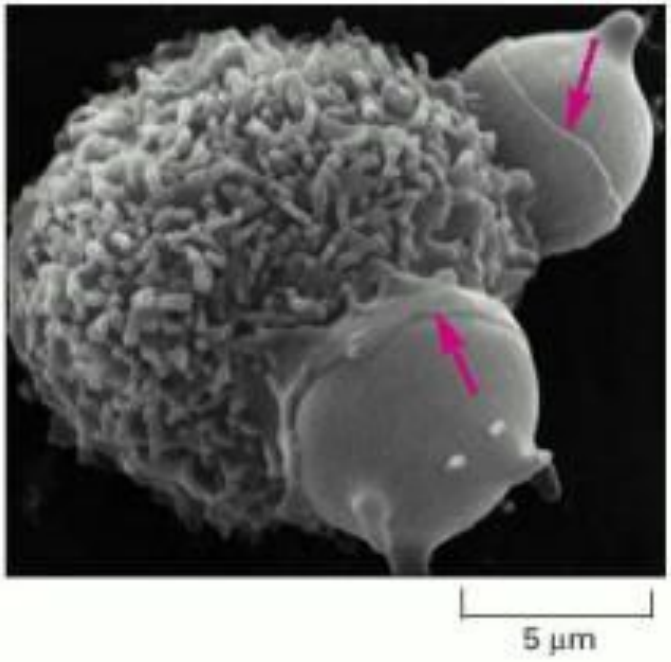
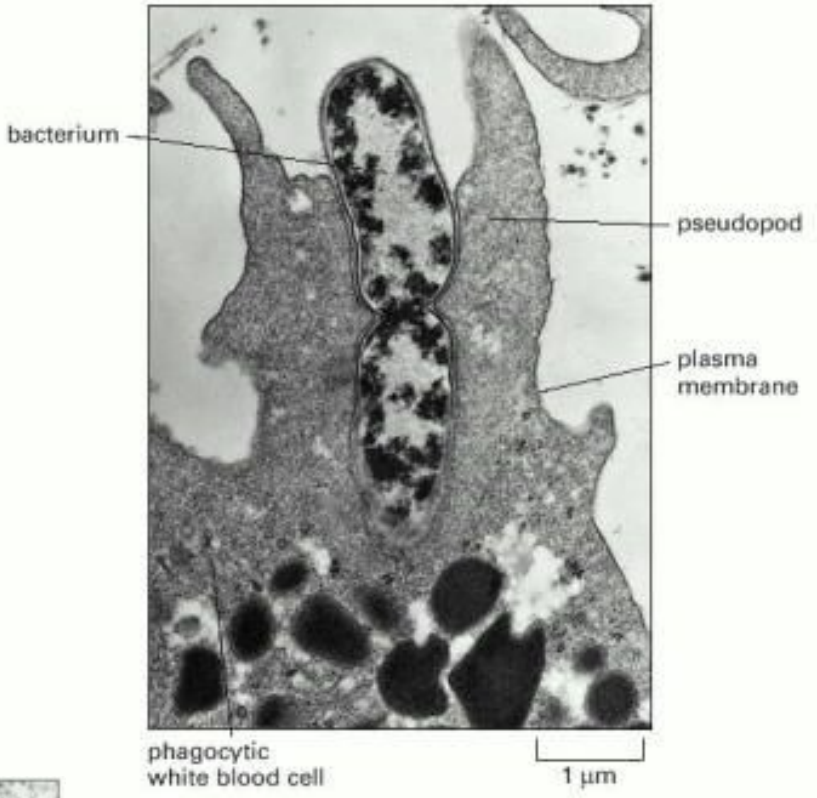
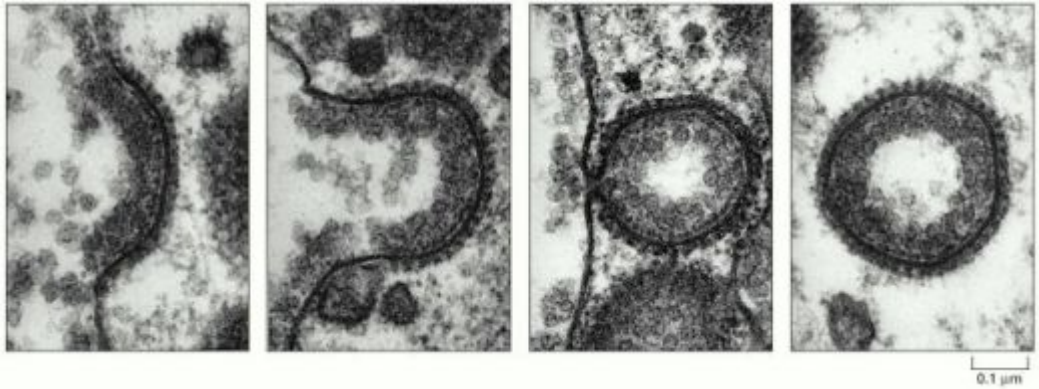
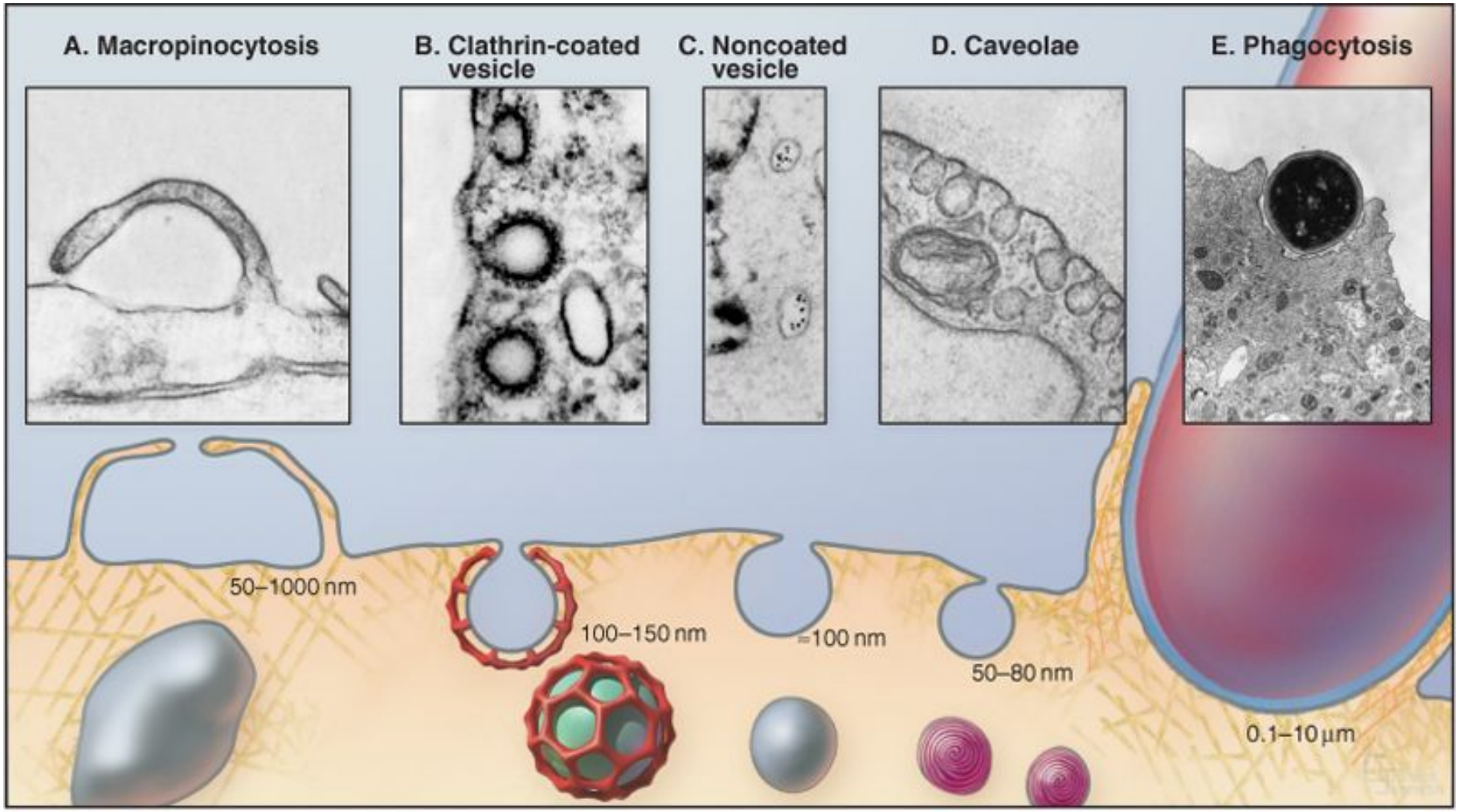
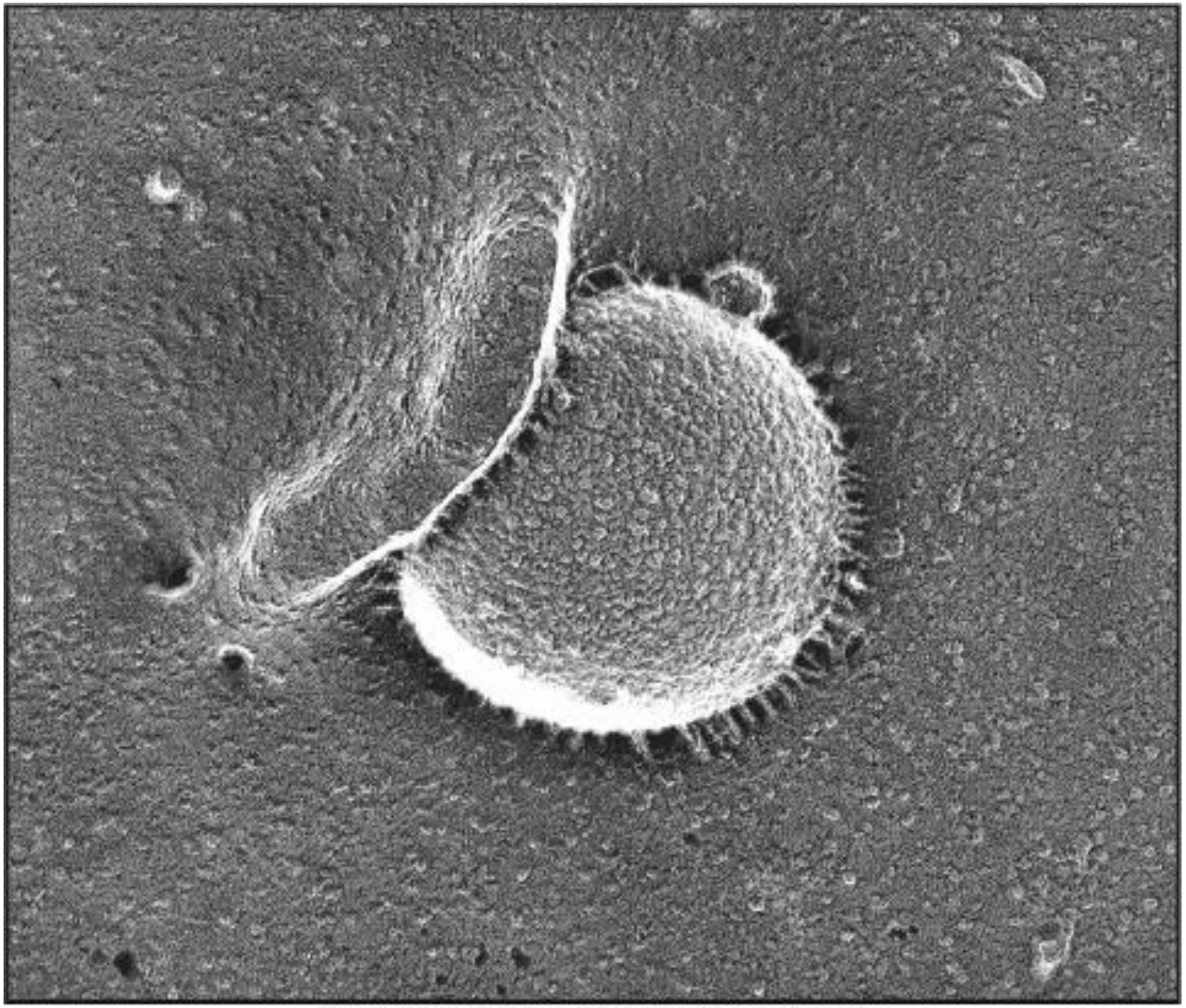
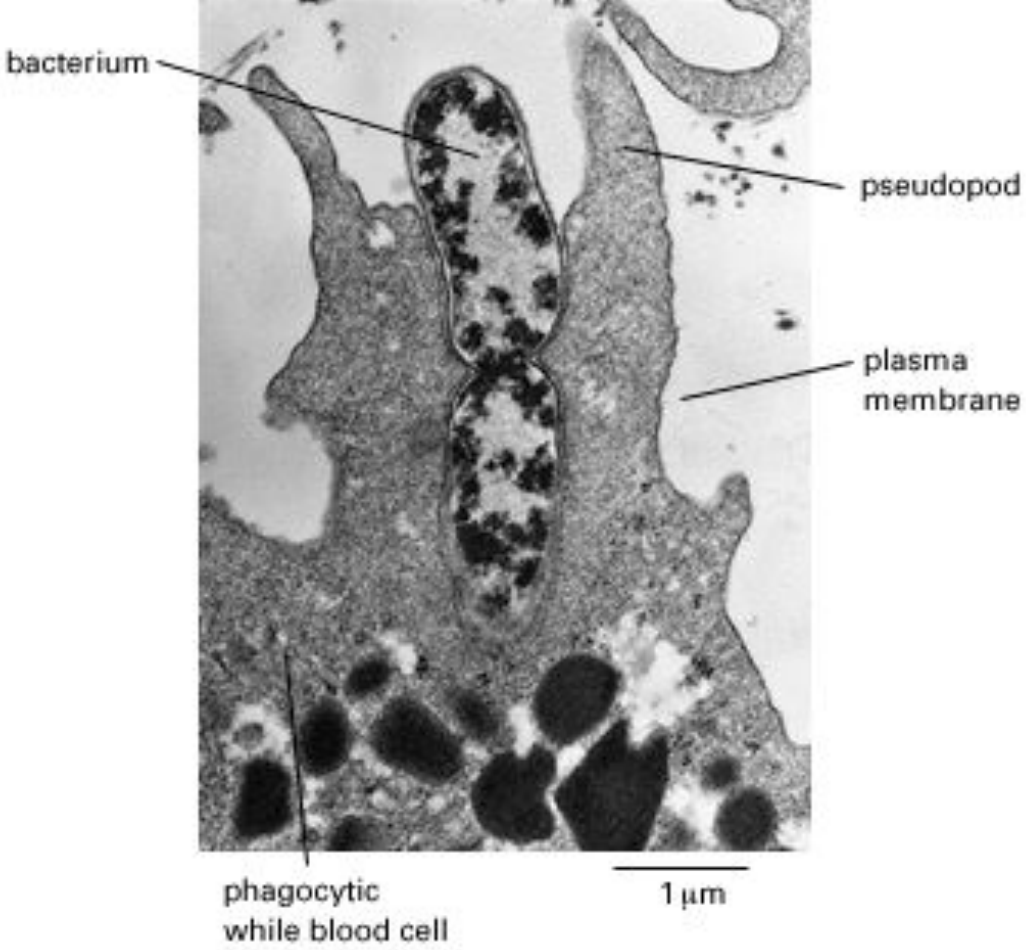

5 µm


bacterium
pseudopod
plasma membrane
phagocytic white blood cell
1 µm


0.1 µm







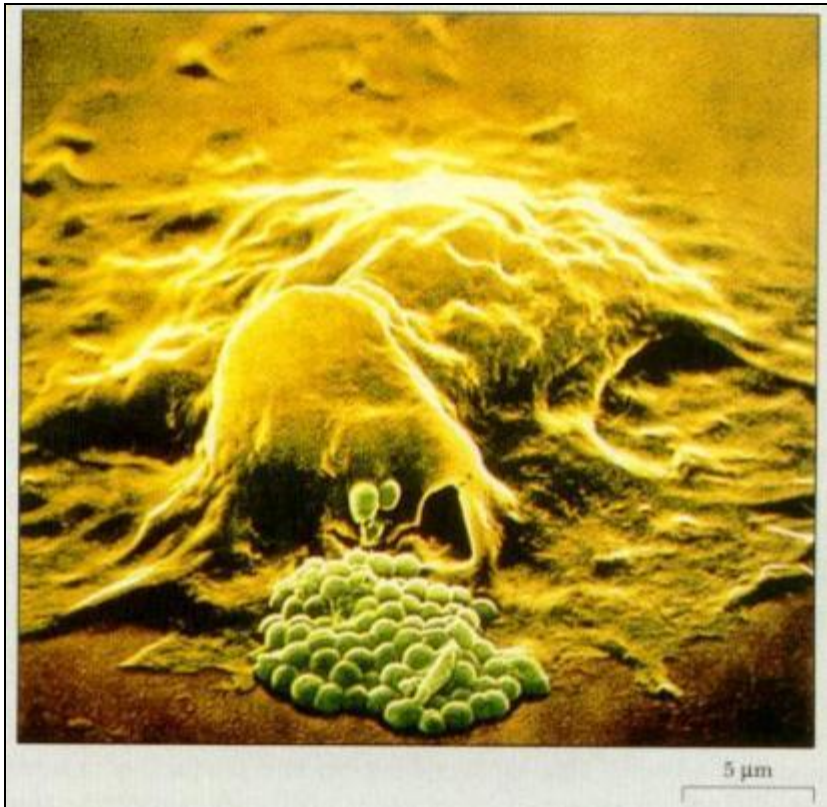
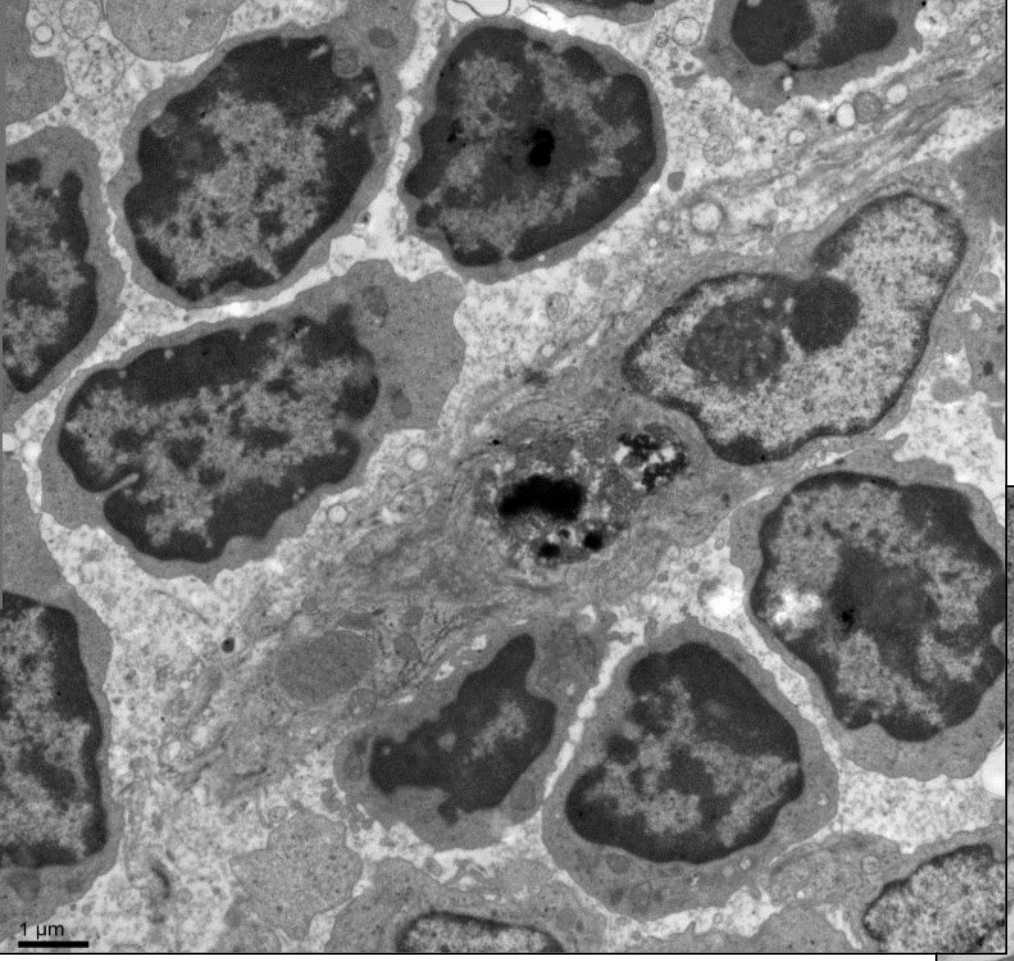
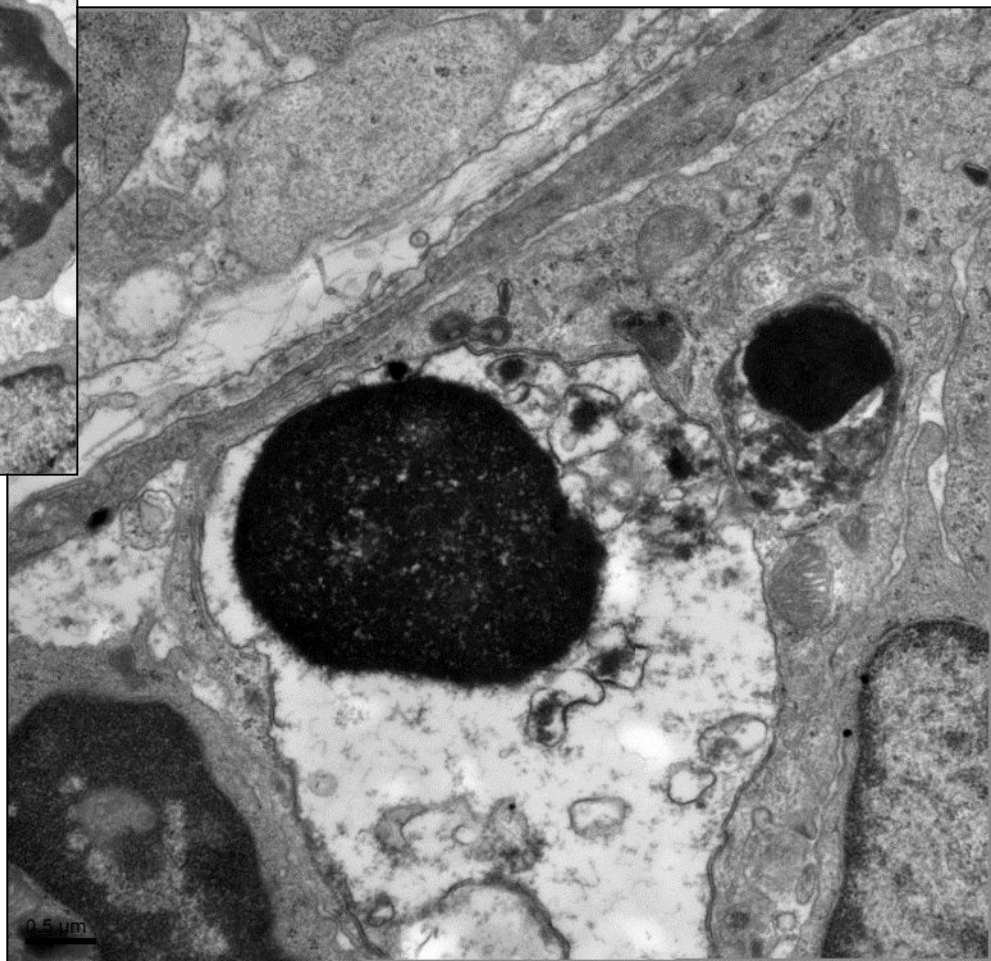


Figure 2 *Pseudopods extend around the foreign microorganism. Extension requires the polymerization of actin into actin filaments.* (Lennart Nilsson)


1 µm


0.5 µm

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- Удаление продуктов деградации

https://www.frontiersin.org/articles/10.3389/fimmu.2020.01097/full

Группы хемоаттрактантов

- Вещества, продуцируемые микроорганизмами (fMLP)
- Противовоспалительные факторы, образующиеся в очаге воспаления (цитокины, лейкотриены, компоненты системы комплемента)
- Вещества, попадающие в межклеточное пространство при нарушении целостности плазмолеммы

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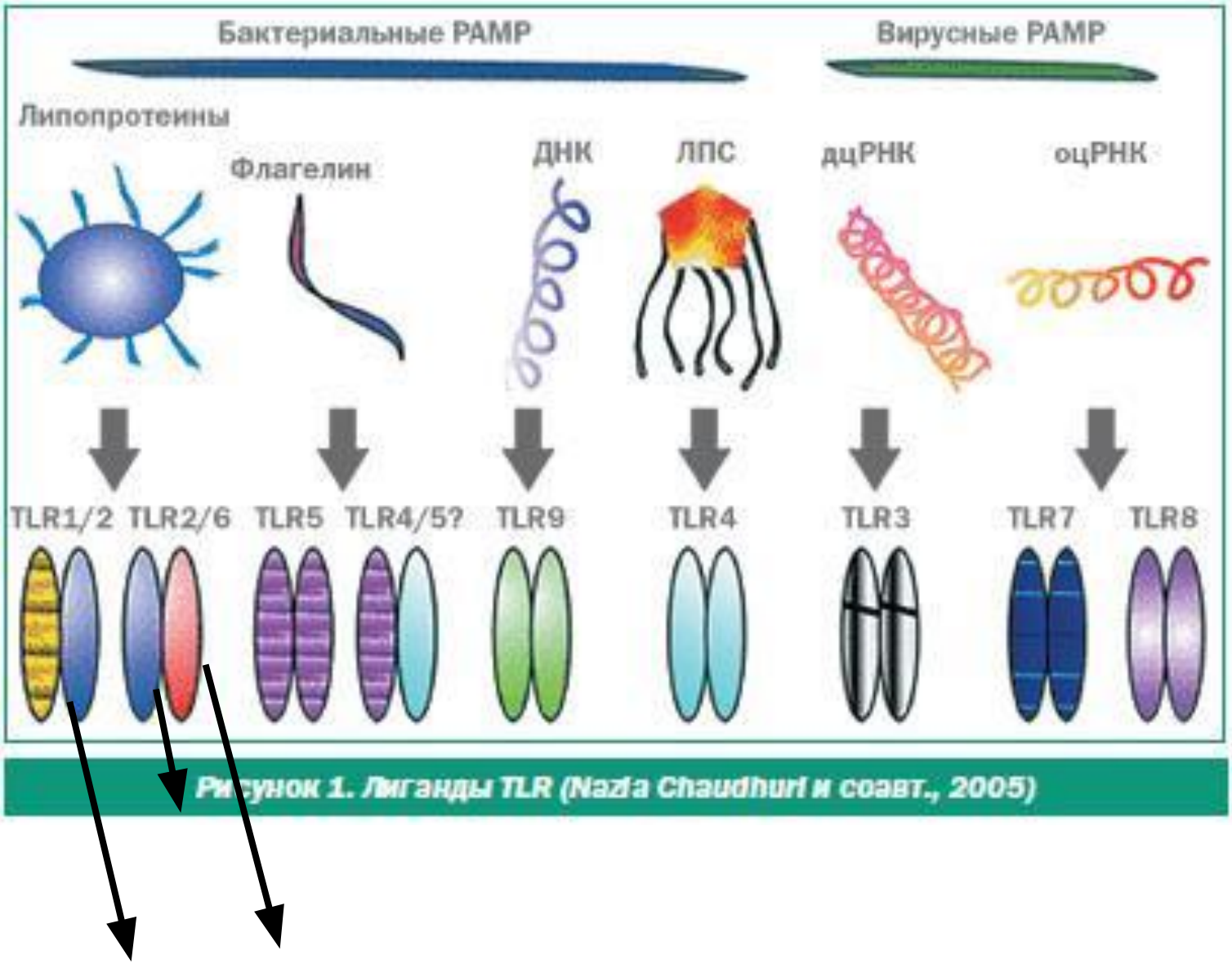
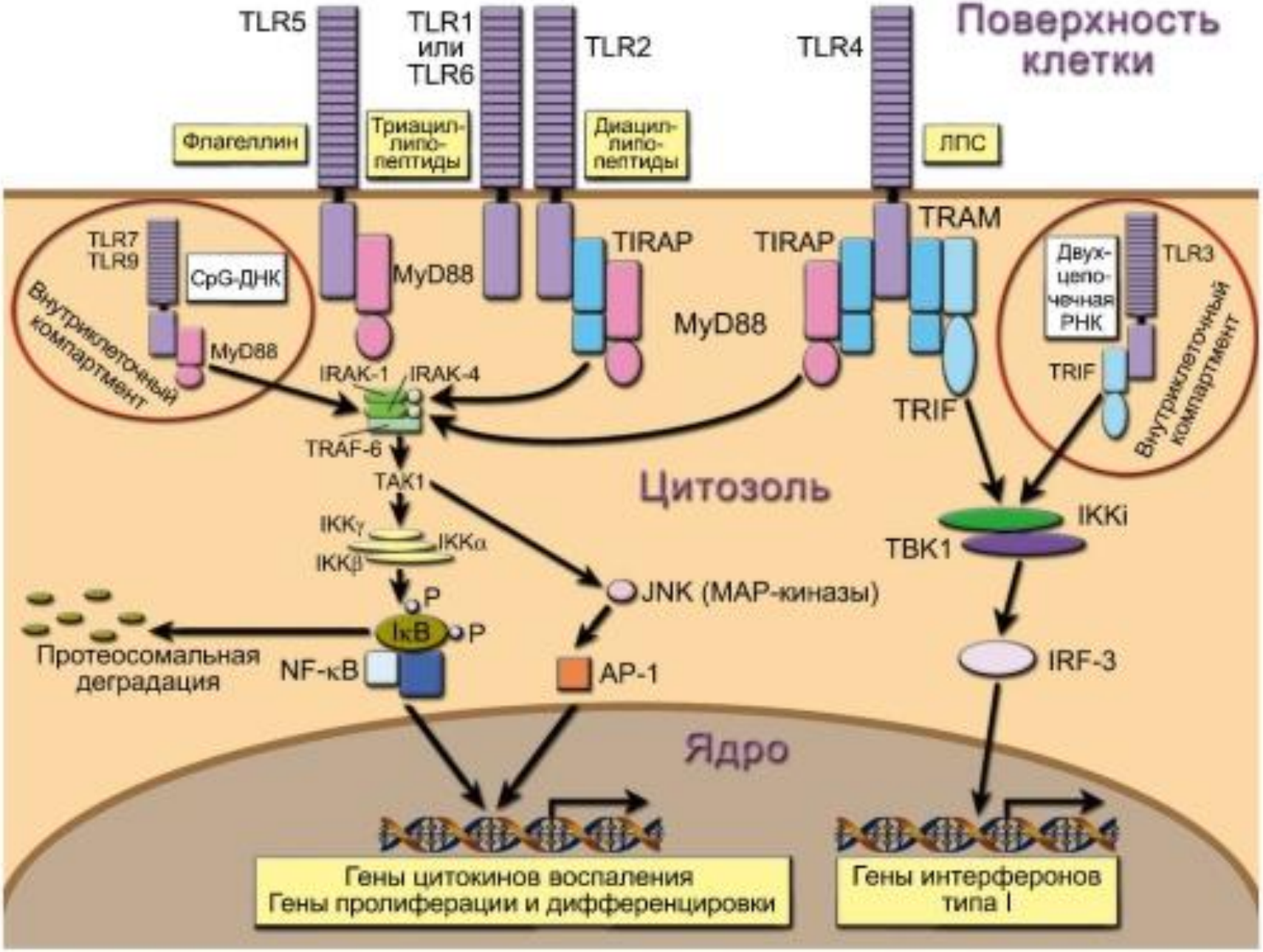
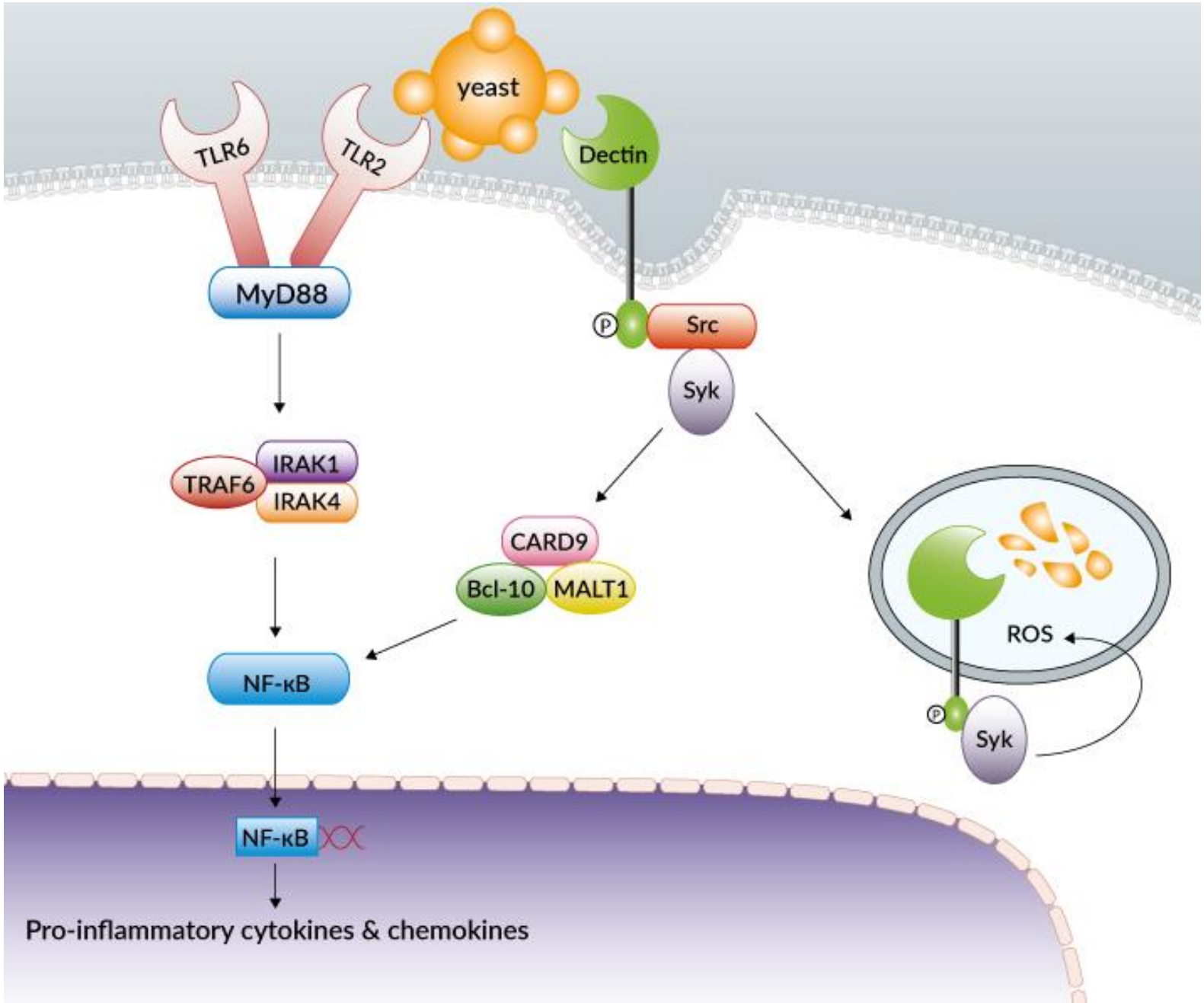
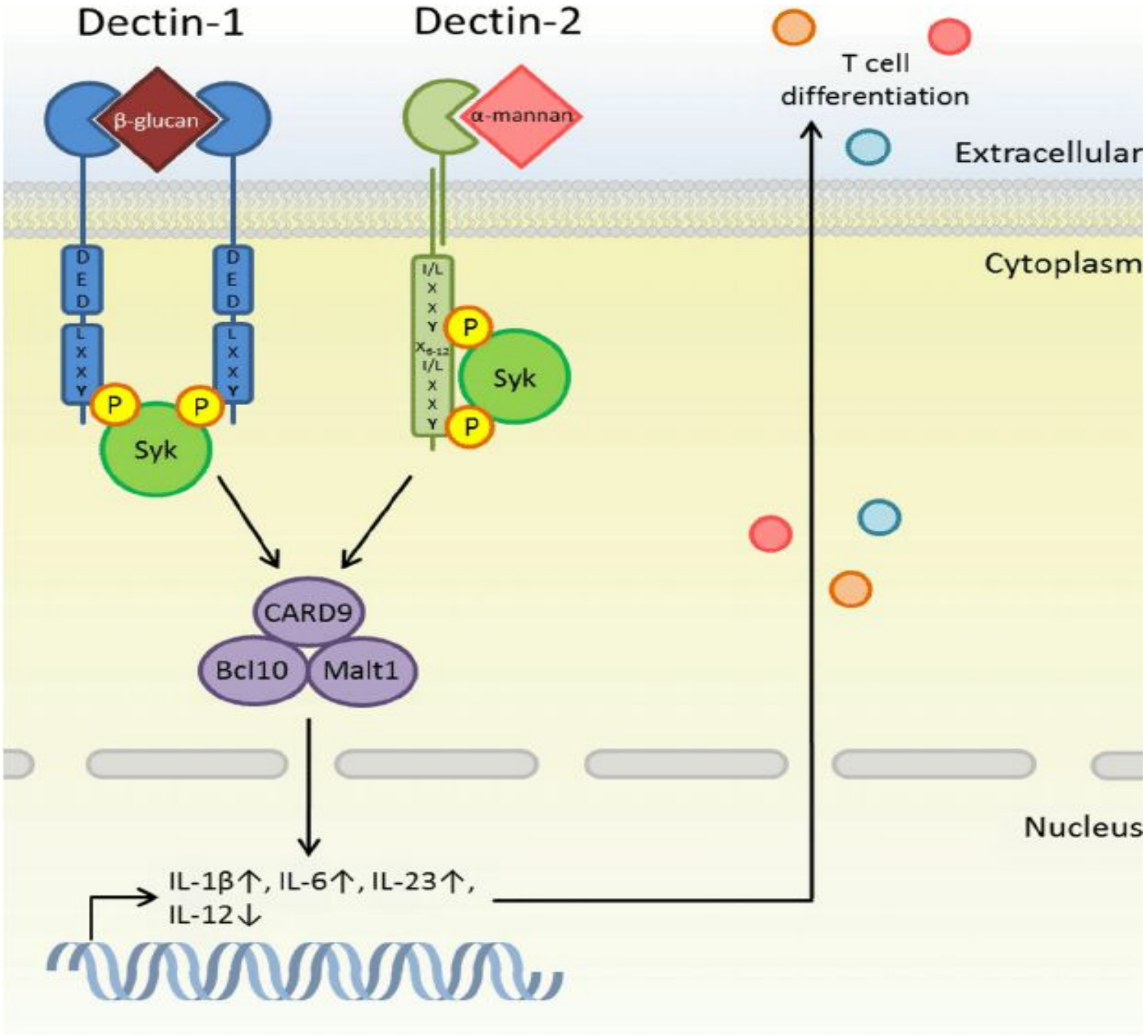


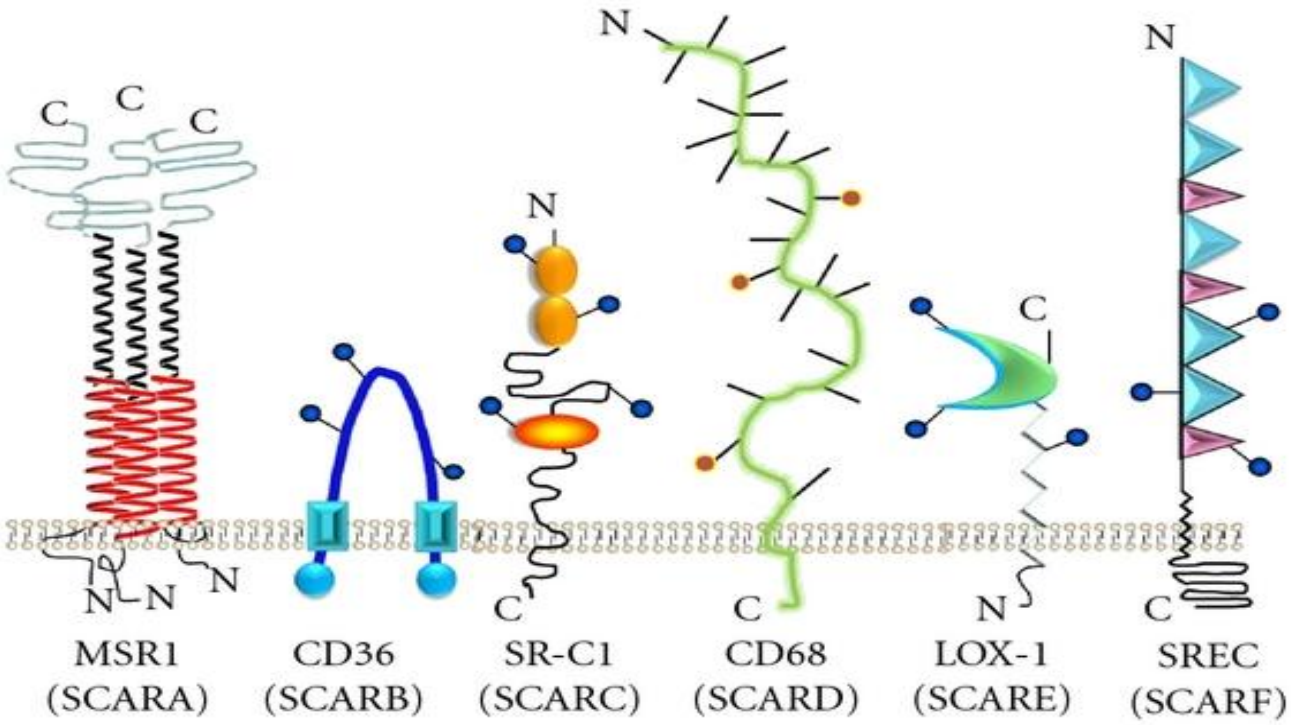
Рисунок 1. Лиганды TLR (Nazia Chaudhuri и соавт., 2005)


TLR5
TLR1 или TLR6
TLR2
TLR4
Поверхность клетки
Флагеллин
Триацил-липо-пептиды
Диацил-липо-пептиды
ЛПС
TLR7 TLR9
CpG-ДНК
Внутриклеточный компартмент
MyD88
TIRAP
TRAM
Двух-цепо-чечная РНК
TLR3
TRIF
IRAK-1
IRAK-4
TRAF-6
TAK1
Цитозоль
IKKγ
IKKα
IKKβ
IKKi
TBK1
P
IκB
JNK (MAP-киназы)
Протеосомальная деградация
NF-κB
AP-1
IRF-3
Ядро
Гены цитокинов воспаления
Гены пролиферации и дифференцировки
Гены интерферонов типа I


yeast
TLR6
TLR2
Dectin
MyD88
P
Src
Syk
IRAK1
TRAF6
IRAK4
CARD9
Bcl-10
MALT1
ROS
NF-κB
P
Syk
NF-κB
Pro-inflammatory cytokines & chemokines


Dectin-1
Dectin-2
β-glucan
α-mannan
T cell
differentiation
Extracellular
Cytoplasm
D
E
D
L
X
X
Y
P
Syk
I/L
X
X
Y
X6-12
CARD9
Bcl10
Malt1
Nucleus
IL-1β↑, IL-6↑, IL-23↑,
IL-12↓

Receptors	Ligands
Pattern-recognition receptors	
Mannose receptor (CD206)	Mannan
Dectin-1 (CLEC7A)	β1,3-glucan
CD14	Lipopolysaccharide-binding protein
Scavenger receptor A (CD204)	Lipopolysaccharide, lipoteichoic acid
CD36	*Plasmodium falciparum*–infected erythrocytes
MARCO	Bacteria



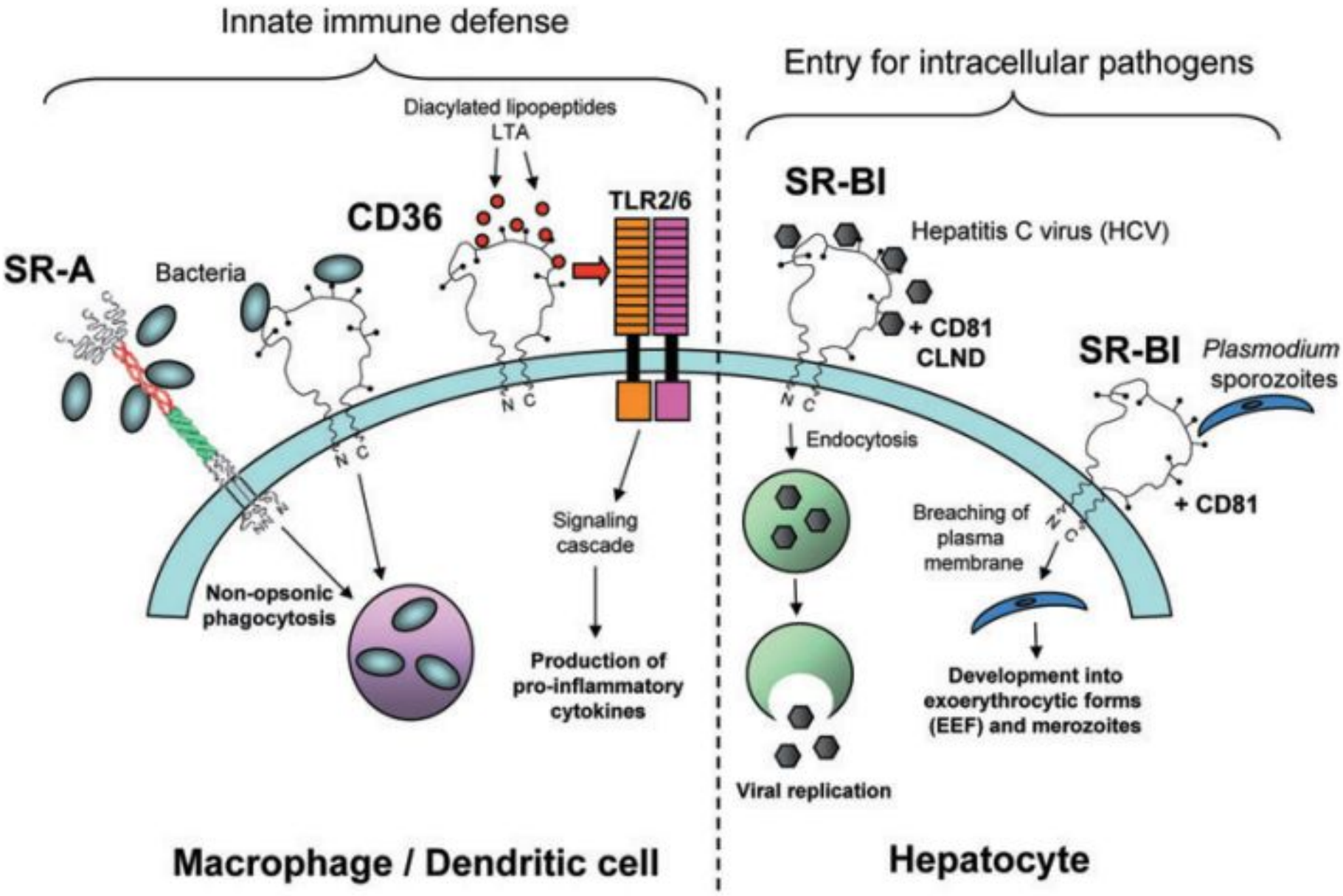
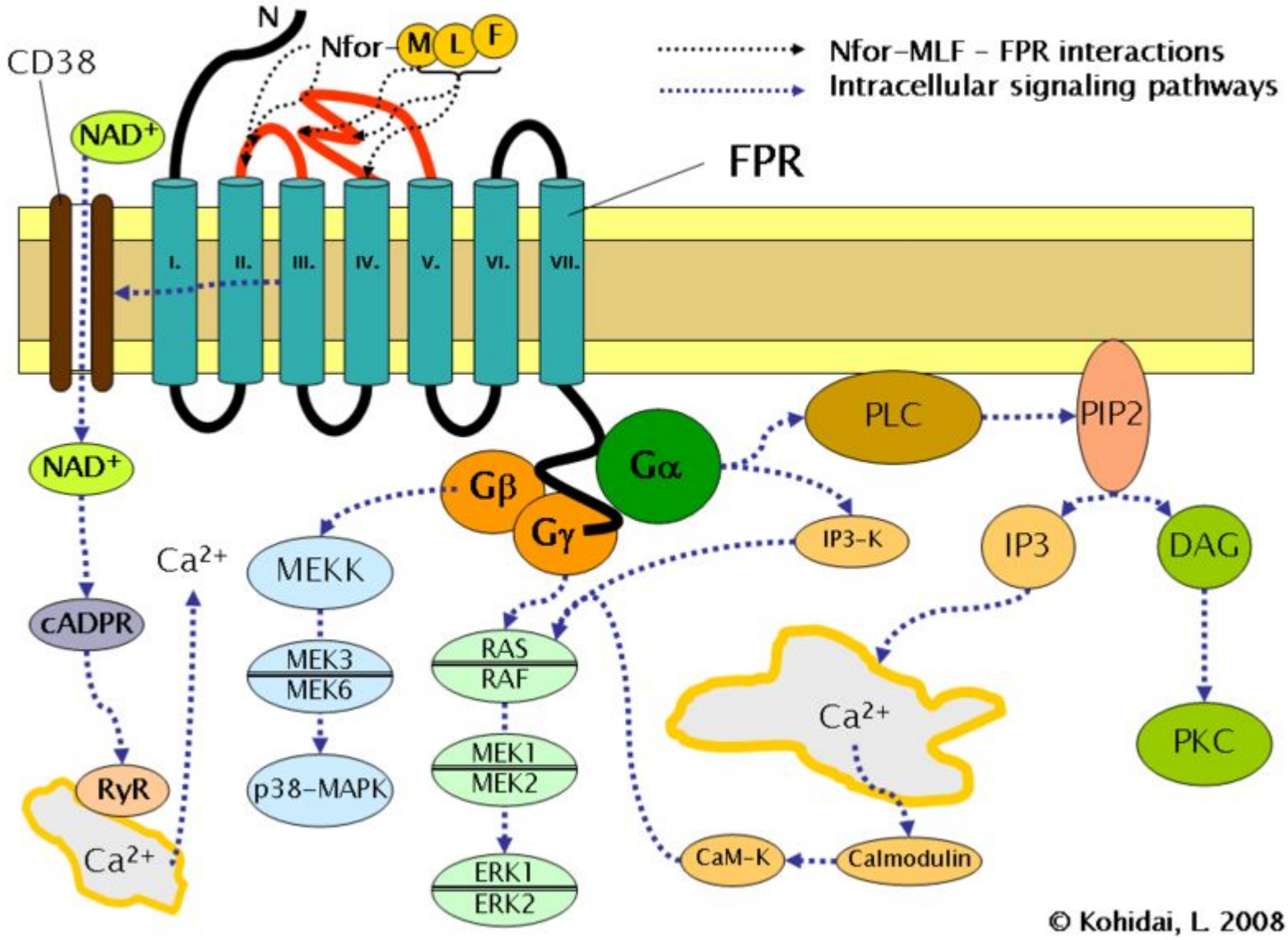
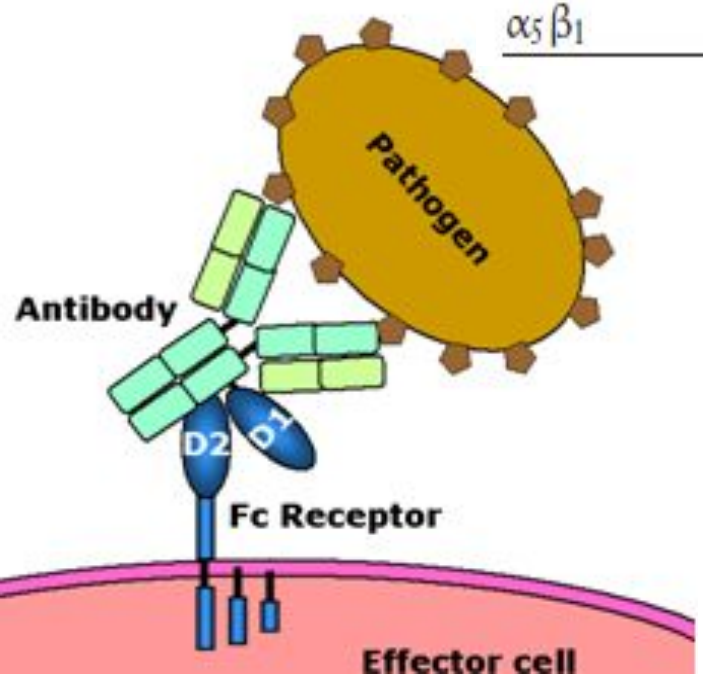


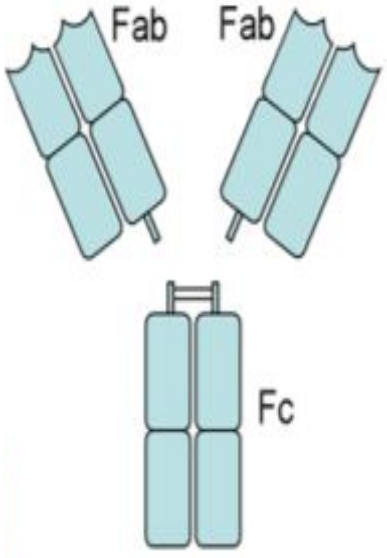
Fig. 1. Summary of the most important functions of SR in the innate immune defence and the role of SR in infections caused by intracellular pathogens such as HCV and *Plasmodium* spp. See text for details.

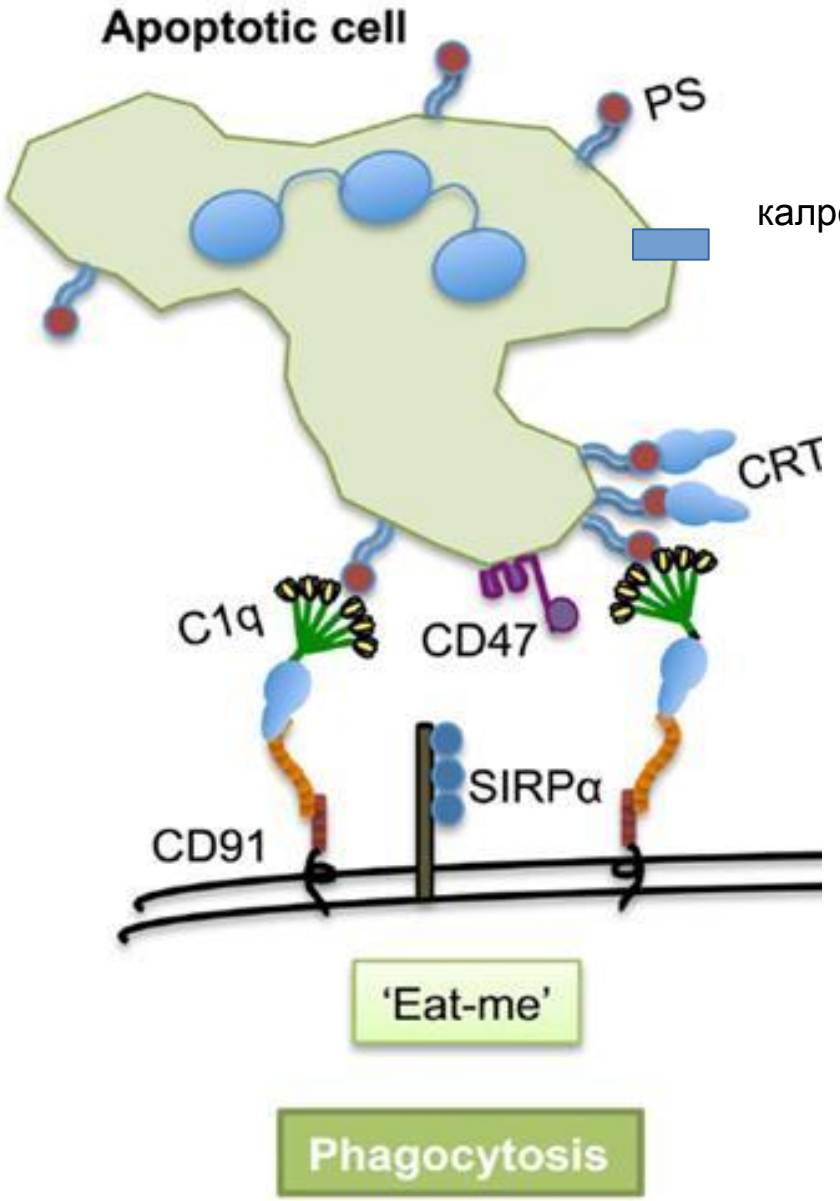
Рецептор к формилметионину



рецептор	опсонин
FcγRI (CD64)	IgG1 = IgG3 > IgG4
FcγRIIa (CD32a)	IgG3 ≥ IgG1 = IgG2
FcγRIIc (CD32c)	IgG
FcγRIIIa (CD16a)	IgG
FcαRI (CD89)	IgA1, IgA2
FcεRI	IgE
CR1 (CD45)	Mannan-binding lectin, C1q, C4b, C3b
CR3 ($\alpha_M\beta_2$, CD11b/CD18, Mac-1)	iC3b
CR4 ($\alpha_V\beta_2$, CD11c/CD18, gp150/95)	iC3b
$\alpha_5\beta_1$	Fibronectin, vitronectin



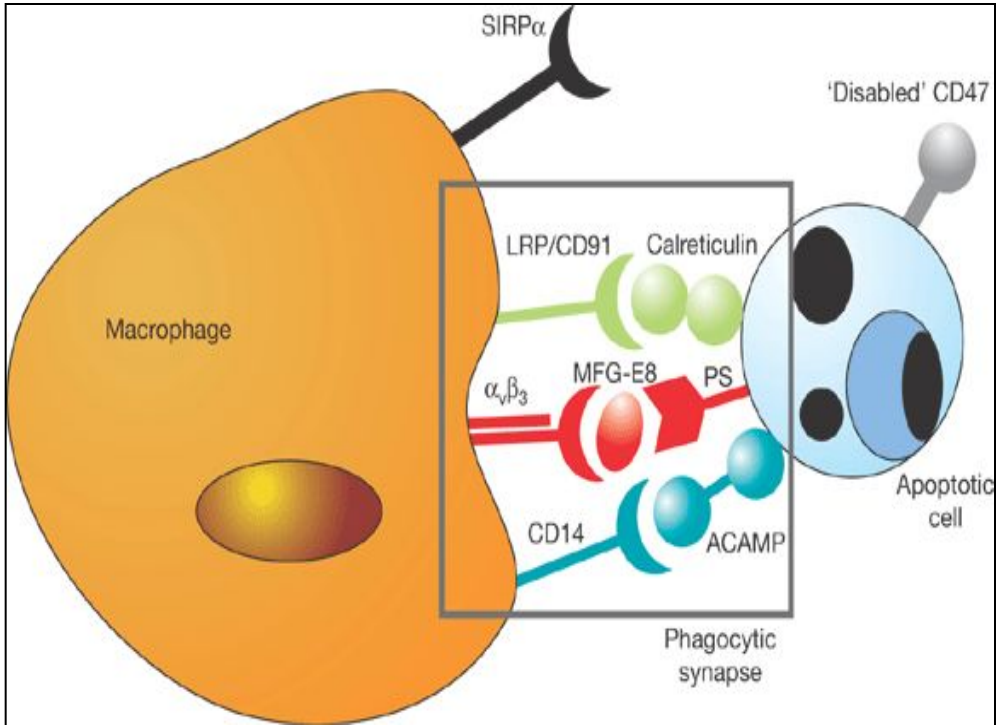


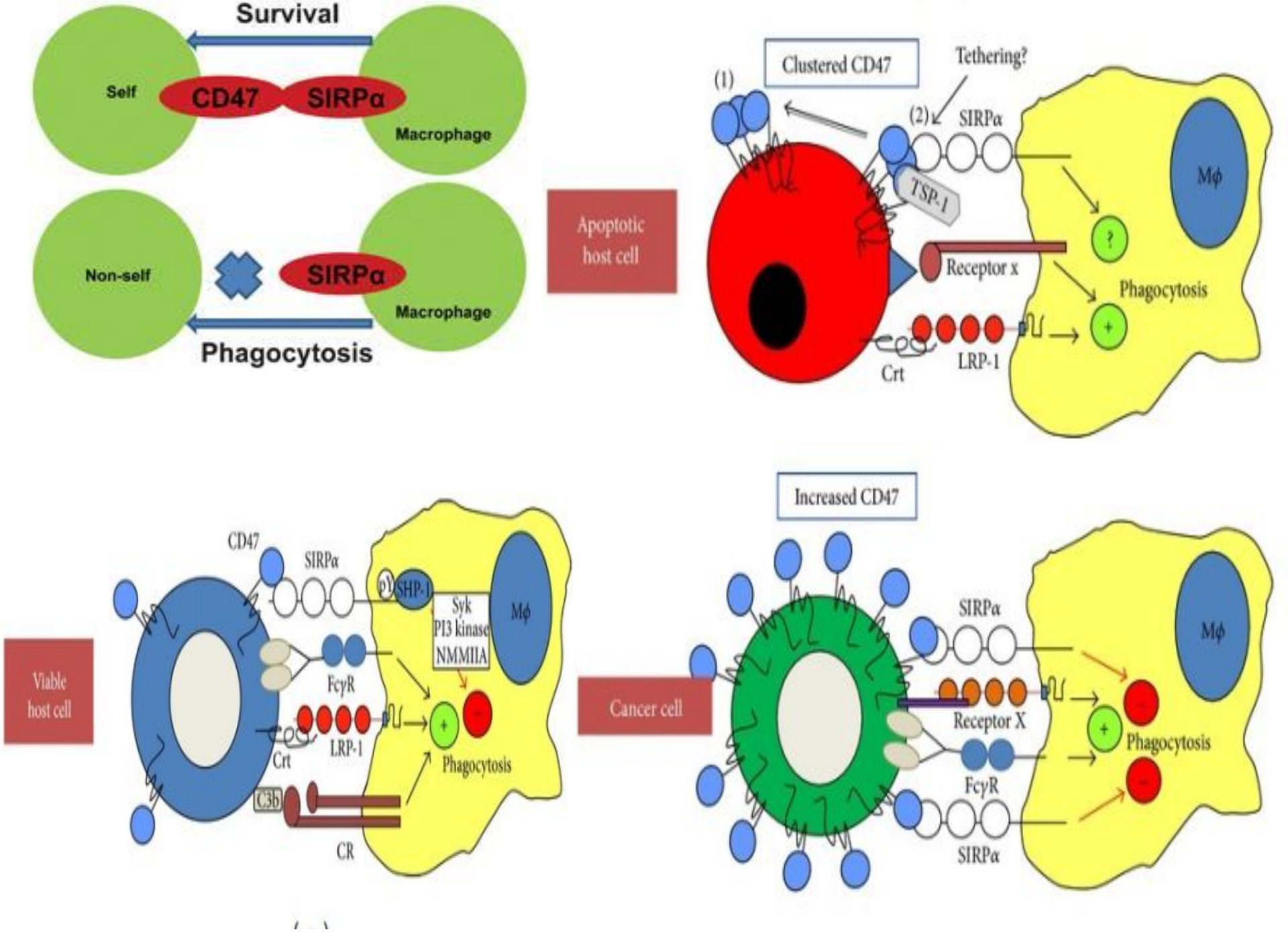


калретикулин

TIM-1	Phosphatidylserine
TIM-4	Phosphatidylserine
BAI1	Phosphatidylserine
Stabilin-2	Phosphatidylserine
Mer	Gas6, protein S
$\alpha_V \beta_3$	MFG-E8
$\alpha_V \beta_5$	Apoptotic cells
CD36	Oxidized lipids

Секретируется макрофагами




Survival
Self
CD47
SIRPα
Macrophage
Non-self
SIRPα
Macrophage
Phagocytosis
Apoptotic host cell
Clustered CD47
Tethering?
(1)
(2)
SIRPα
TSP-1
Mϕ
?
Receptor x
Phagocytosis
+
Crt
LRP-1
Viable host cell
CD47
SIRPα
pY
SHP-1
Syk
PI3 kinase
NMMIIA
Mϕ
FcγR
LRP-1
Crt
+
−
Phagocytosis
C3b
CR
Cancer cell
Increased CD47
SIRPα
Mϕ
Receptor X
+
−
Phagocytosis
FcγR
SIRPα

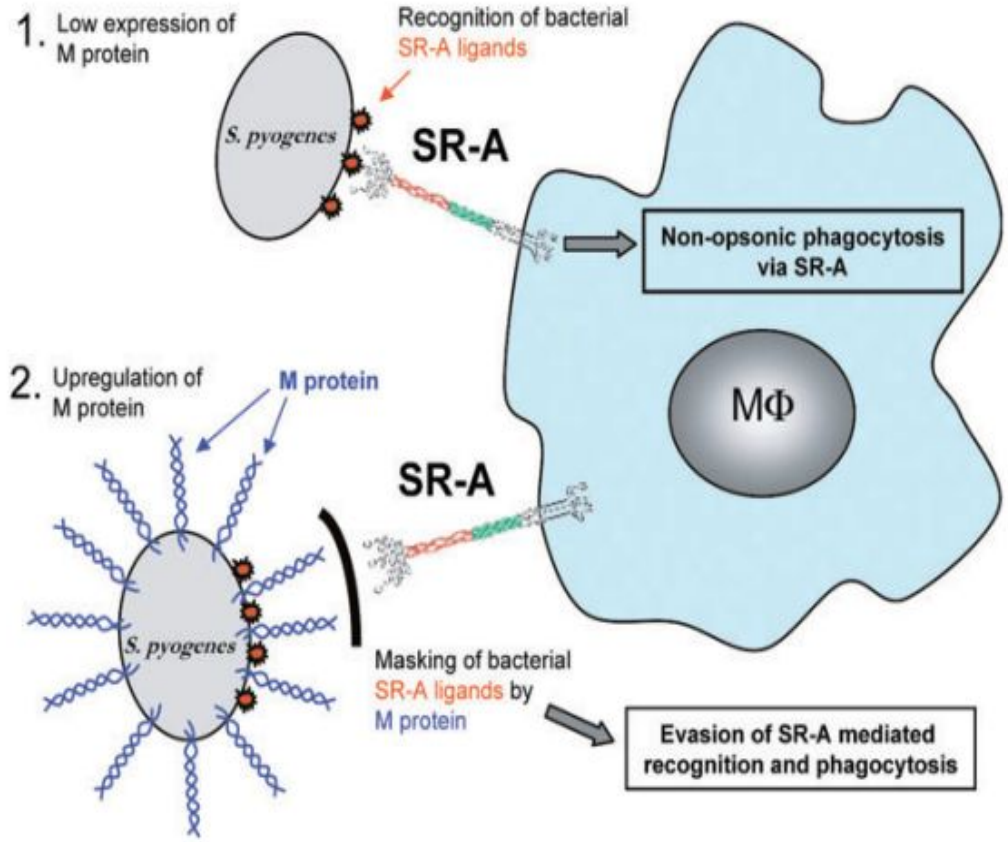


Fig. 2. Model of evasion mechanism in *Streptococcus pyogenes* to avoid SR-A-mediated recognition and non-opsonic phagocytosis by МФ. (1) At low expression of the surface M protein, the SR-A ligand(s) at the bacterial surface are exposed, resulting in SR-A-mediated recognition and phagocytosis. (2) When M protein is expressed at high levels, it prevents SR-A-mediated phagocytosis of *S. pyogenes* by masking the ligand(s) for SR-A at the bacterial surface. See text for references.

 Cellular Microbiology, **11**, 1160–1169

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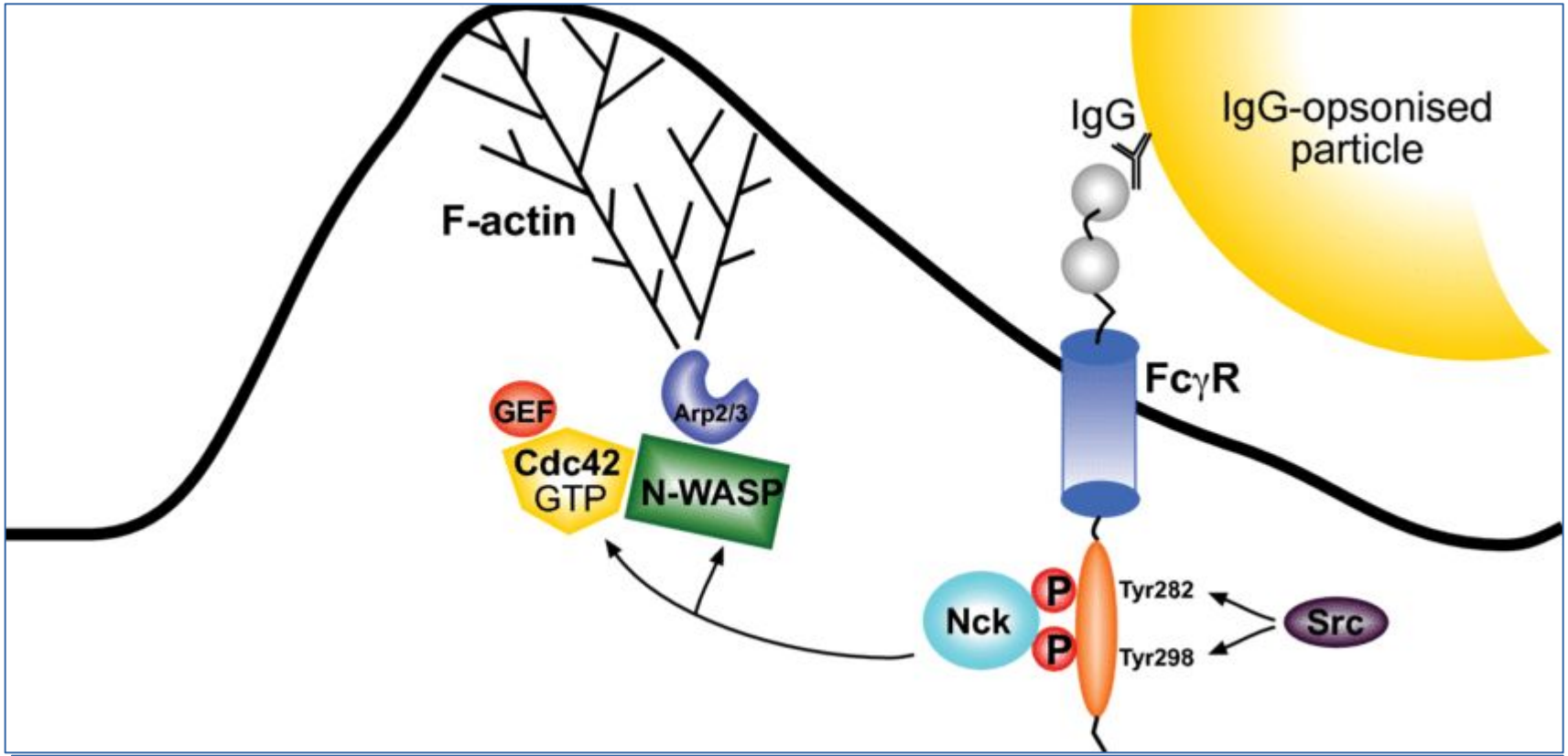
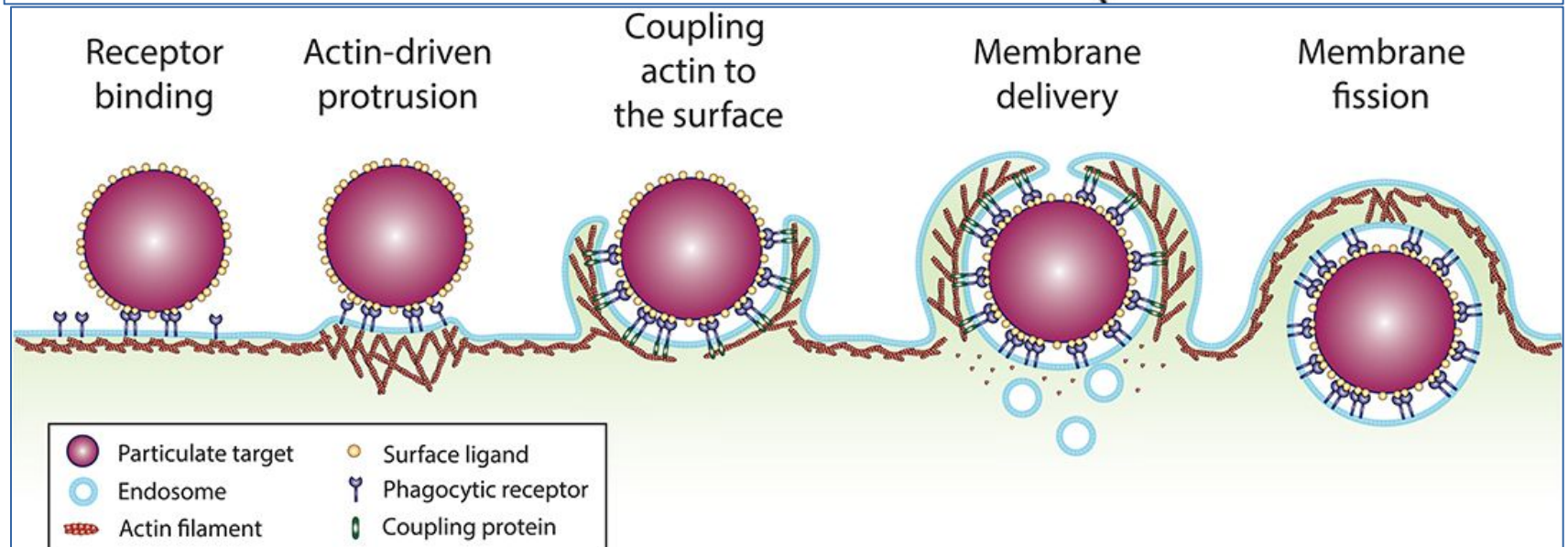
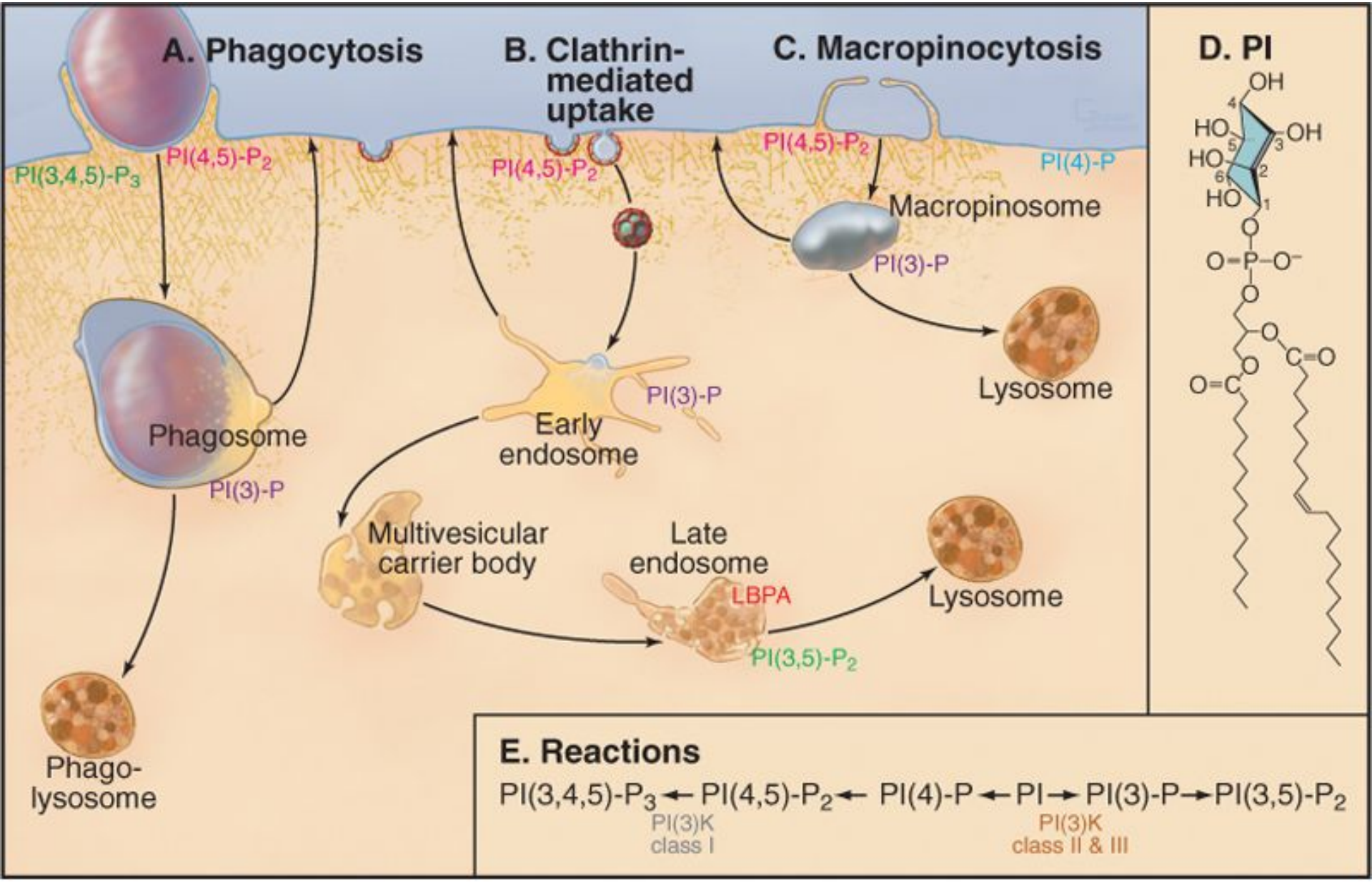
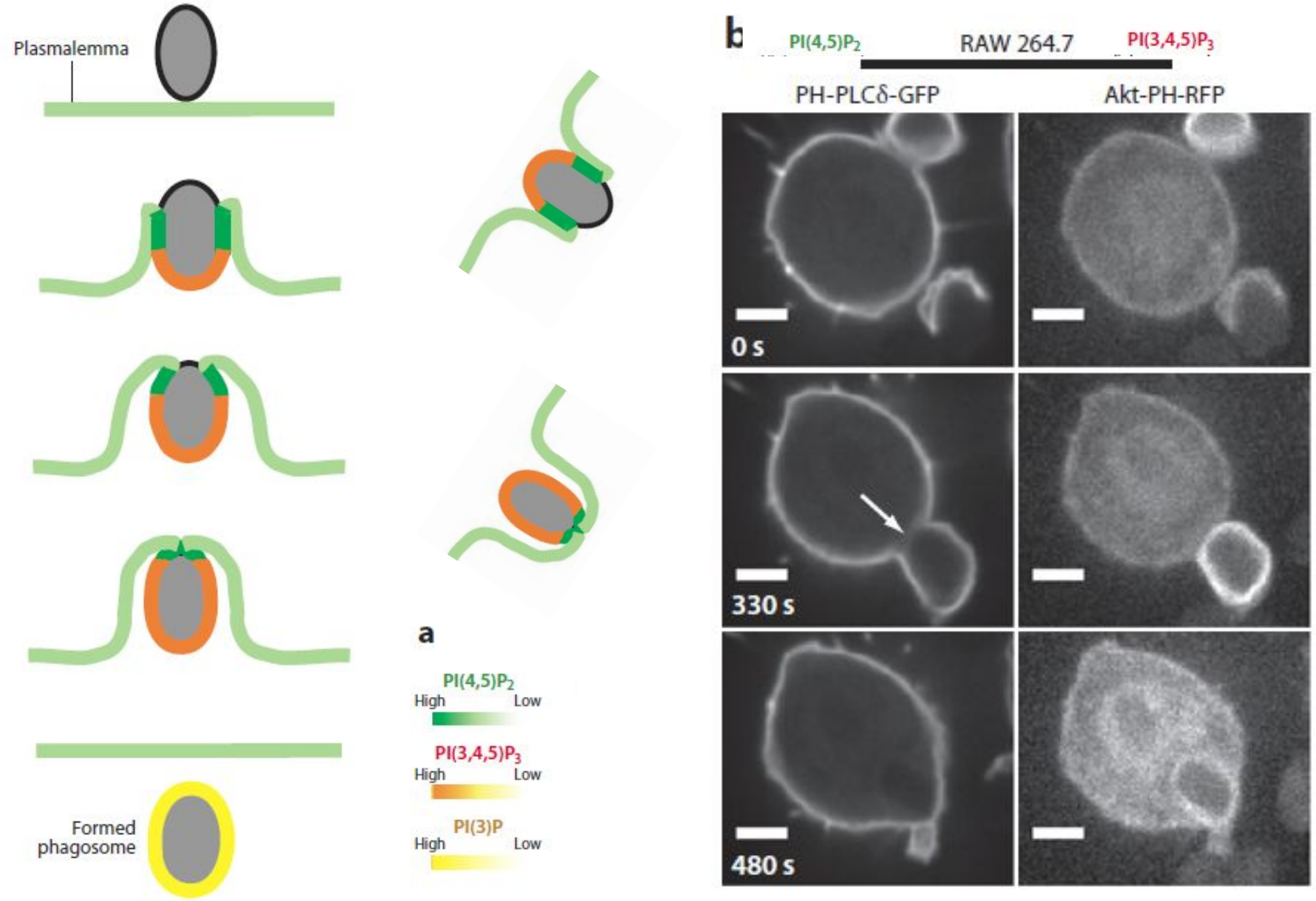
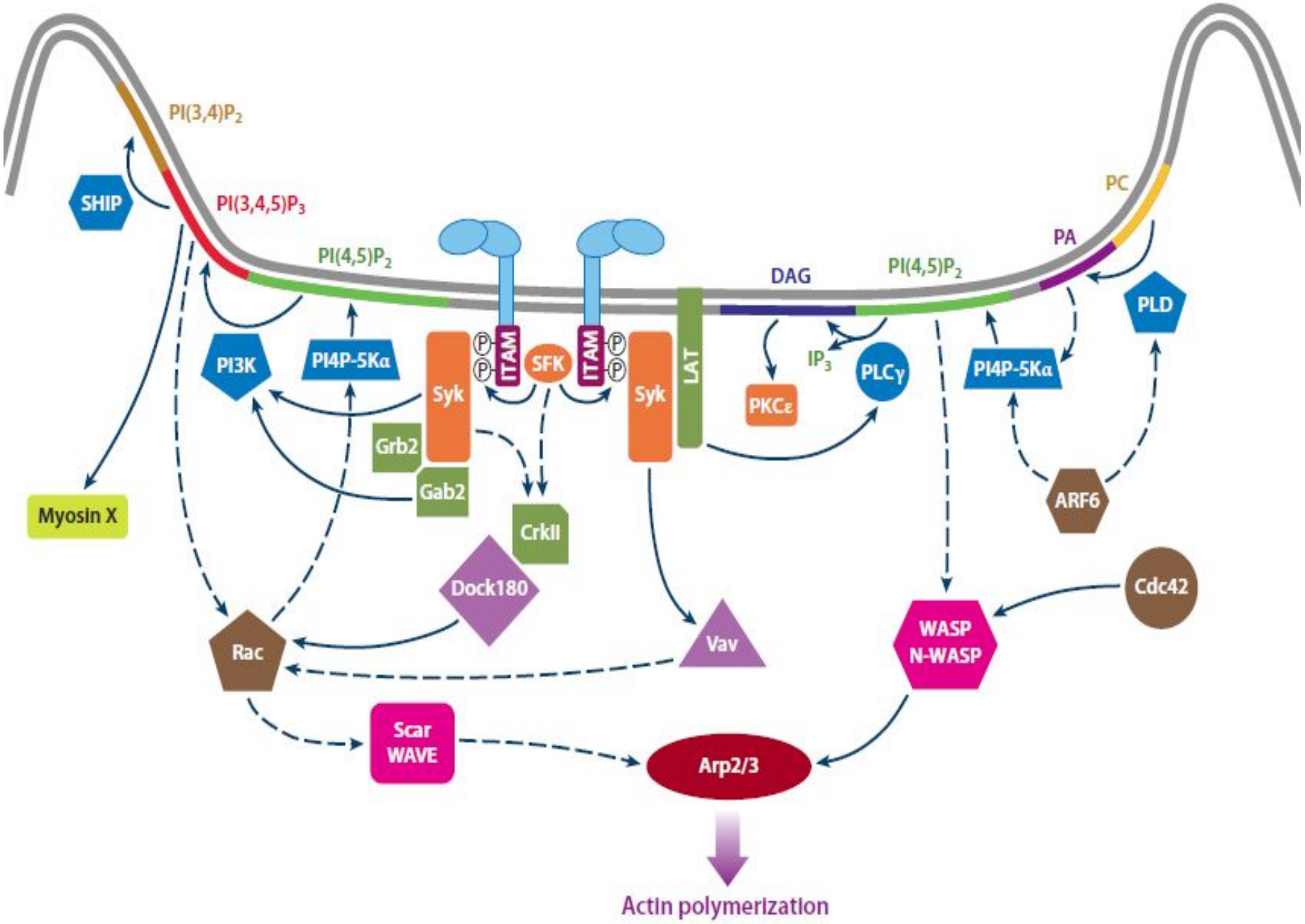
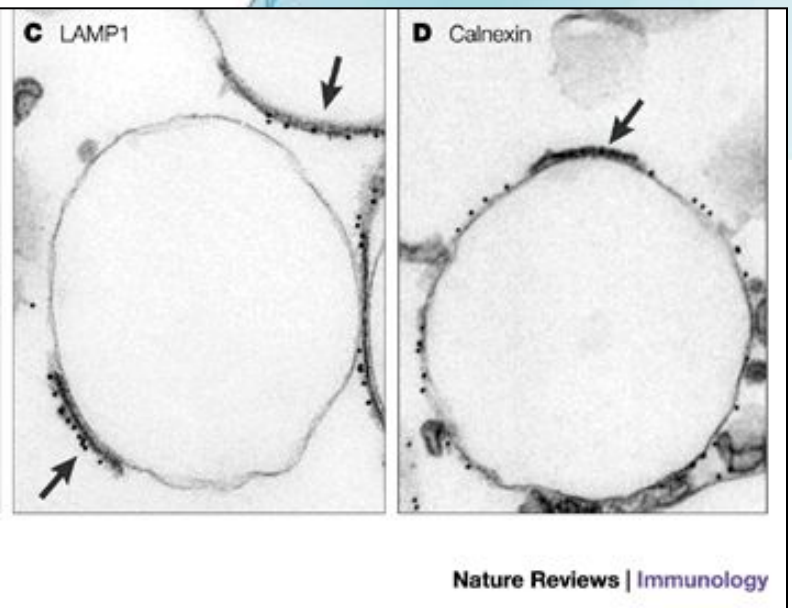

IgG
IgG-opsonised particle
F-actin
FcγR
GEF
Arp2/3
Cdc42
GTP
N-WASP
Nck
P
P
Tyr282
Tyr298
Src

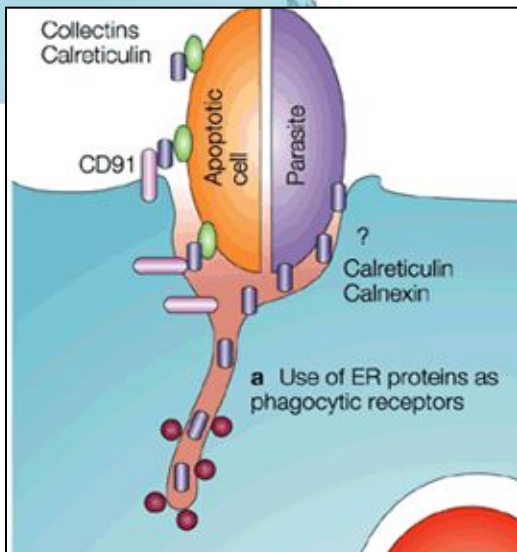

Receptor binding
Actin-driven protrusion
Coupling actin to the surface
Membrane delivery
Membrane fission
Particulate target
Endosome
Actin filament
Surface ligand
Phagocytic receptor
Coupling protein

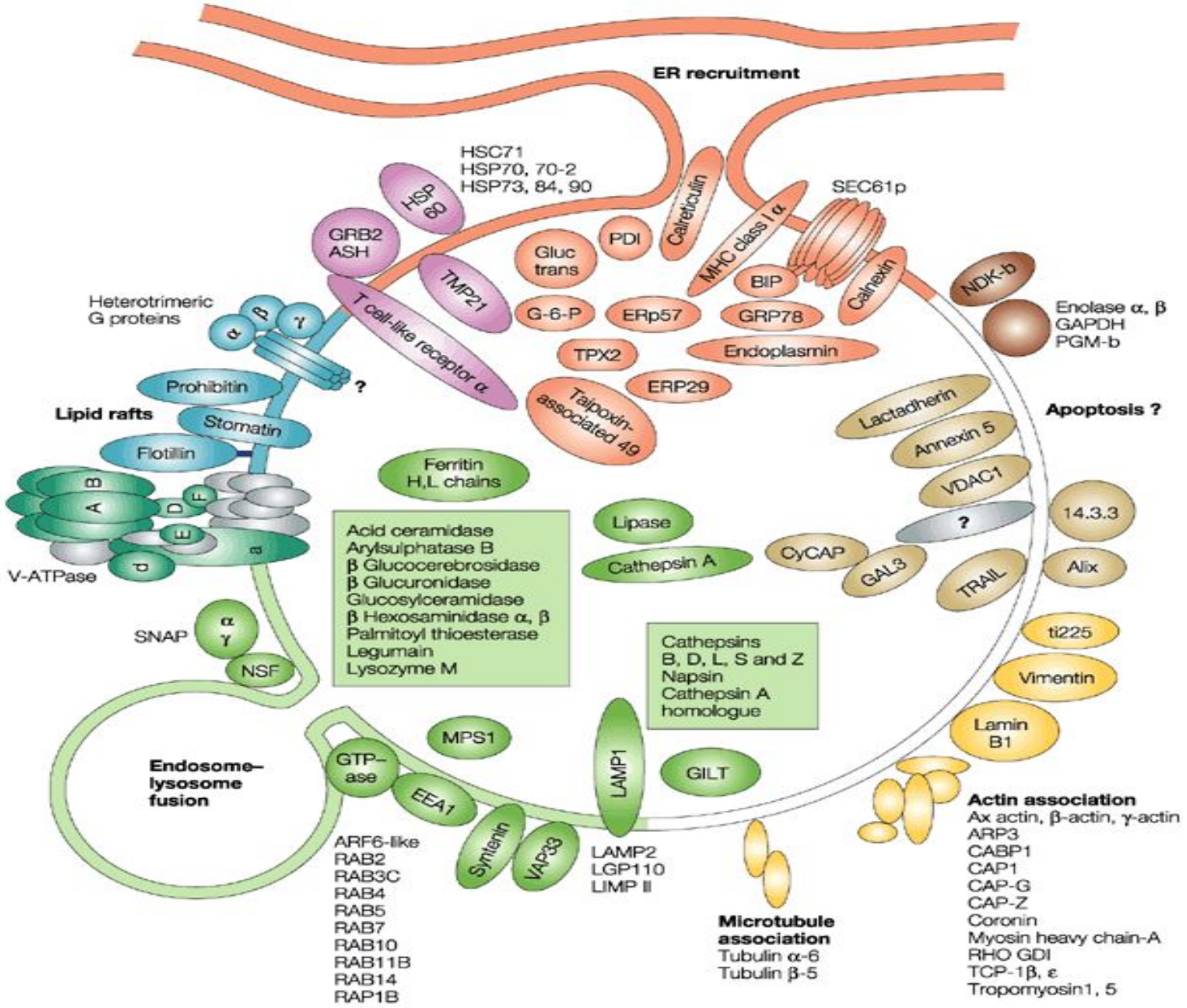


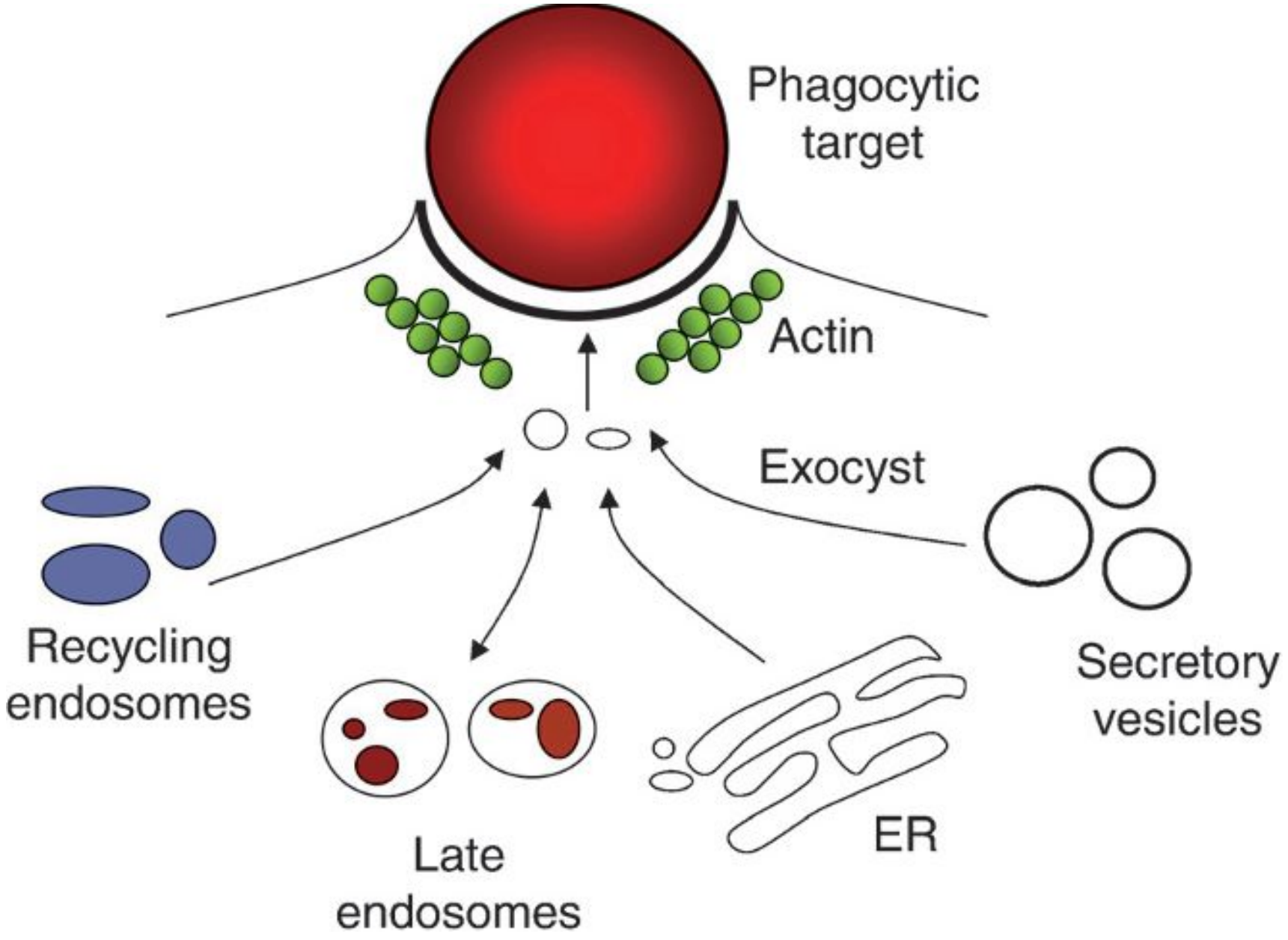

Plasmalemma
Formed phagosome
a
PI(4,5)P2
High
Low
PI(3,4,5)P3
High
Low
PI(3)P
High
Low
b
PI(4,5)P2
RAW 264.7
PI(3,4,5)P3
PH-PLCδ-GFP
Akt-PH-RFP
0 s
330 s
480 s


PI(3,4)P2
SHIP
PI(3,4,5)P3
PI(4,5)P2
DAG
PI(4,5)P2
PC
PA
PLD
PI3K
PI4P-5Kα
ITAM
SFK
ITAM
Syk
LAT
Syk
IP3
PLCγ
PKCε
PI4P-5Kα
Grb2
Gab2
CrkII
ARF6
Myosin X
Dock180
Cdc42
Rac
Vav
WASP
N-WASP
Scar
WAVE
Arp2/3
Actin polymerization

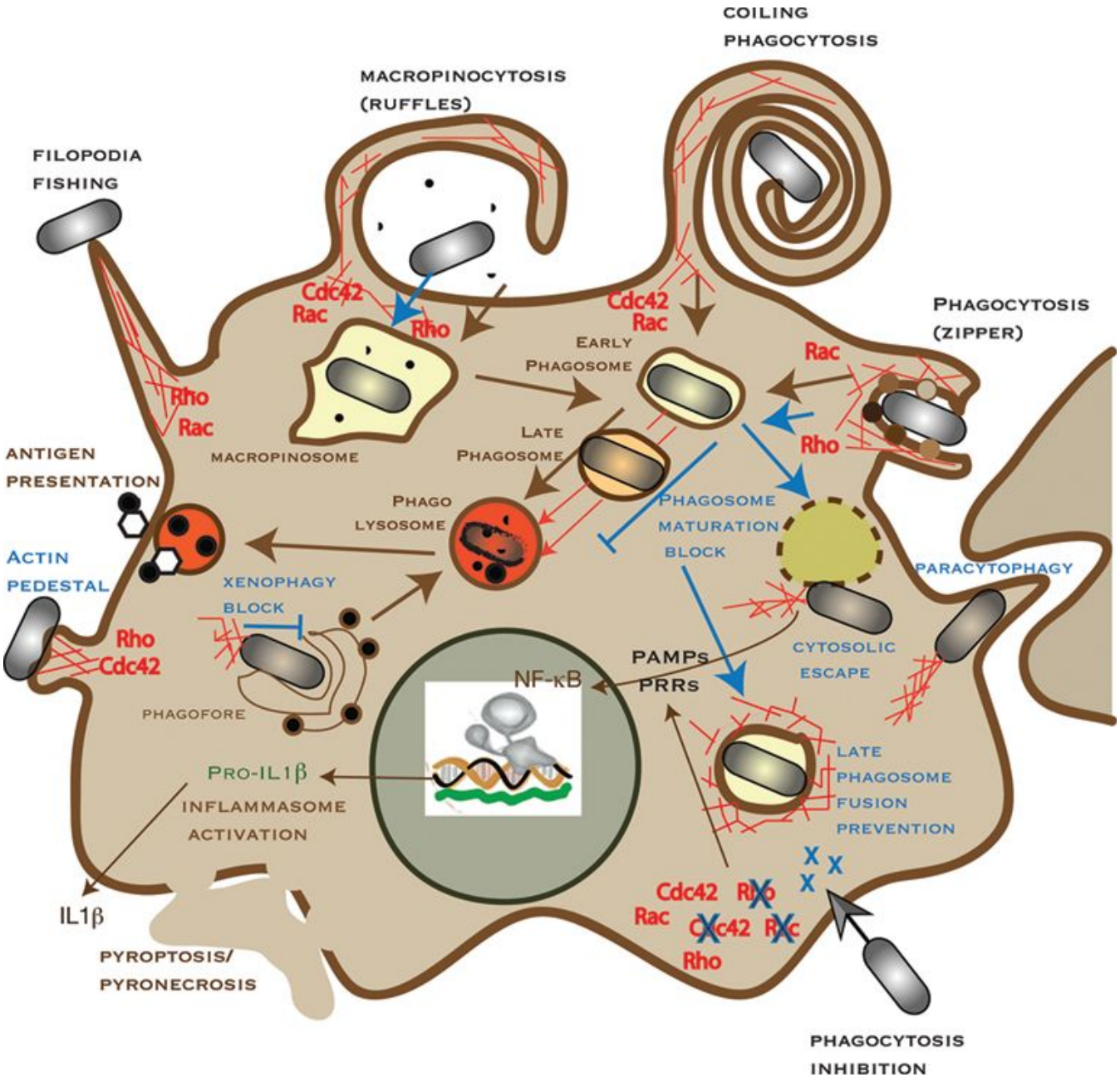

C LAMP1
D Calnexin
Nature Reviews | Immunology


Collectins
Calreticulin
CD91
Apoptotic cell
Parasite
?
Calreticulin
Calnexin
a Use of ER proteins as phagocytic receptors


ER recruitment
HSC71
HSP70, 70-2
HSP73, 84, 90
HSP 90
GRB2
ASH
Calreticulin
MHC class I α
SEC61p
Gluc trans
PDI
TMP21
BIP
Calnexin
NDK-b
Enolase α, β
GAPDH
PGM-b
G-6-P
ERp57
GRP78
Heterotrimeric
G proteins
α
β
γ
T cell-like receptor α
TPX2
Endoplasmin
ERP29
Taipoxin-associated 49
Prohibitin
?
Lipid rafts
Stomatin
Flotillin
Lactadherin
Annexin 5
Apoptosis ?
VDAC1
Ferritin
H,L chains
A
B
D
F
E
a
b
V-ATPase
Acid ceramidase
Arylsulphatase B
β Glucocerebrosidase
β Glucuronidase
Glucosylceramidase
β Hexosaminidase α, β
Palmitoyl thioesterase
Legumain
Lysozyme M
Lipase
Cathepsin A
CyCAP
GAL3
?
14.3.3
TRAIL
Alix
SNAP
α
γ
NSF
Cathepsins
B, D, L, S and Z
Napsin
Cathepsin A
homologue
ti225
Vimentin
Lamin
B1
MPS1
GTP–
ase
EEA1
Endosome–
lysosome
fusion
LAMP1
GILT
Actin association
Ax actin, β-actin, γ-actin
ARP3
CABP1
CAP1
CAP-G
CAP-Z
Coronin
Myosin heavy chain-A
RHO GDI
TCP-1β, ε
Tropomyosin1, 5
Syntenin
VAP33
ARF6-like
RAB2
RAB3C
RAB4
RAB5
RAB7
RAB10
RAB11B
RAB14
RAP1B
LAMP2
LGP110
LIMP II
Microtubule
association
Tubulin α-6
Tubulin β-5


Phagocytic target
Actin
Exocyst
Recycling endosomes
Secretory vesicles
Late endosomes
ER

Механизмы захвата



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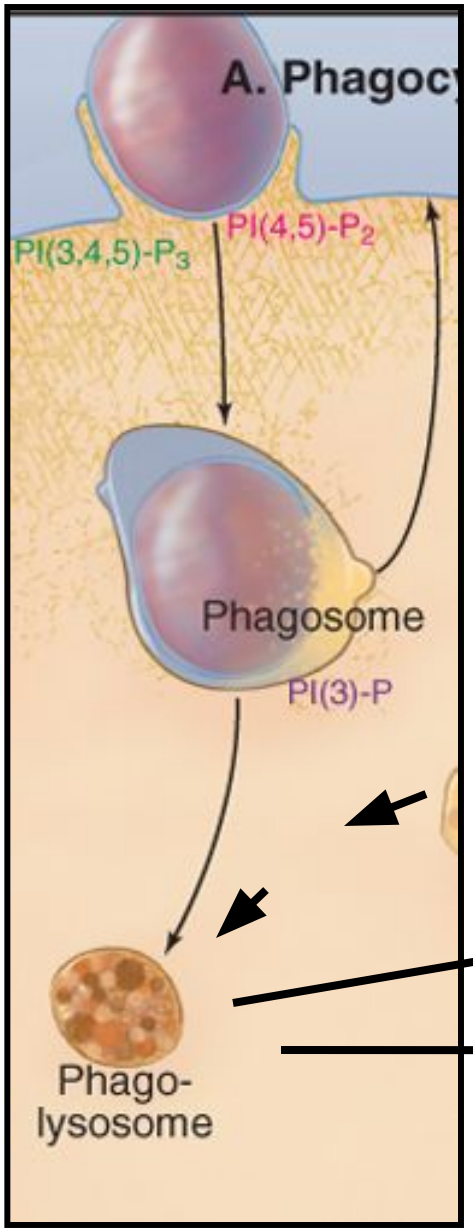
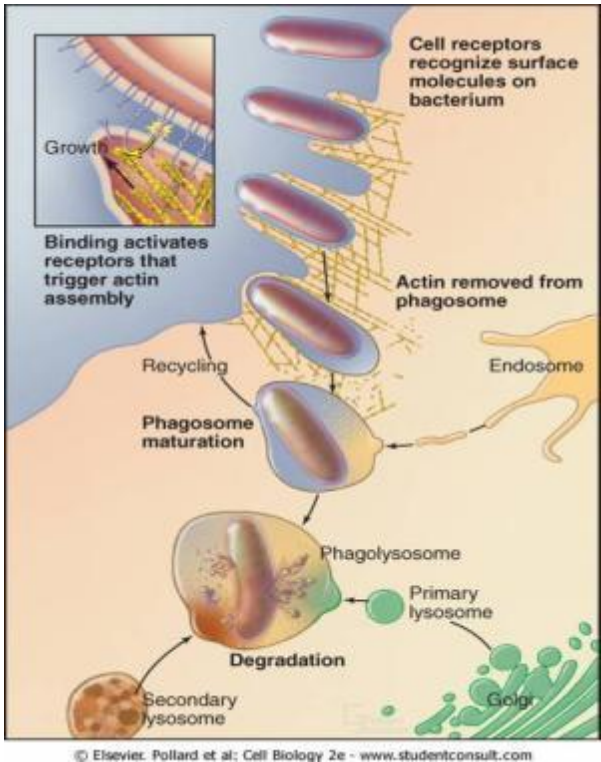


PI(4)-P ← PI → PI(3)-P → PI(3,5)-P_2

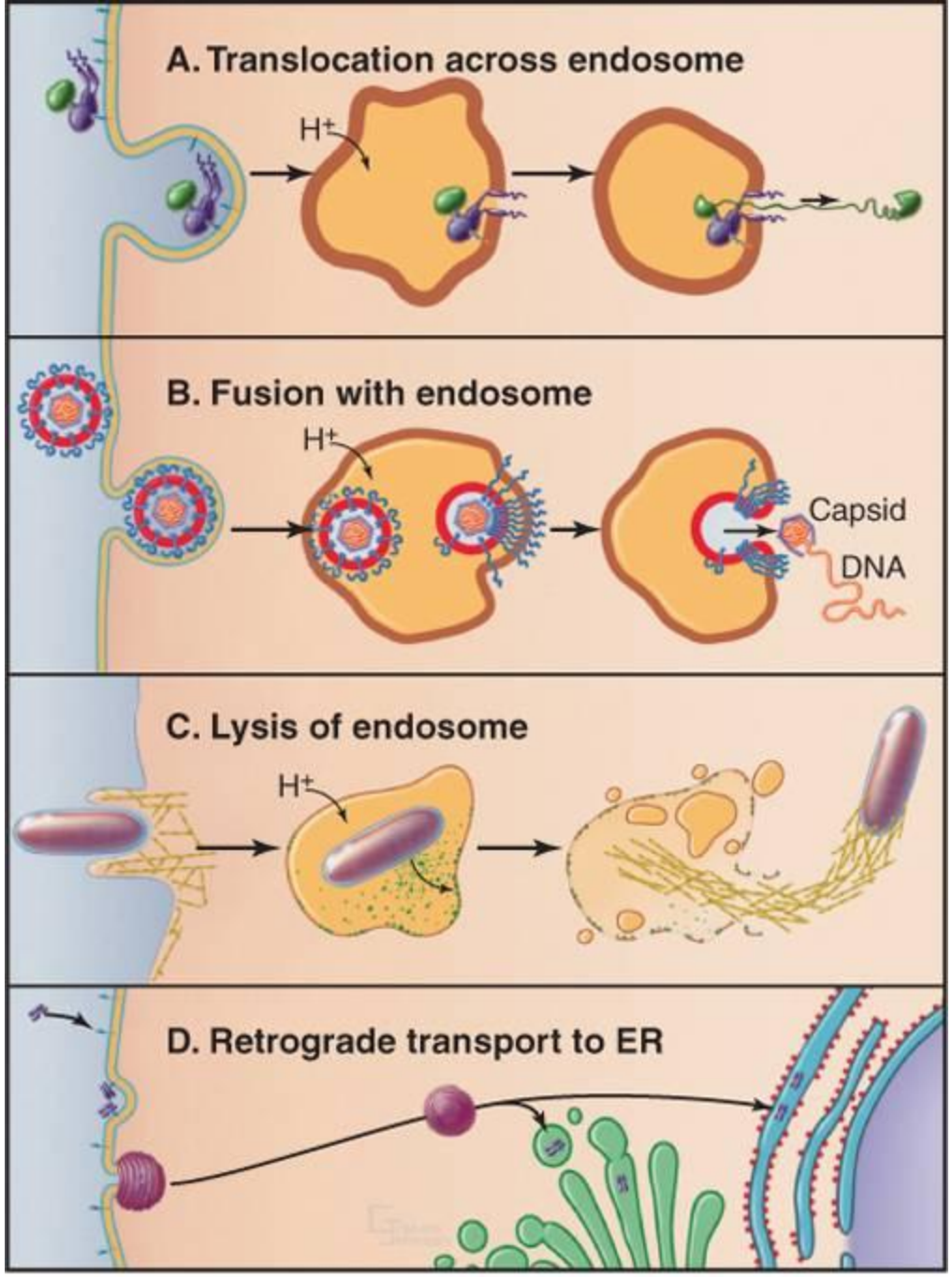
PI(3)K
class II & III

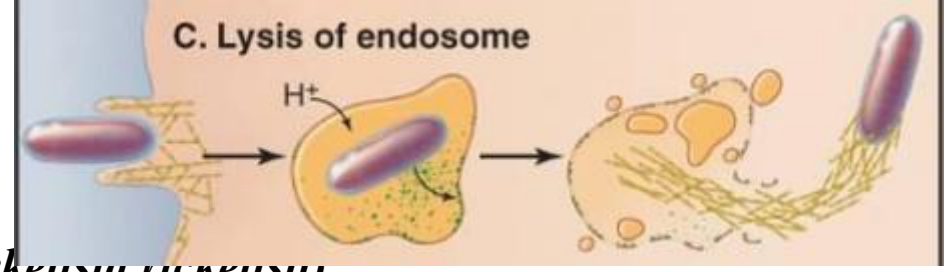
Расщепление содержимого фаголизосом

- Активные формы кислорода (NADPH-оксидаза)
- Галоидсодержащие соединения (миелопероксидаза)
- Азотистые метаболиты (NO-синтаза)
- Катионные белки (лизоцим, серпроцидины, лактоферрин, BPI-протеины)
- Бактерицидные пептиды (дефензины, кателицидины)
- Факторами, обеспечивающие локальное закисление (V-АТФаза)
- Другие ферменты



Способы выживания





"Escape "

Секреция токсинов, которые разрушают мембрану фагосом *(Shigella flexneri, Listeria monocytogenes, Rickettsia rickettsii)*

"Dodge"

Вход в клетку через альтернативный, патоген-специфичный путь *(Salmonella typhimurium, Legionella pneumophila, Chlamydia trachomatis)*

Ингибирование слияния фагосомы с лизосомами *(S. typhimurium, Mycobacterium tuberculosis)*

Ингибирование закисления фаголизосомы (*Mycobacterium* species)

"Stand and Fight"

Репликация при низком pH *(Coxiella burnetii, S. typhimurium)*

Усиление рапарации ДНК – выживание при оксидативном стрессе *(S. typhimurium)*

Защита с помощью патогенспецифичных факторов *(C. burnetii, S. typhimurium)*

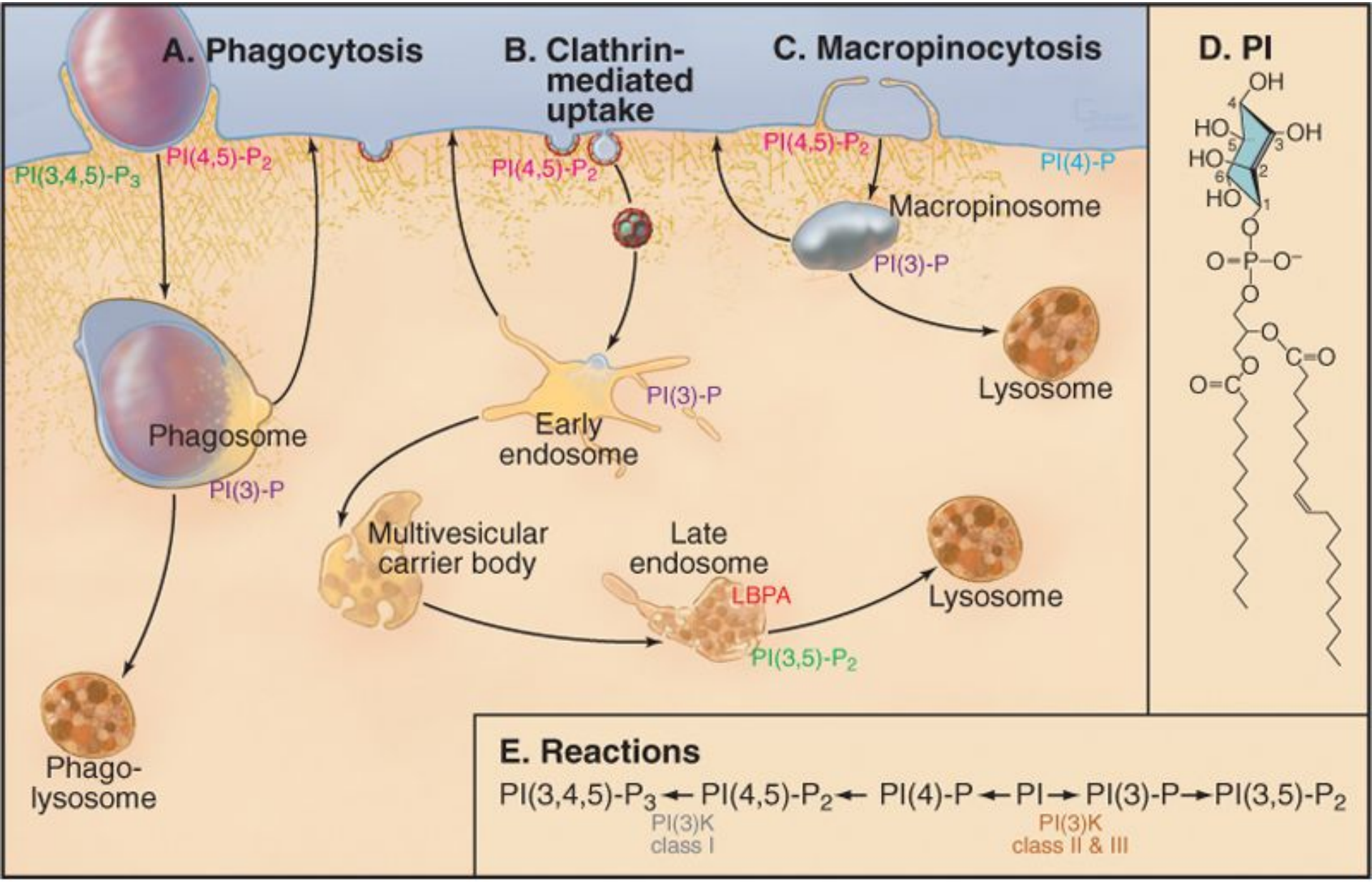
Нарушение процессинга и презентации бактериальных антигенов *(S. typhimurium)*

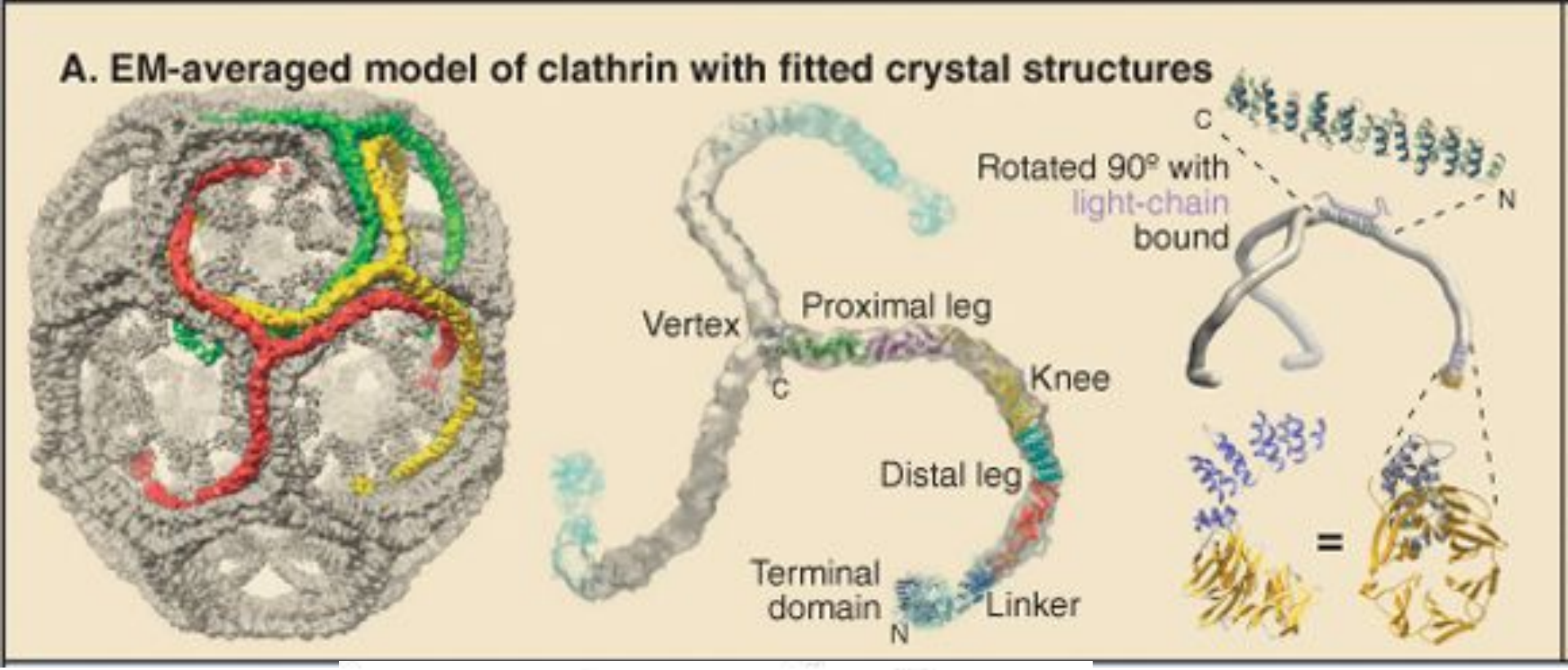
Effectors	Functions	Species
Inhibition of attachment		
Protein A	Binds Fc region, preventing normal interaction with FcγR	*Staphylococcus aureus*
Capsule	Prevents complement deposition	*Cryptococcus neoformans*, *Streptococcus pneumoniae*, *Escherichia coli* K1, *Klebsiella pneumoniae*, *Neisseria meningitidis*, *S. aureus*, *Haemophilus influenzae*, *Treponema pallidum*
M proteins	Prevents binding to CRs	*Streptococcus pyogenes*
YadA	Prevents deposition of C3b	*Yersinia enterocolitica*
Inhibition of signaling		
YopH	Tyrosine phosphatase for Cas, Fyb, SKAP-HOM, paxillin, and FAK	*Yersinia* sp.
YopE	GAP for RhoA, Rac, and Cdc42	*Yersinia* sp.
YopT	Cysteine protease of Rho, Rac, and Cdc42	*Yersinia* sp.
YpkA (YopO)	Serine/threonine kinase of actin, RhoA, and Rac	*Yersinia* sp.
ExoT	GAP for RhoA, Rac, and Cdc42	*Pseudomonas aeruginosa*
ExoS	GAP for RhoA, Rac, and Cdc42	*Pseudomonas aeruginosa*
EspJ	Inhibits FcγR- and CR3-mediated phagocytosis	*Escherichia coli*
EspB	Inhibits myosin–actin interactions	*Escherichia coli*
EspH	Inactivates Rho GEFs	*Escherichia coli*
T4SS	Delays phagocytosis	*Helicobacter pylori*
LspA1 and -2	Inhibit Src-family kinases	*Haemophilus ducreyi*
Nef	Inhibits membrane delivery to the phagosome	HIV-1

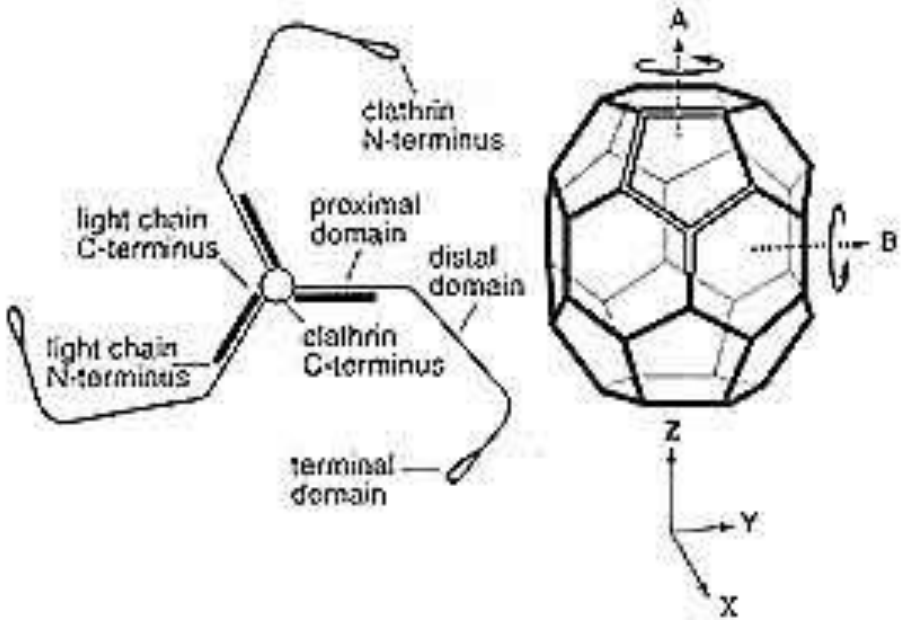
Table 3 Representative human pathogens and the biochemical properties of pathogen-containing phagosom

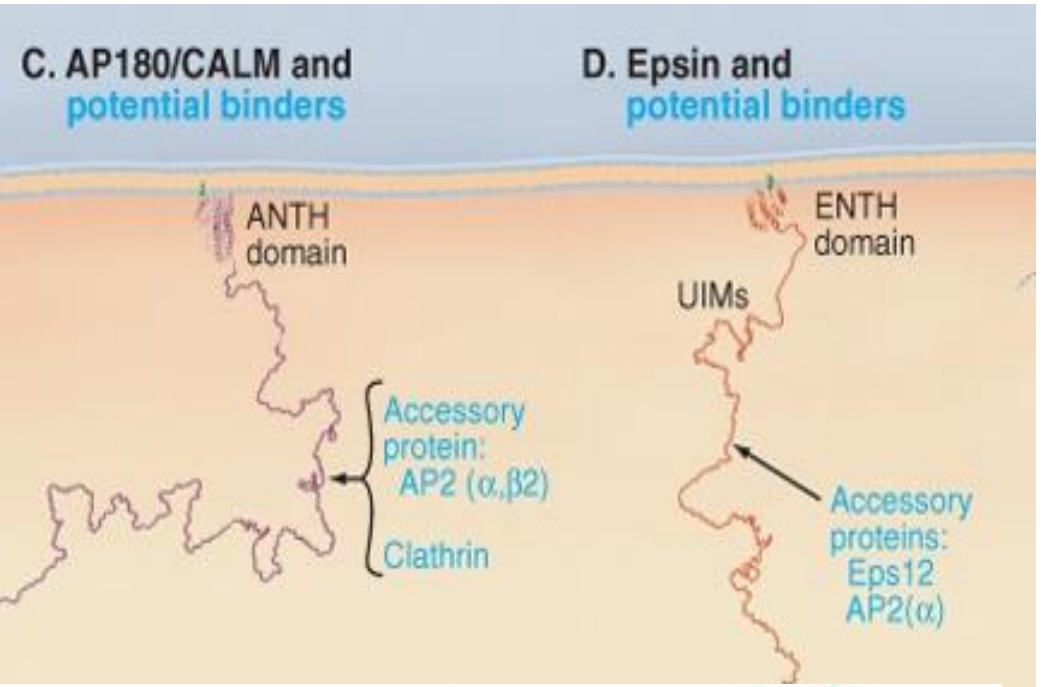
Strategy	Organism	Mechanisms of survival and phagosome properties
Altered phagosome maturation	*Mycobacterium tuberculosis*	Phagosome is mildly acidic and continuously interacts with recycling endosomes bearing the TfRs that provide the bacteria with iron *M. tuberculosis*–containing phagosomes are Rab5 positive but devoid of PI(3)P and EEA1
		Maturation arrest is mediated by the expression of numerous effector proteins (e.g., SapM and PknG) and lipids (e.g., lipoarabinomannan)
	Burkholderia cenocepacia	Delay maturation of their vacuole
		B. cenocepacia–containing phagosomes acquire early markers [i.e., Rab5, PI(3)P, and EEA1], but Rab7 activation and phagosome acidification are perturbed
		LAMP proteins are eventually acquired, indicating lysosomal fusion
		Require the expression of unknown bacterial effectors secreted through type IV and/or type VI secretion systems
	Coxiella burnetii	Internalized *C. burnetii* transit through Rab5- and Rab7-positive compartments Ultimately reside within an acidic lysosome-like compartment Bacteria-containing vacuole acquires markers of autophagy (e.g., LC3), indicating intersection with autophagosomes, ostensibly for nutrient acquisition
	Histoplasma capsulatum	Evade formation of late phagosomes and phagolysosome fusion Perturb V-ATPase activity, blocking acidification, which prevents vesicular fusion and the acquisition of lysosomal markers (i.e., LAMP-2)
	Leishmania donovani and *L. major*	*Leishmania* spp. impair phagosome maturation by blocking the fusion of late endosomes and lysosomes The blockade in maturation requires the expression of a unique surface glycolipid, LPG F-actin accumulation around the parasite-containing phagosome also occurs in an LPG-dependent manner, ostensibly to form a cage that blocks fusion of late endosomes and lysosomes

Strategy	Organism	Mechanisms of survival and phagosome properties
	Theileria parva	Rapidly escape phagosomes through an unknown mechanism and replicate in the cytosol Induce uncontrolled proliferation of infected cells, and through the expression of the protein TaSE, attach to host cell microtubules to disseminate between daughter cells
Genesis of a unique vacuole	*Chlamydia trachomatis*	Upon phagocytosis, *C. trachomatis* construct a unique vacuole, termed the inclusion, in which the bacteria replicate Inclusion is devoid of early and late phagosome markers (Rab5 and Rab7, respectively) and does not resemble a proper phagosome
		Many effector proteins (e.g., IncA) are required for *C. trachomatis* to usurp host cell functions and to construct its inclusion
	Toxoplasma gondii	Invade phagocytes and reside in a unique vacuole that, although derived from the host cell plasma membrane, is largely devoid of host transmembrane proteins The vacuole does not acidify, and *T. gondii* induces the formation of a pore in its vacuole to gain access to diffusible nutrients from the host Host cell microfilaments and vimentin associate with the *T. gondii*–containing vacuole, ostensibly to dock it in proximity
Phagosome lysis	*Listeria monocytogenes*	Express a pore-forming toxin, LLO, that in conjunction with various lipases solubilizes the limiting membrane of the phagosome Maturation of the phagosome is rapidly prevented by LLO-dependent pore formation and perturbation of luminal H^+ and Ca^{2+} concentrations
	Shigella flexneri	Lyse phagosomes in which they reside, entering the cytosol and disseminating via actin-based motility Phagosome escape requires the function of the Mxi-Spa type III secretion system and the secreted effector proteins IpaB, IpaC, and IpaD

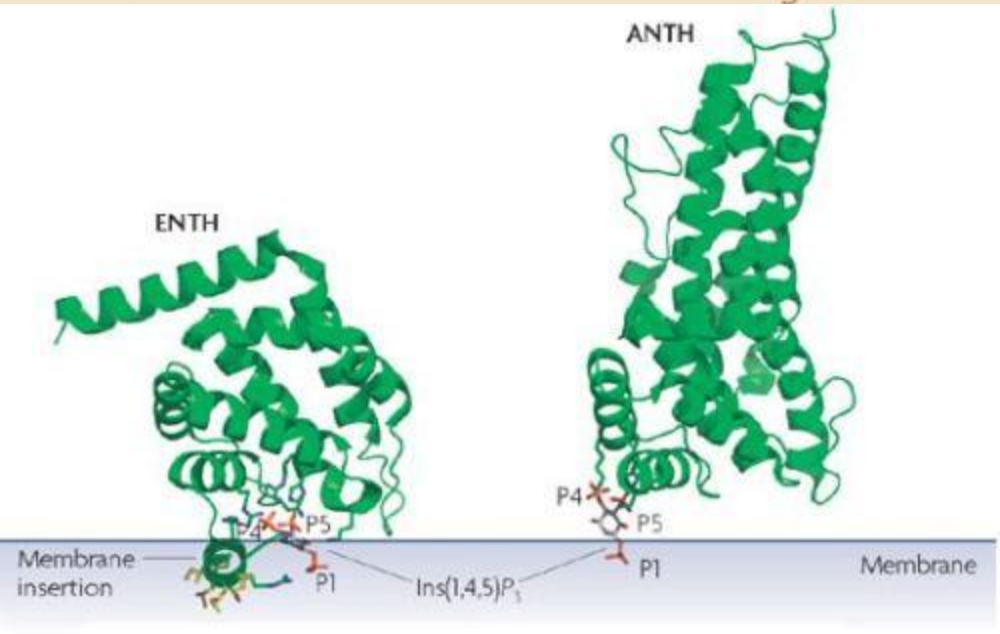


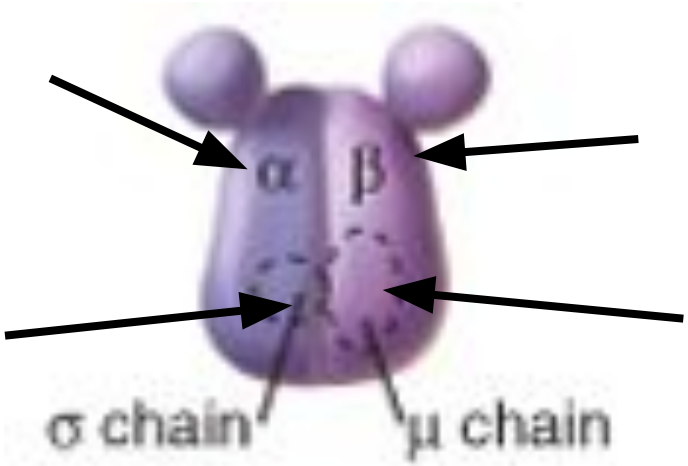

A. EM-averaged model of clathrin with fitted crystal structures
Vertex
Proximal leg
Knee
Distal leg
Terminal domain
Linker
C
N
Rotated 90° with light-chain bound
C
N
=

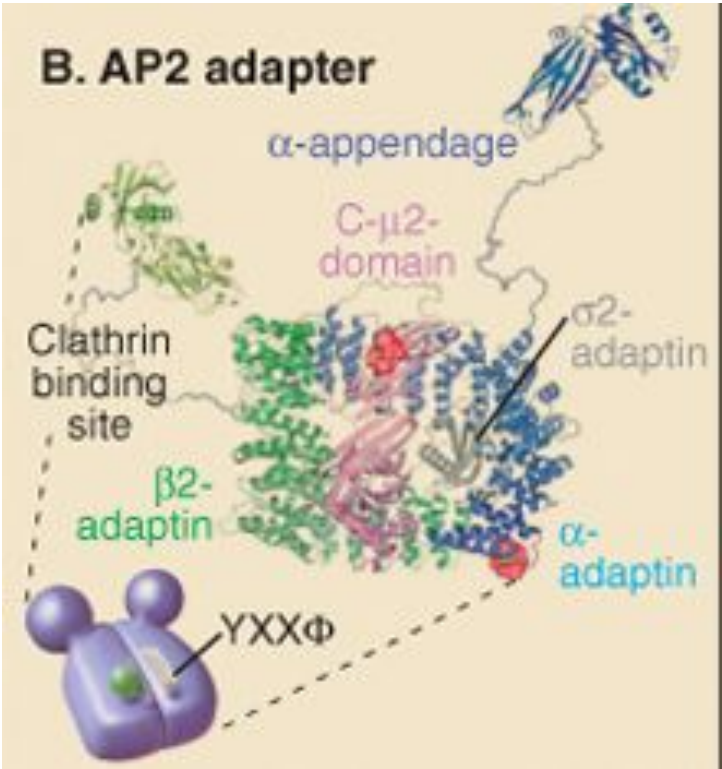

clathrin N-terminus
light chain C-terminus
proximal domain
distal domain
light chain N-terminus
clathrin C-terminus
terminal domain
A
B
Z
Y
X

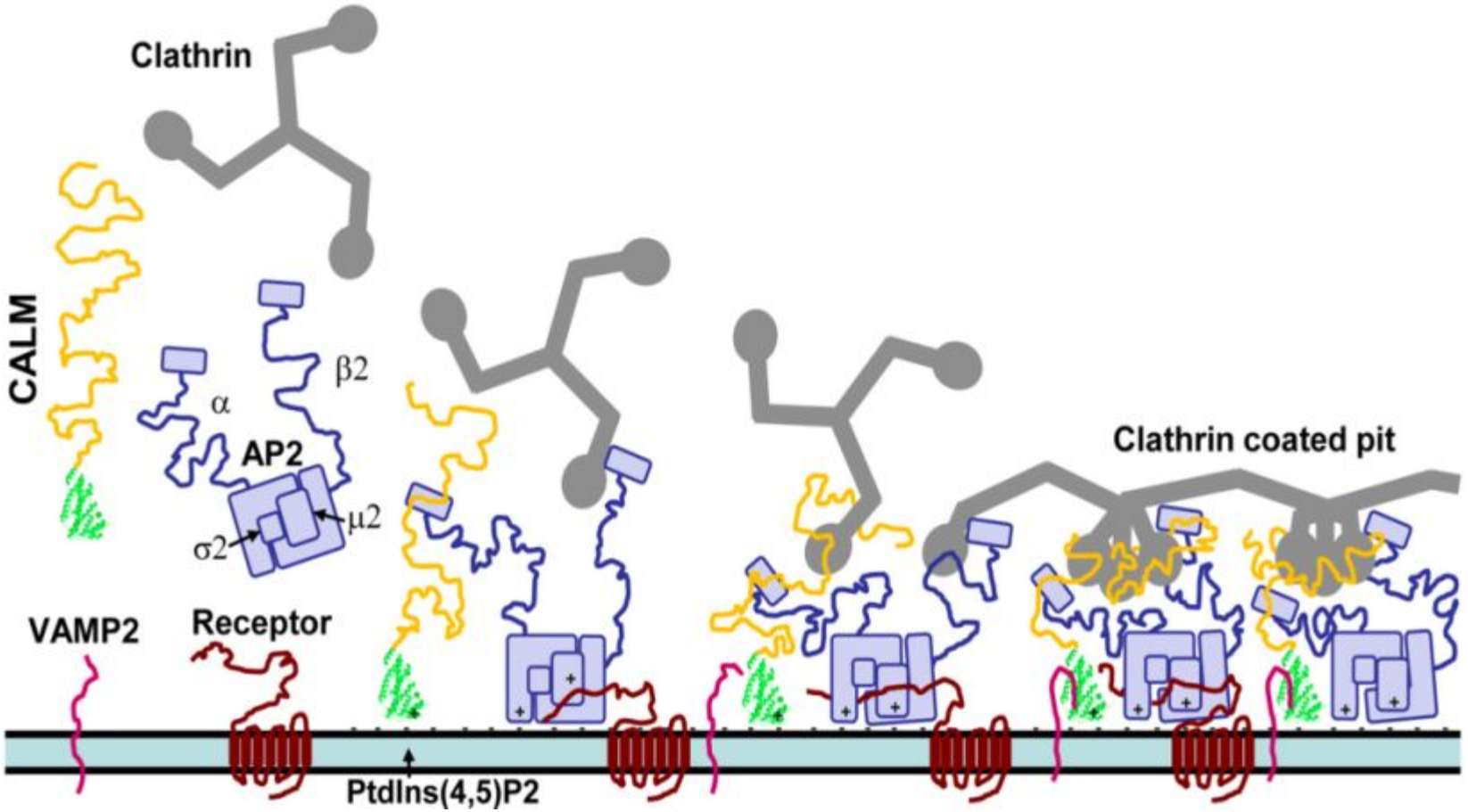

C. AP180/CALM and
potential binders
ANTH
domain
Accessory
protein:
AP2 (α,β2)
Clathrin
D. Epsin and
potential binders
ENTH
domain
UIMs
Accessory
proteins:
Eps12
AP2(α)

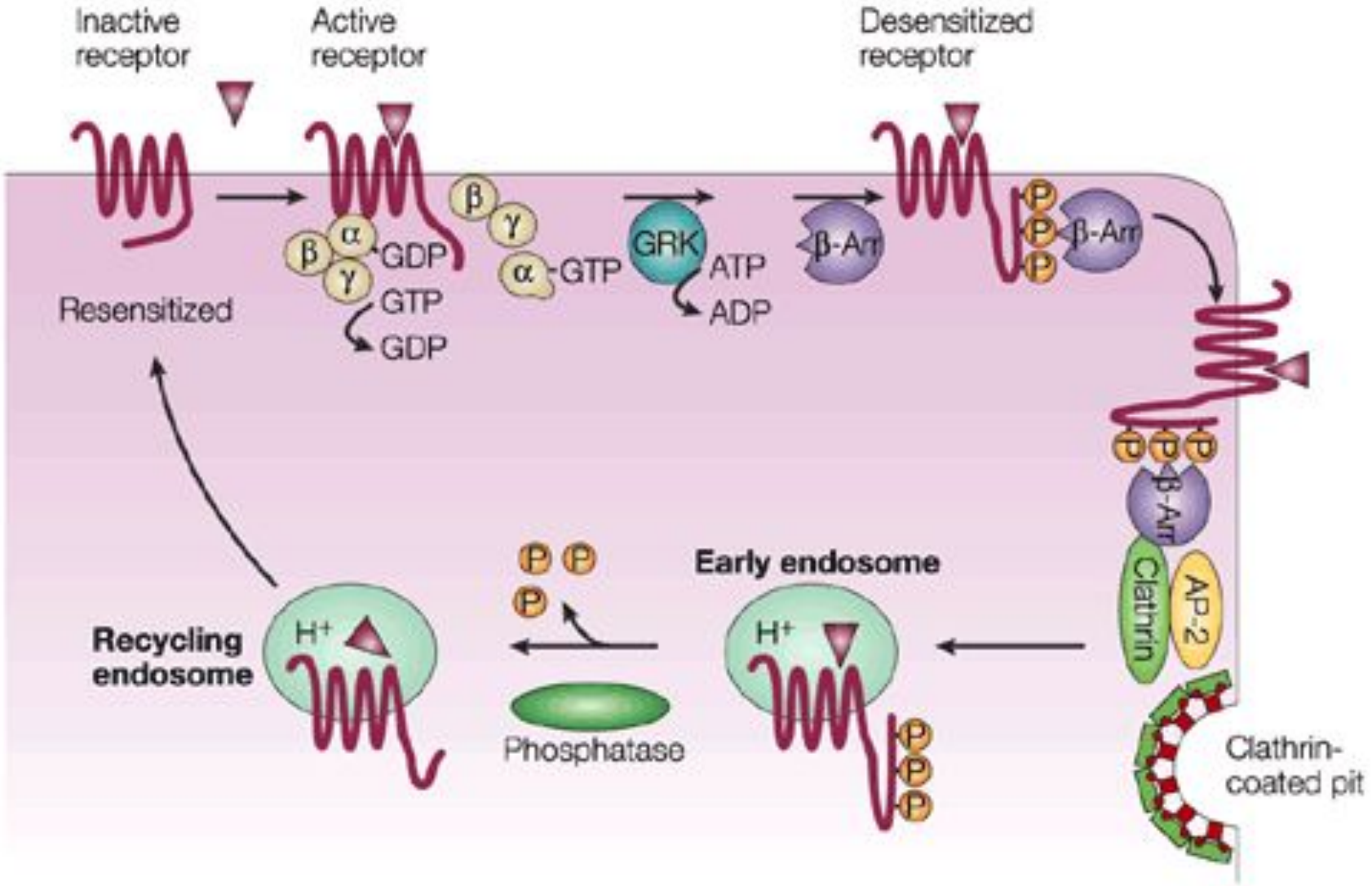

α
β
σ chain
μ chain


ENTH
ANTH
P4
P5
P4
P5
P1
P1
Membrane
insertion
Ins(1,4,5)P3
Membrane


α
β
σ chain
μ chain


B. AP2 adapter
α-appendage
C-μ2-domain
σ2-adaptin
Clathrin binding site
β2-adaptin
α-adaptin
YXXΦ


Clathrin
CALM
α
β2
AP2
μ2
σ2
VAMP2
Receptor
Clathrin coated pit
PtdIns(4,5)P2



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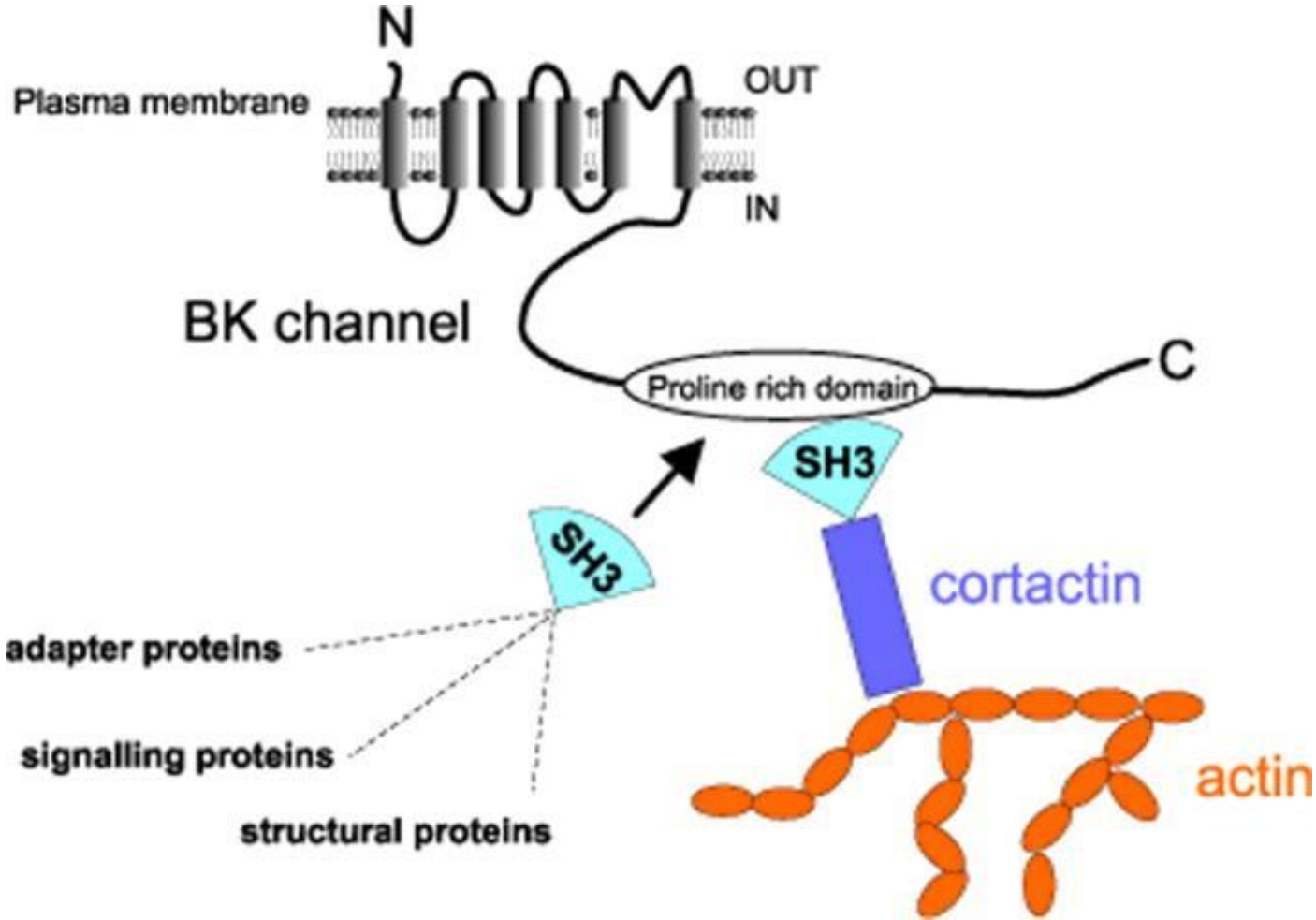
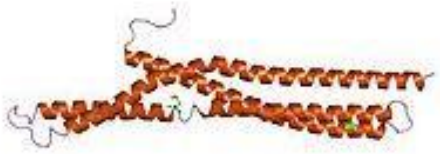
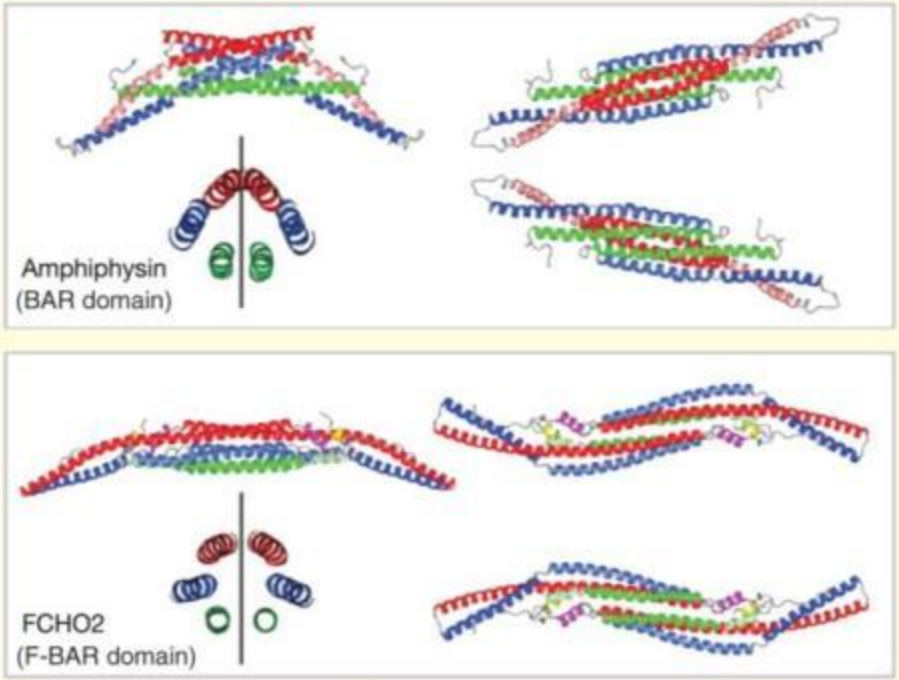

N
Plasma membrane
OUT
IN
BK channel
Proline rich domain
C
SH3
SH3
cortactin
adapter proteins
signalling proteins
structural proteins
actin



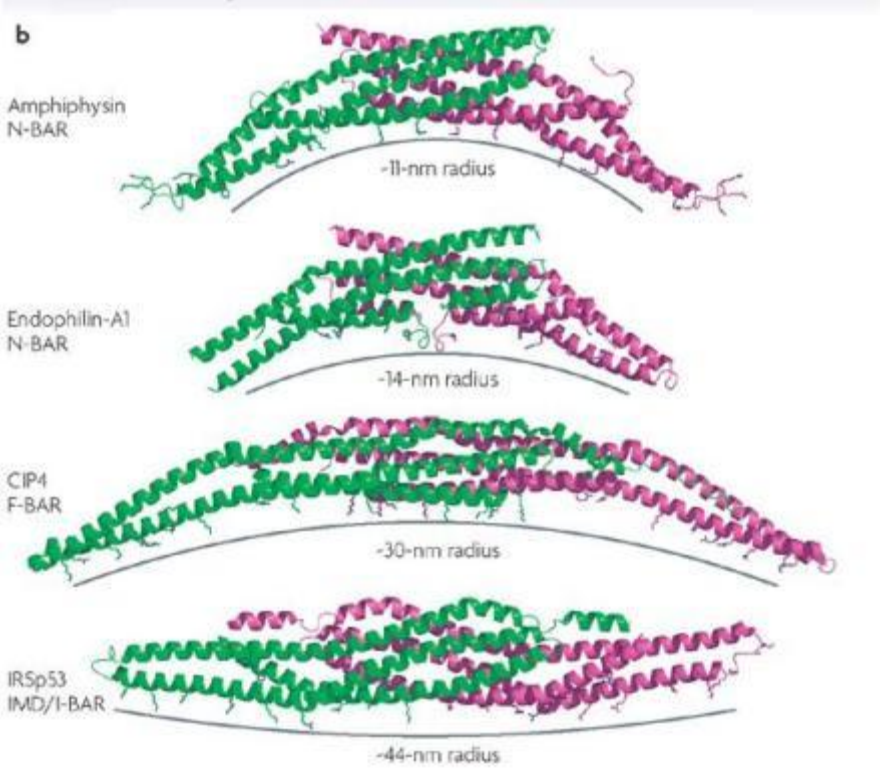
SH3 domains	**Amphiphysin, endophilin**
N-BAR	**Amphiphysin, endophilin, BRAP1/bin2 , nadrin**
F-BAR	**Syndapin/pacsin**

Crystal structure



(from Henne et al., 2007)

- F-BAR domains curve less sharply than BAR domains, correlating with the formation of broader membrane tubules
- Thus different BAR domain relatives might bind to and shape different parts of budding vesicles



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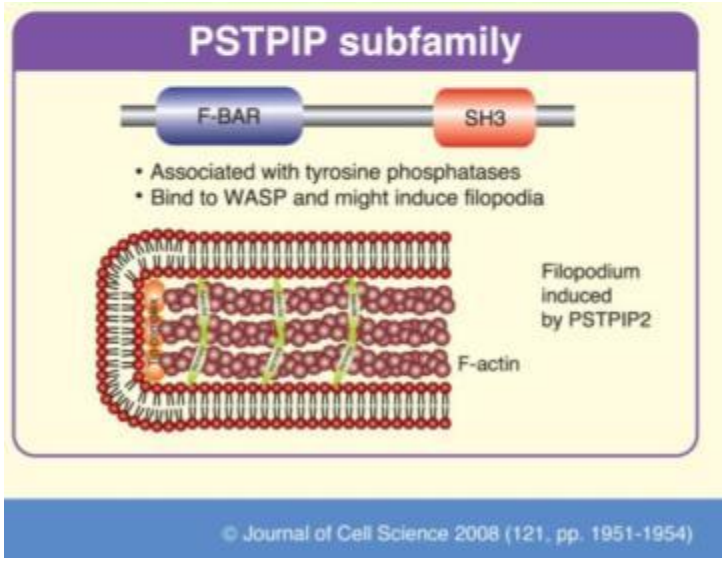
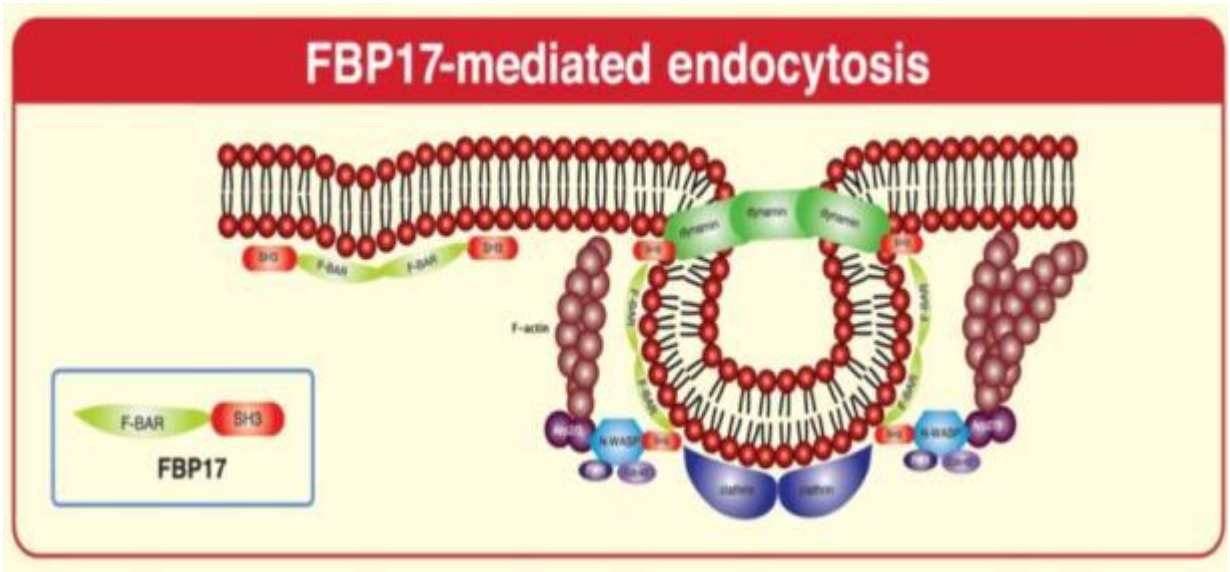
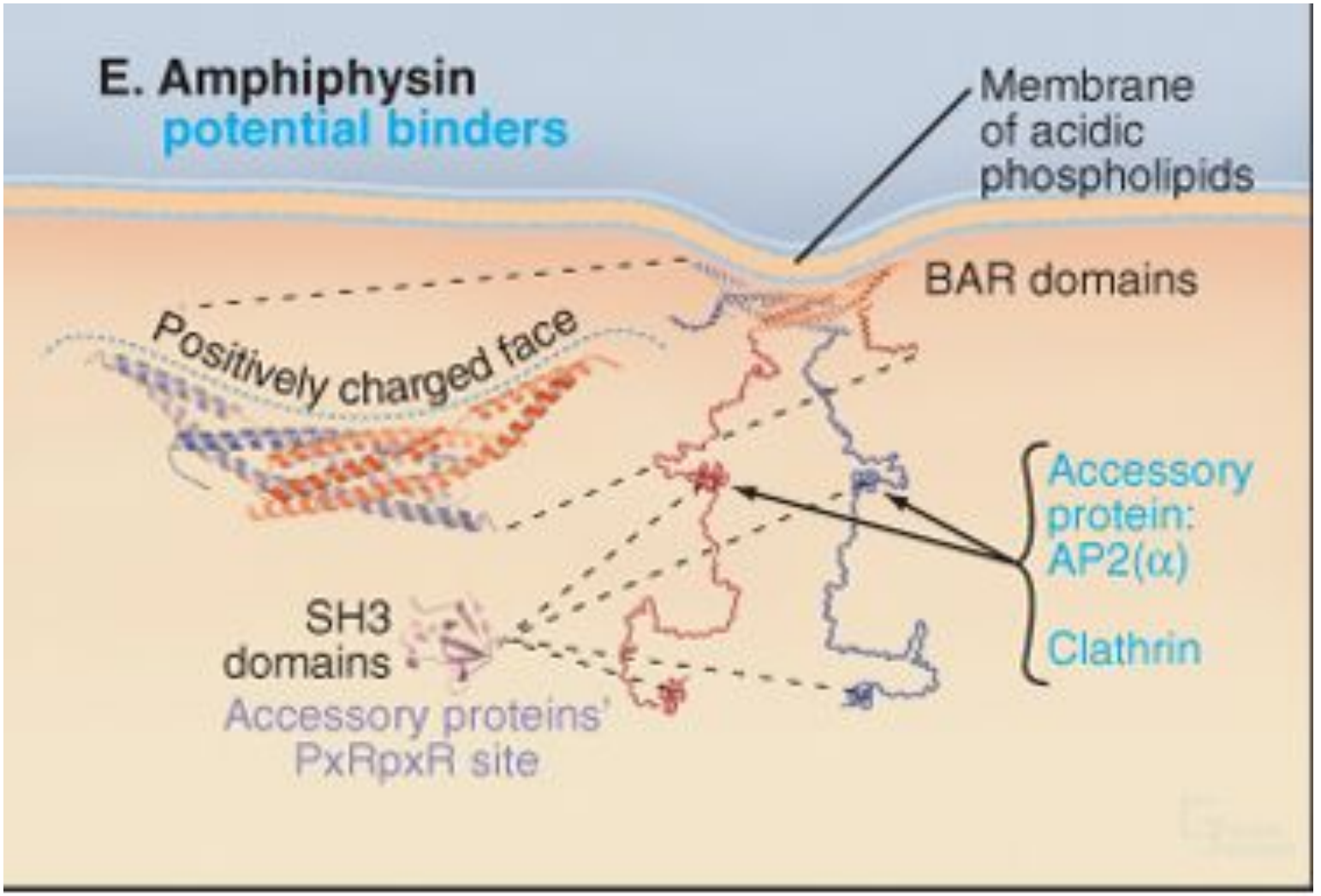
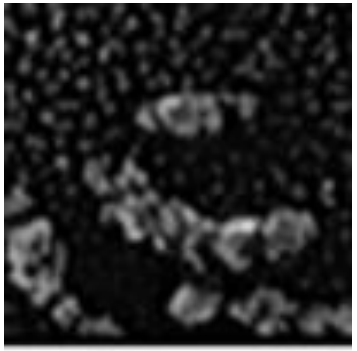
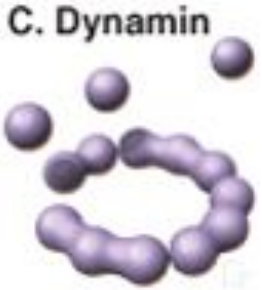


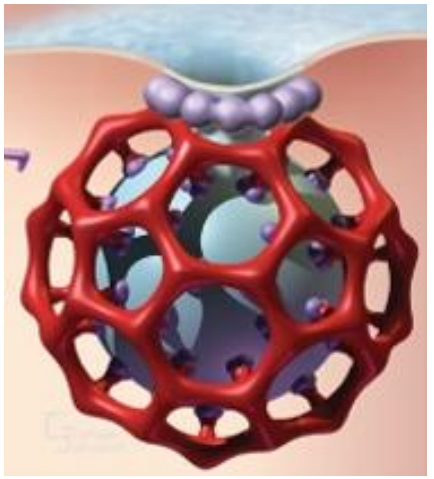


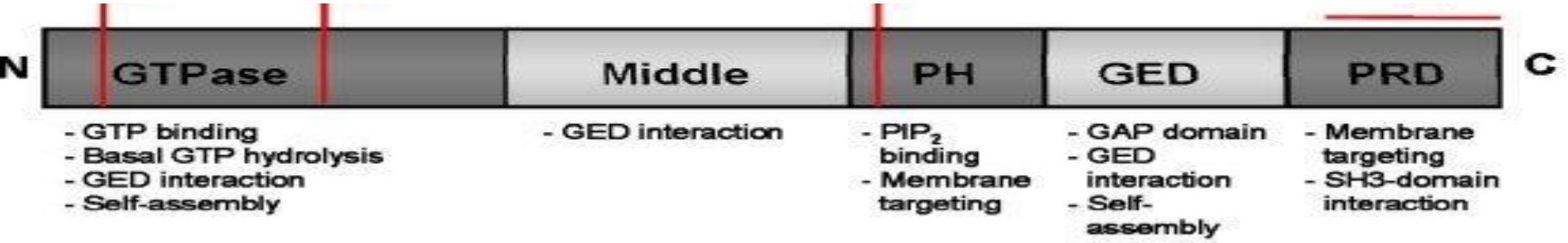


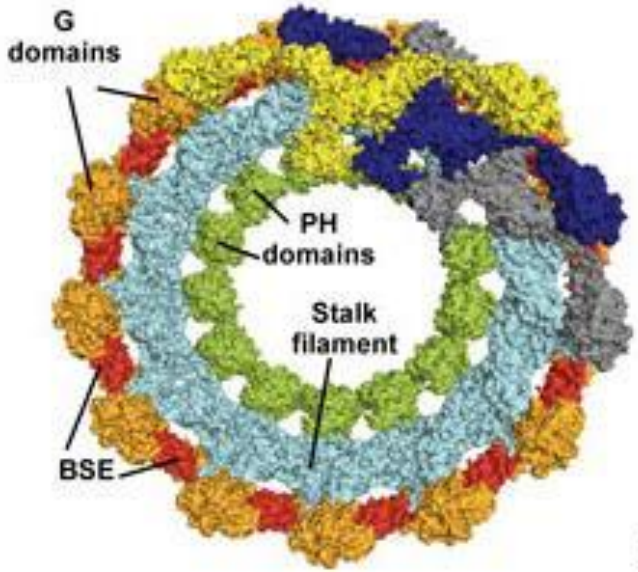


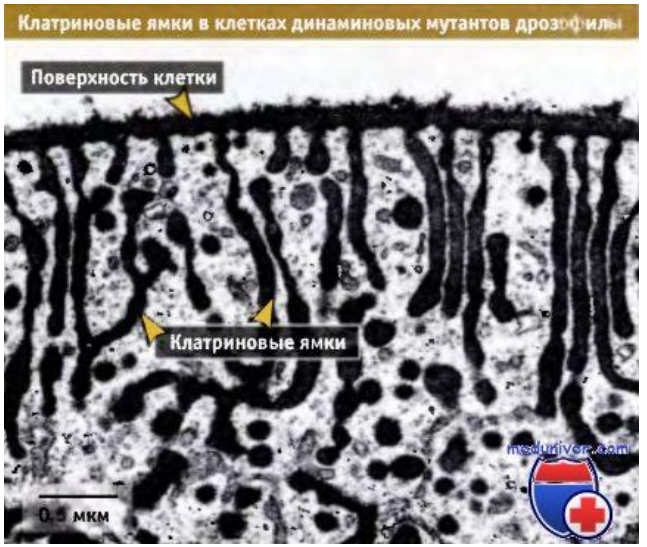
C. Dynamin

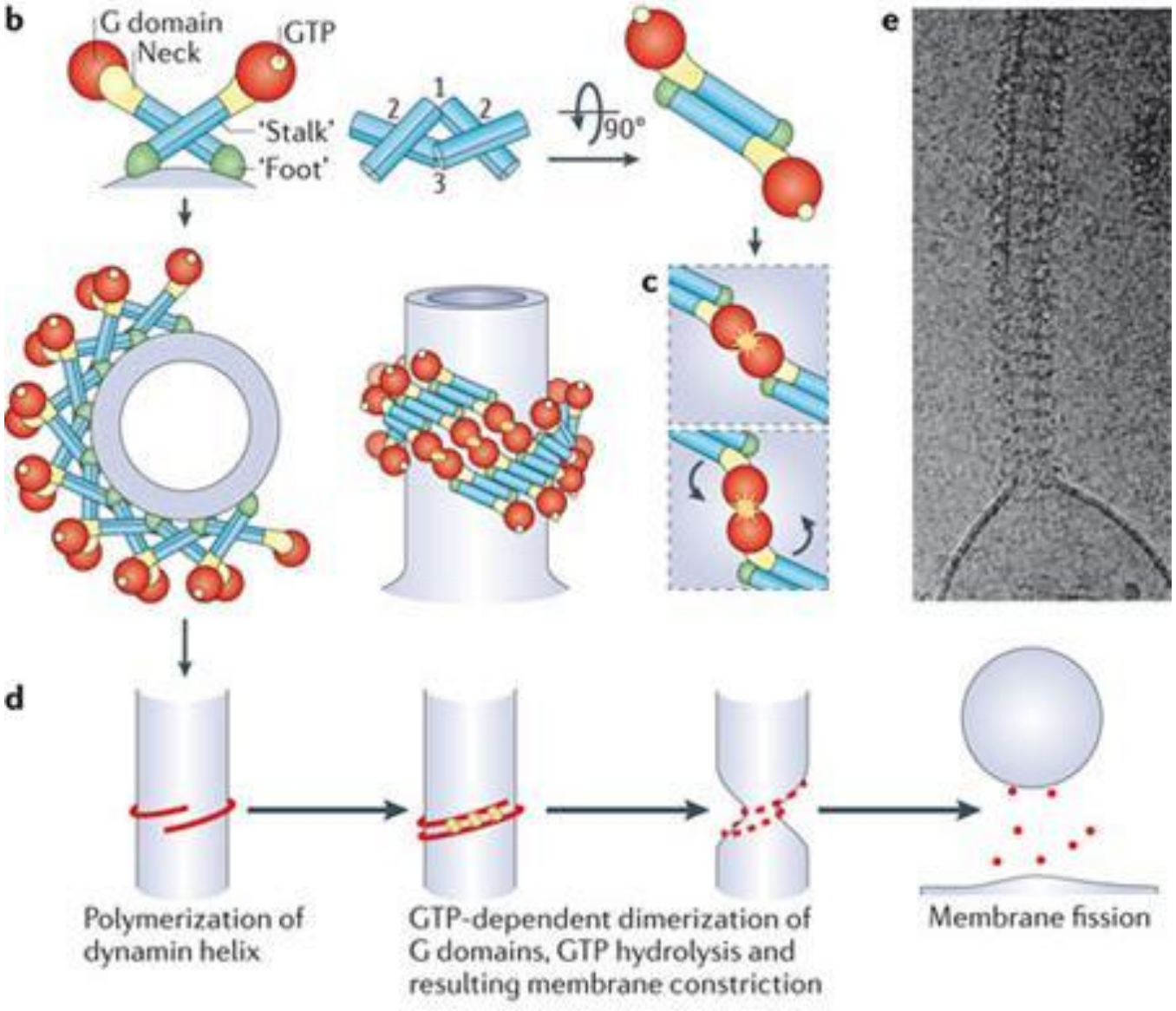

C. Dynamin

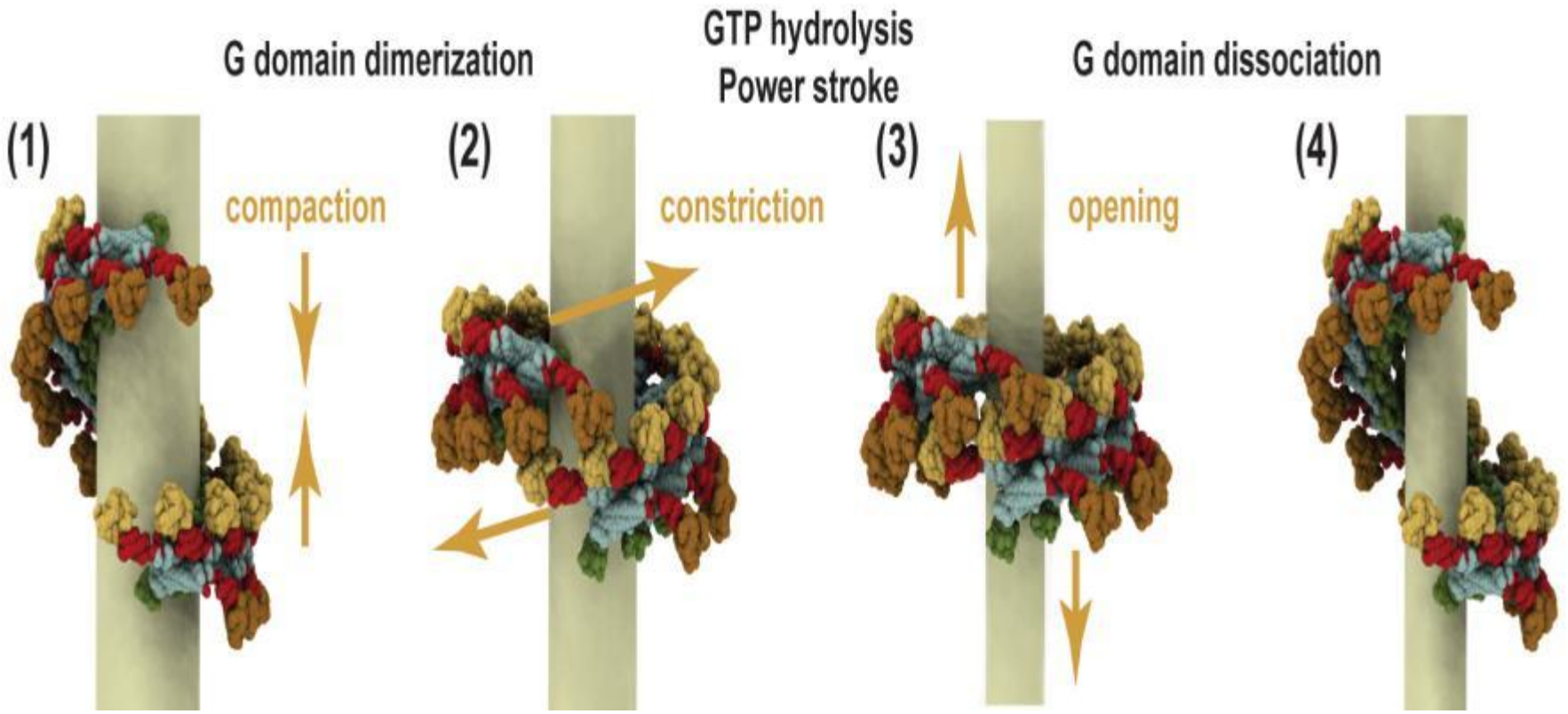


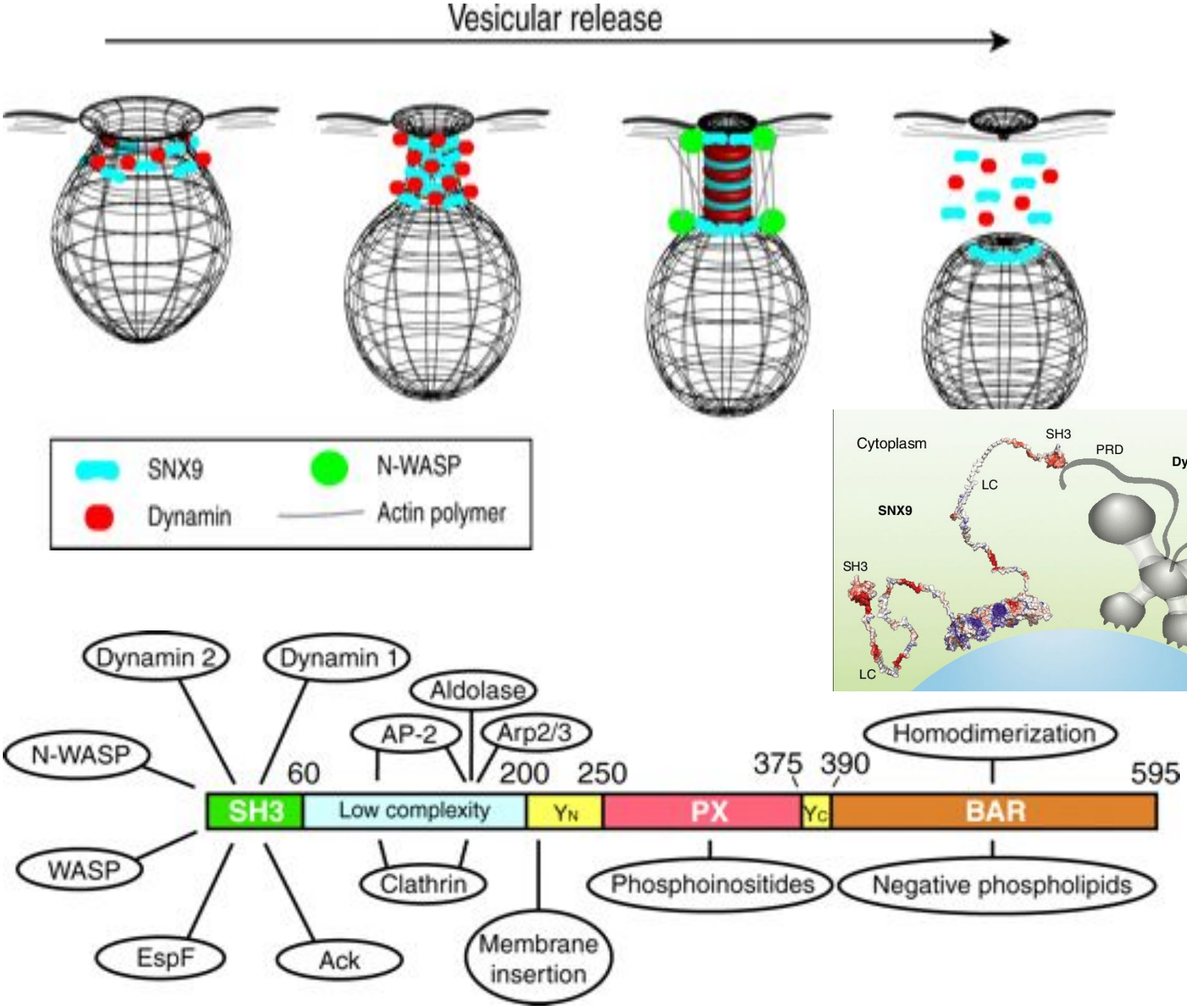

N
GTPase
Middle
PH
GED
PRD
C
- GTP binding
- Basal GTP hydrolysis
- GED interaction
- Self-assembly
- GED interaction
- PIP_2 binding
- Membrane targeting
- GAP domain
- GED interaction
- Self-assembly
- Membrane targeting
- SH3-domain interaction

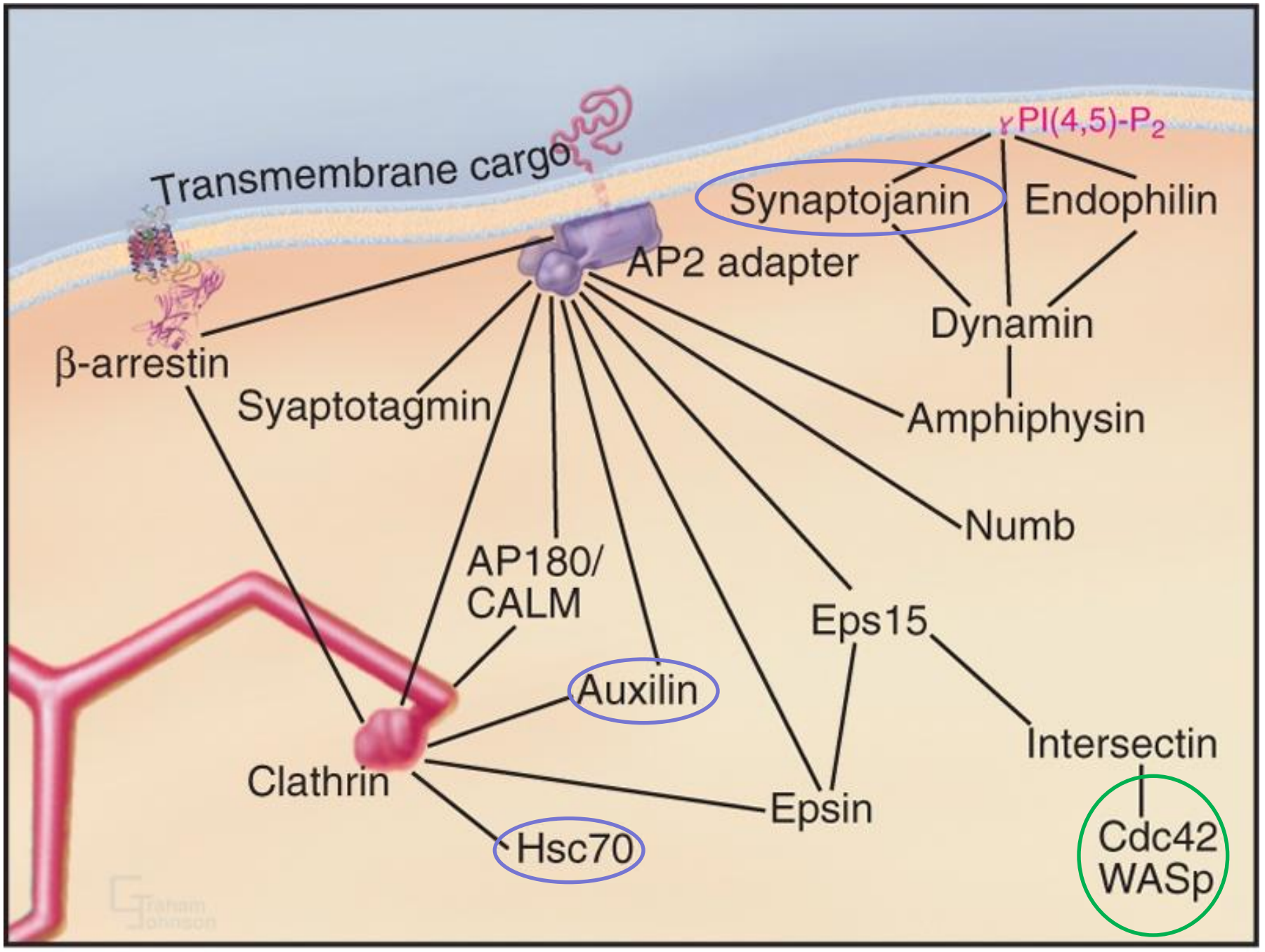

G domains
PH domains
Stalk filament
BSE

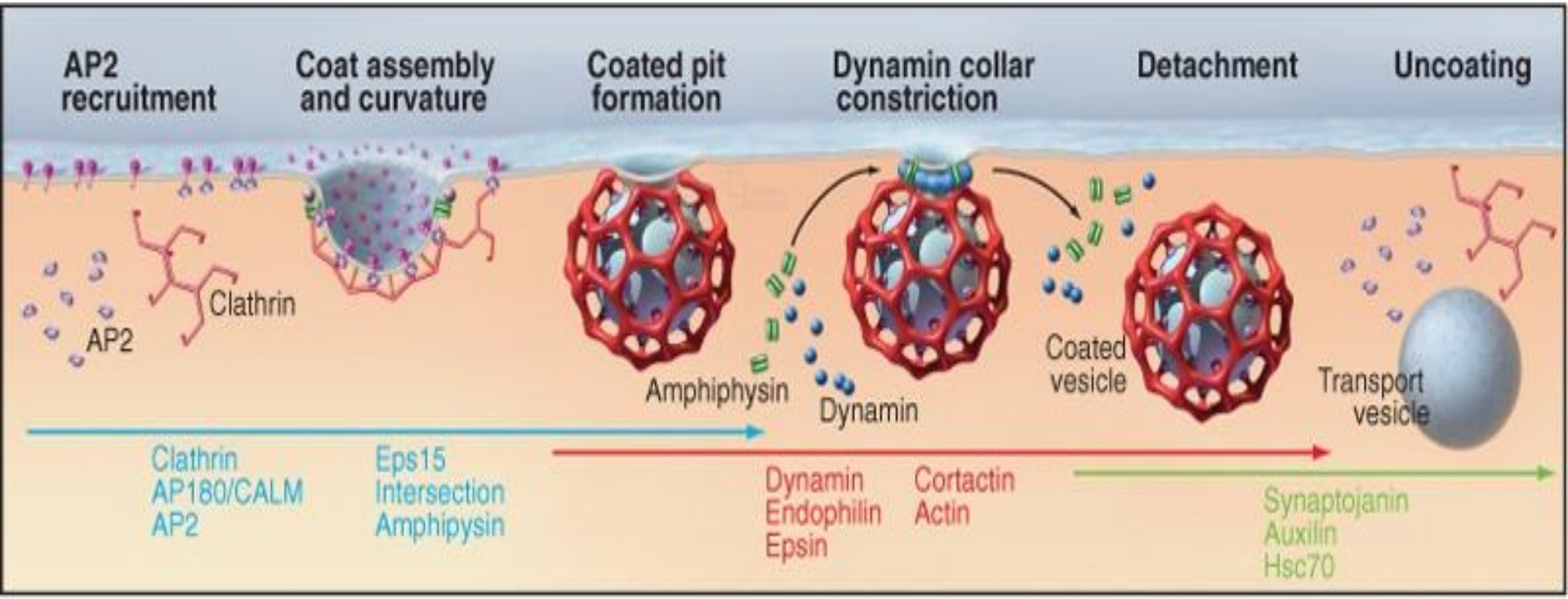

Клатриновые ямки в клетках динаминовых мутантов дрозофилы
Поверхность клетки
Клатриновые ямки
0.5 мкм

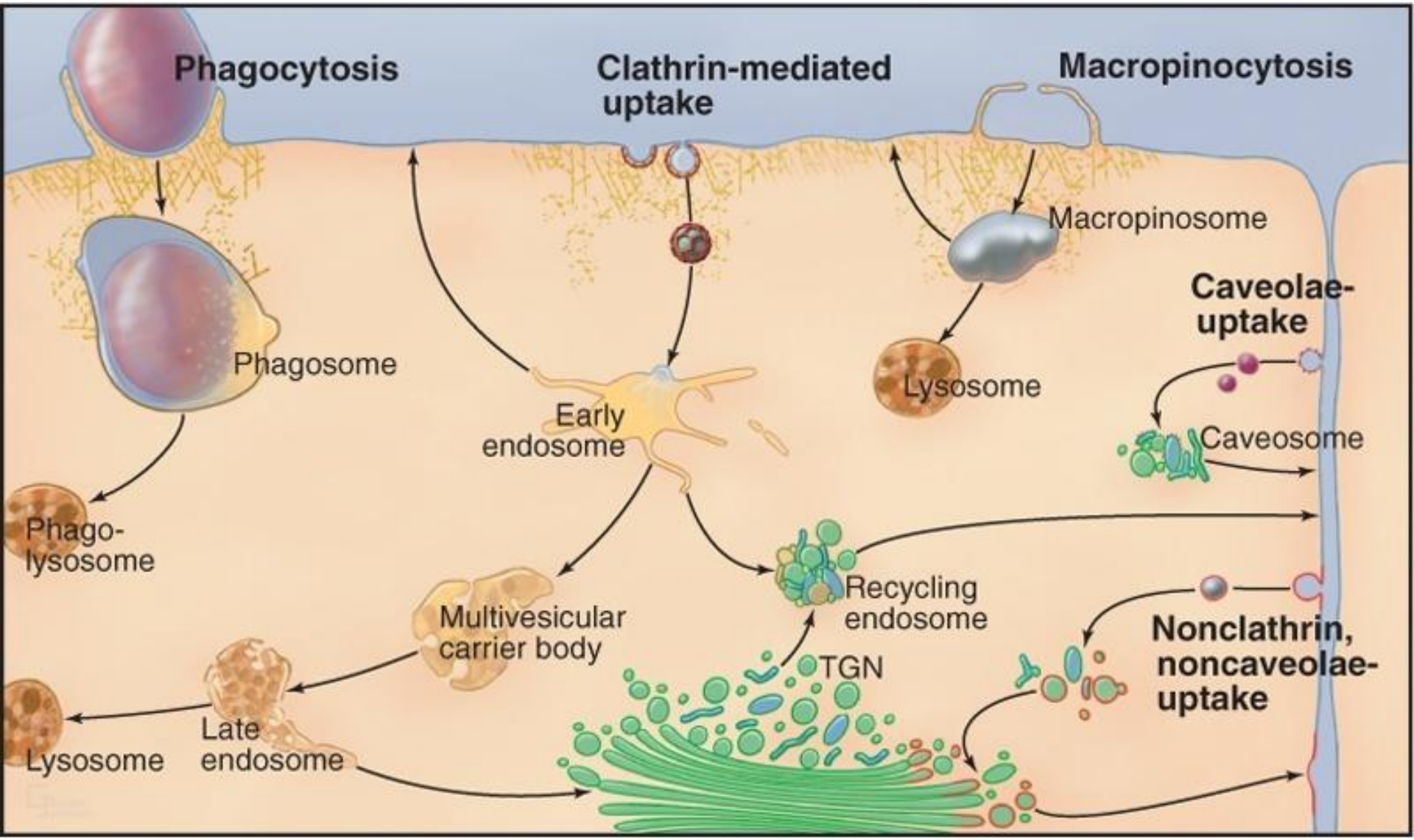

b
G domain
Neck
GTP
'Stalk'
'Foot'
1
2
2
3
90°
c
e
d
Polymerization of dynamin helix
GTP-dependent dimerization of G domains, GTP hydrolysis and resulting membrane constriction
Membrane fission

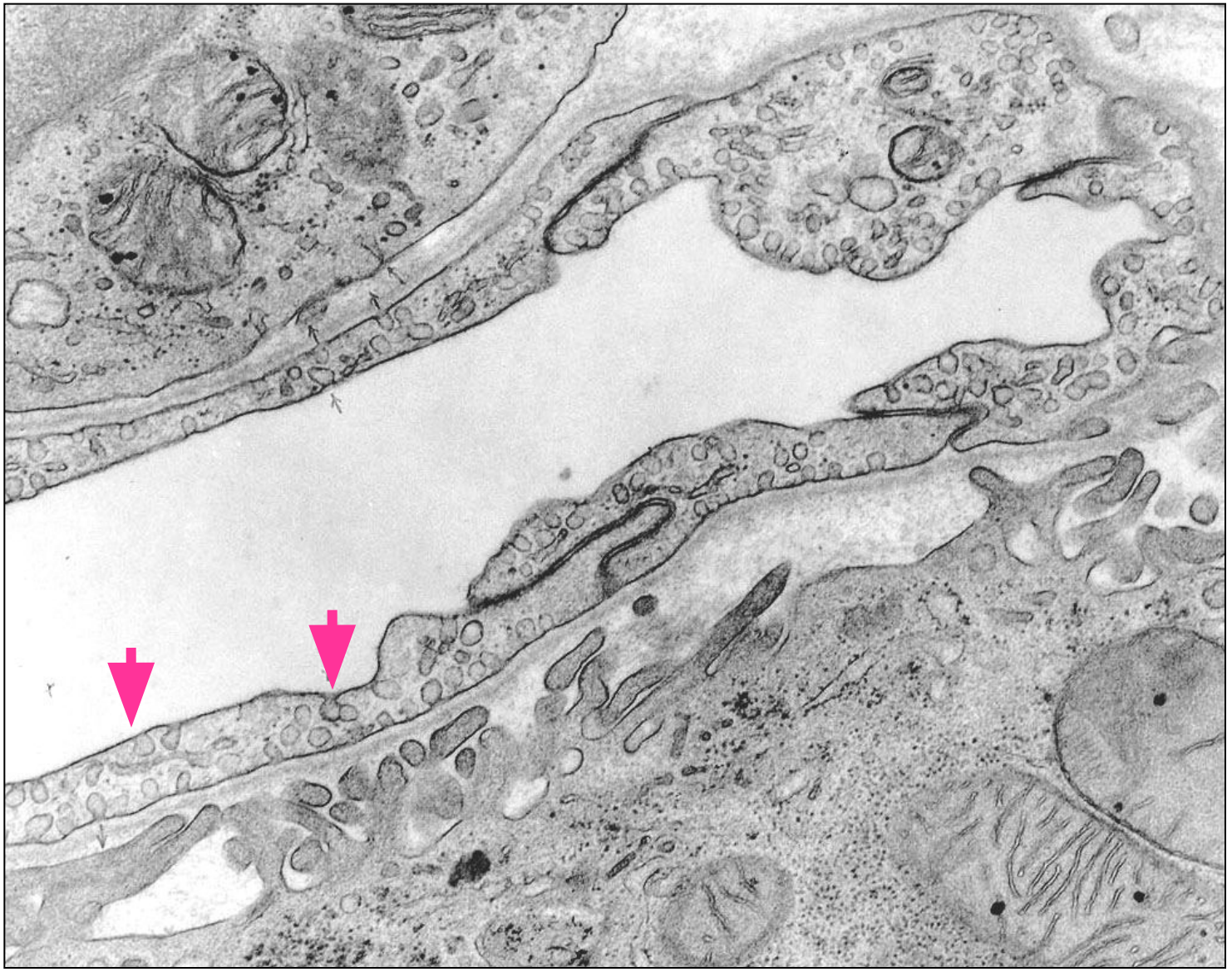

G domain dimerization
GTP hydrolysis
Power stroke
G domain dissociation
(1)
compaction
(2)
constriction
(3)
opening
(4)

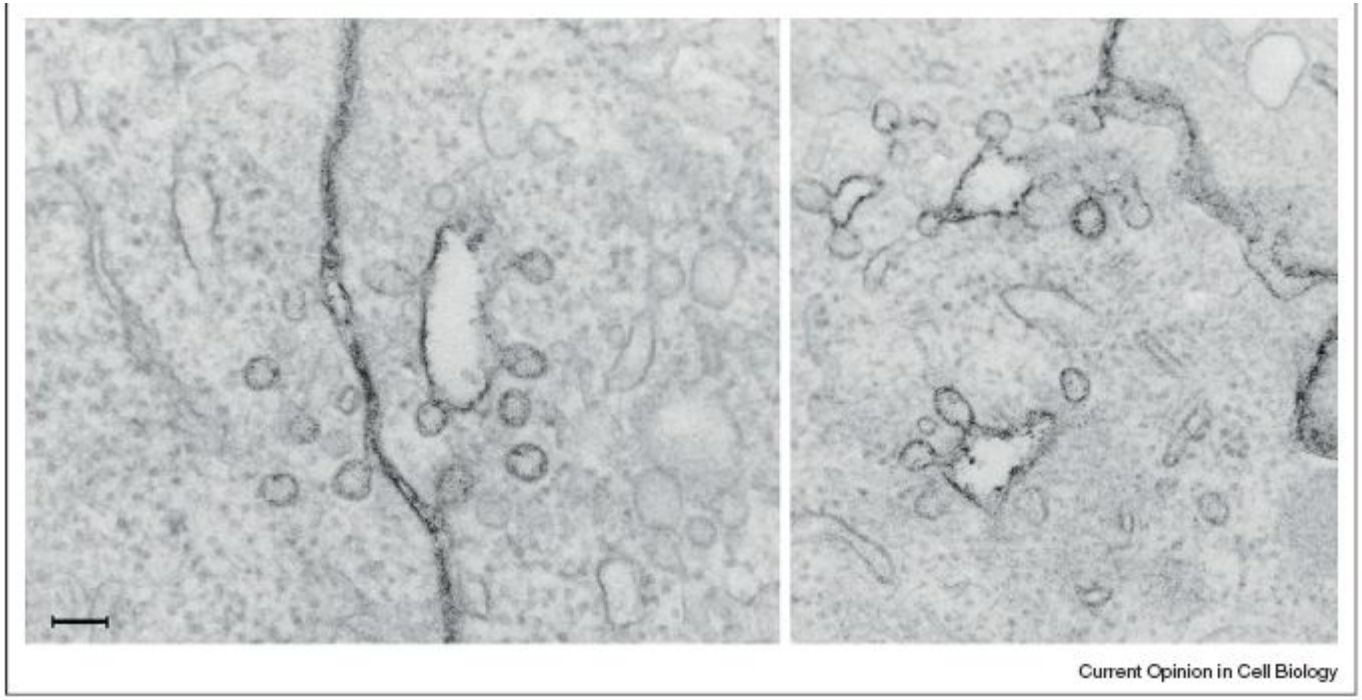

Vesicular release
SNX9
Dynamin
N-WASP
Actin polymer
Cytoplasm
SH3
PRD
Dynamin
LC
SNX9
SH3
LC
Dynamin 2
Dynamin 1
Aldolase
AP-2
Arp2/3
N-WASP
Homodimerization
60
200
250
375
390
595
SH3
Low complexity
YN
PX
YC
BAR
WASP
Clathrin
Phosphoinositides
Negative phospholipids
EspF
Ack
Membrane insertion





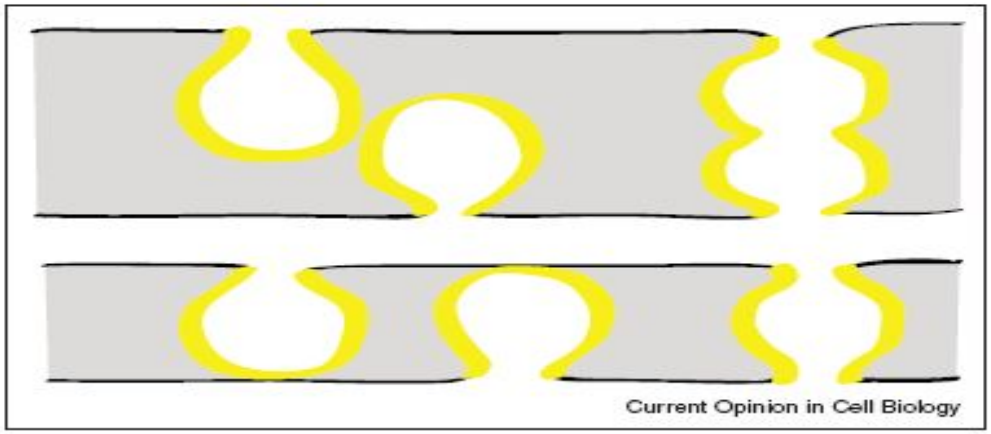


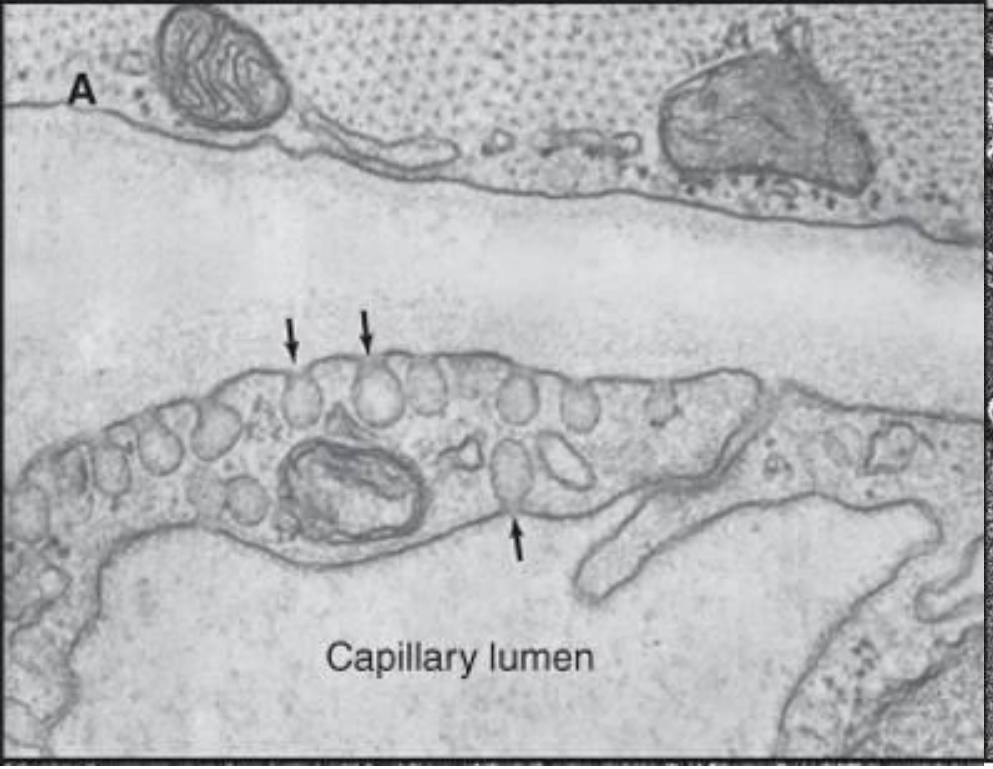


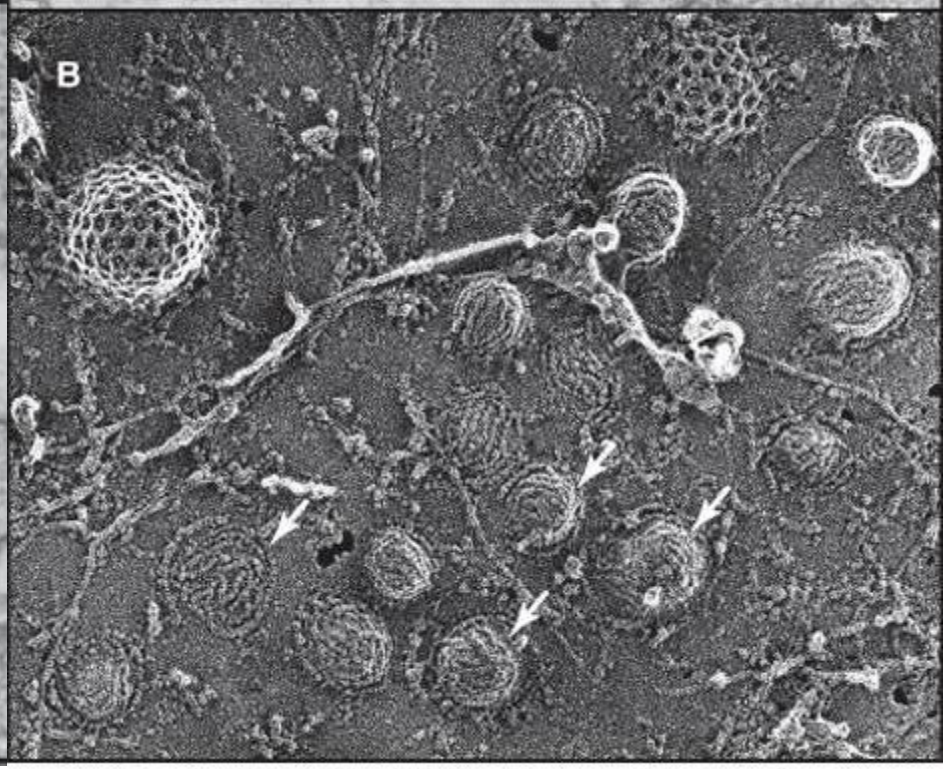


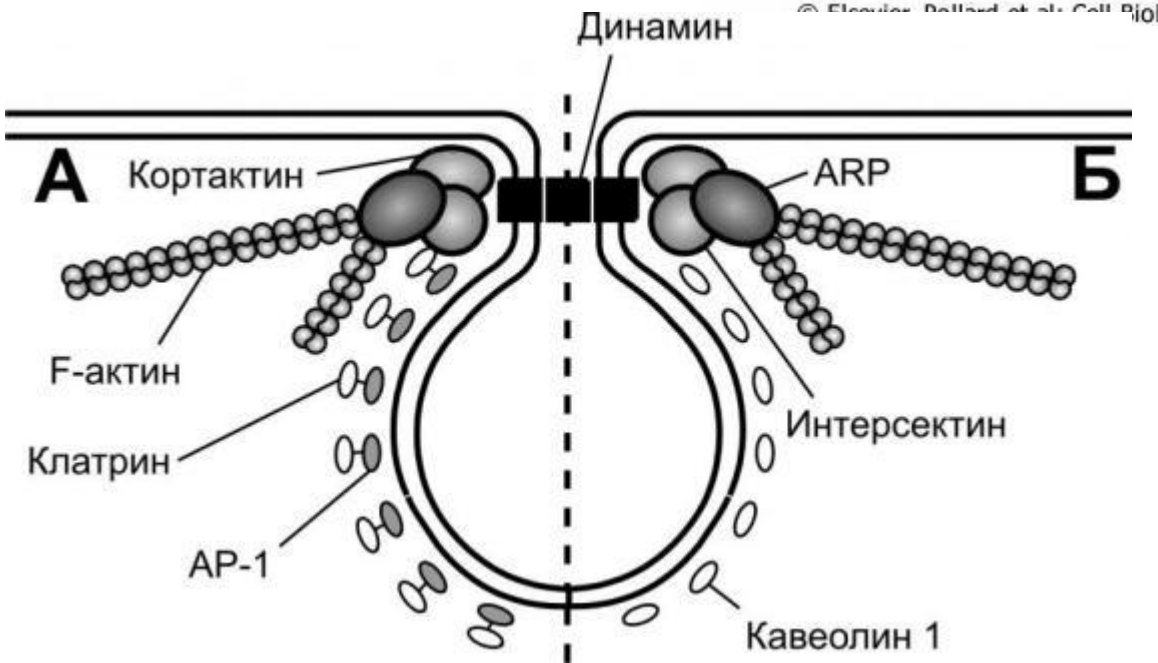
The vacuolar structures with associated caveolae apparently freely localized in the cytoplasm could easily be interpreted as special caveolar endosomes, or caveosomes. However, fixation in the presence of the surface marker ruthenium red clearly shows that the structures are surface-connected, for example, invaginations of the plasma membrane with associated caveolae, and have nothing to do with internalization of caveolae. Bar, 100 nm.

Figure 3

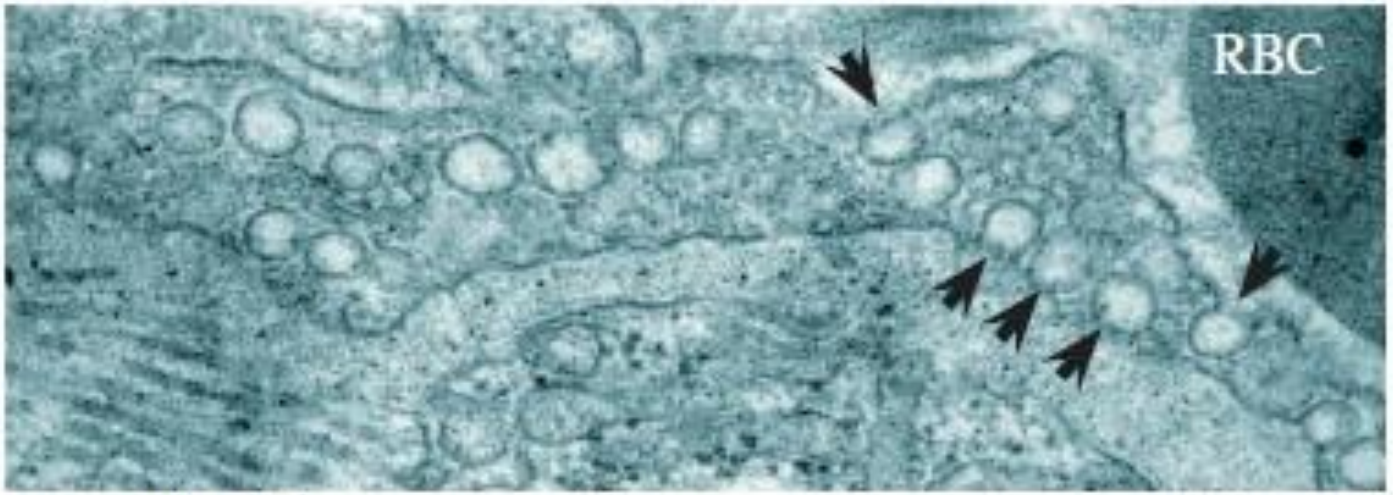




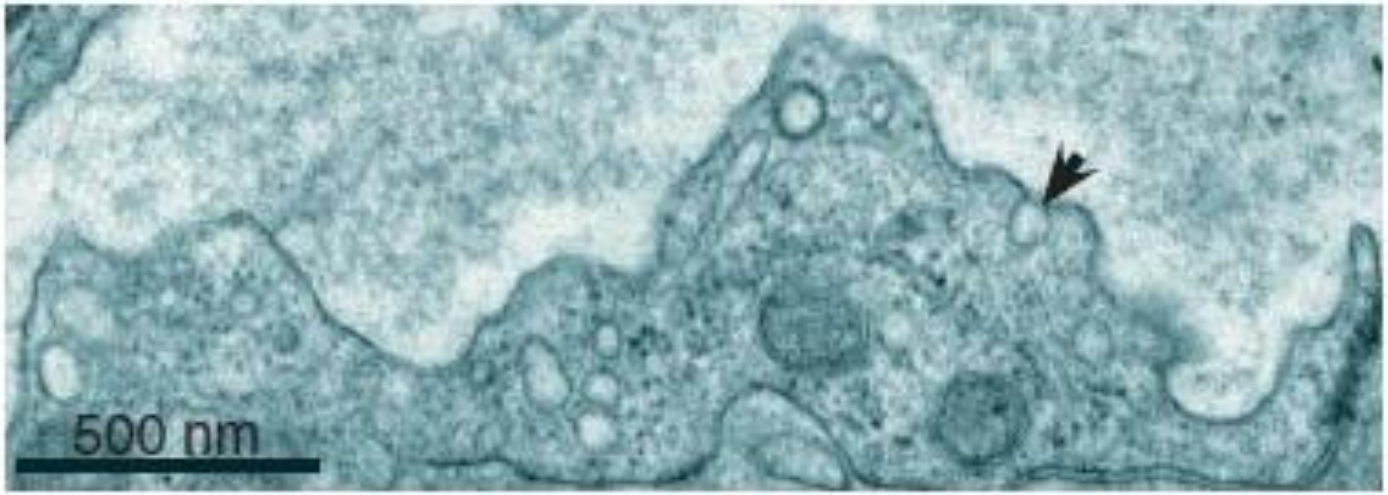


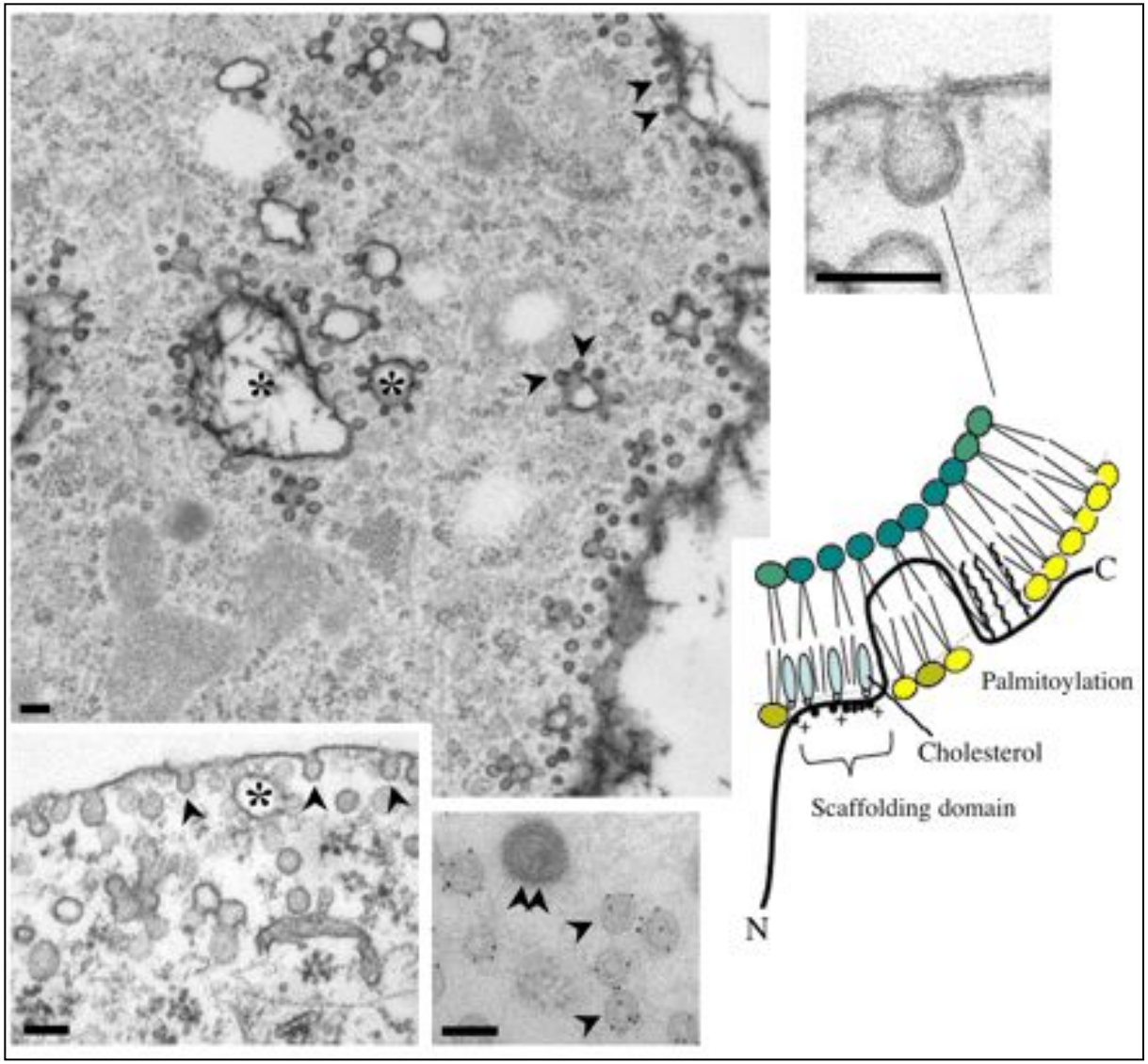


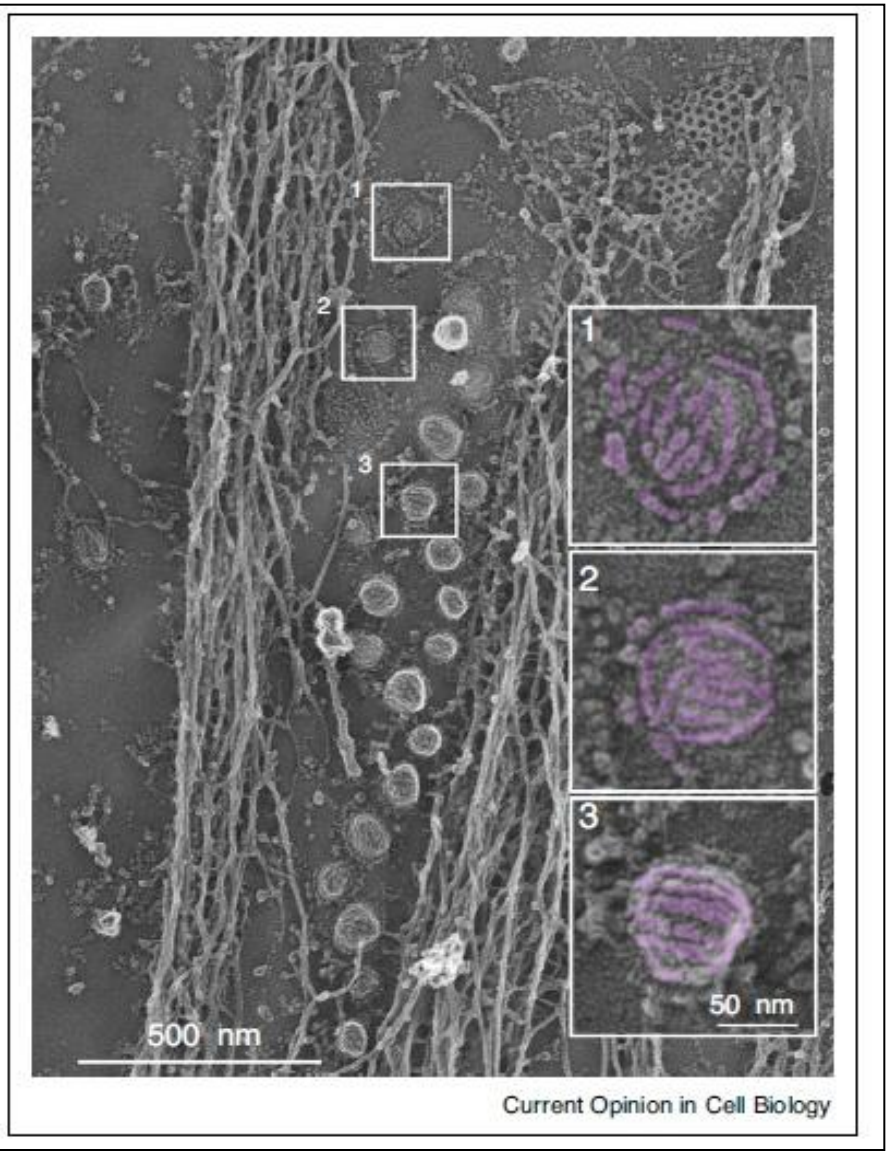
caveolin $1^{+/+}$



caveolin $1^{-/-}$




C
Palmitoylation
Cholesterol
Scaffolding domain
N


1
2
3
1
2
3
500 nm
50 nm
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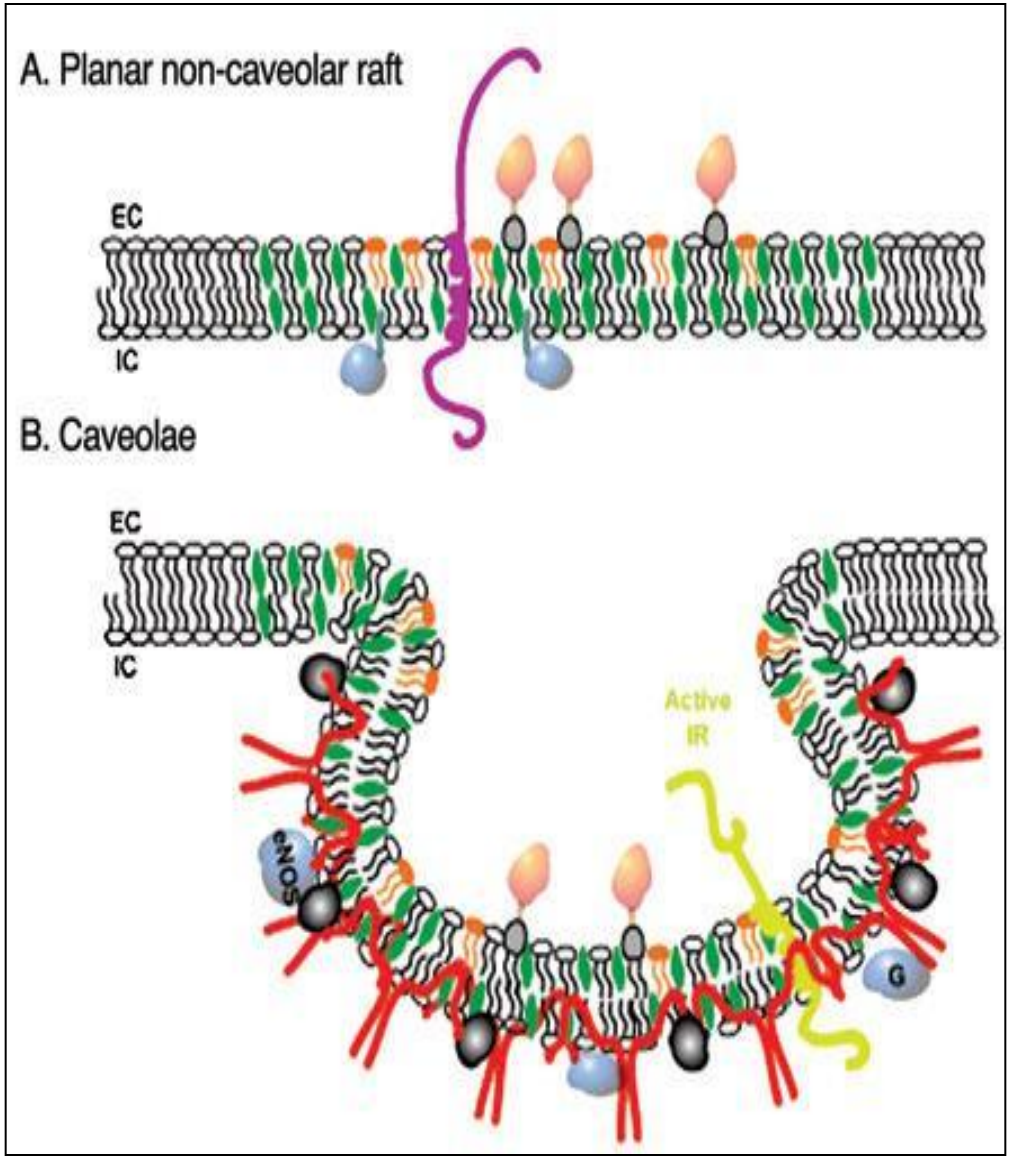
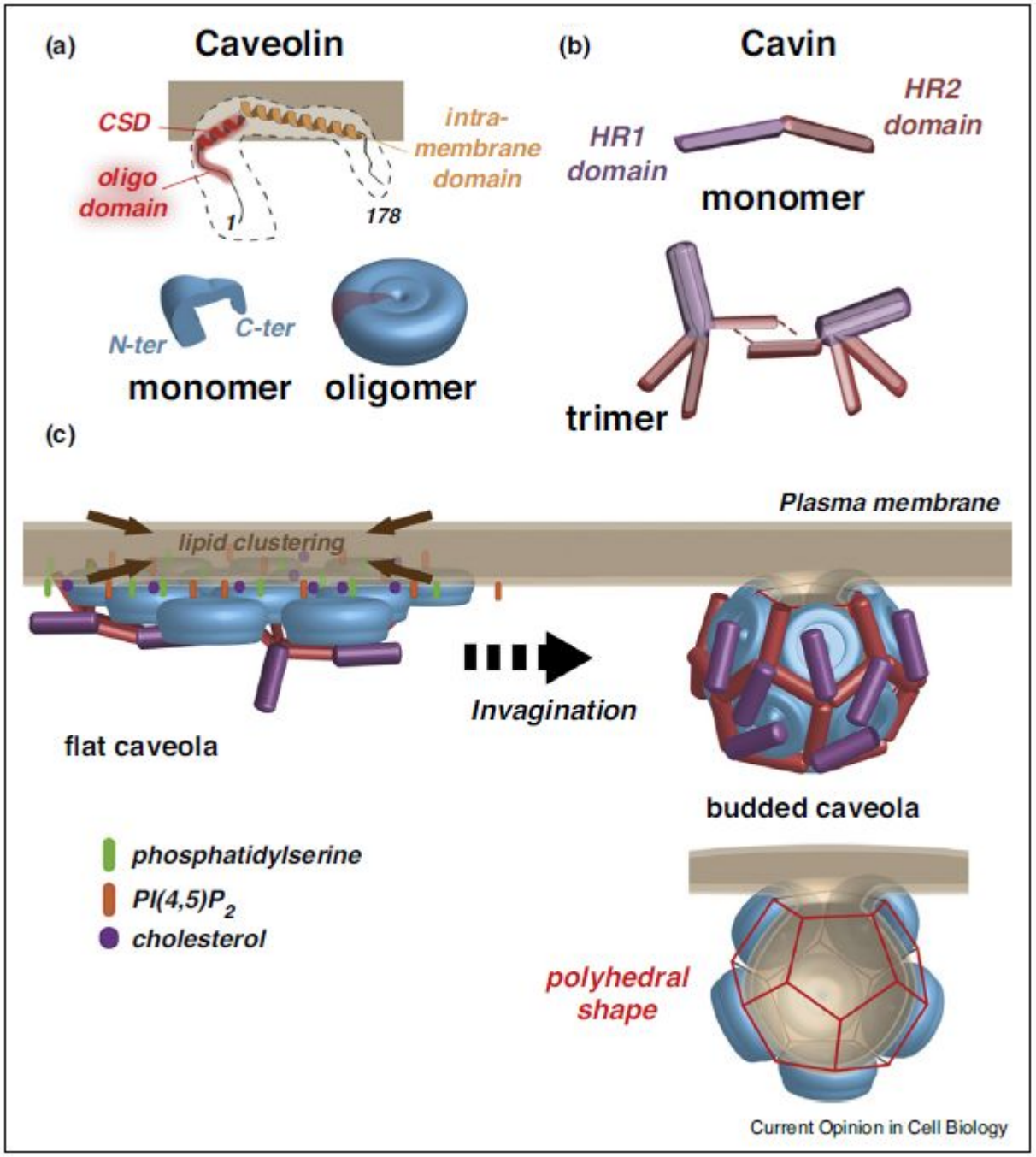
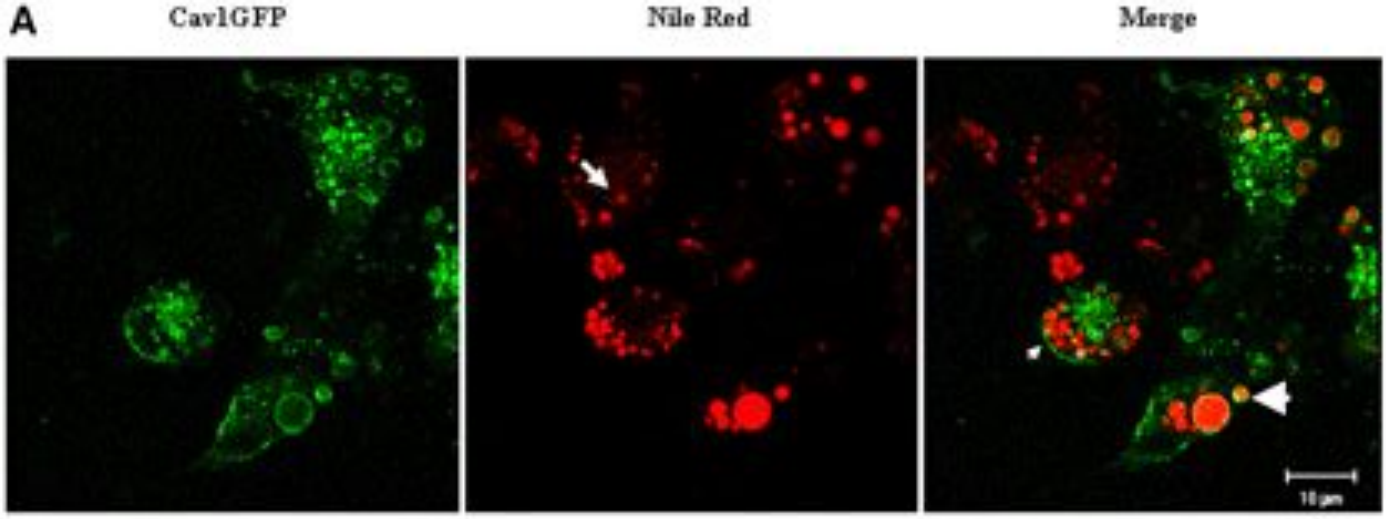
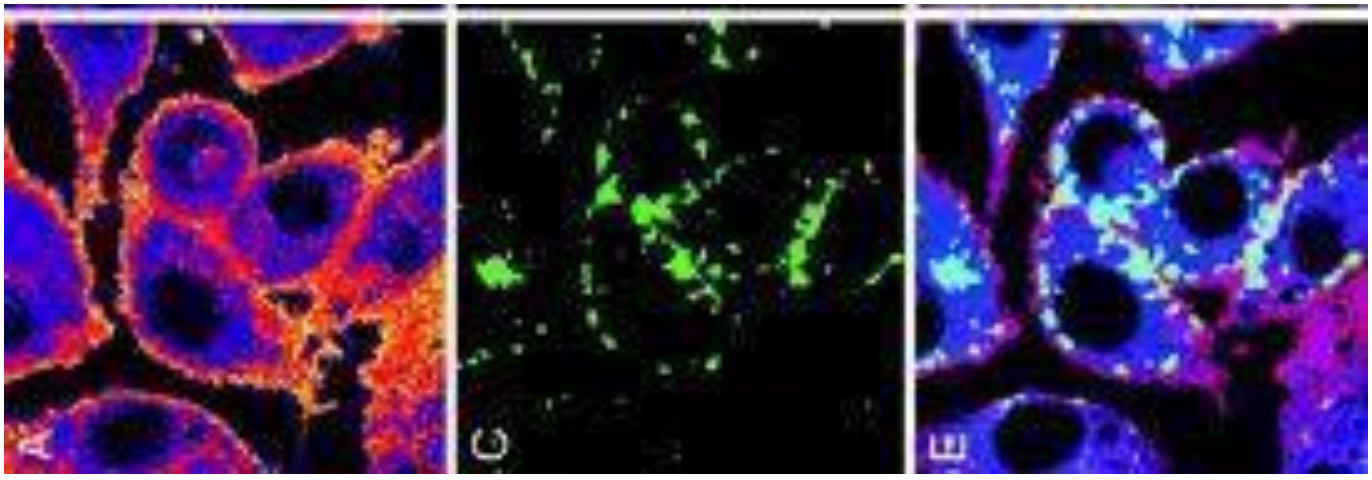
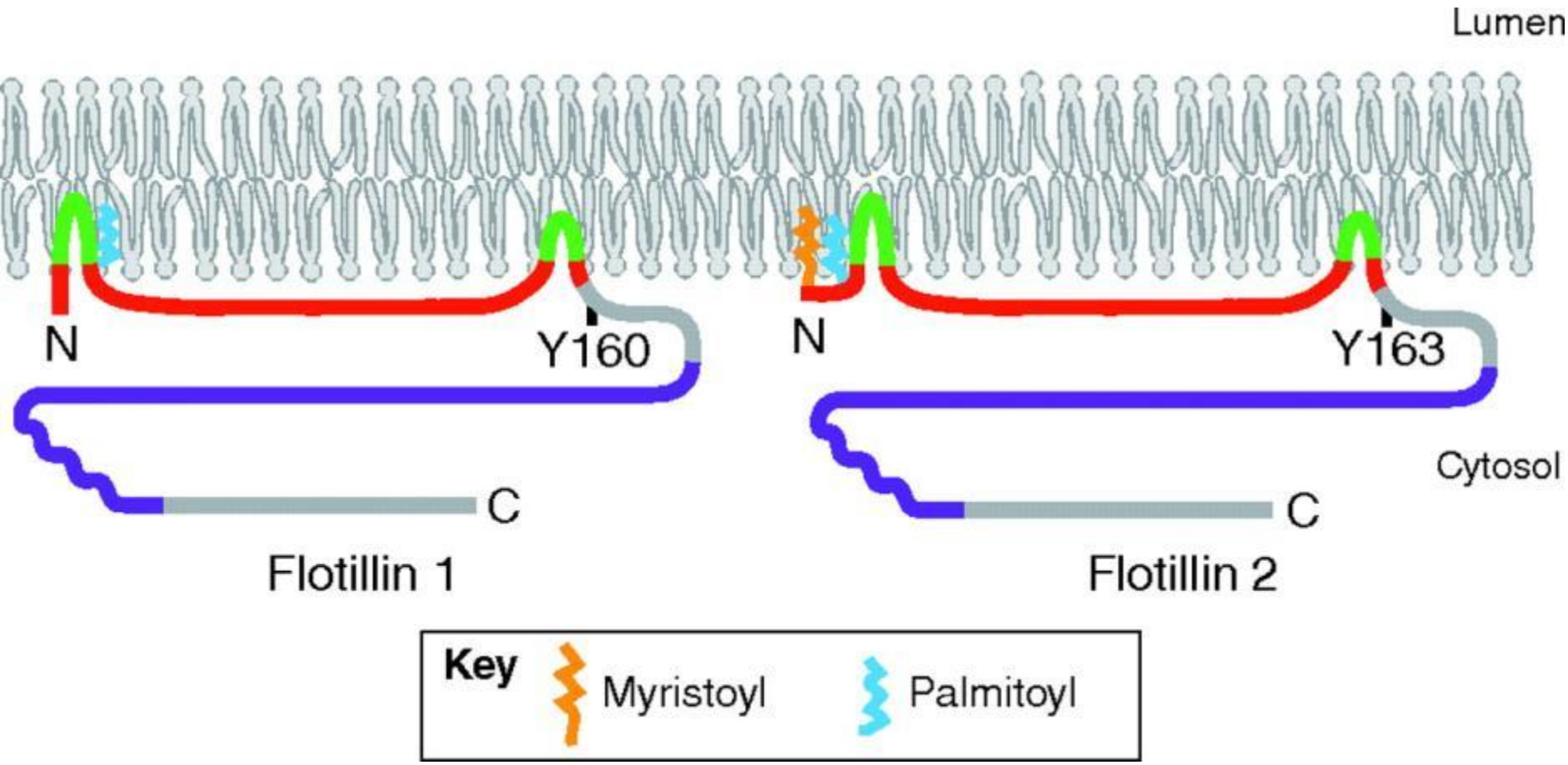
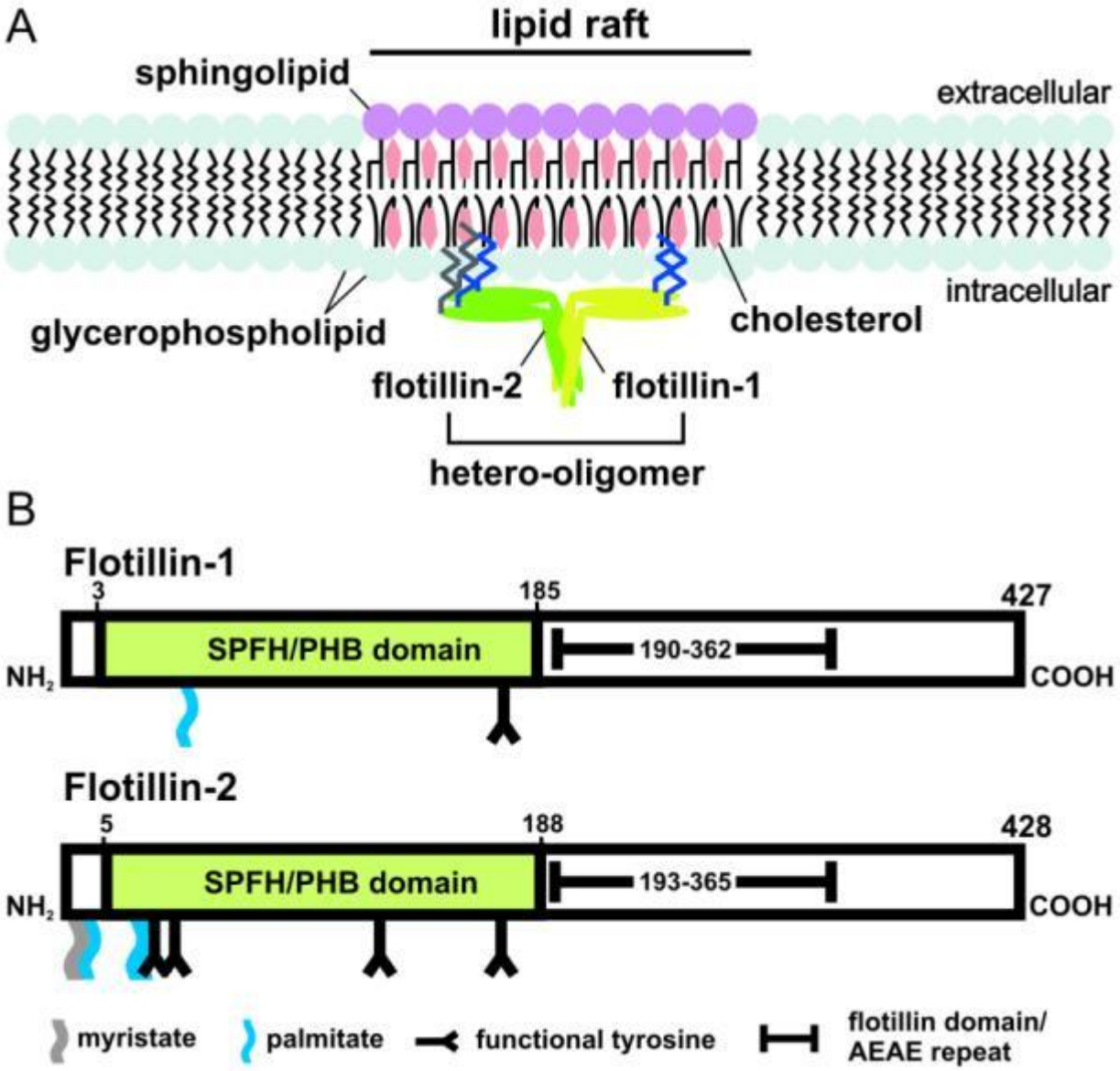

A. Planar non-caveolar raft
EC
IC
B. Caveolae
EC
IC
Active
IR
eNOS
G

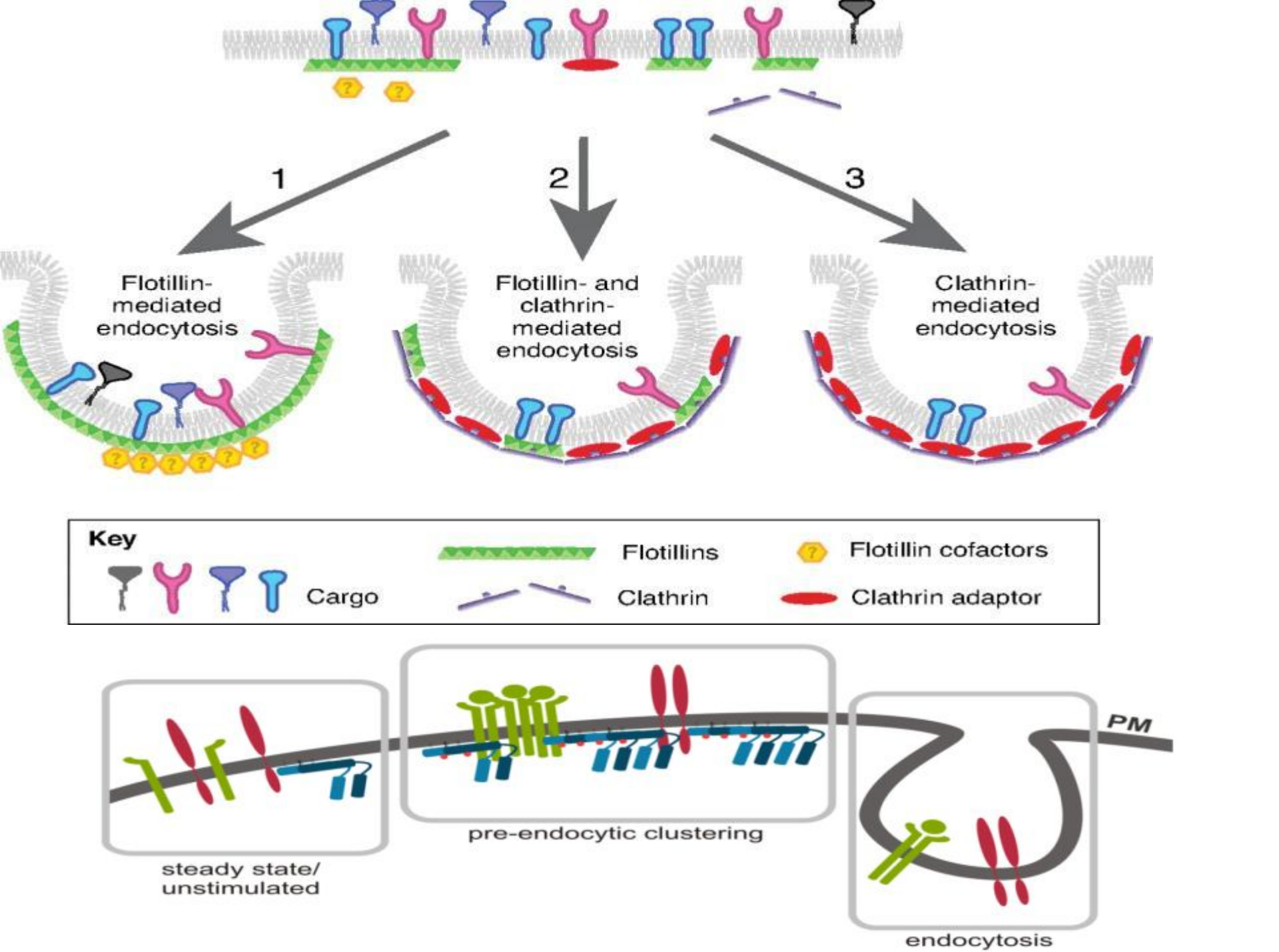

(a)
Caveolin
CSD
oligo domain
intra-membrane domain
1
178
N-ter
C-ter
monomer
oligomer
(b)
Cavin
HR2 domain
HR1 domain
monomer
trimer
(c)
Plasma membrane
lipid clustering
flat caveola
Invagination
budded caveola
phosphatidylserine
PI(4,5)P2
cholesterol
polyhedral shape
Current Opinion in Cell Biology

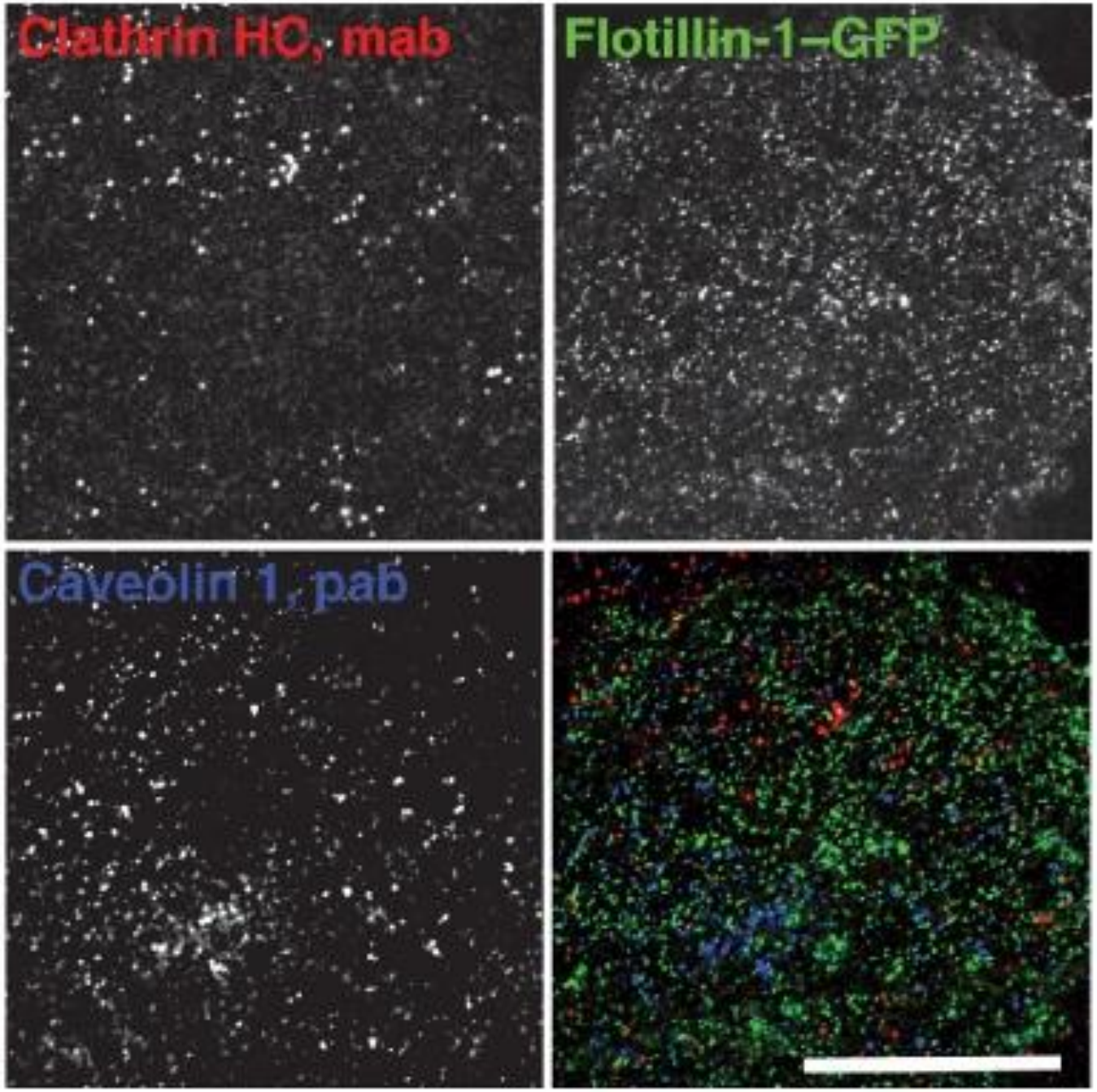

A
Cav1GFP
Nile Red
Merge

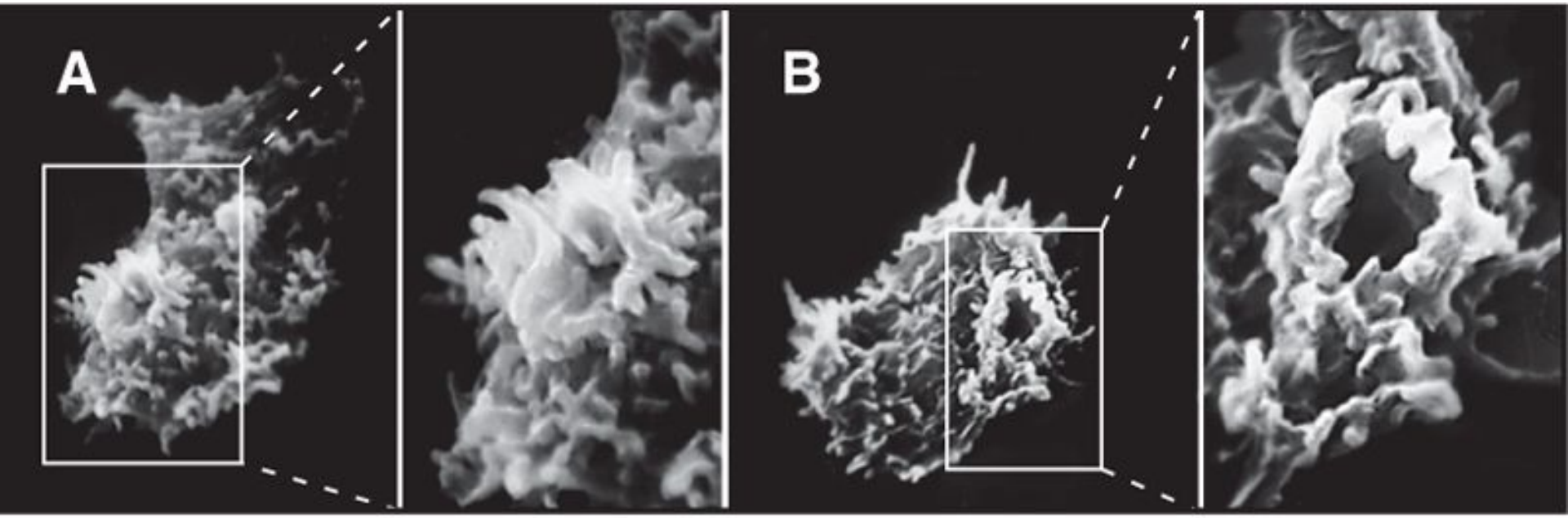


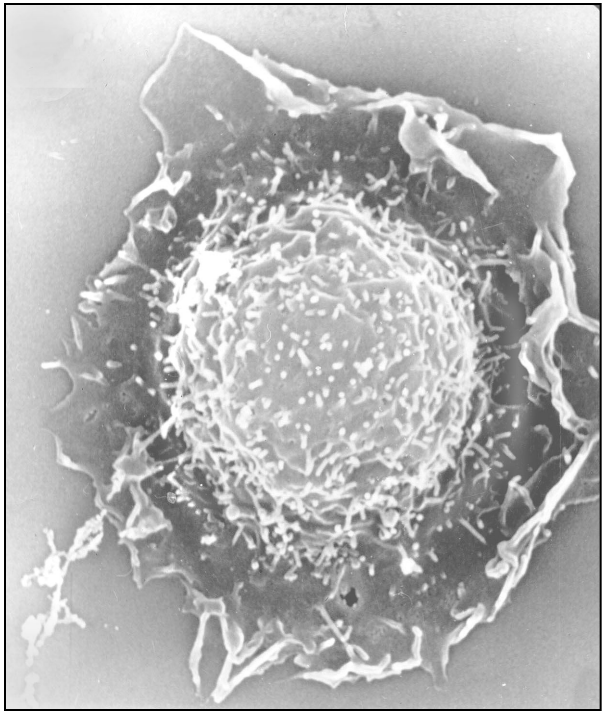

Lumen
N
Y160
C
Flotillin 1
N
Y163
C
Flotillin 2
Cytosol
Key
Myristoyl
Palmitoyl

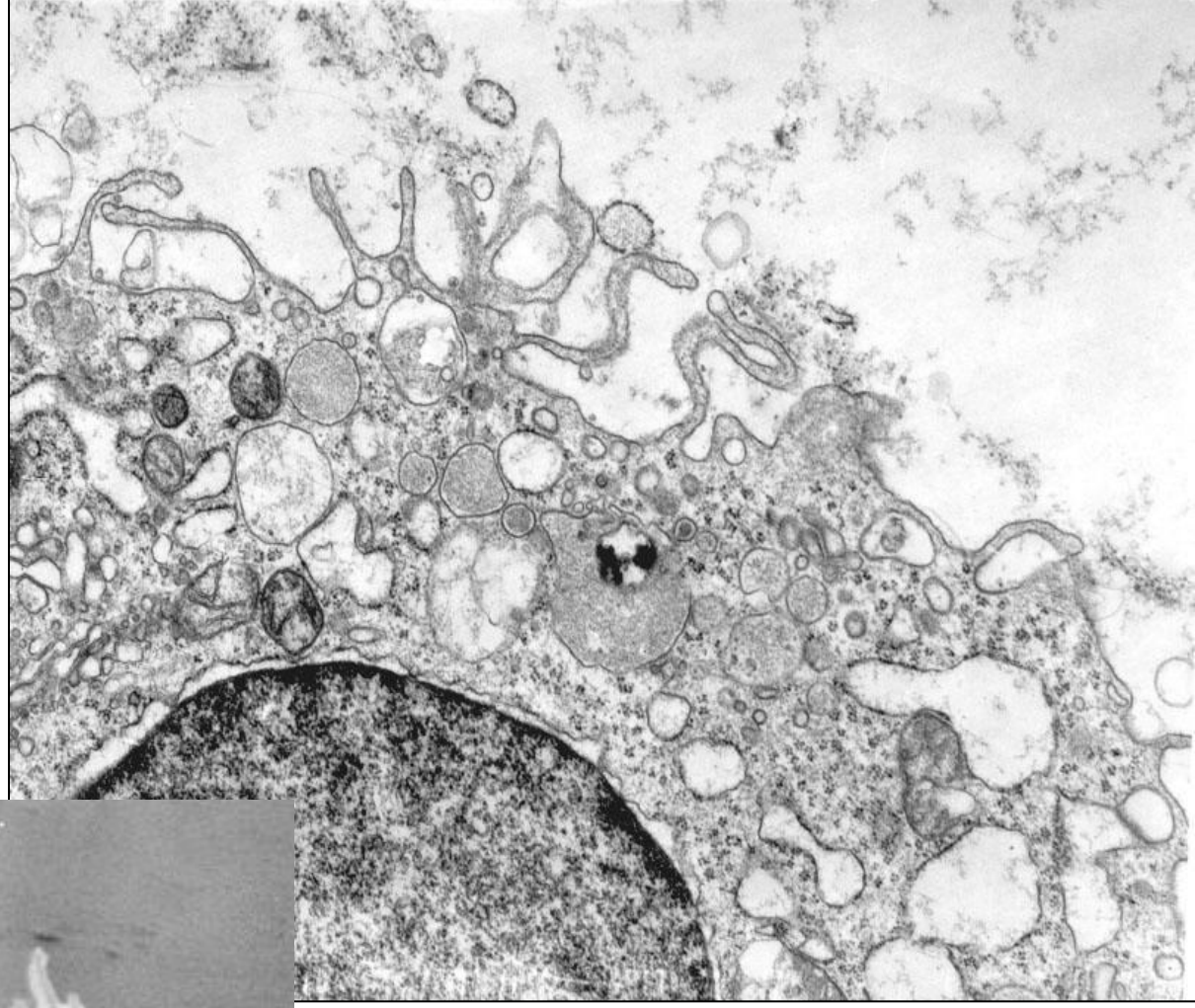

A
lipid raft
sphingolipid
extracellular
intracellular
glycerophospholipid
cholesterol
flotillin-2
flotillin-1
hetero-oligomer
B
Flotillin-1
3
185
427
SPFH/PHB domain
190-362
NH2
COOH
Flotillin-2
5
188
428
SPFH/PHB domain
193-365
NH2
COOH
myristate
palmitate
functional tyrosine
flotillin domain/
AEAE repeat

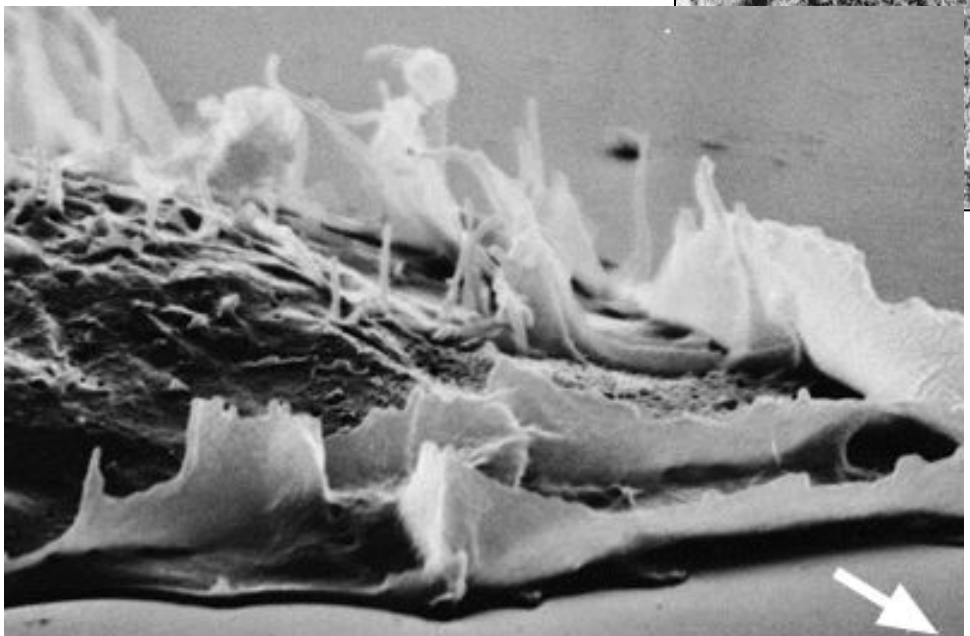

1
2
3
Flotillin-mediated endocytosis
Flotillin- and clathrin-mediated endocytosis
Clathrin-mediated endocytosis
Key
Cargo
Flotillins
Clathrin
Flotillin cofactors
Clathrin adaptor
steady state/ unstimulated
pre-endocytic clustering
endocytosis
PM

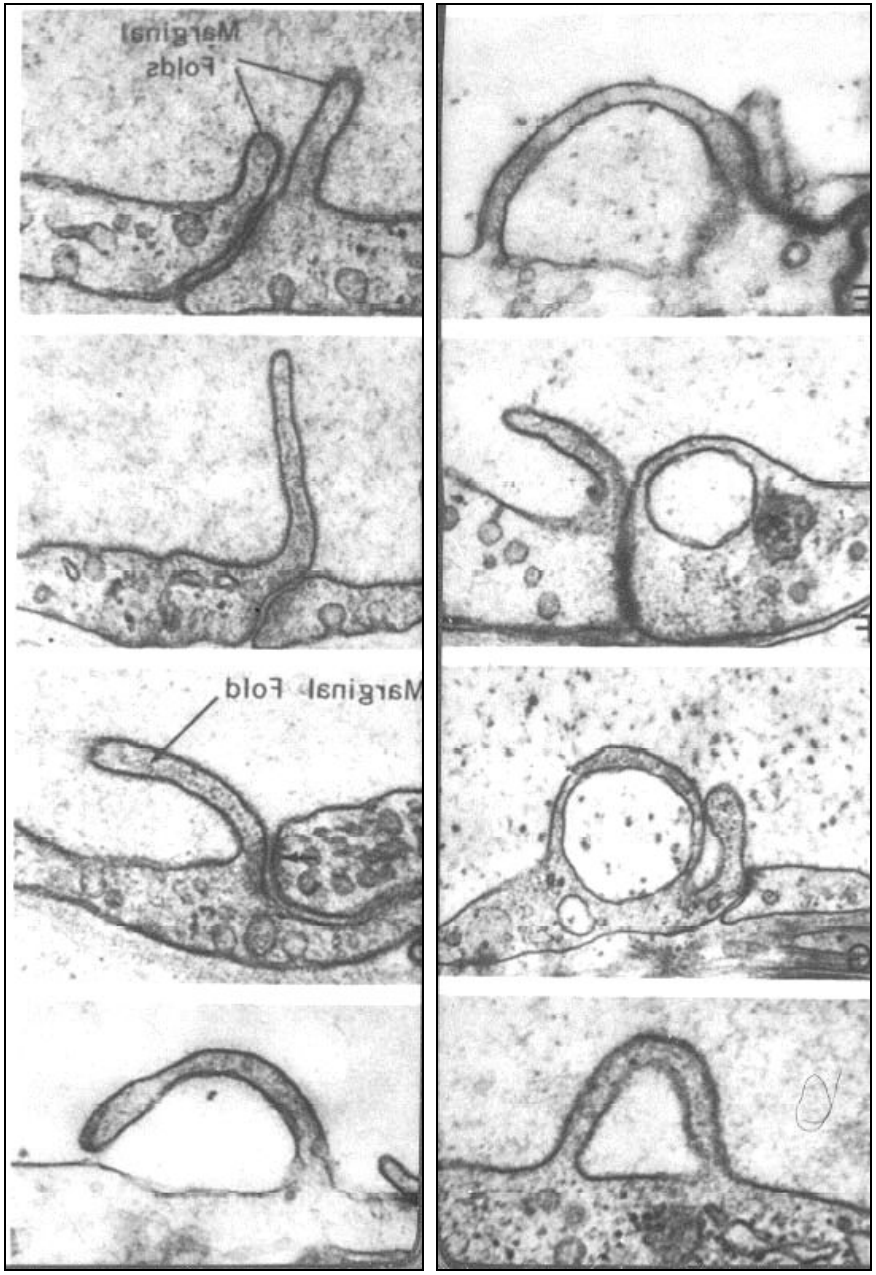

Clathrin HC, mab
Flotillin-1–GFP
Caveolin 1, pab

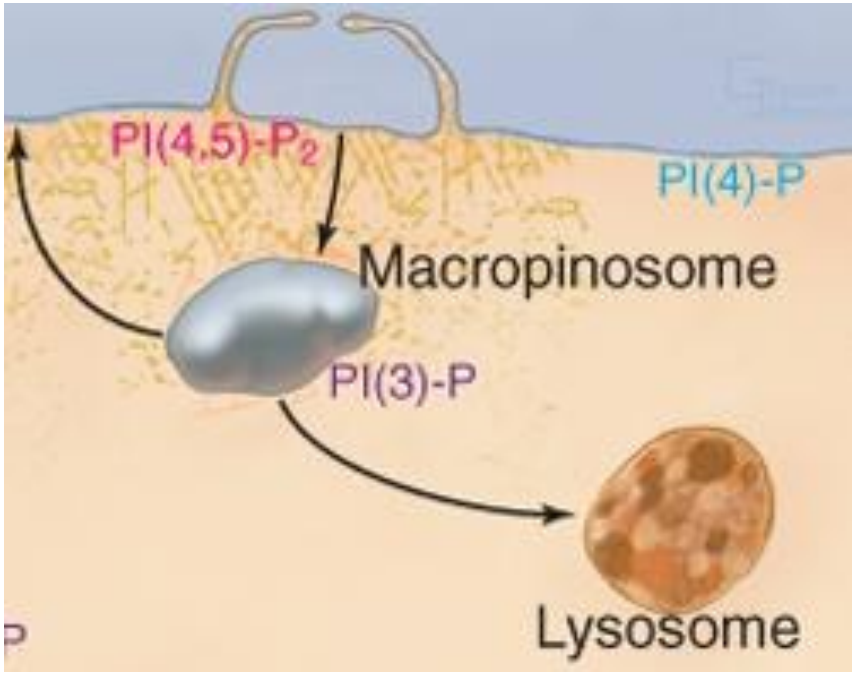


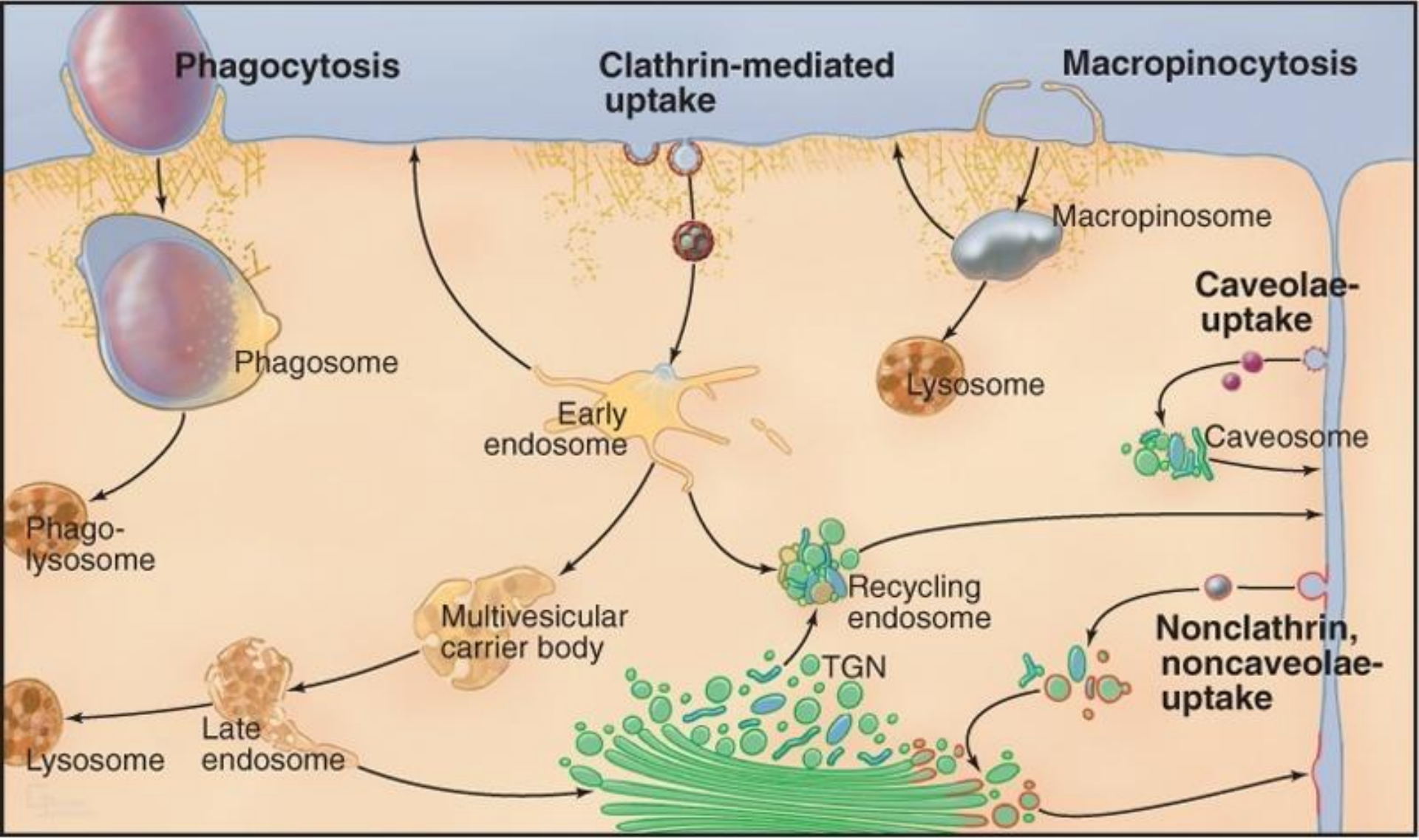


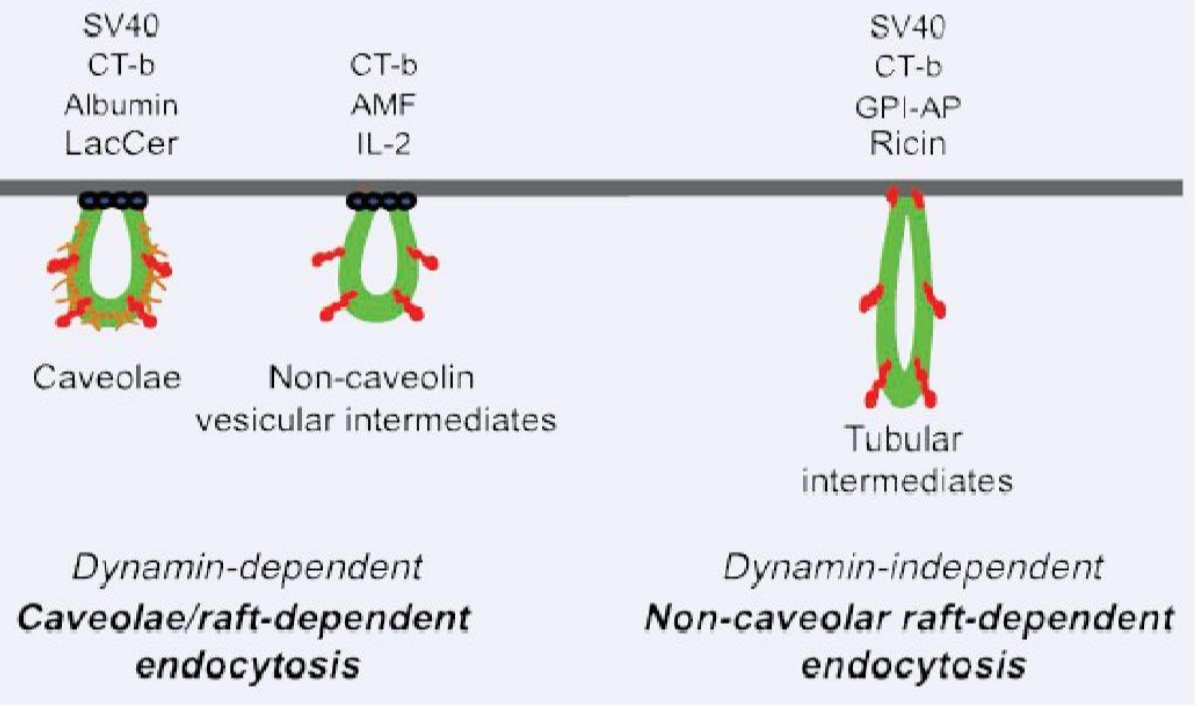


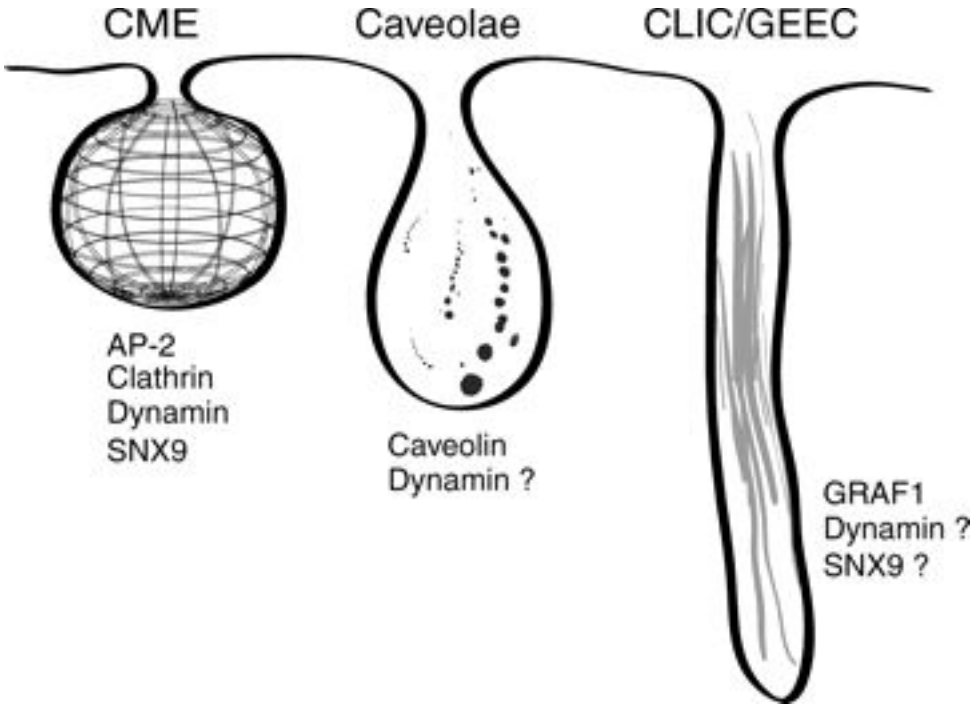



Marginal Folds
Marginal Fold


PI(4,5)-P2
PI(4)-P
Macropinosome
PI(3)-P
Lysosome

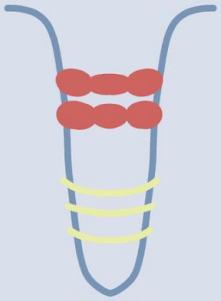



SV40
CT-b
Albumin
LacCer
CT-b
AMF
IL-2
SV40
CT-b
GPI-AP
Ricin
Caveolae
Non-caveolin
vesicular intermediates
Tubular
intermediates
Dynamin-dependent
Caveolae/raft-dependent
endocytosis
Dynamin-independent
Non-caveolar raft-dependent
endocytosis


CME
Caveolae
CLIC/GEEC
AP-2
Clathrin
Dynamin
SNX9
Caveolin
Dynamin ?
GRAF1
Dynamin ?
SNX9 ?

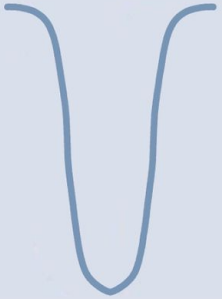
In lipid-rafts membrane domain

Caveolae-dependent Endocytosis



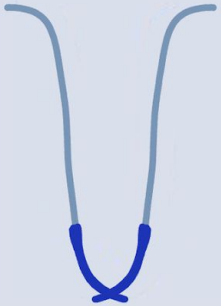
Main regulators:
Caveolin
Dynamin
Cavins
Actin

CLIC/GEEC pathway Endocytosis



Main regulators:
Cdc42
Actin

Fillotin pathway Endocytosis



Main regulators:
Flotillin
Actin

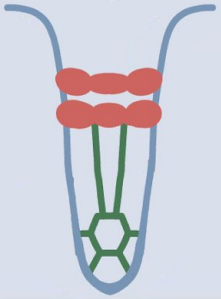
Other Endocytosis pathways

Pathways dependent on small GTPases

Main regulators:
Cdc42
Arf1
Arf6
RhoA

Non-lipid rafts membrane domain

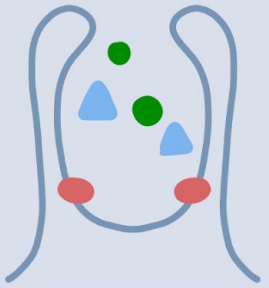
Clathrin-mediated Endocytosis



Main regulators:
Clathrin
Dynamin
AP2
Eps15
Epsin

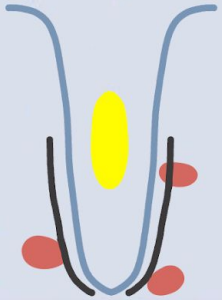
Mixed membrane domains

Micropinocytosis



Main regulators:
Dyn-2
Actin
BARs
Kinases

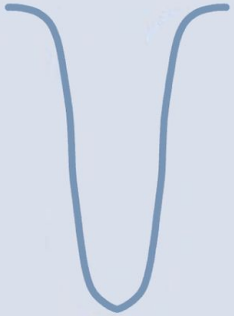
Phagocytosis



Main regulators:
Dyn-2
Actin

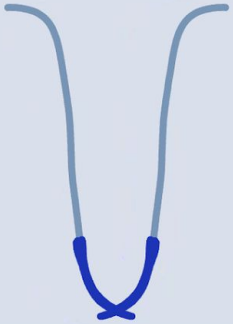
Clathrin and dynamin independent

CLIC/GEEC pathway Endocytosis



Main regulators:
Cdc42
Actin

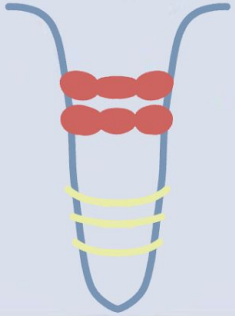
Fillotin pathway Endocytosis



Main regulators:
Flotillin
Actin

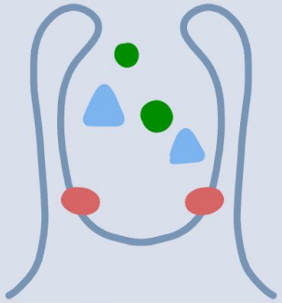
Clathrin-independent and dynamin -dependent

Caveolae-dependent endocytosis



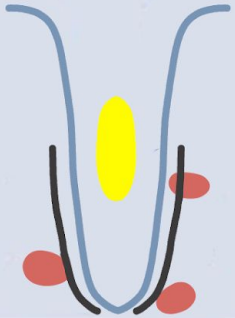
Main regulators:
Caveolin
Dynamin
Cavins
Actin

Micropinocytosis



Main regulators:
Dyn-2
Actin
BARs
Kinases

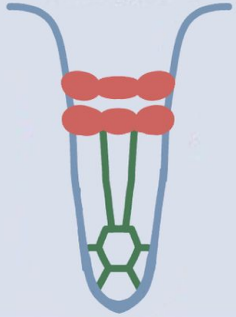
Phagocytosis



Main regulators:
Dyn-2
Actin

Clathrin and dynamin dependent

Clathrin-mediated endocytosis

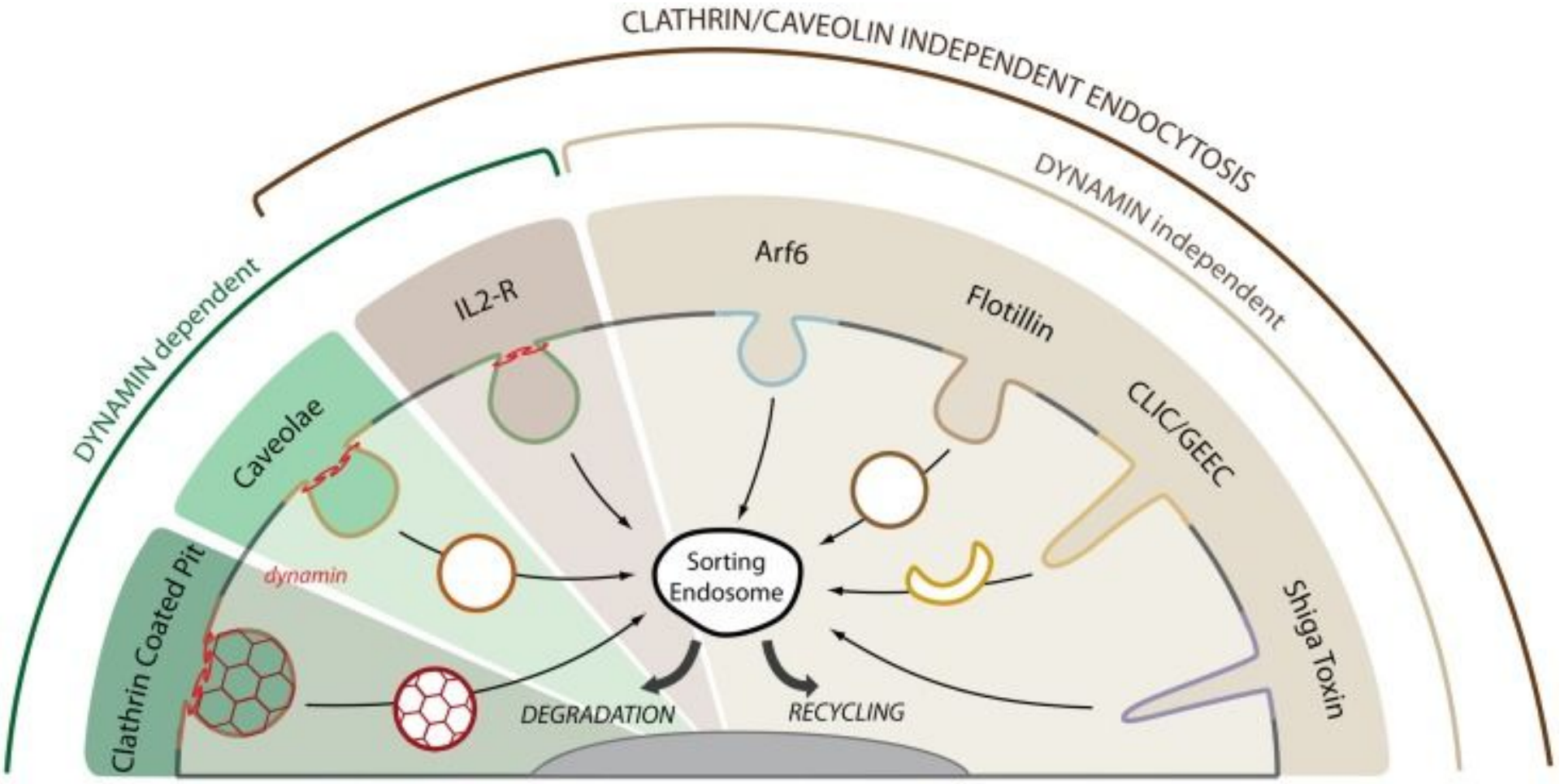


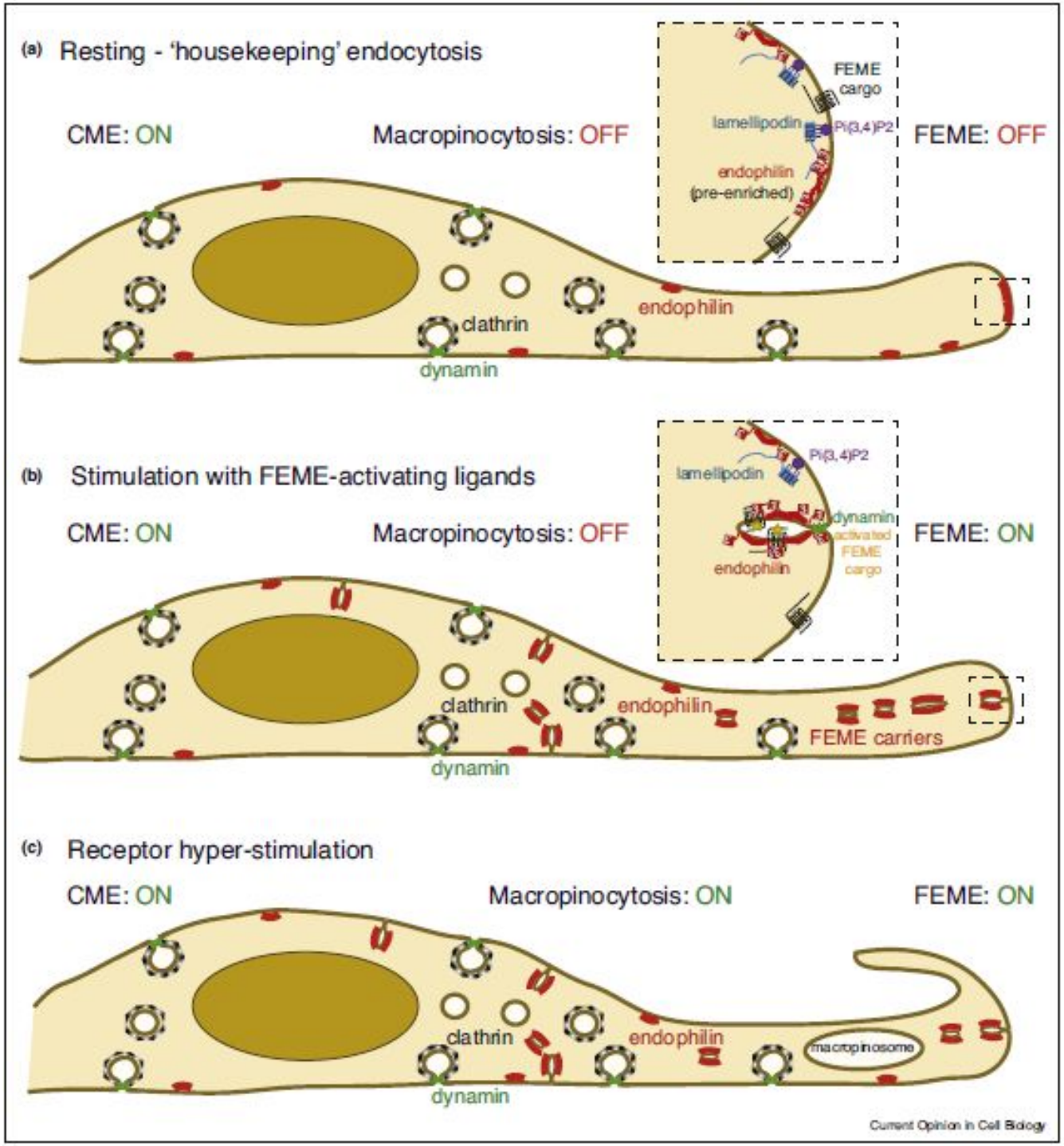
Main regulators:
Clathrin
Dynamin
AP2
Eps15
Epsin

Morphology	Structural components		Cargo	Additional associated proteins
	Involvement of dynamin	Involvement of small GTPases		
Vesicular, flasked-shaped	Yes	Unclear	SV40	Actin, caveolins, PTRF/cavin-1, Src
Vesicular	Both dynamin-dependence and dynamin-independence reported	Unclear	Cholera toxin B, CD59, proteoglycans	Actin, flotillin-1/2
Tubular	No	Cdc42, Arf1	Fluid uptake, cholera toxin B, GPI-APs, VacA toxin	Actin, GRAF1, ARHGAP10
Vesicular	Yes	RhoA, Rac1	IL-2Rβ, γc-cytokine receptor, HIV-1, C2 toxin	Pak 1/2
Tubular	Both dynamin-dependence and dynamin-independence reported	Arf6	MHC I, coxsackievirus A9, carboxypeptidase E, GPI-APs	Unclear
Ruffles and large vesicles	No	Rac1, Cdc42, Arf6	Fluid uptake, pathogens	Actin, Abi1, CtBP1/BARS, PI3K, Pak 1, Ras, Src, SNX-PX-BAR proteins

Defining features of CIE pathways

Feature	Caveolae [34]	Arf6 regulated	CLIC/GEEC	RhoA regulated
Major regulator	Cav1/Cav3	Arf6 [6,23]	Cdc42/Arf1 [7,43]	RhoA [5]
Carrier	50–80 nm smooth, flask-shaped (chemically fixed)	Large, tubular [49]	100–200 nm ring-shaped Clathrin-independent carrier (CLIC) [12]	50–60 nm smooth, vesicular [5]
Dynamin	Dependent	Independent [6]	Independent [7,12]	Dependent [5,25]
Cargo	Lipid-rafts	MHCI, Tac [6]	GPI-AP [7]	IL2R [5]


CLATHRIN/CAVEOLIN INDEPENDENT ENDOCYTOSIS
DYNAMIN independent
DYNAMIN dependent
Arf6
IL2-R
Flotillin
CLIC/GEEC
Caveolae
Clathrin Coated Pit
dynamin
Sorting Endosome
Shiga Toxin
DEGRADATION
RECYCLING


(a) Resting - 'housekeeping' endocytosis
CME: ON
Macropinocytosis: OFF
FEME: OFF
FEME cargo
lamellipodin
PI(3,4)P2
endophilin (pre-enriched)
clathrin
endophilin
dynamin
(b) Stimulation with FEME-activating ligands
CME: ON
Macropinocytosis: OFF
FEME: ON
PI(3,4)P2
lamellipodin
dynamin activated FEME cargo
endophilin
clathrin
endophilin
FEME carriers
dynamin
(c) Receptor hyper-stimulation
CME: ON
Macropinocytosis: ON
FEME: ON
clathrin
endophilin
macropinosome
dynamin
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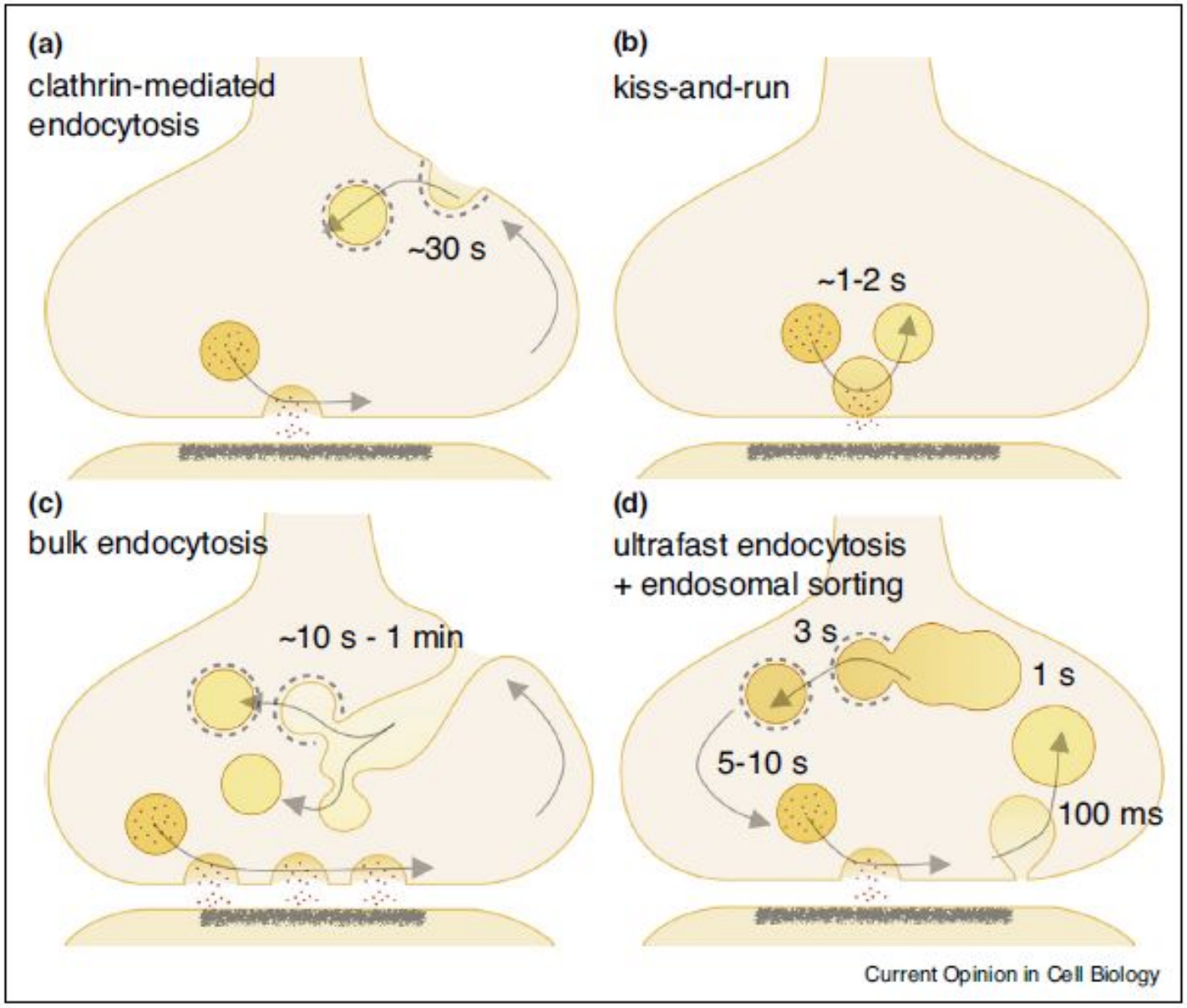
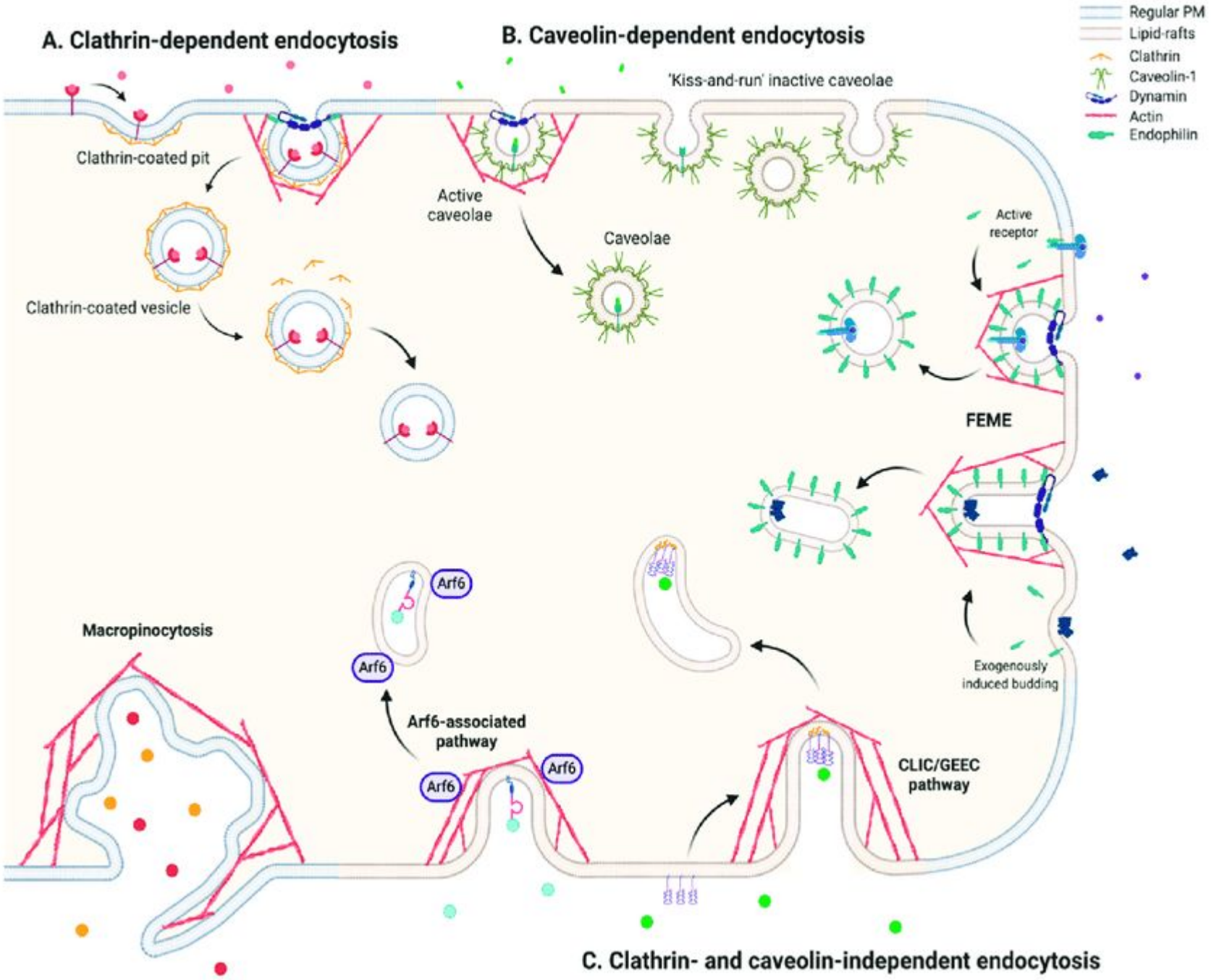
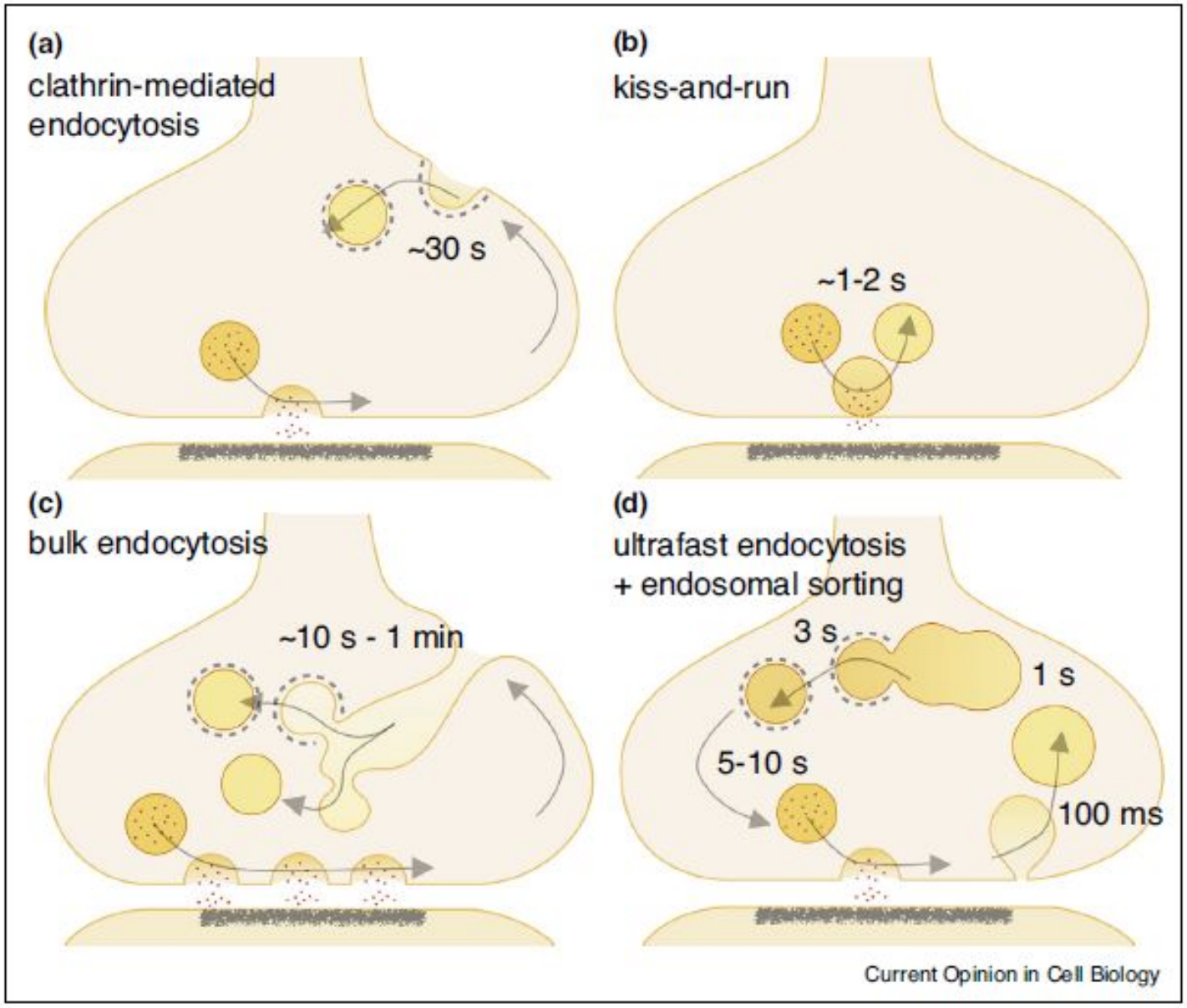
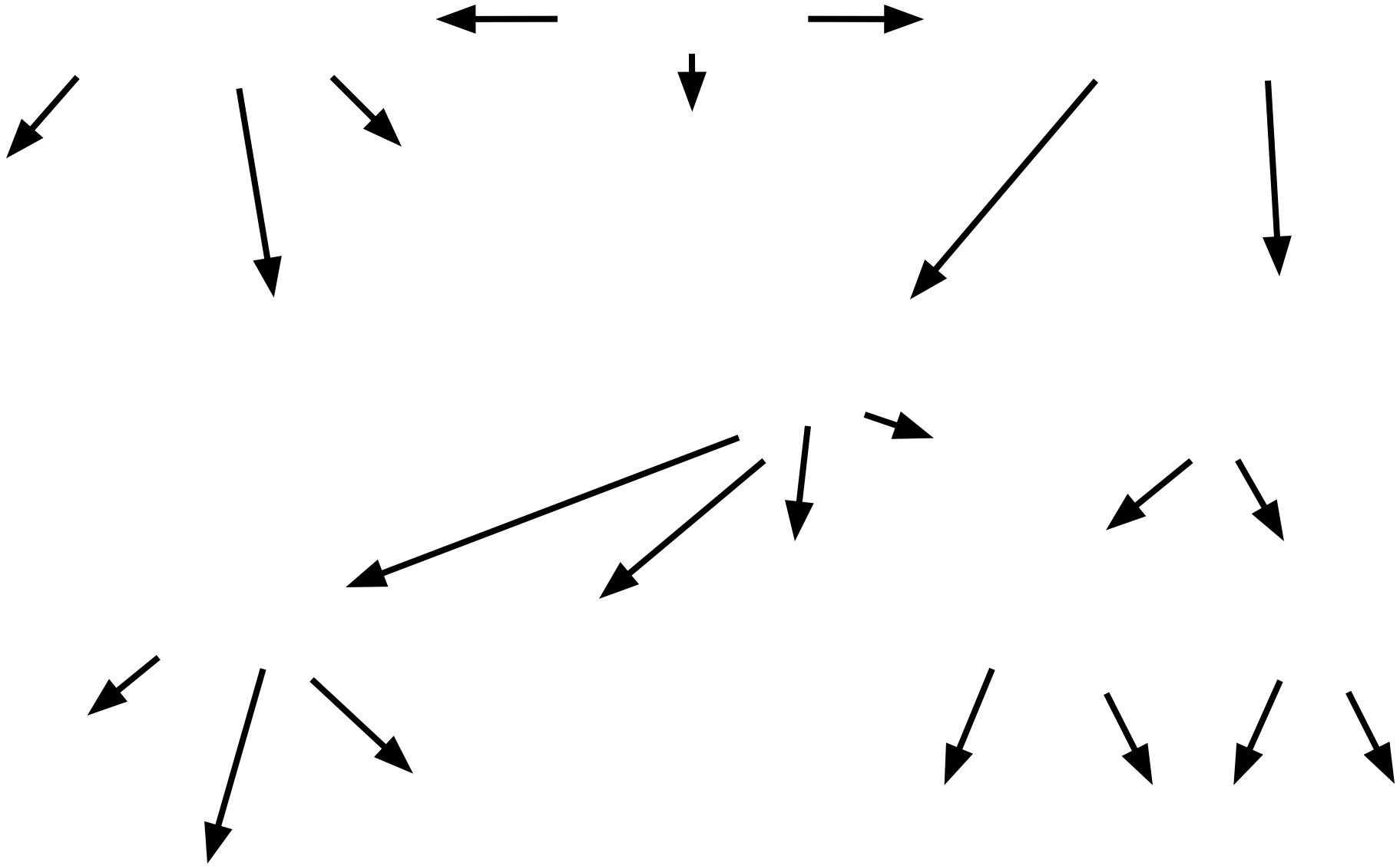
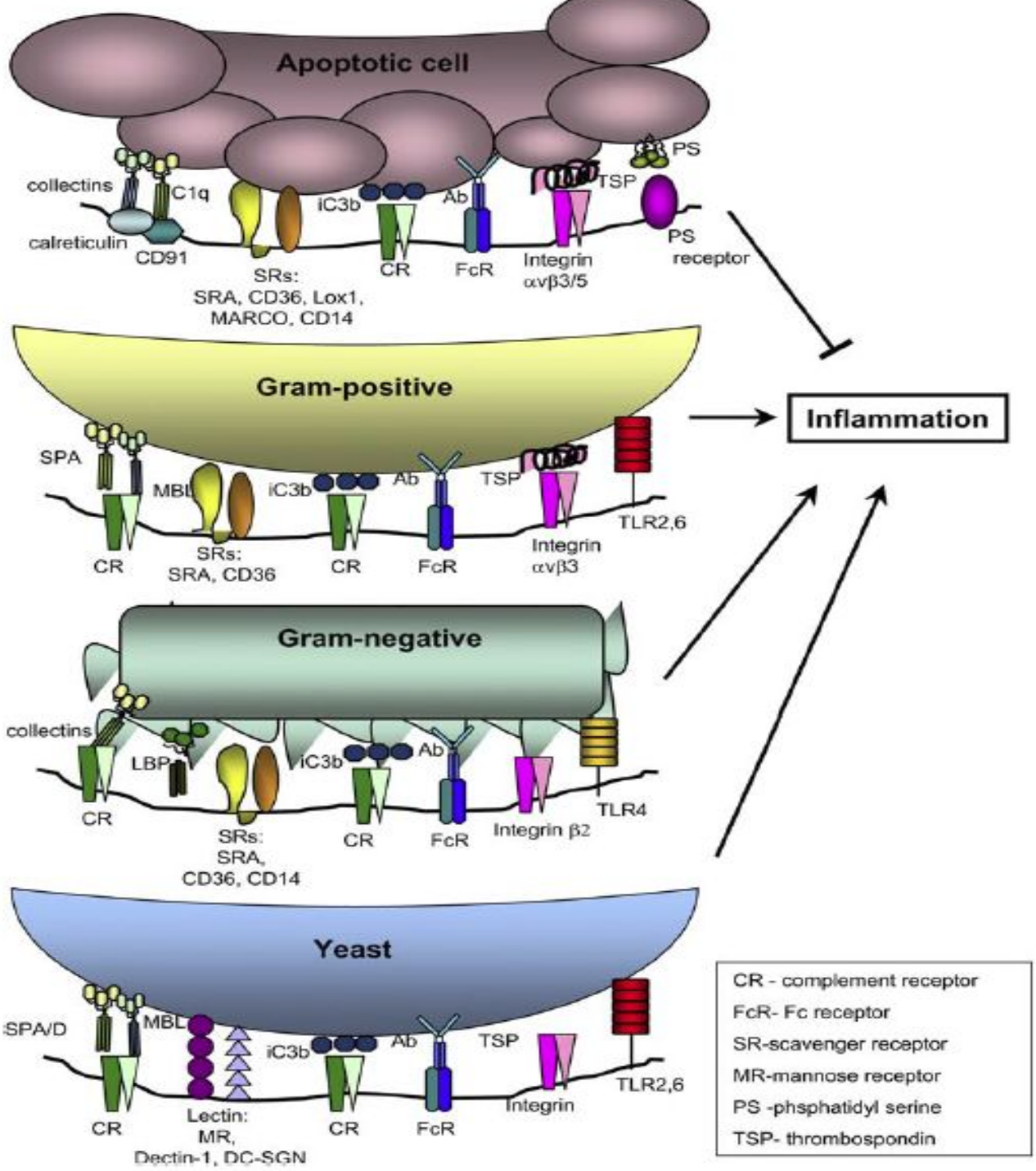

(a)
clathrin-mediated
endocytosis
~30 s
(b)
kiss-and-run
~1-2 s
(c)
bulk endocytosis
~10 s - 1 min
(d)
ultrafast endocytosis
+ endosomal sorting
3 s
1 s
5-10 s
100 ms
Current Opinion in Cell Biology


A. Clathrin-dependent endocytosis
B. Caveolin-dependent endocytosis
'Kiss-and-run' inactive caveolae
Regular PM
Lipid-rafts
Clathrin
Caveolin-1
Dynamin
Actin
Endophilin
Clathrin-coated pit
Active caveolae
Caveolae
Active receptor
Clathrin-coated vesicle
FEME
Arf6
Arf6
Macropinocytosis
Exogenously induced budding
Arf6-associated pathway
Arf6
Arf6
CLIC/GEEC pathway
C. Clathrin- and caveolin-independent endocytosis


(a)
clathrin-mediated
endocytosis
~30 s
(b)
kiss-and-run
~1-2 s
(c)
bulk endocytosis
~10 s - 1 min
(d)
ultrafast endocytosis
+ endosomal sorting
3 s
1 s
5-10 s
100 ms
Current Opinion in Cell Biology




Apoptotic cell
collectins
C1q
calreticulin
CD91
SRs:
SRA, CD36, Lox1,
MARCO, CD14
iC3b
CR
Ab
FcR
TSP
Integrin
αvβ3/5
PS
PS
receptor
Gram-positive
SPA
MBL
SRs:
SRA, CD36
CR
iC3b
CR
Ab
FcR
TSP
Integrin
αvβ3
TLR2,6
Inflammation
Gram-negative
collectins
LBP
CR
SRs:
SRA,
CD36, CD14
iC3b
CR
Ab
FcR
Integrin β2
TLR4
Yeast
SPA/D
MBL
Lectin:
MR,
Dectin-1, DC-SGN
iC3b
CR
Ab
FcR
TSP
Integrin
TLR2,6
CR - complement receptor
FcR- Fc receptor
SR-scavenger receptor
MR-mannose receptor
PS -phsphatidyl serine
TSP- thrombospondin