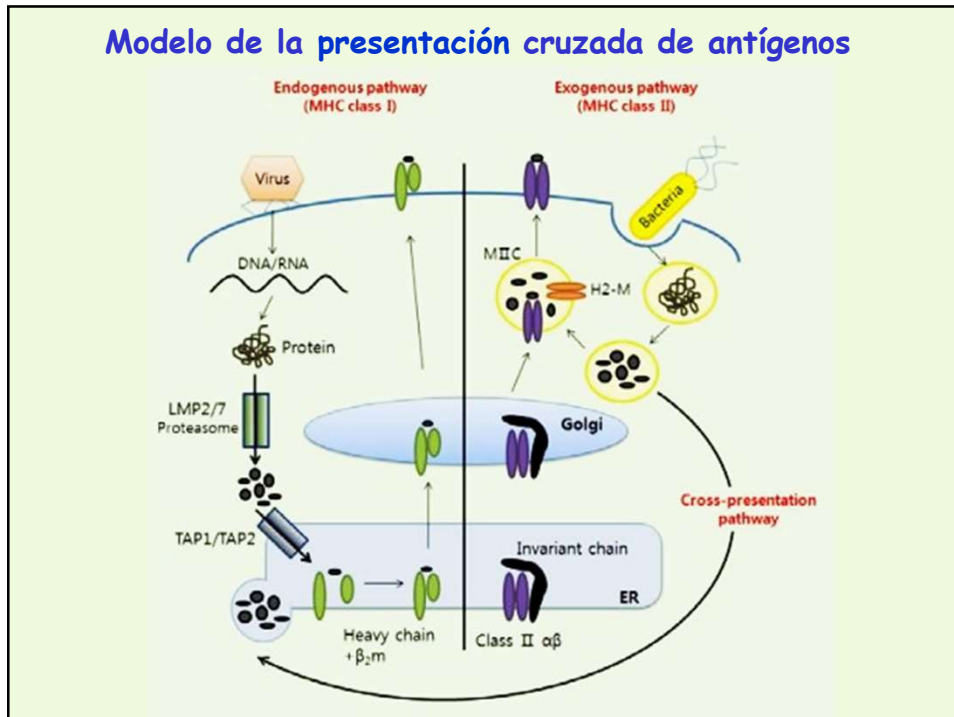
58

Modelo general para la presentación de antígenos



59

Modelo de la presentación cruzada de antígenos



60