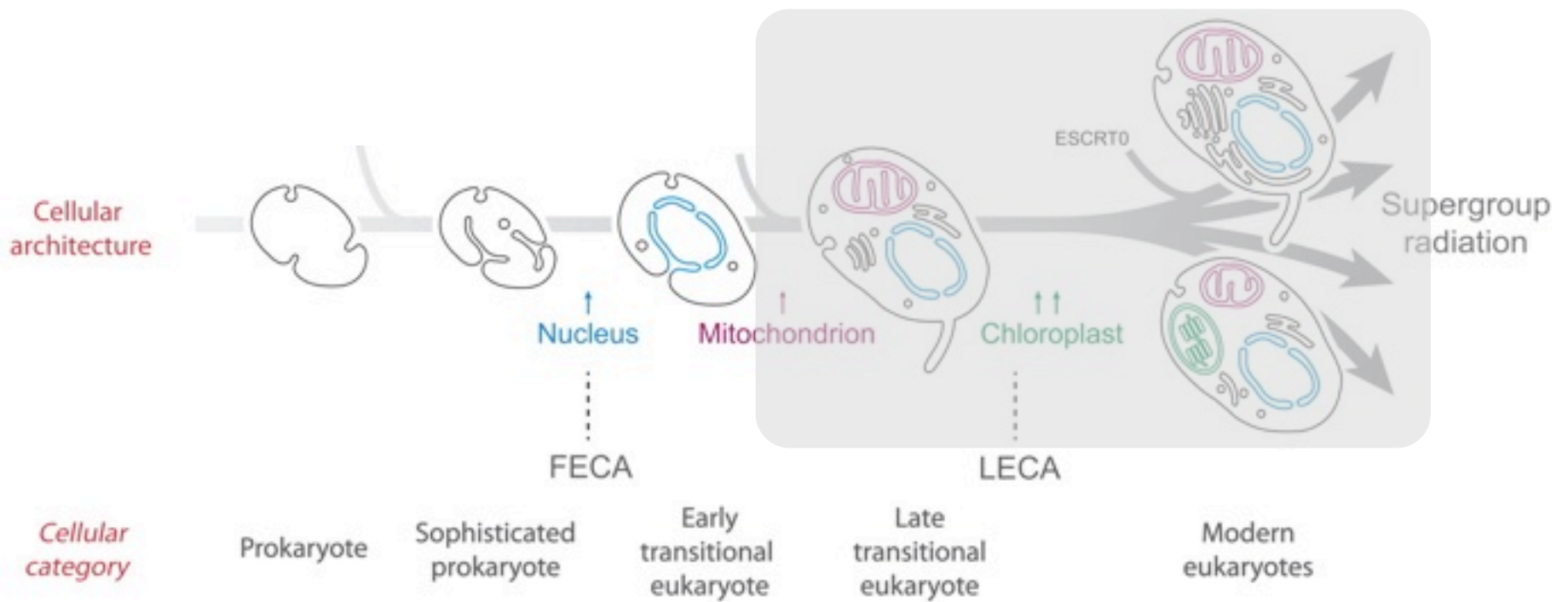
An electron micrograph showing a large, roughly circular cell with a prominent, lighter-colored central compartment. This compartment is surrounded by a thin membrane and contains a dense network of fine, parallel filaments. The surrounding cytoplasm is darker and contains various organelles, including smaller circular vesicles and larger, more complex structures. The overall appearance is that of a highly organized, compartmentalized cell.

Evolutionary origins of compartmentalized cells  
ICTS  
Bangalore, Feb. 2012

**Microbiology's  
platypus**

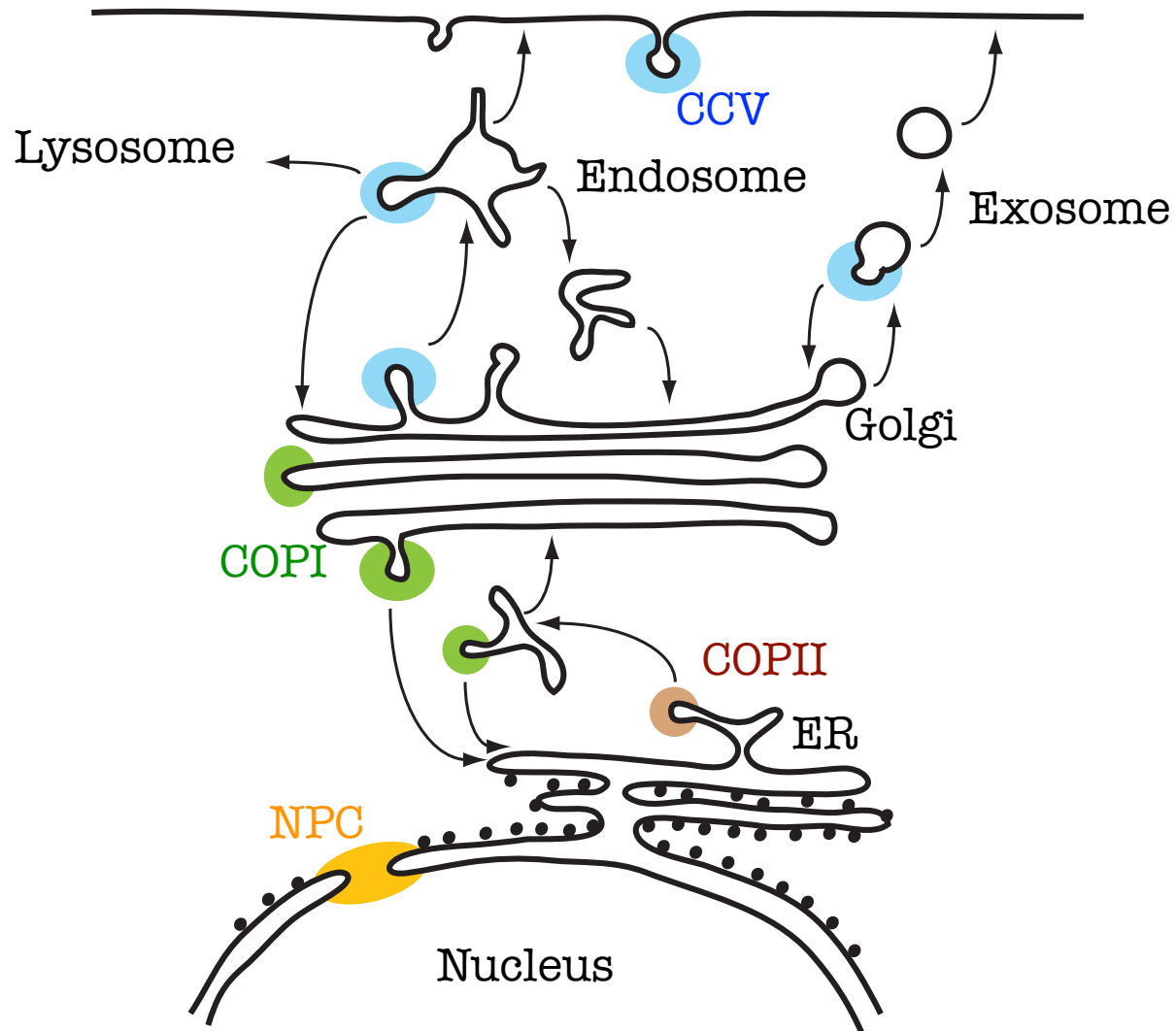
**Damien Devos  
EMBL, Heidelberg  
Germany**

# Before the endosymbionts



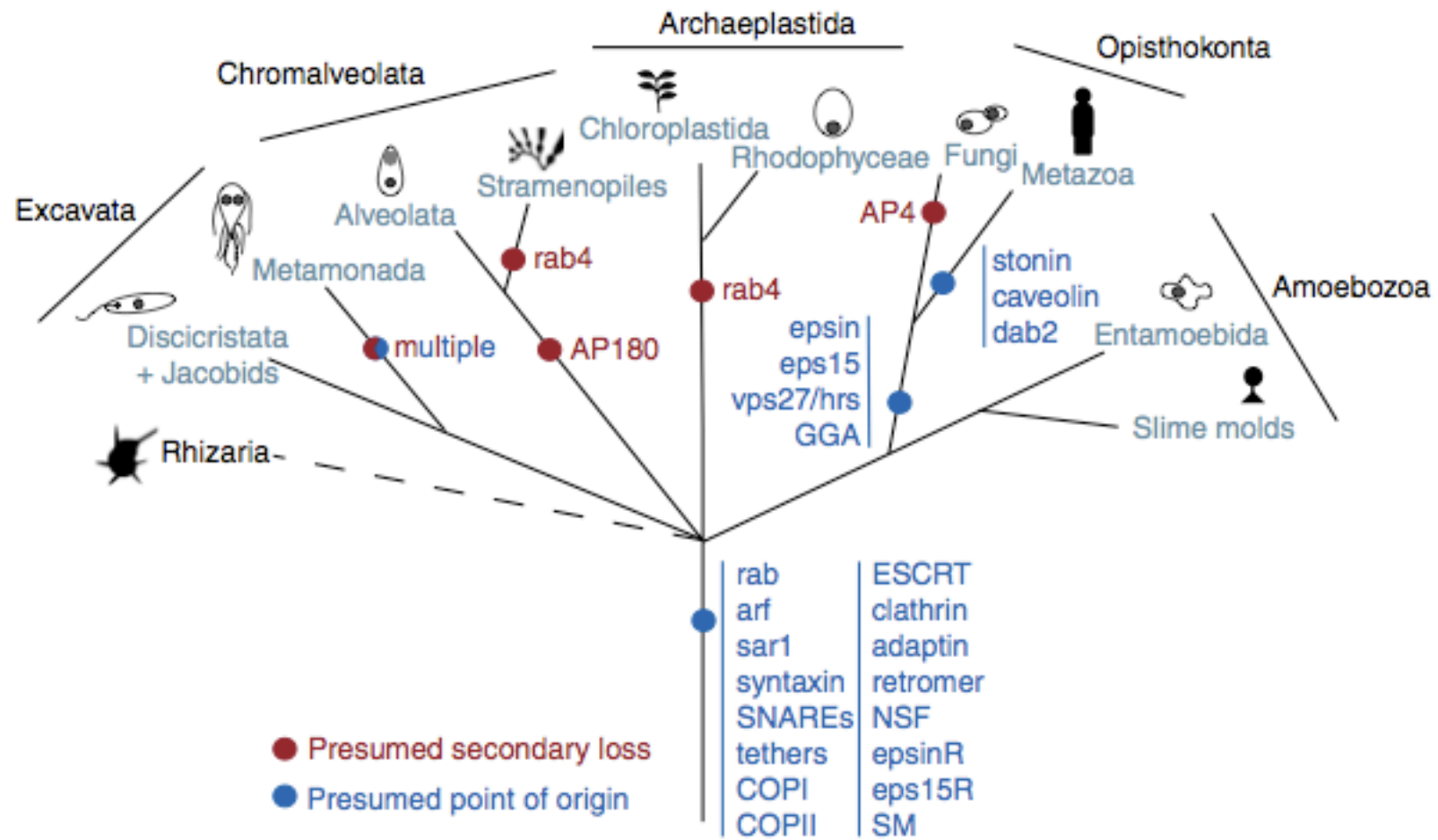
Field et al., JCB 2011

# Eukaryotic Membrane Systems

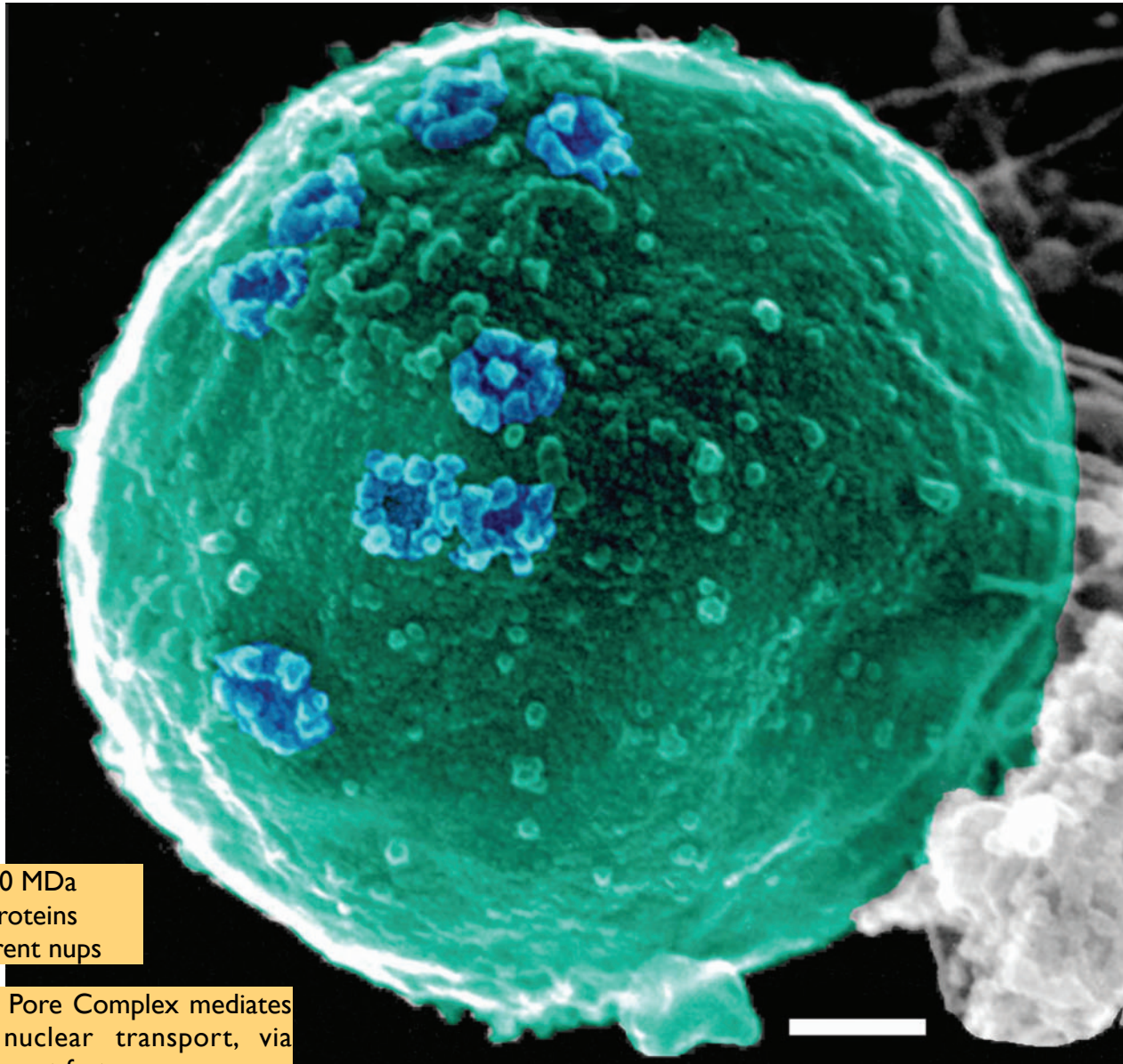




# LECA already had a complex endomembrane system including nucleus and NPC



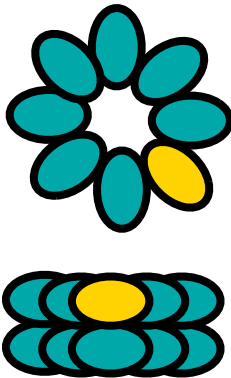
# The Nuclear Pore Complex































~50-100 MDa  
~480 proteins  
~30 different nups

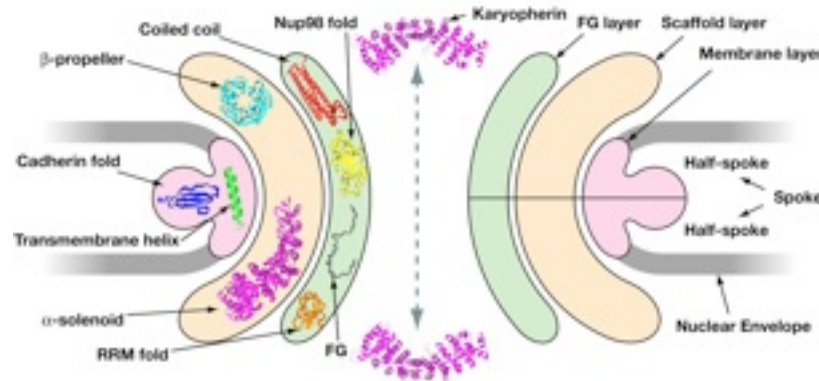
The Nuclear Pore Complex mediates all known nuclear transport, via cognate transport factors.

Scale bar: 100 nm































# Simplified organization of the NPC

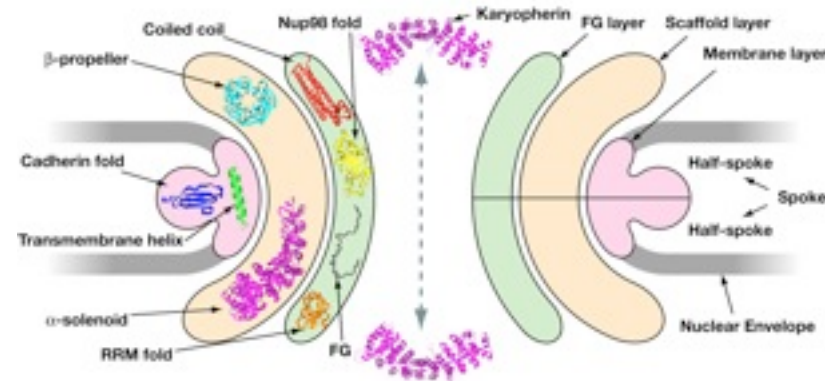
	Pom34
	Ndc1
	Pom152
	Sec13
	Seh1
	Nup145C
	Nup84
	Nup85
	Nic96
	Nup188
	Nup192
	Nup120
	Nup133
	Nup157
	Nup170
	Nup82
	Nup159
	Nup49
	Nup57
	Nsp1
	Nup145N
	Nup100
	Nup116
	Nup53
	Nup59
	Nup42
	Nup60
	Nup1



Devos et al., PNAS 2006; Alber et al., Nature 2007

# Simplified organization of the NPC





























		Pom34
		Ndc1
		Pom152
beta-propeller		Sec13
		Seh1
SPAH (Stacked pairs of alpha-helices)		Nup145C
		Nup84
		Nup85
		Nup86
		Nup188
		Nup192
		Nup120
		Nup133
		Nup157
		Nup170
		Nup82
		Nup159
		Nup49
		Nup57
		Nsp1
		Nup145N
		Nup100
		Nup116
		Nup53
		Nup59
		Nup42
		Nup60
		Nup1

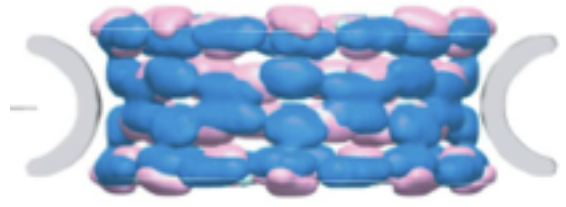
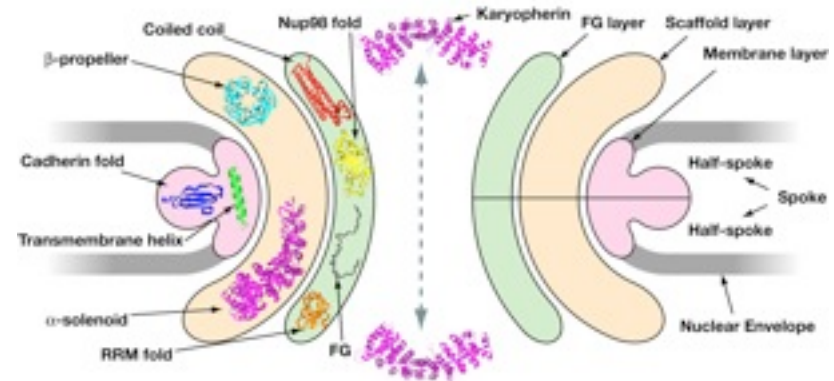


Devos et al., PNAS 2006; Alber et al., Nature 2007



# Simplified organization of the NPC





























		Pom34
		Ndc1
beta-propeller		Pom152
		Sec13
		Seh1
SPAH (Stacked pairs of alpha-helices)		Nup145C
		Nup84
		Nup85
		Nic96
		Nup188
		Nup192
		Nup120
		Nup133
		Nup157
		Nup170
		Nup82
		Nup159
		Nup49
		Nup57
		Nsp1
		Nup145N
		Nup100
		Nup116
		Nup53
		Nup59
		Nup42
		Nup60
		Nup1

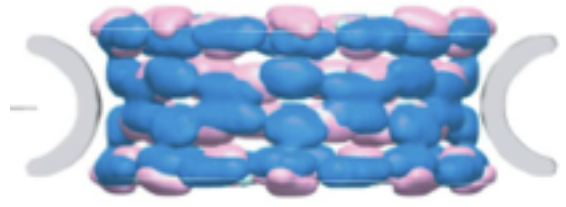
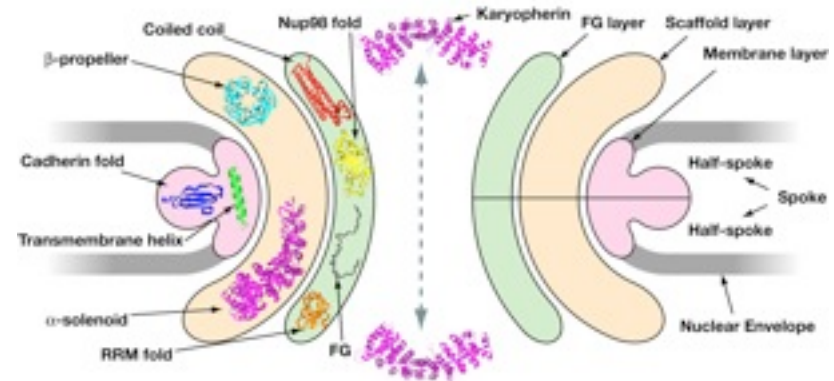


Devos et al., PNAS 2006; Alber et al., Nature 2007



# Simplified organization of the NPC

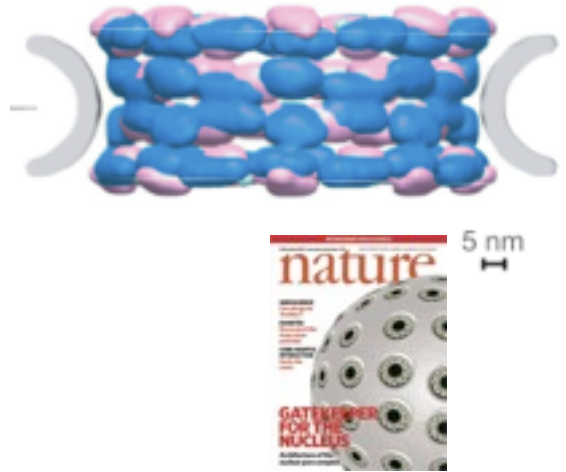
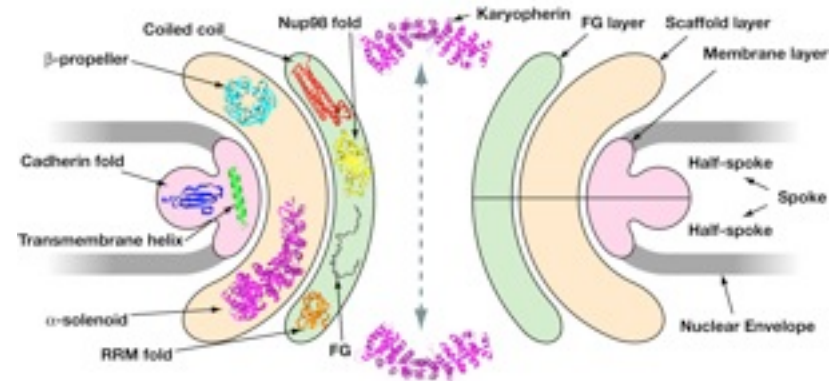
		Pom34
		Ndc1
		Pom152
beta-propeller		Sec13
		Seh1
SPAH (Stacked pairs of alpha-helices)		Nup145C
		Nup84
		Nup85
		Nic96
		Nup188
		Nup192
		Nup120
		Nup133
		Nup157
		Nup170
		Nup82
		Nup159
		Nup49
		Nup57
		Nsp1
		Nup145N
		Nup100
		Nup116
		Nup53
		Nup59
		Nup42
		Nup60
		Nup1



Devos et al., PNAS 2006; Alber et al., Nature 2007

# Simplified organization of the NPC

		Pom34
		Ndc1
		Pom152
beta-propeller		Sec13
		Seh1
SPAH (Stacked pairs of alpha-helices)		Nup145C
		Nup84
		Nup85
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		Nup120
		Nup133
		Nup157
		Nup170
		Nup82
		Nup159
		Nup49
		Nup57
		Nsp1
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		Nup59
		Nup42
		Nup60
		Nup1



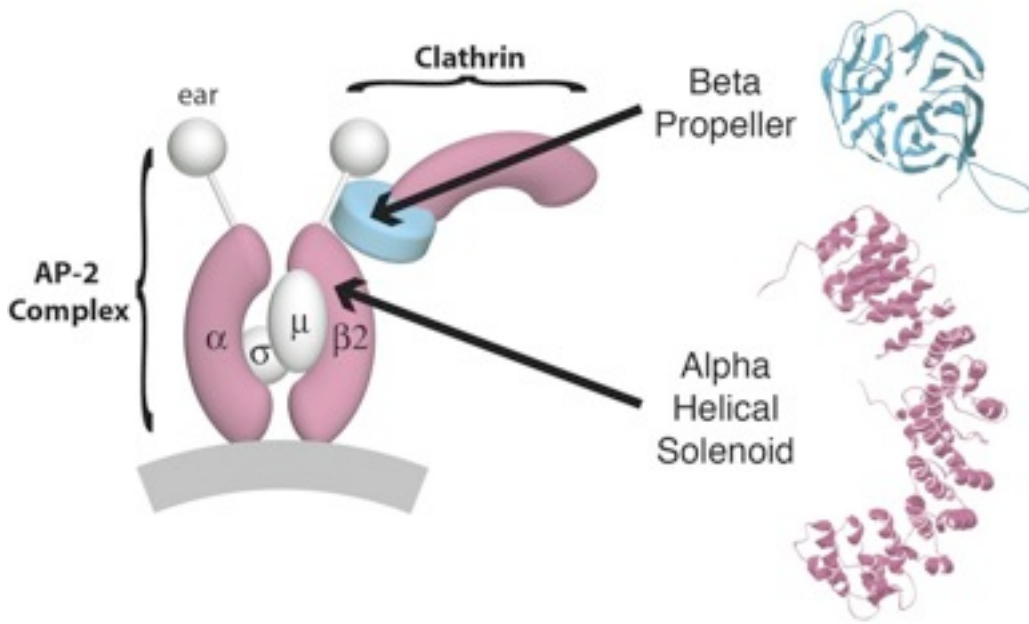
Particular architecture restricted to eukaryotic proteins involved in NPC or coated vesicles

Devos et al., PNAS 2006; Alber et al., Nature 2007

# NPC and Coated Vesicle share a unique architecture

## EXAMPLE

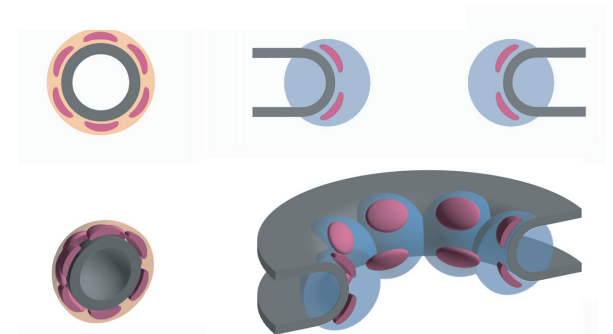
### Clathrin/AP-2 Complex



## FOLDS

CCVs	COPI	COPII	NPC
<b>Clathrin-N</b>	<b>α-subunit-N</b>	<b>Sec31-N</b>	<b>Nup120-N</b>
	<b>β'-subunit-N</b>	Sec13	<b>Nup133-N</b>
		Seh1	Sec13
			Seh1
<b>Clathrin-C</b>	<b>α-subunit-C</b>	<b>Sec31-C</b>	<b>Nup120-C</b>
α-subunit	<b>β'-subunit-C</b>		<b>Nup133-C</b>
β-subunit	β-subunit		Nup85
γ-subunit	γ-subunit		Nup84
δ-subunit	ε-subunit		Nup145C
ε-subunit			

Membrane coats architecture  
(Nt-propeller + Ct-SPAH)



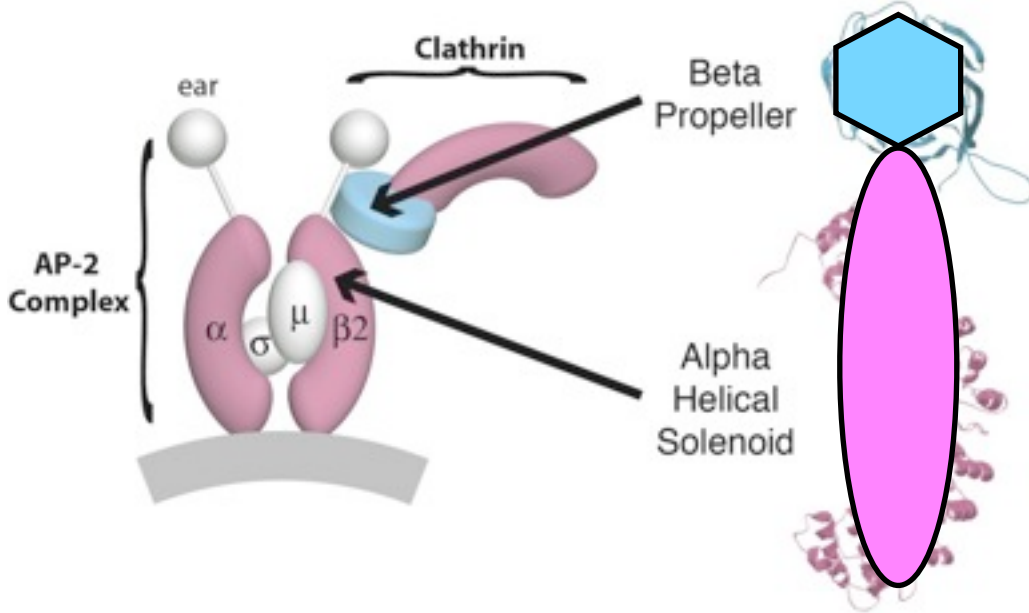
Devos et al., PLoS Biology 2004



# NPC and Coated Vesicle share a unique architecture

## EXAMPLE

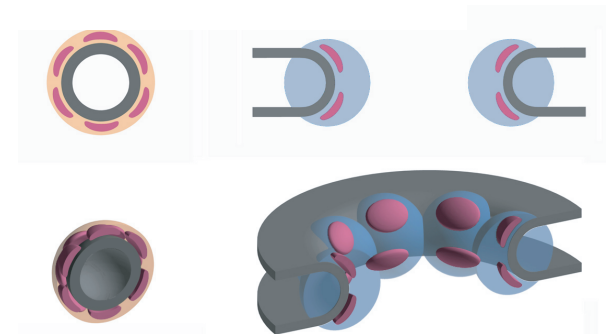
### Clathrin/AP-2 Complex



## FOLDS

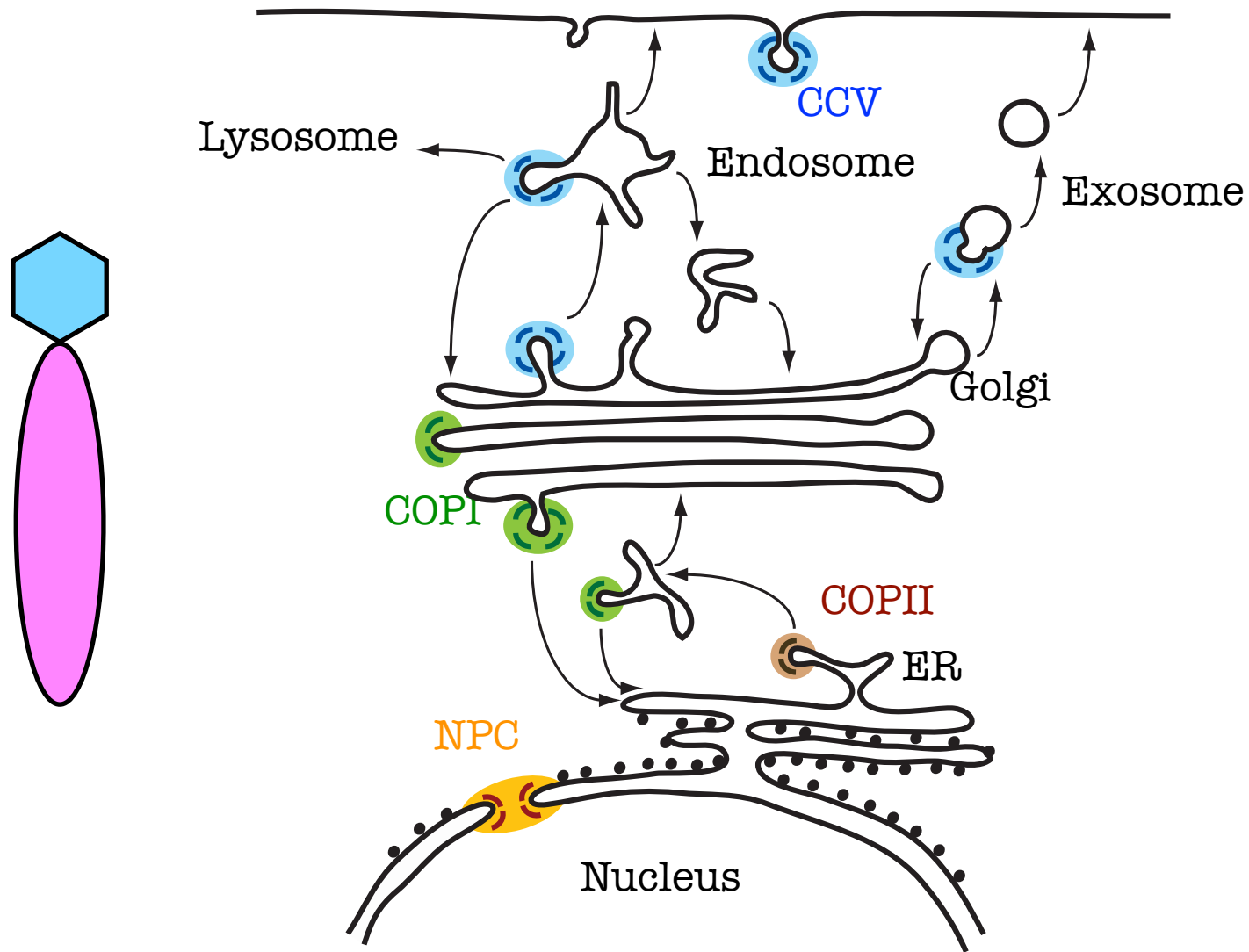
CCVs	COPI	COPII	NPC
<b>Clathrin-N</b>	<b><math>\alpha</math>-subunit-N</b>	<b>Sec31-N</b>	<b>Nup120-N</b>
	<b><math>\beta'</math>-subunit-N</b>	Sec13	<b>Nup133-N</b>
		Seh1	Sec13
			Seh1
<b>Clathrin-C</b>	<b><math>\alpha</math>-subunit-C</b>	<b>Sec31-C</b>	<b>Nup120-C</b>
$\alpha$ -subunit	<b><math>\beta'</math>-subunit-C</b>		<b>Nup133-C</b>
$\beta$ -subunit	$\beta$ -subunit		Nup85
$\gamma$ -subunit	$\gamma$ -subunit		Nup84
$\delta$ -subunit	$\epsilon$ -subunit		Nup145C
$\epsilon$ -subunit			

Membrane coats architecture  
(Nt-propeller + Ct-SPAH)



Devos et al., PLoS Biology 2004

# MC Proteins in Eukaryotic endomembrane complexes



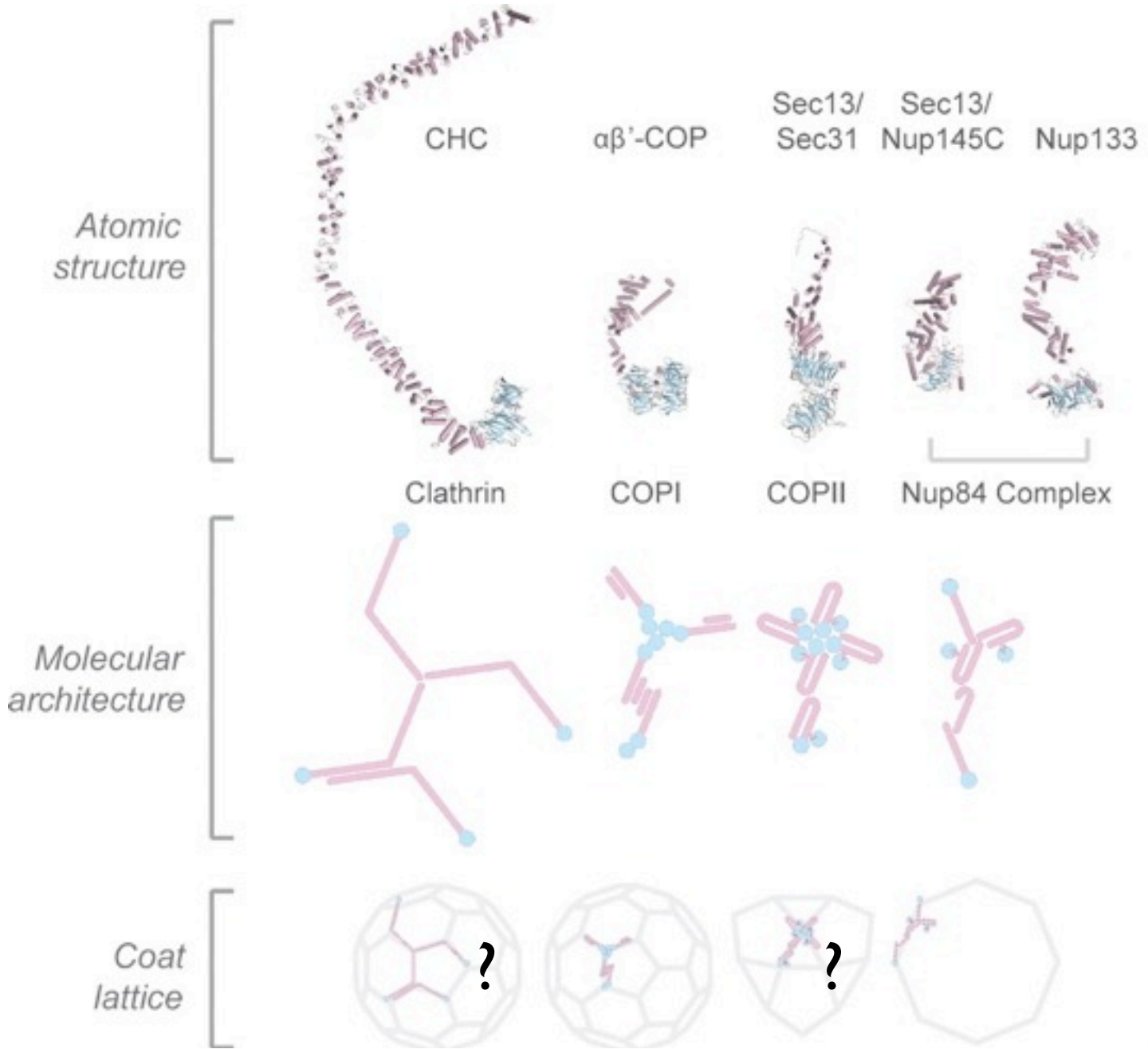
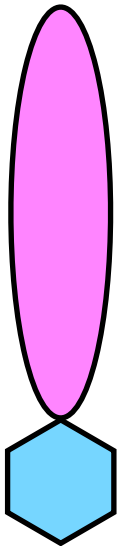
Devos et al., *PLoS Biology* 2004

# Similarities and differences between MC proteins



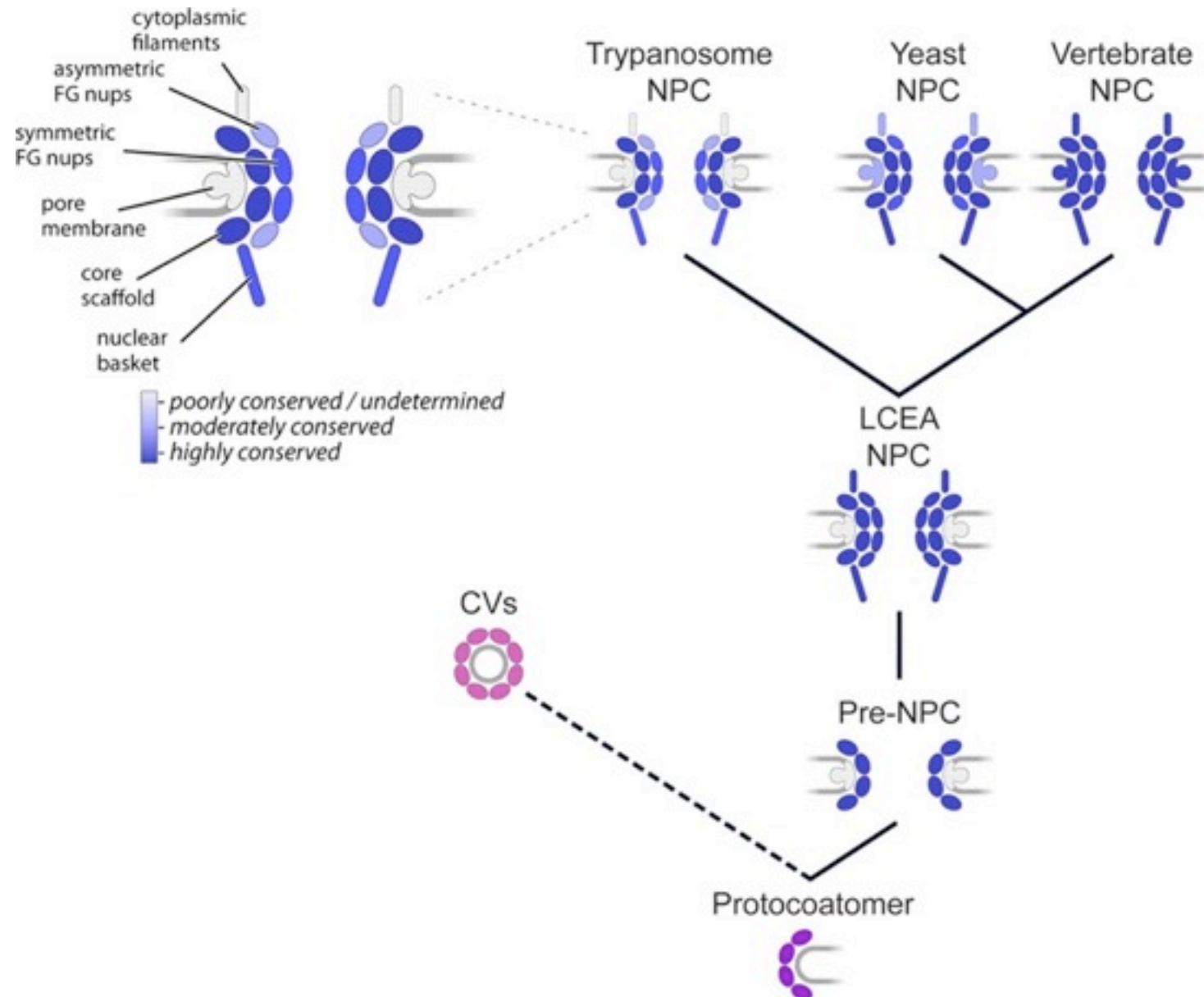


# NPC lattice and assembly/disassembly



Field et al., JCB 2011

# Architecture Conserved from the Last Common Eukaryotic Ancestor



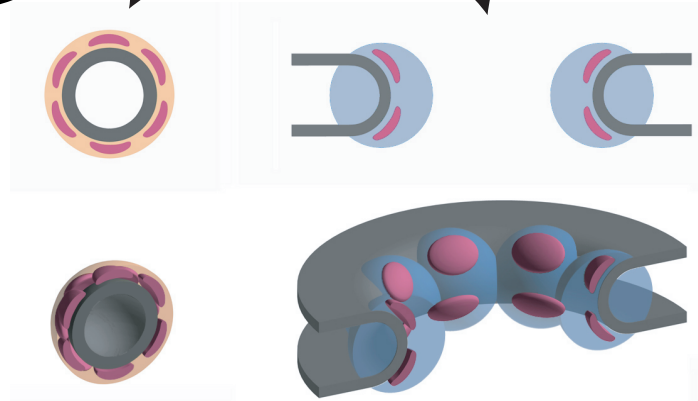
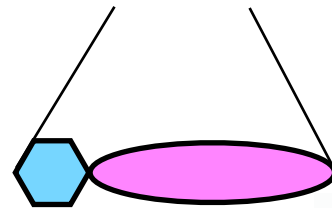
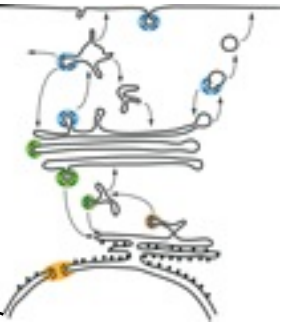
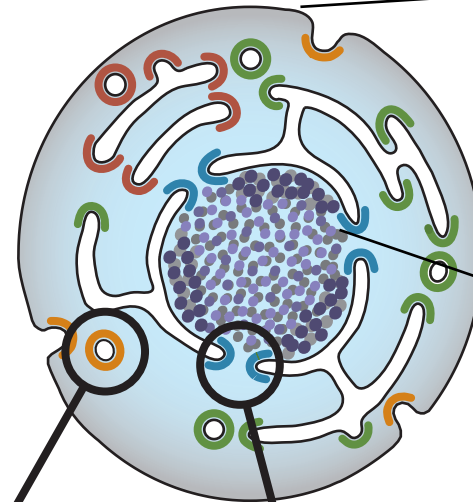
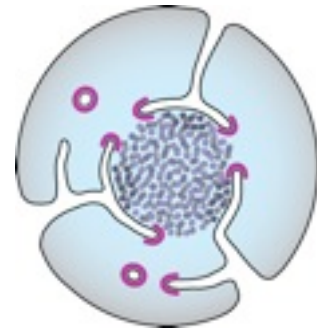
DeGrasse et al., Mol. Cell. Proteom. 2009

# The Protoconformer Hypothesis

Prokaryote

Early Eukaryote

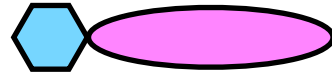
Modern Eukaryote



Devos et al., *PLoS Biology* 2004



# Membrane Coat Proteins

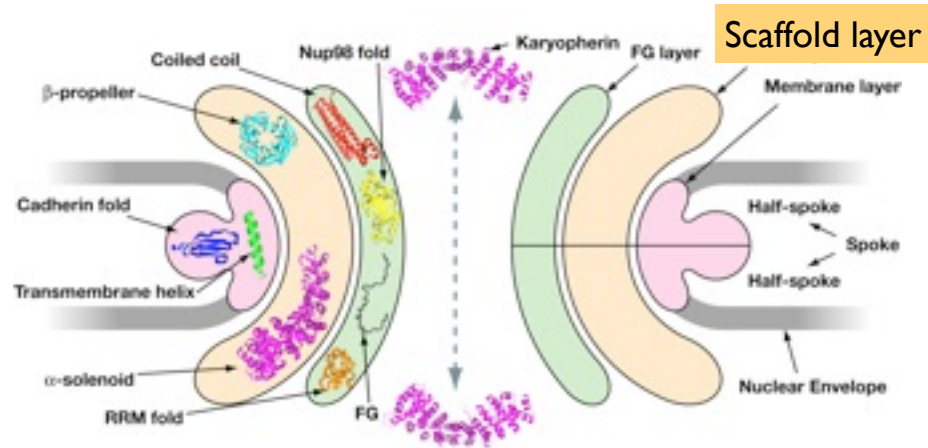


Essential to the integrity of each compartment

Scaffold

Earliest steps of eukaryotic evolution

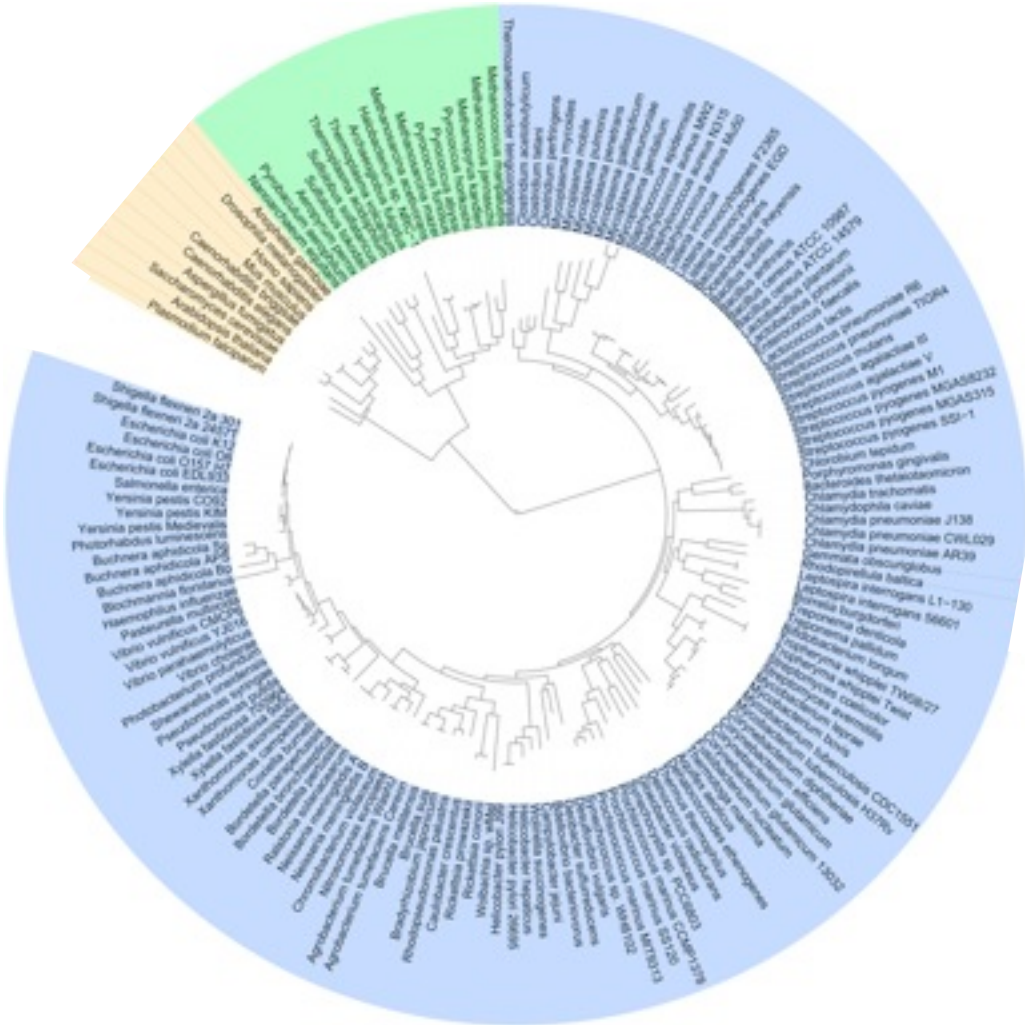
Ancestor of the eukaryotes



Devos et al., *PLoS Biology* 2004

# Searching for the origin of Euk MCs

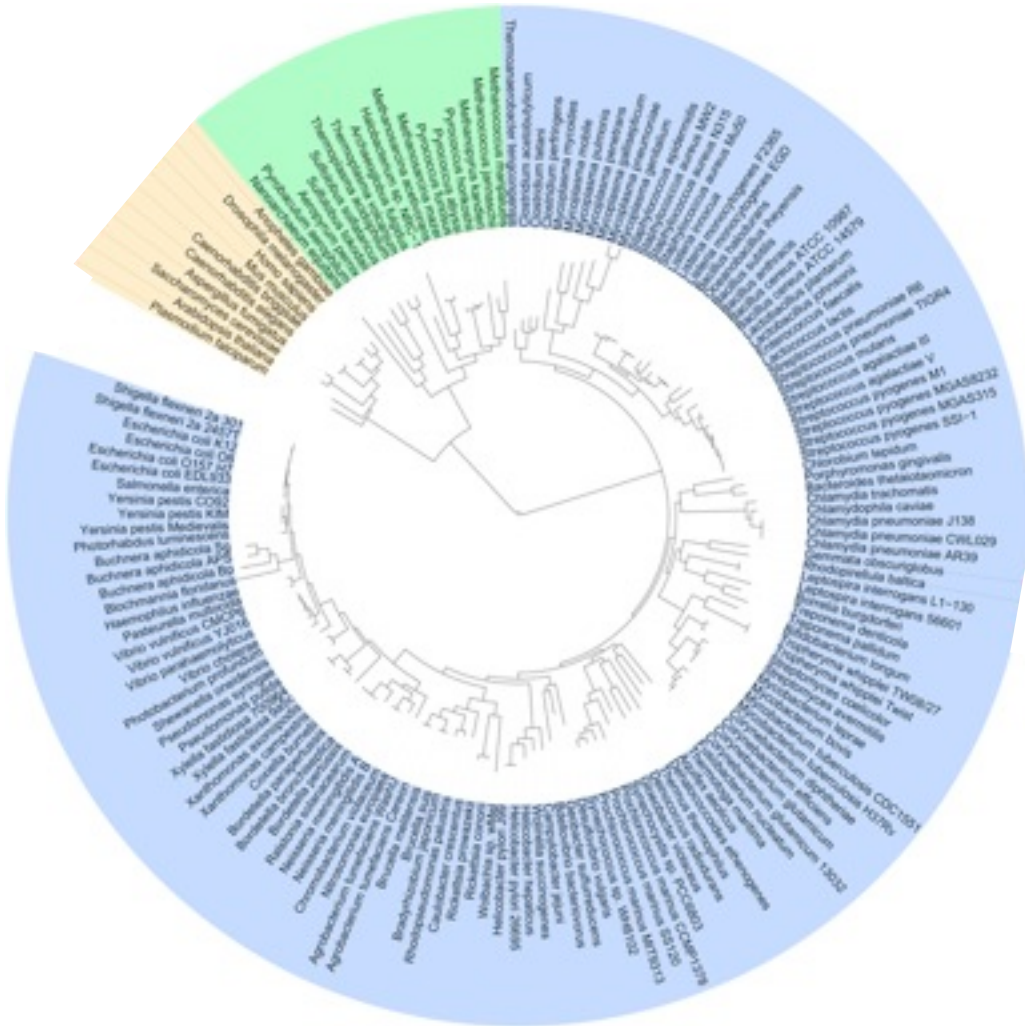
Fold assignments  
>200 complete genomes  
~1x10<sup>9</sup> sequence



Santarella et al., PLoS Biology 2010

# Searching for the origin of Euk MCs

Fold assignments  
>200 complete genomes  
~1x10<sup>9</sup> sequence

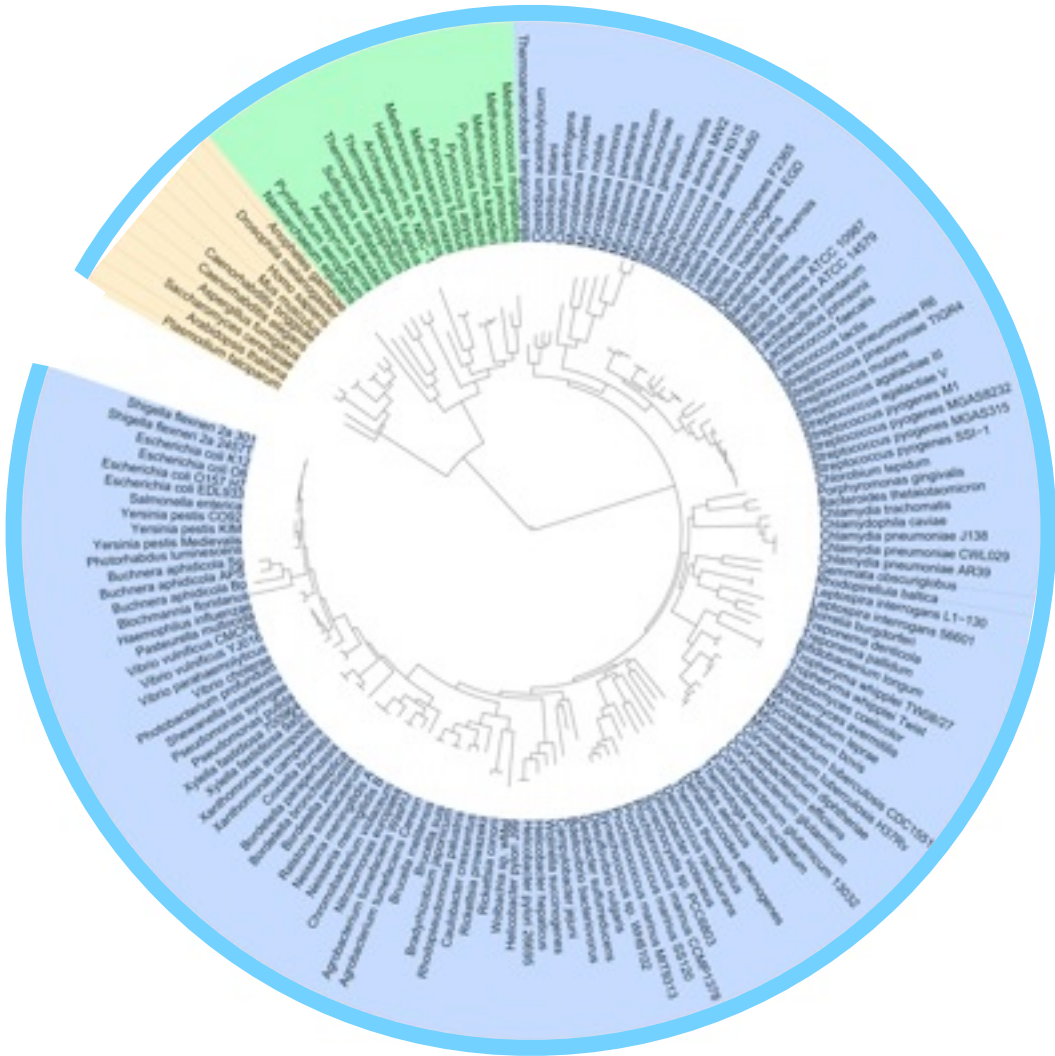


Eukarya  
Archea  
Bacteria



# Searching for the origin of Euk MCs

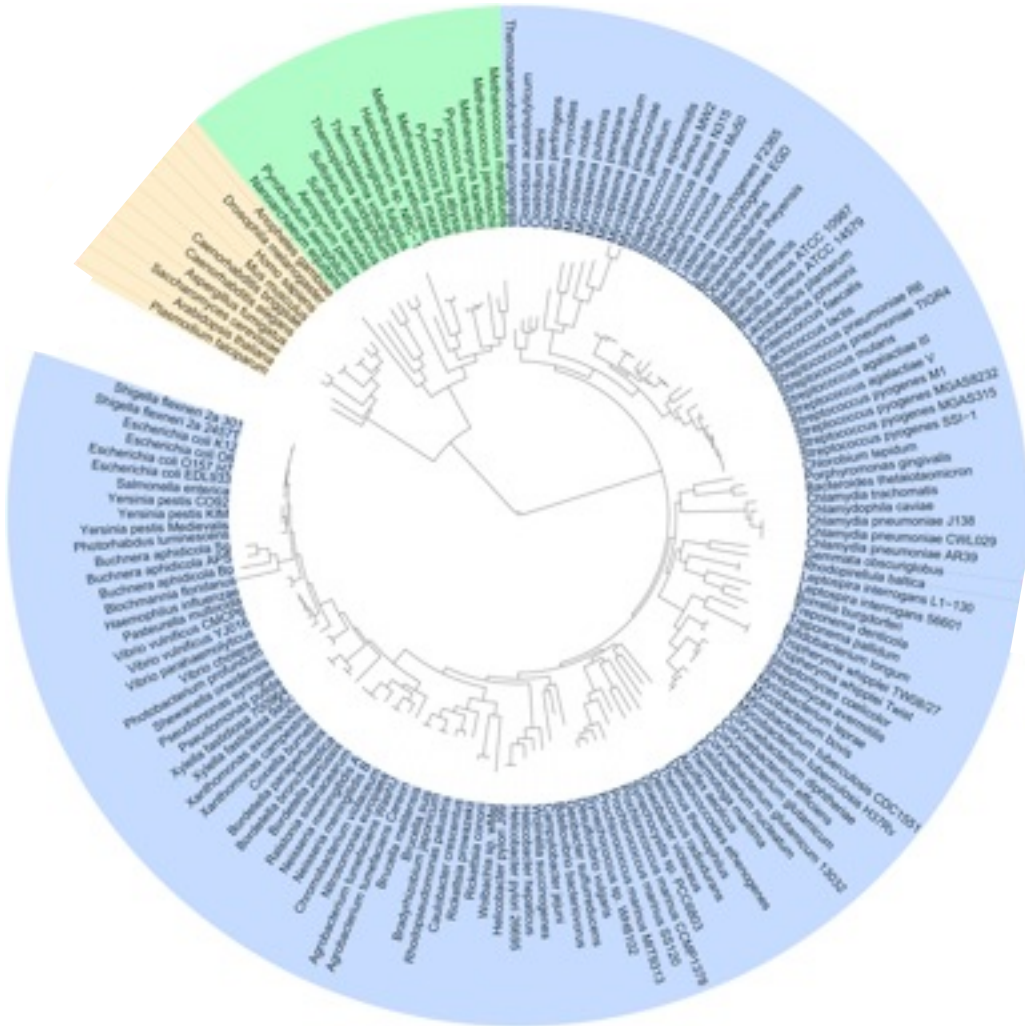
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Eukarya  
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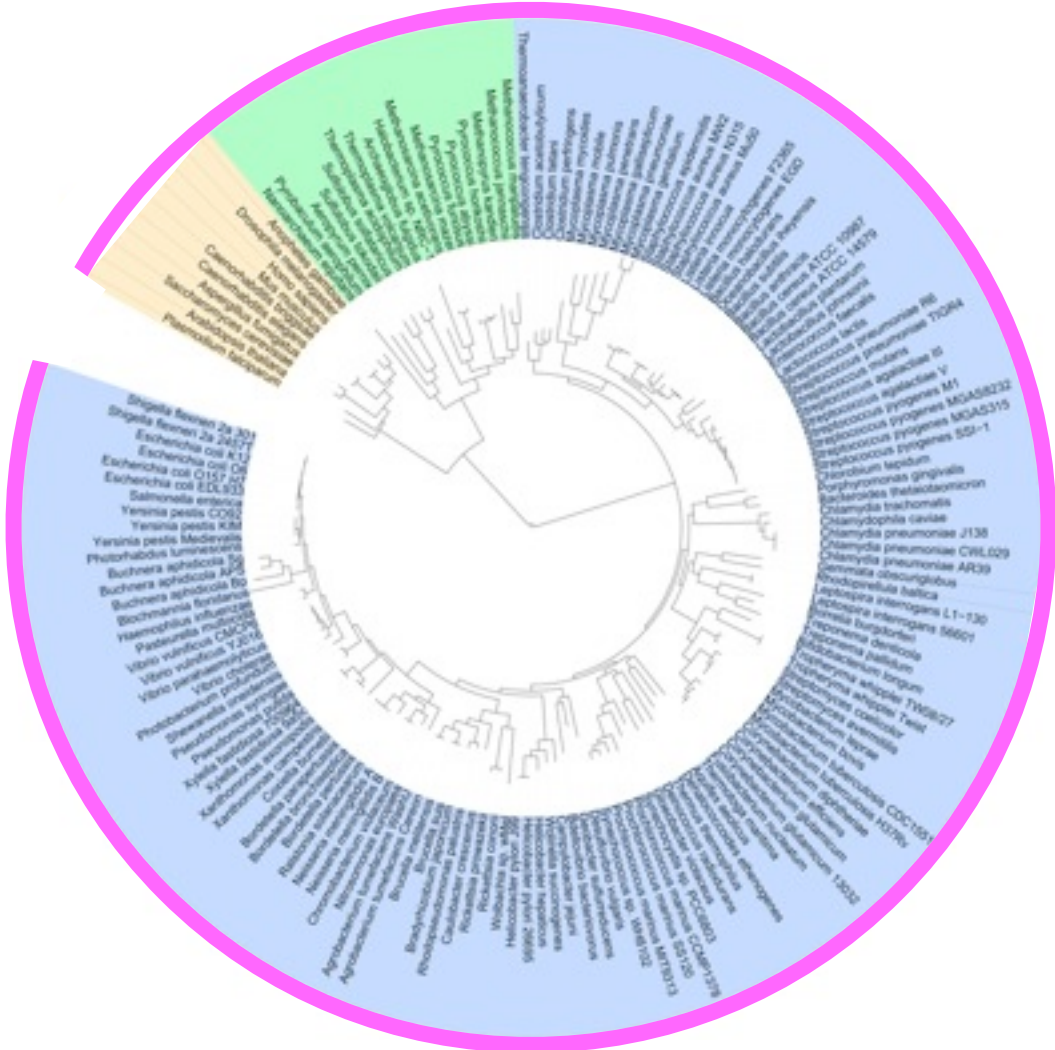
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Eukarya  
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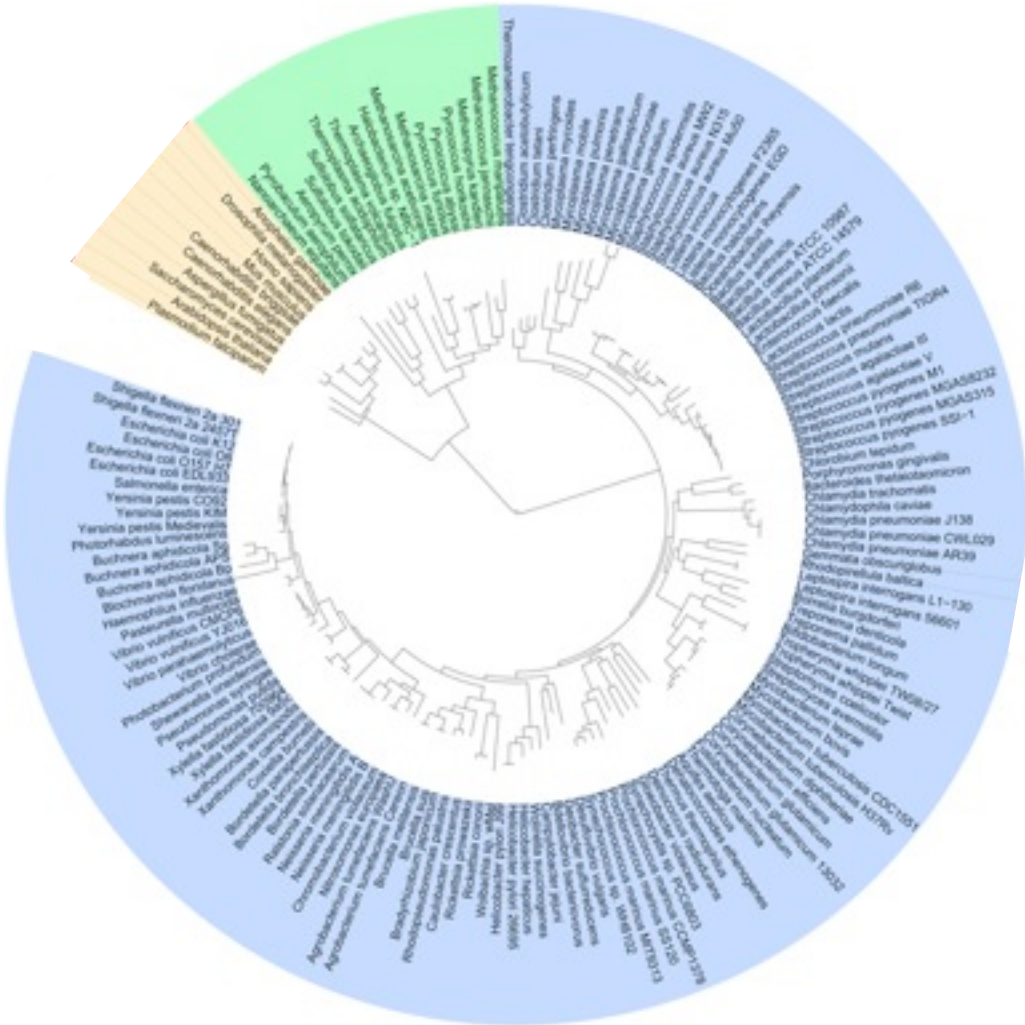
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Eukarya  
Archea  
Bacteria

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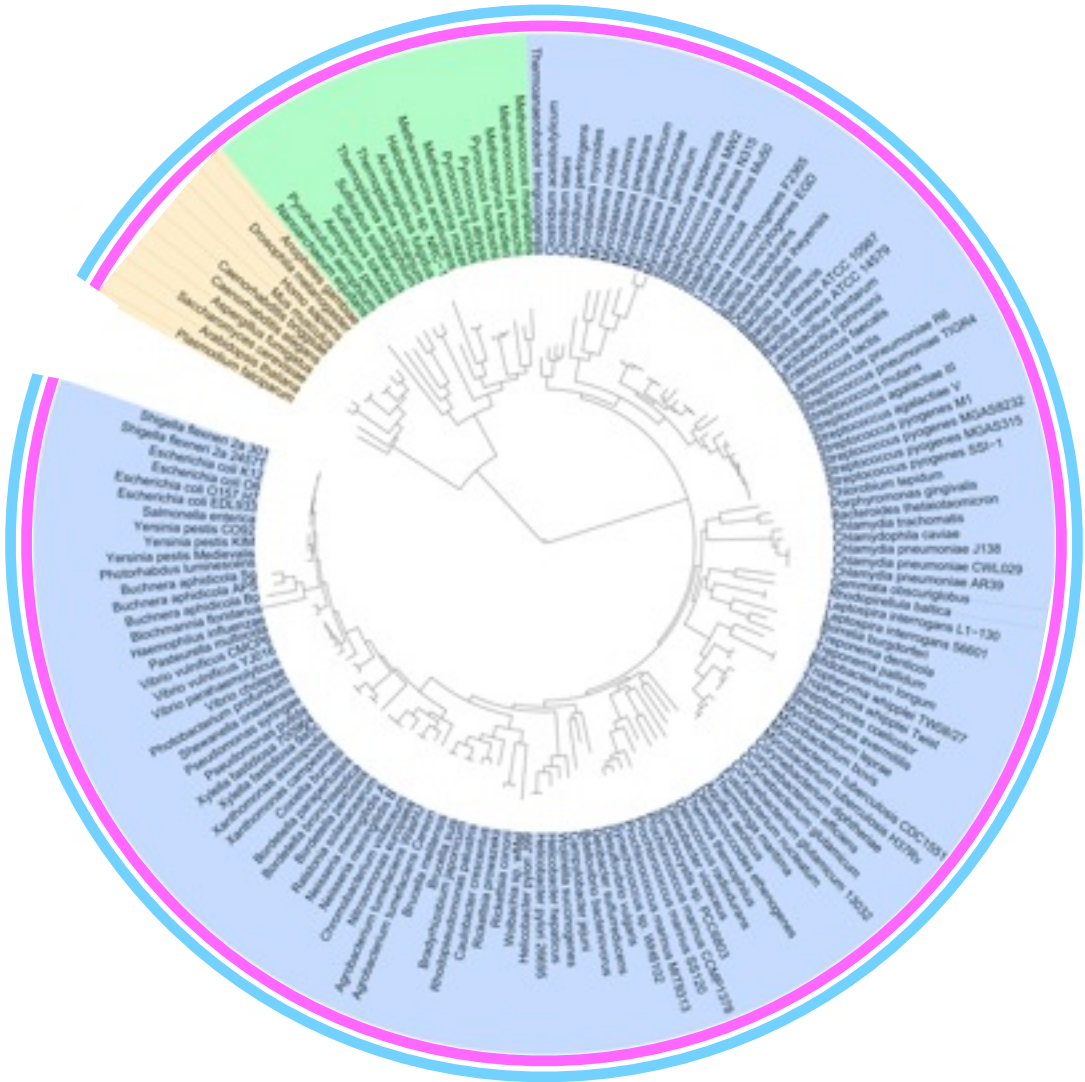


Eukarya  
 Archea  
 Bacteria



# Searching for the origin of Euk MCs

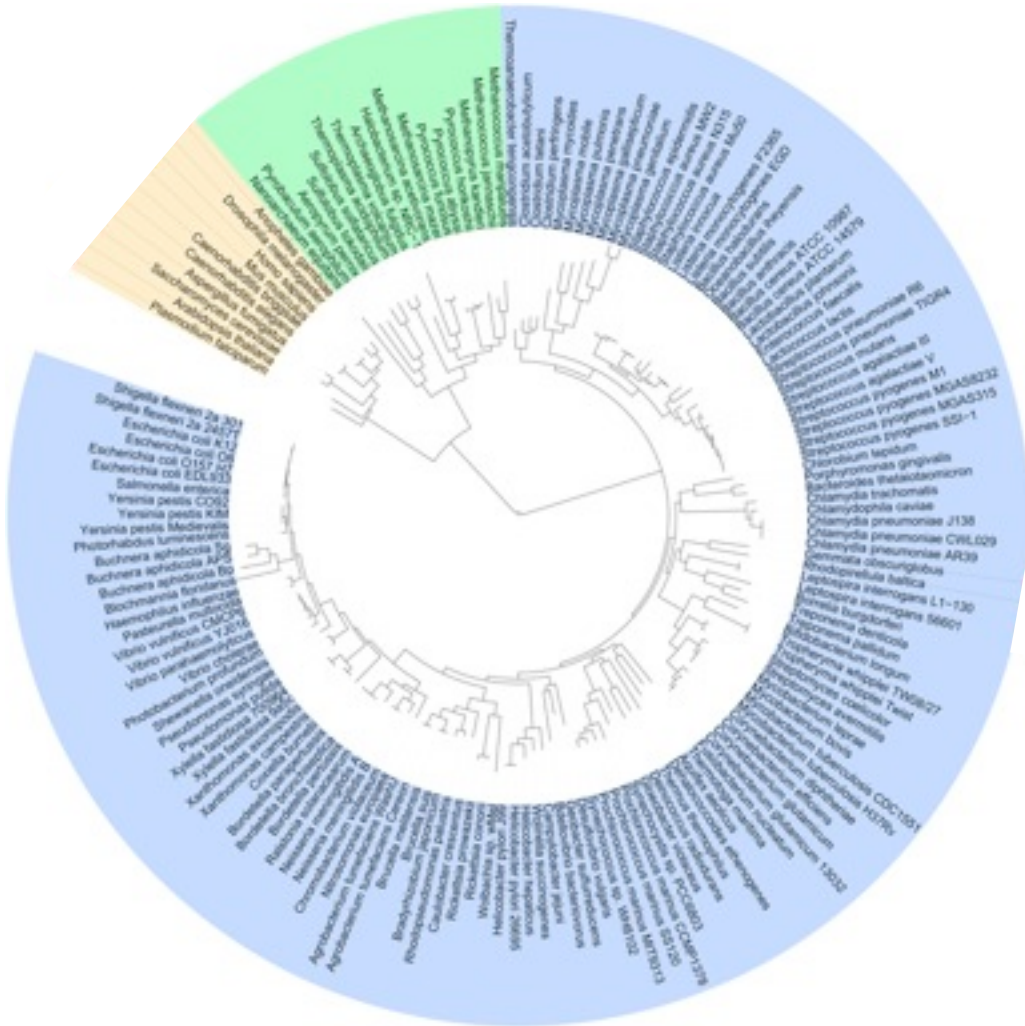
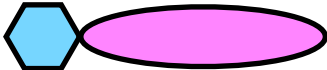
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Eukarya  
Archea  
Bacteria

# Searching for the origin of Euk MCs

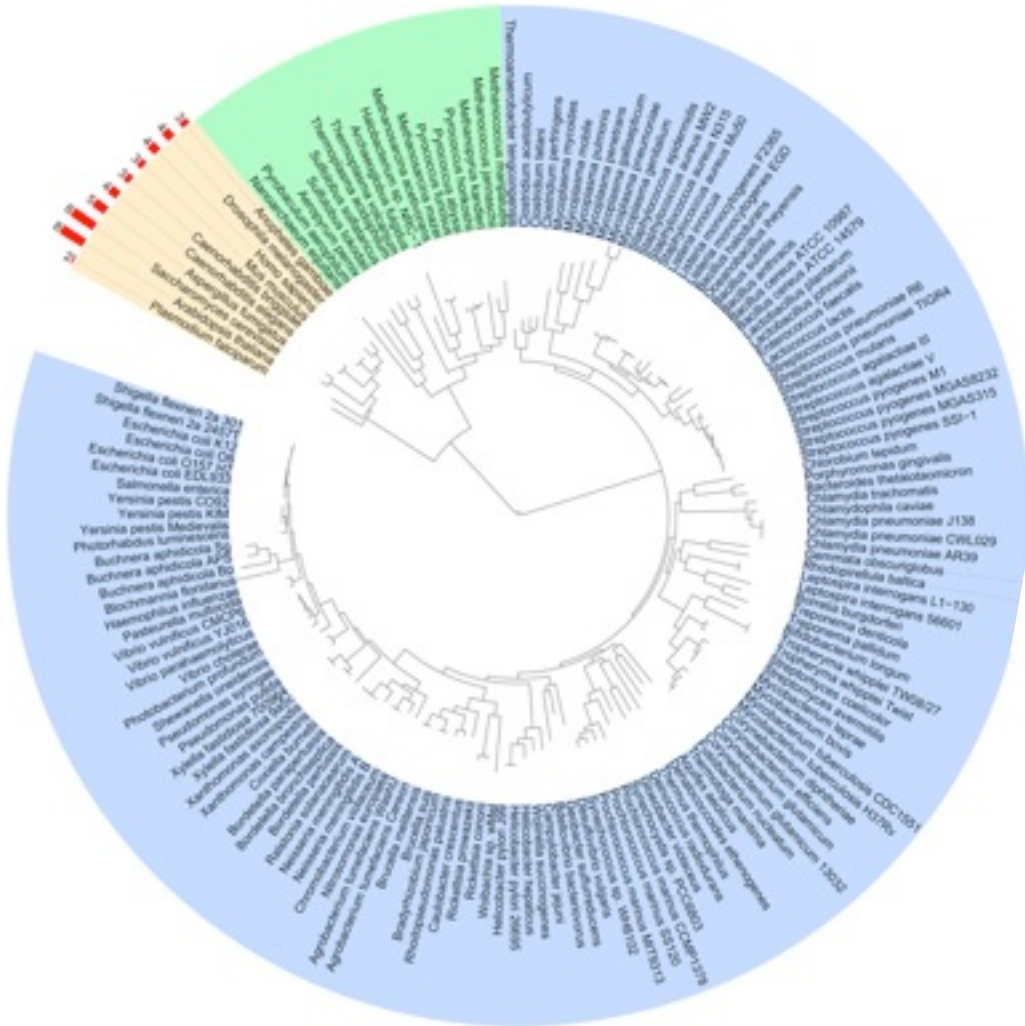
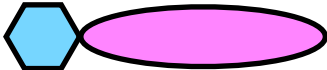
Fold assignments  
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Eukarya  
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# Searching for the origin of Euk MCs

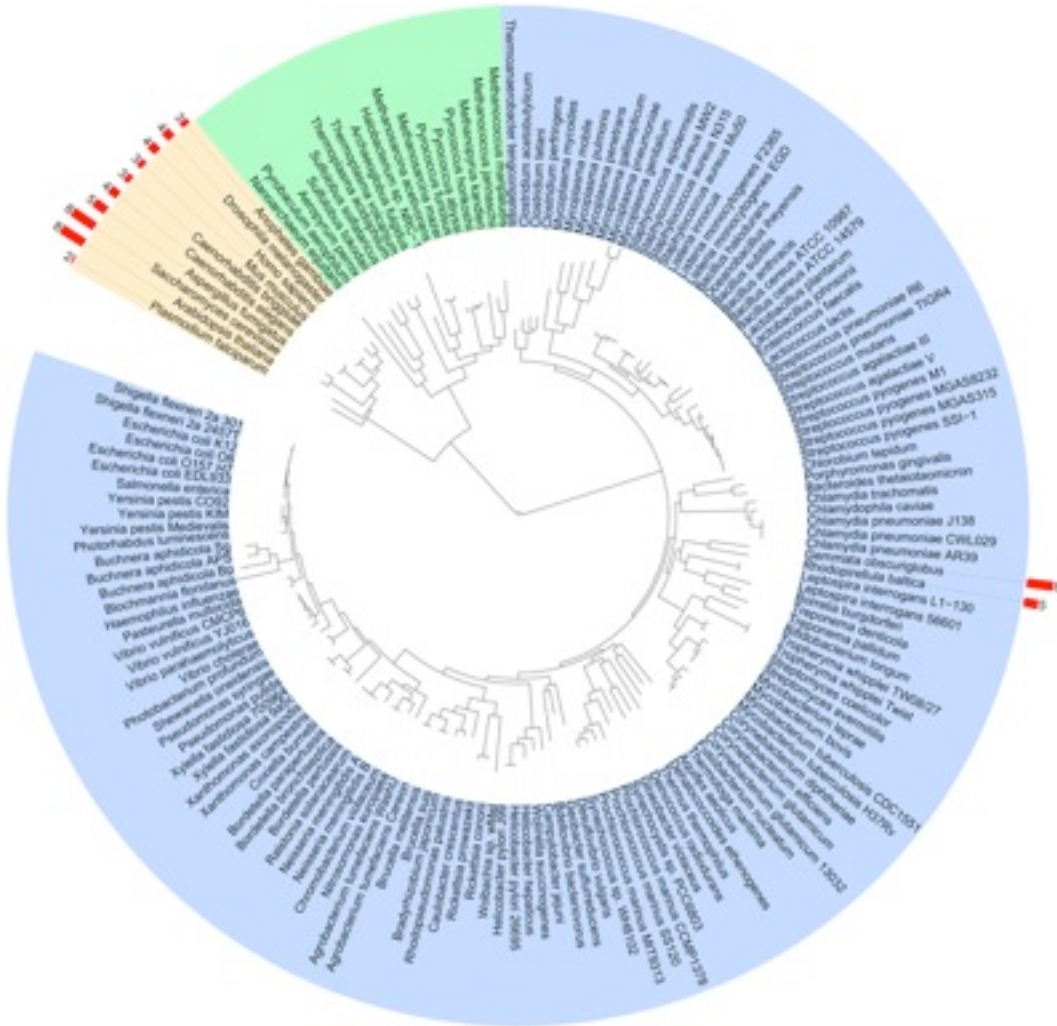
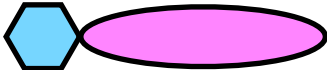
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Eukarya  
Archea  
Bacteria

# Searching for the origin of Euk MCs

Fold assignments  
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Eukarya  
 Archea  
 Bacteria

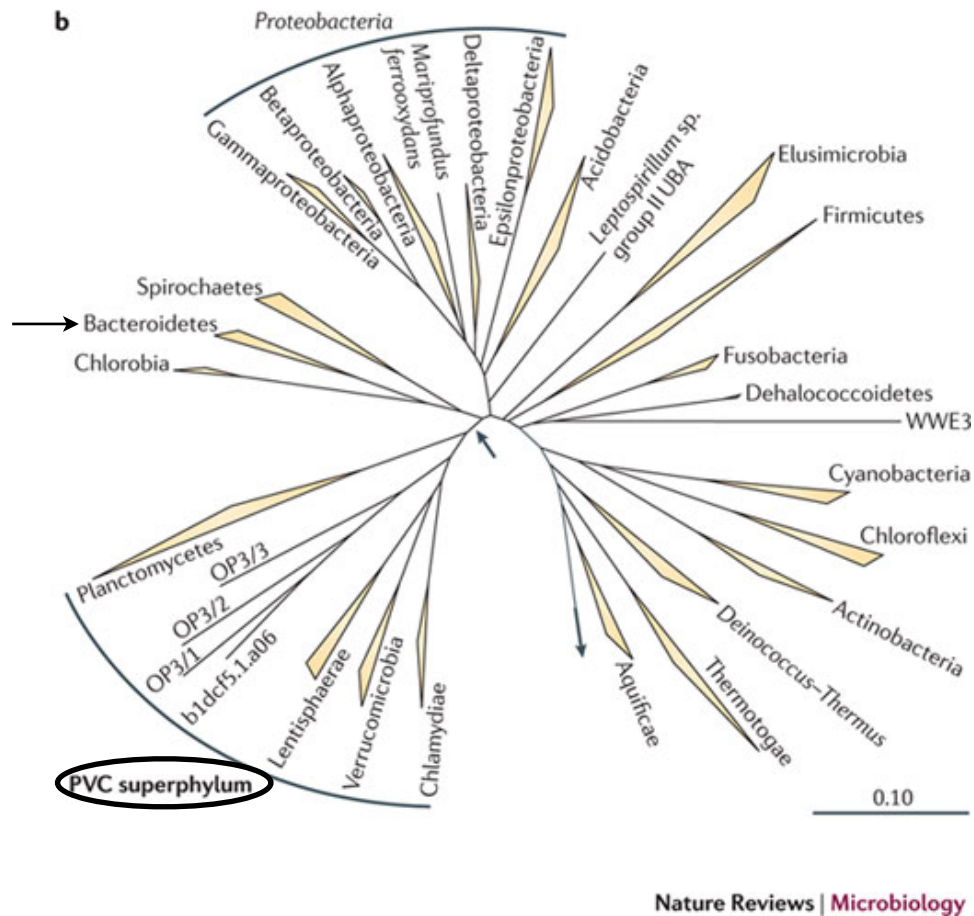


# MC Proteins in bacteria

Species	Phylum	Number of MCs
<i>Chlamydophila felis</i> Fe/C-56	C	0
<i>Candidatus Protochlamydia amoebophila</i> UWE25	C	0
<i>Chlamydia muridarum</i> Nigg	C	0
<i>Victivallis vadensis</i> BAA-548	L	0
<i>Lentisphaera araneosa</i> HTCC2155	L	9
<i>Candidatus Kuenenia stuttgartiensis</i>	P	0
<i>Blastopirellula marina</i> DSM 3645	P	11
<i>Planctomyces maris</i> DSM 8797	P	11
<i>Rhodopirellula baltica</i> SH 1	P	5
<i>Gemmata obscuriglobus</i> UQM 2246	P	8
<i>Akkermansia muciniphila</i> BAA-835	V	0
<i>Methylococcus burtonii</i> V4	V	0
<i>Opitutaceae</i> bacterium TAV2	V	0
<i>Opitutus terrae</i> PB90-1	V	0
<i>Pedosphaera parvula</i> Ellin514	V	9
<i>Verrucomicrobium spinosum</i>	V	16
<i>Chthoniobacter flavus</i> Ellin428	V	14

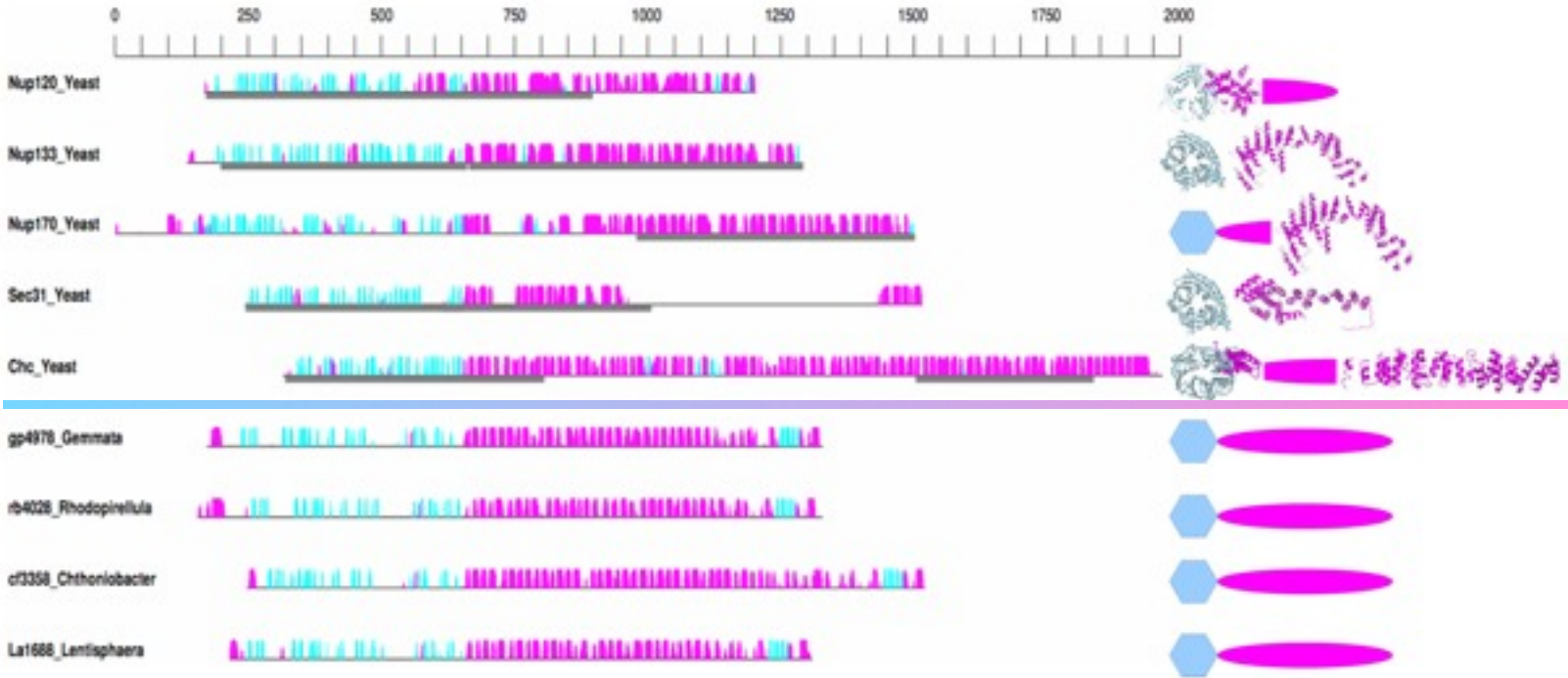
V: Verrucomicrobia, L: Lentisphaerae, P: Planctomycetes, C: Chlamydiae

# The PVC bacterial super-phylum



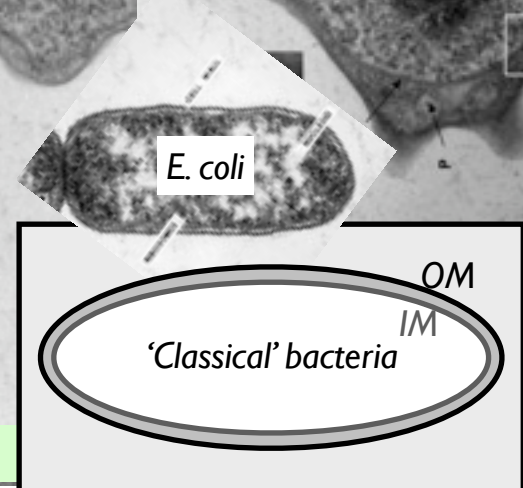
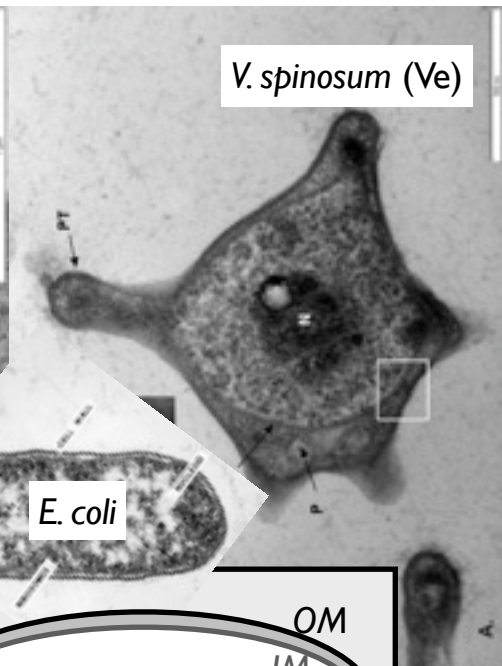
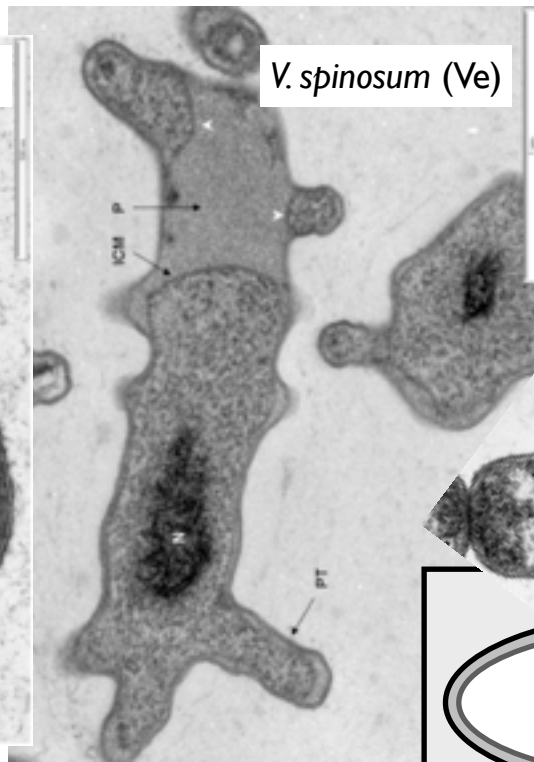
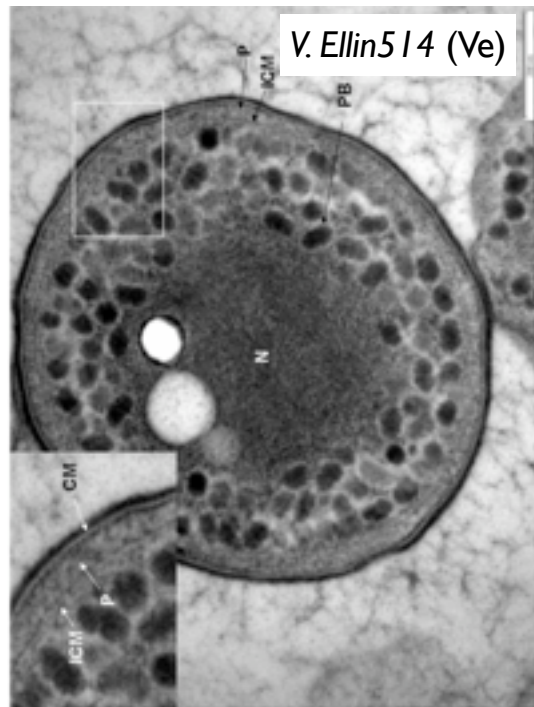
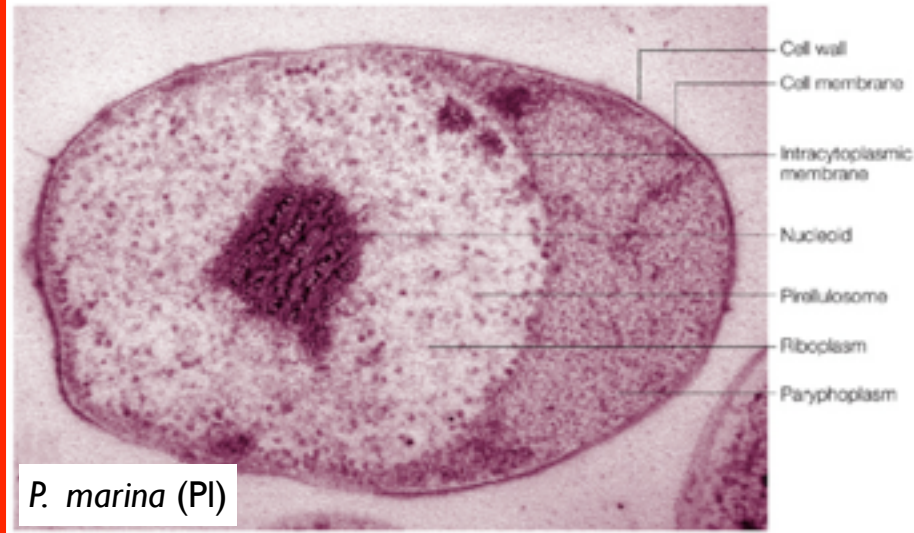
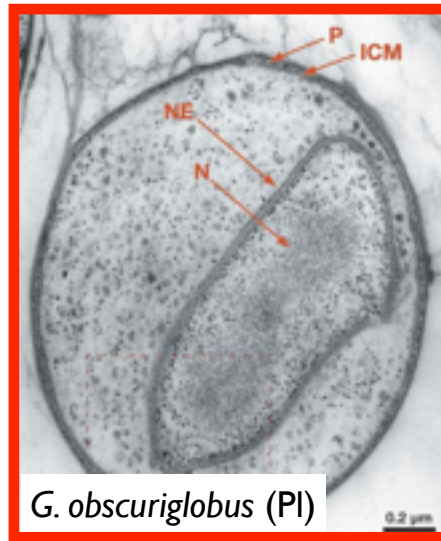
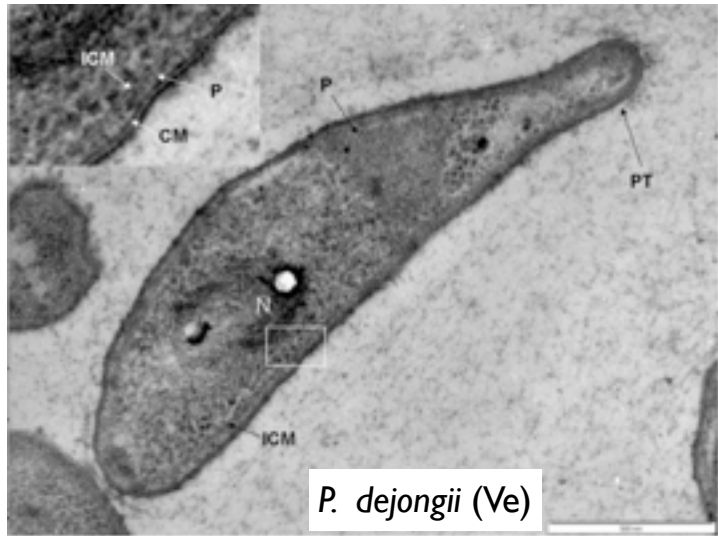
Fuerst & Sagulenko *Nat Rev Microbiol* 2011

# Bacterial proteins have the MC architecture



Santarella et al., PLoS Biology 2010

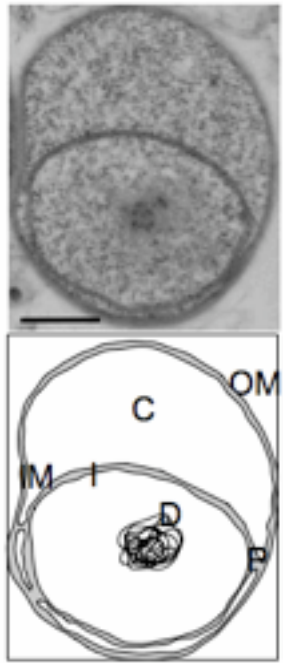
# PVC: The Compartmentalized Bacteria



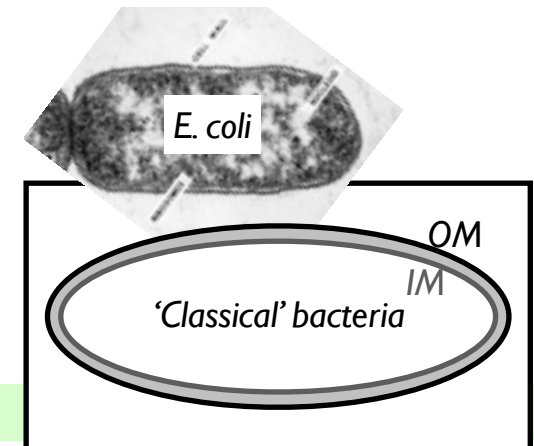
Lee et al., BMC Microbiology 2009



# Gemmata obscuriglobus endomembrane variability

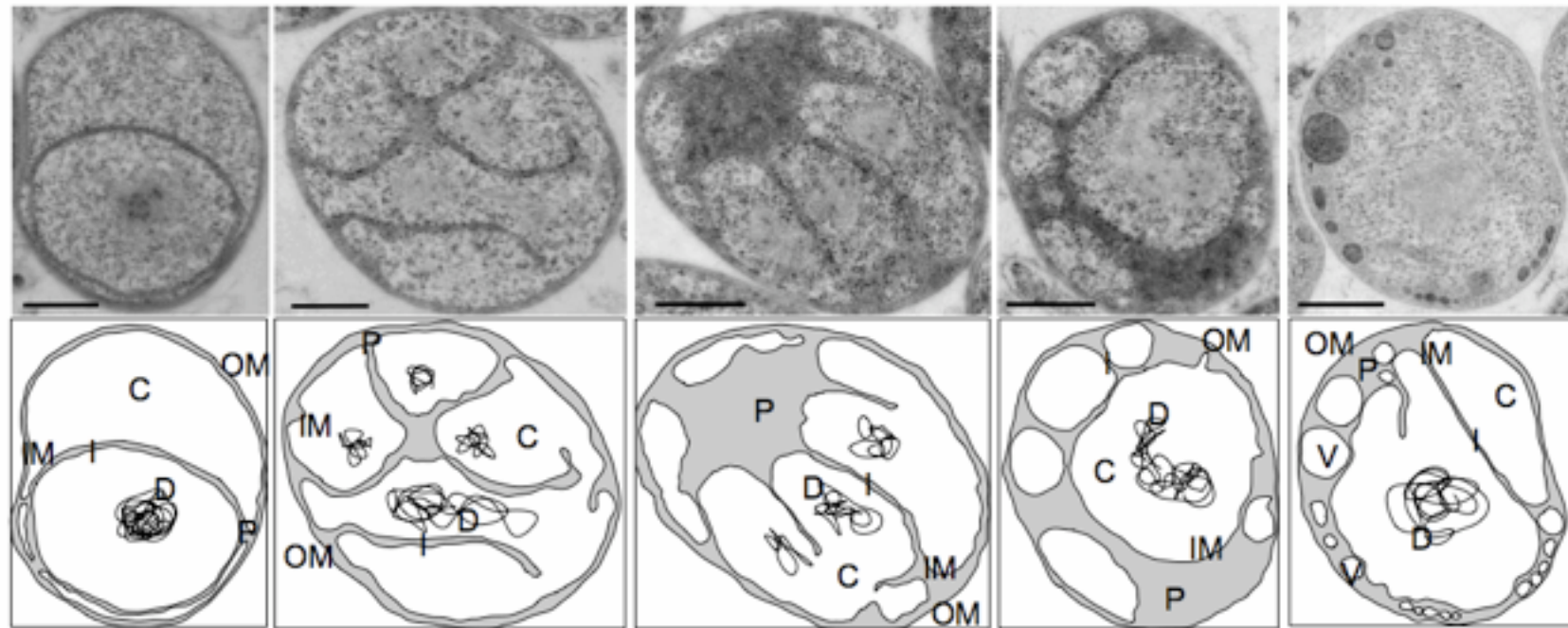


- ✓ C: Cytoplasm
- ✓ P: Periplasm
- ✓ IM: Inner membrane
- ✓ OM: Outer membrane
- ✓ I: Invagination (of the IM)
- ✓ D: DNA

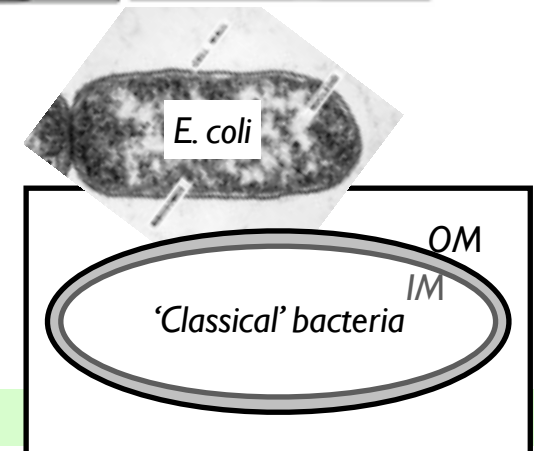


Santarella et al., PLoS Biology 2010

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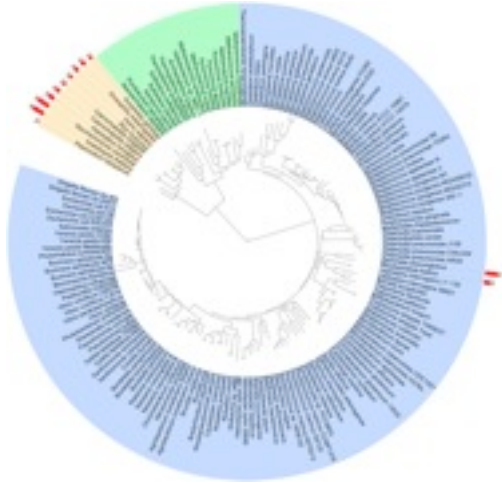
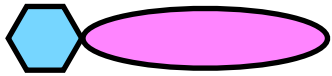


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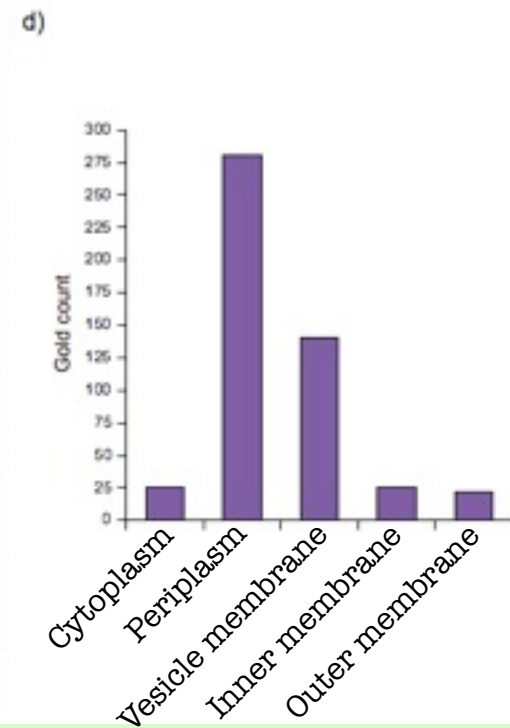
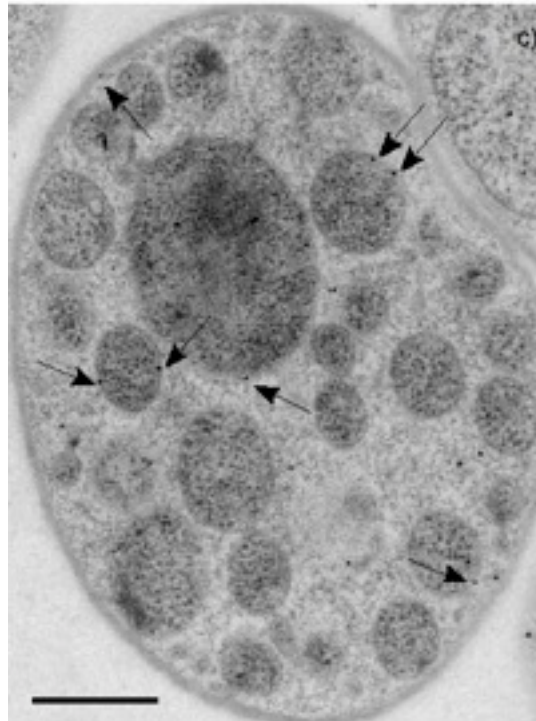
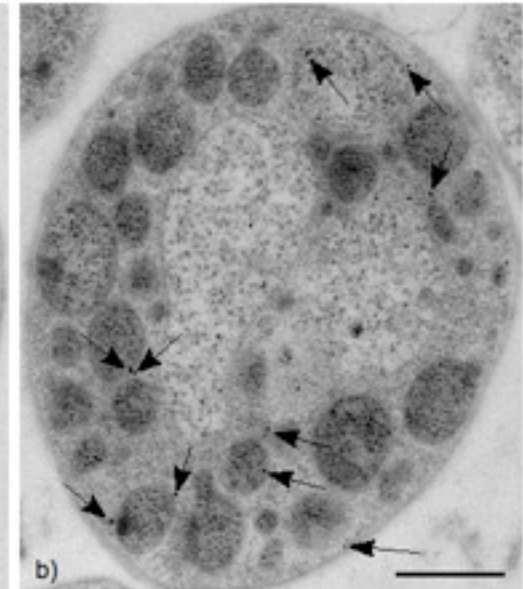
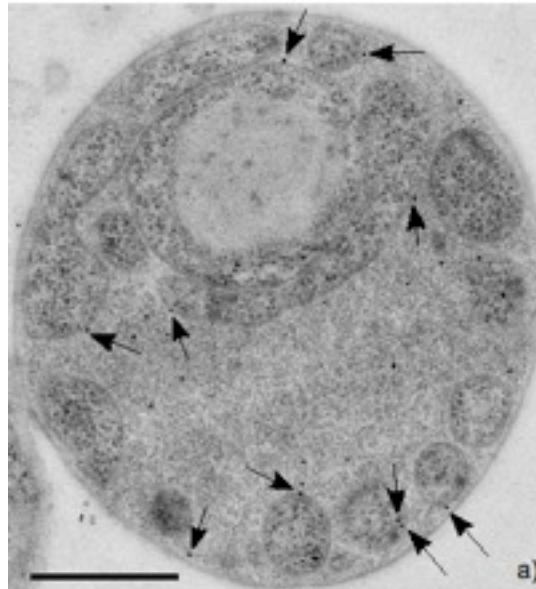
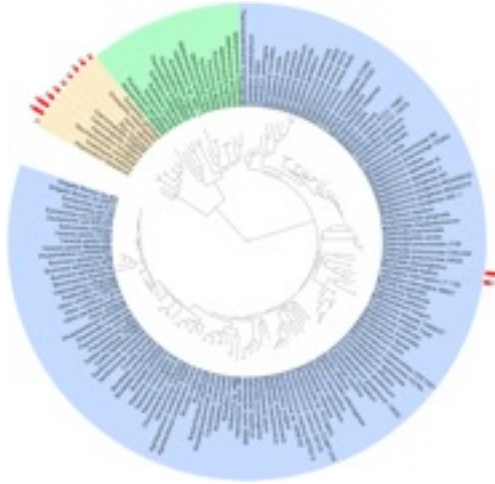
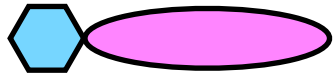


Santarella et al., PLoS Biology 2010

# Bacterial MC at the vesicle membranes



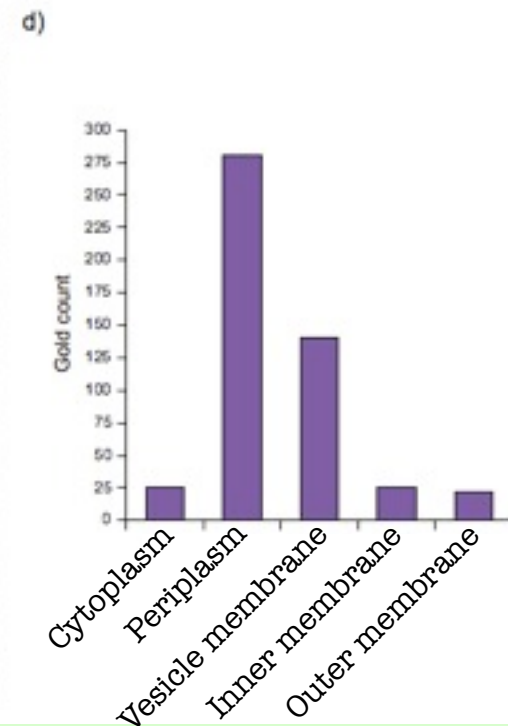
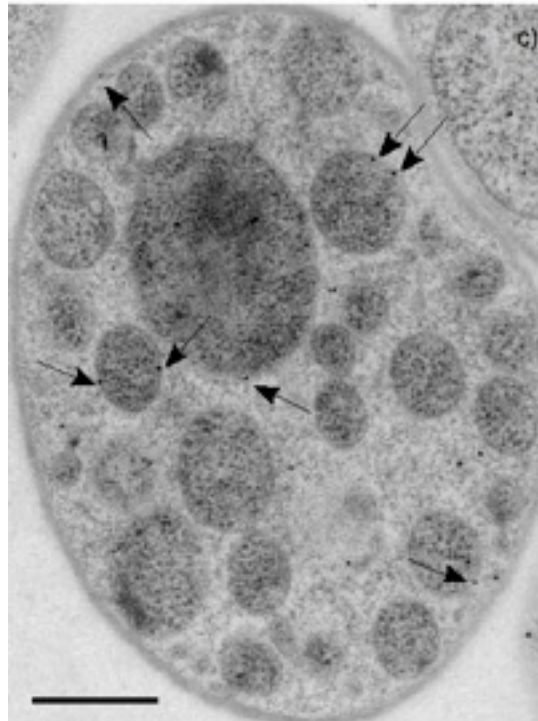
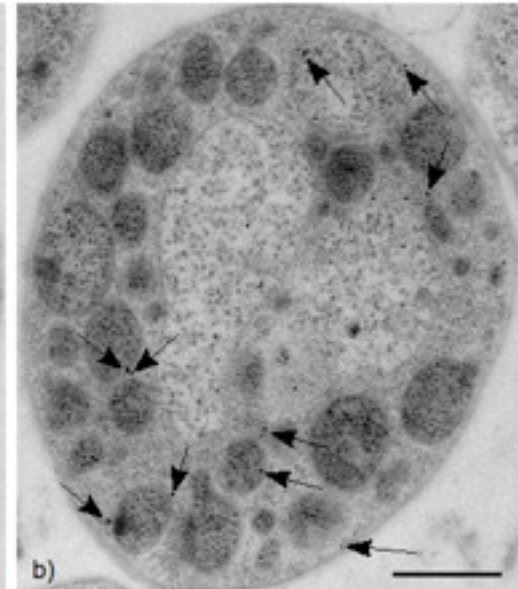
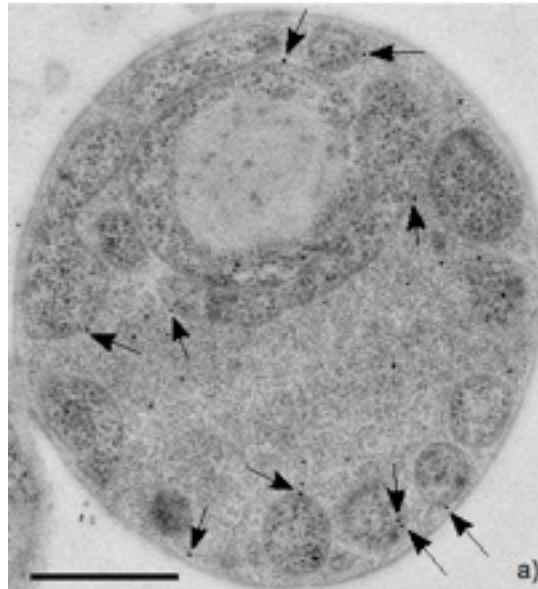
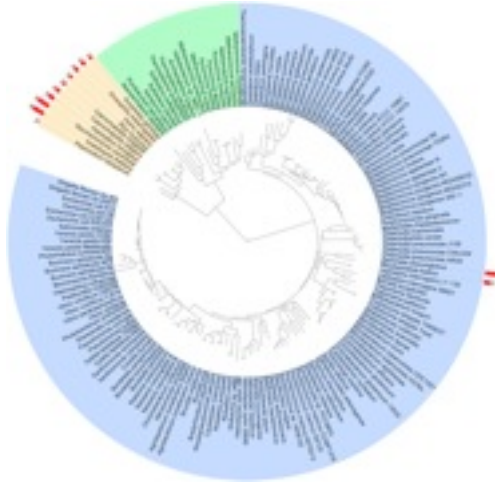
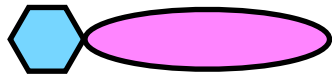
# Bacterial MC at the vesicle membranes



Santarella et al., PLoS Biology 2010



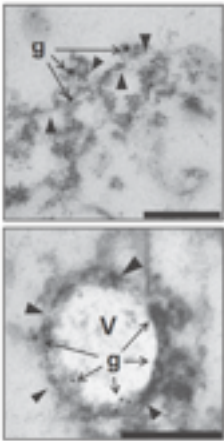
# Bacterial MC at the vesicle membranes



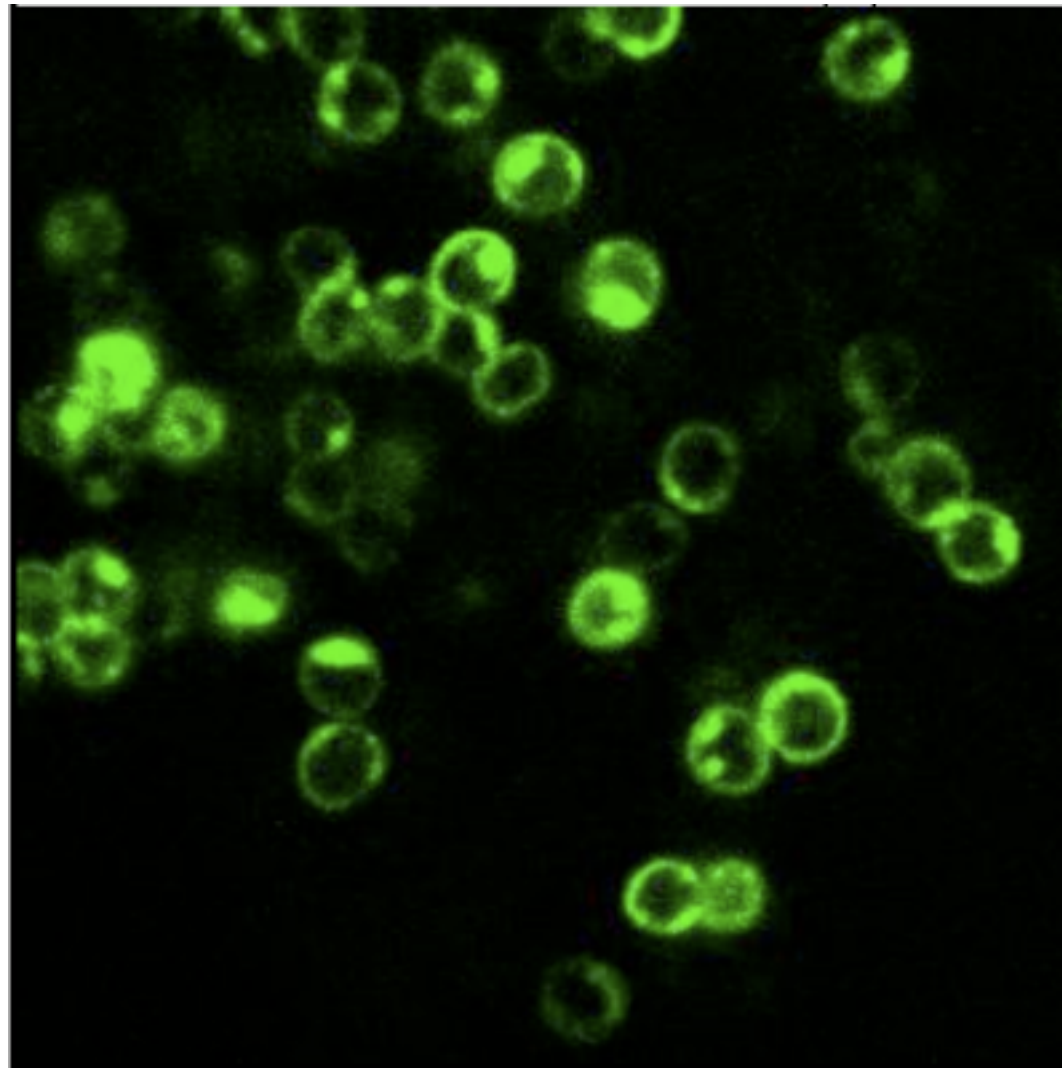
Bacterial endomembrane system  
unlike any other bacterial one  
sustain by eukaryotic-like  
membrane coats

Santarella et al., PLoS Biology 2010

# Endocytosis in *G. obscuriglobus*

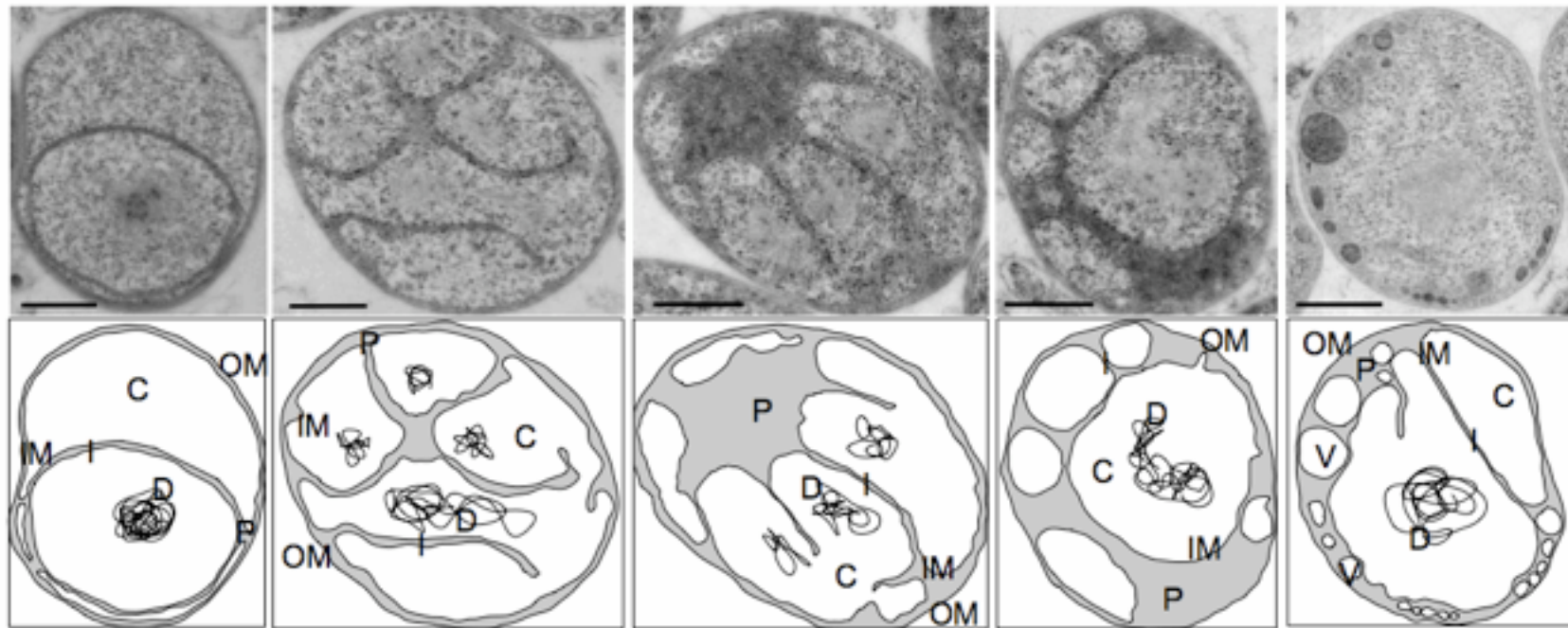


MCs associated  
to vesicles



# Gemmata obscuriglobus

## The compartmentalized bacteria?



- ✓ C: Cytoplasm
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- ✓ D: DNA

Scale bars: 500nm

Santarella et al., PLoS Biology 2010



# Gemmata 3D

Sections 250nm  
Technai F30 300kv (FEL)  
Dual axis tilt series  
IMOD  
1130 slices/5

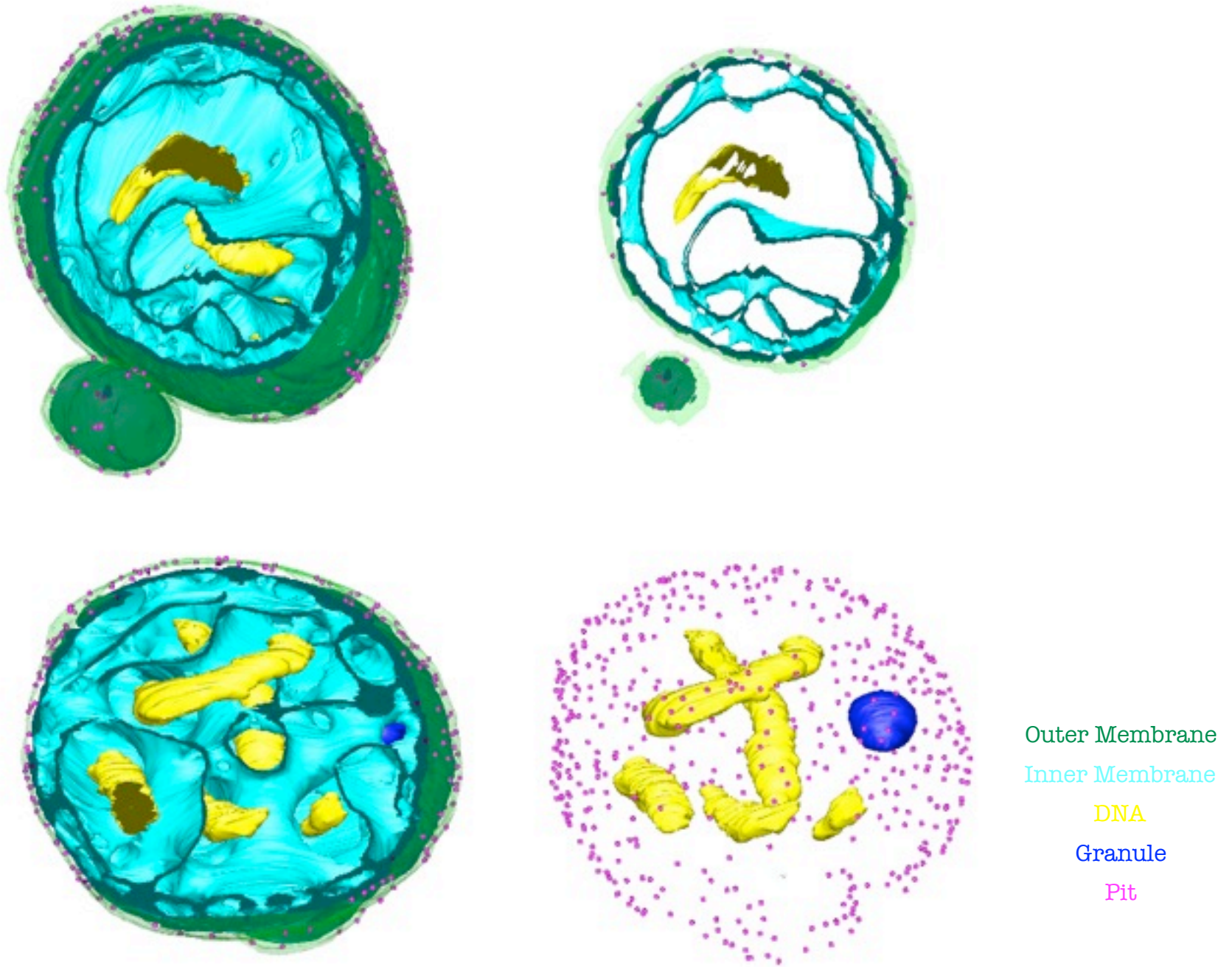


Outer Membrane  
Inner Membrane  
DNA  
Granule  
Pit

Prugnaller et al., in preparation.

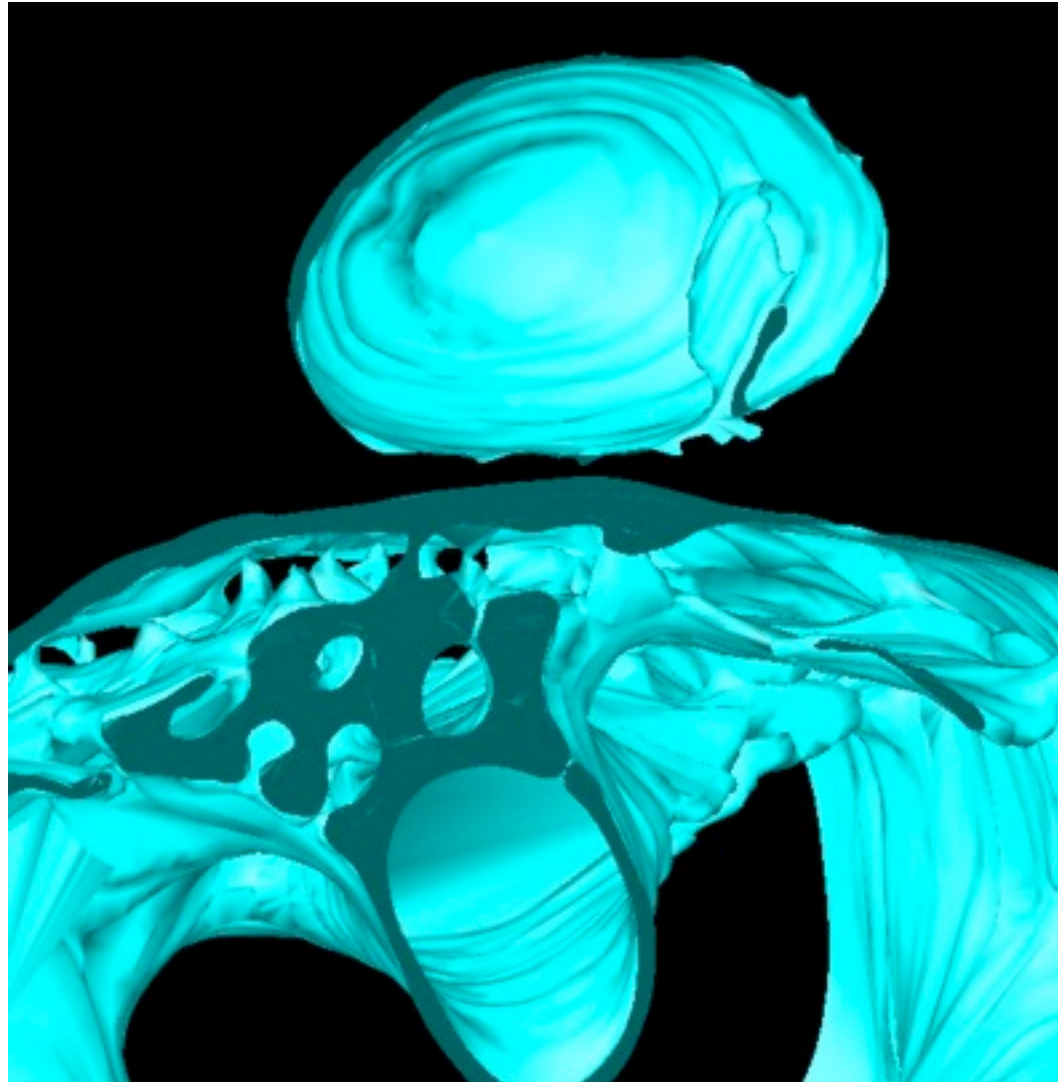


# No bacterial nucleus



Prugnaller et al., in preparation.

## Bud and neck



Prugnaller et al., in preparation.

# Bud neck



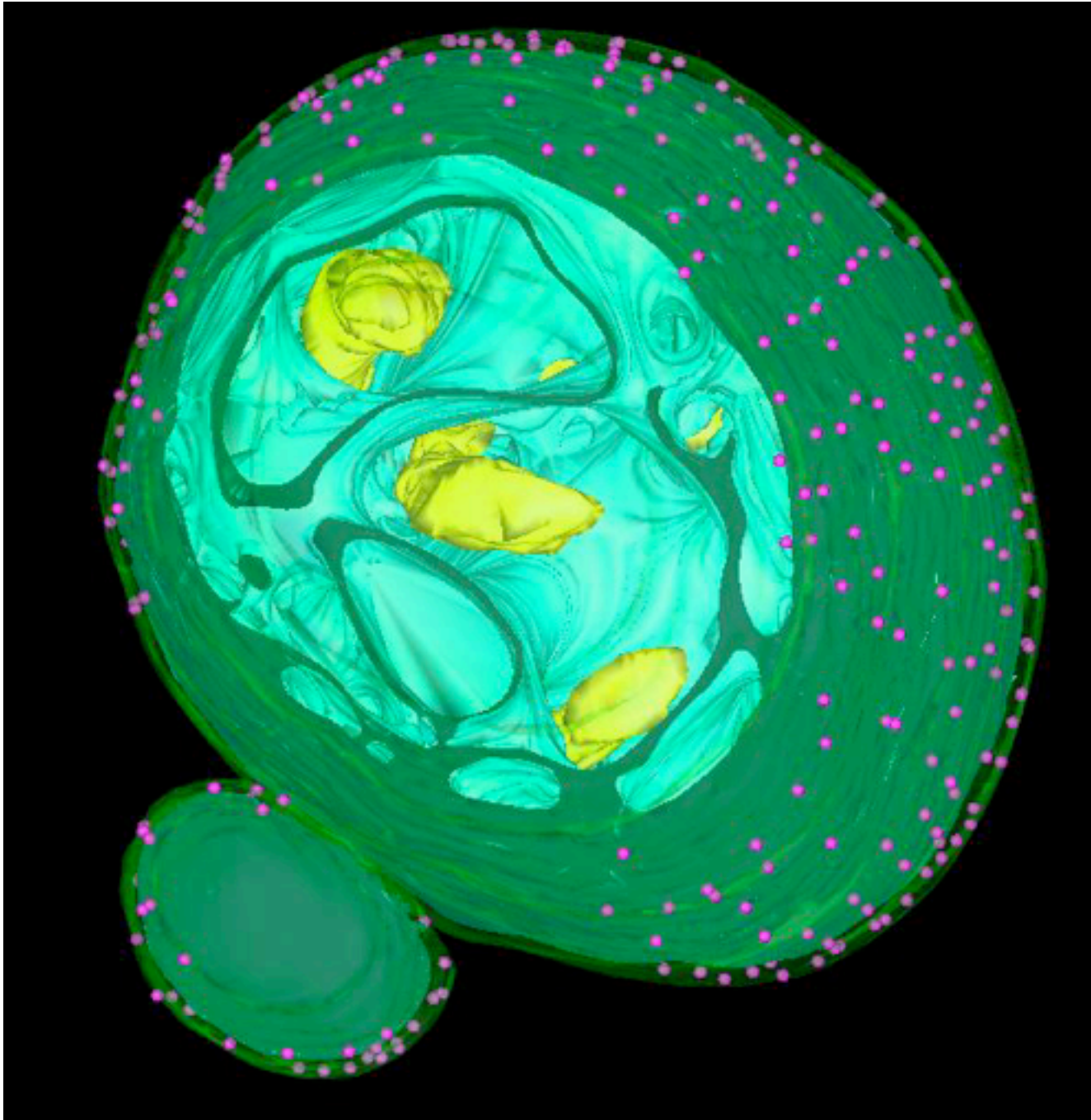
Scale bar: 100nm

Prugnaller et al., in preparation.



# Gemmata 3D

Sections 250nm  
Technai F30 300kv (FEI)  
Dual axis tilt series  
IMOD  
1130 slices/5



Outer Membrane  
Inner Membrane  
DNA  
Granule  
Pit

Prugnaller et al., in preparation.



# Gemmata 3D conclusions

Extensive membrane organisation

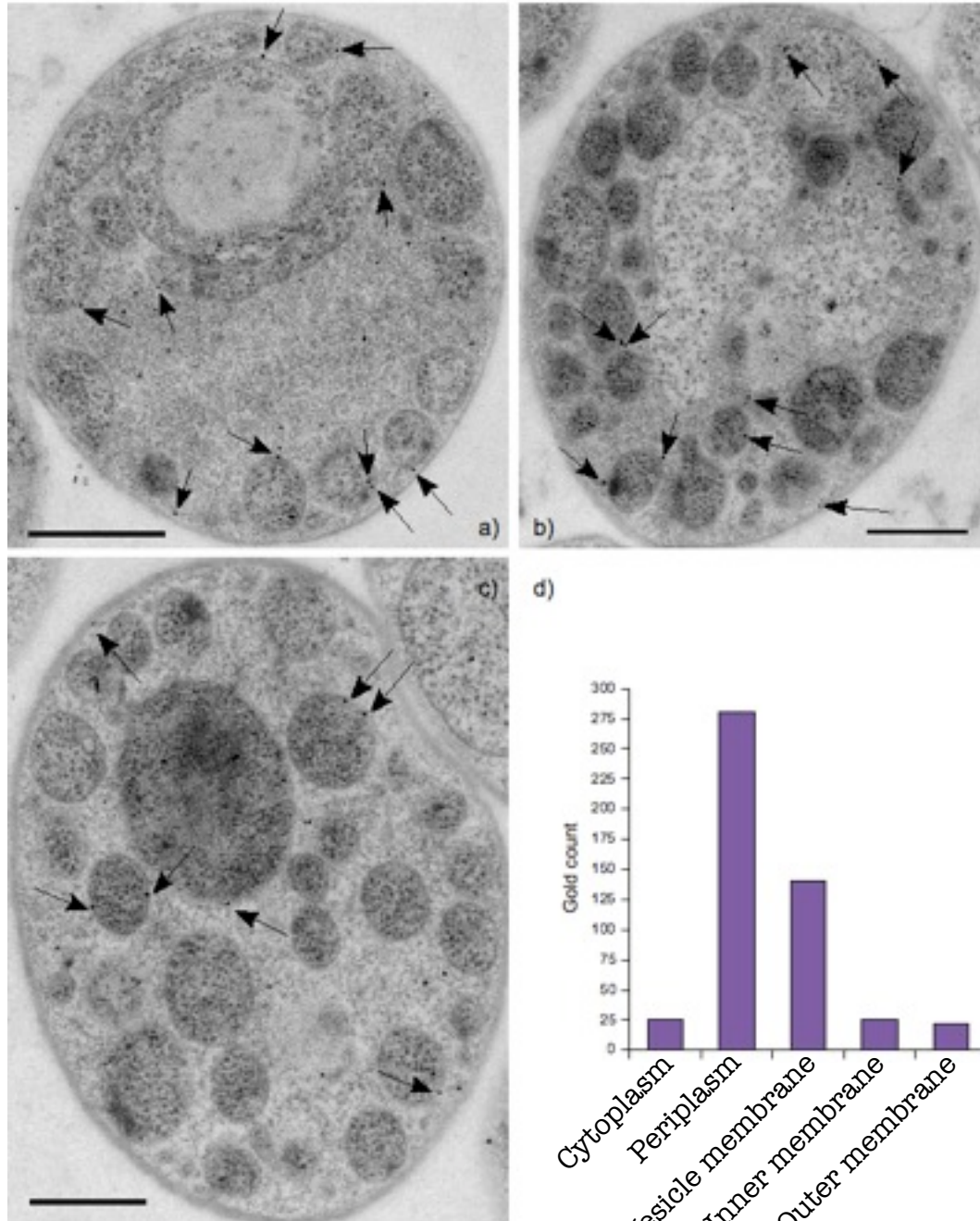
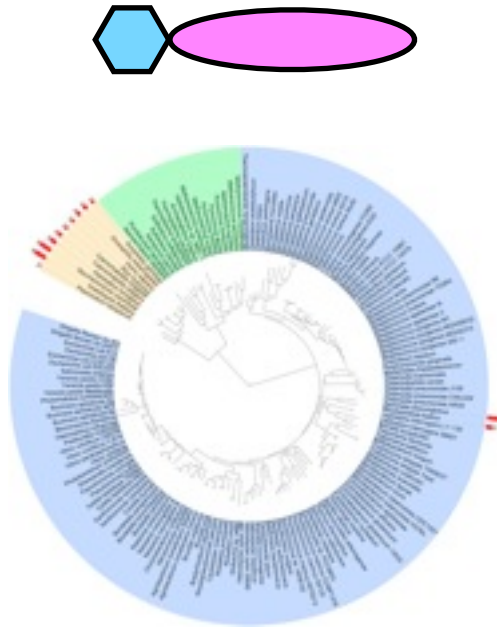
No compartments

No nucleus

Several chromosomes

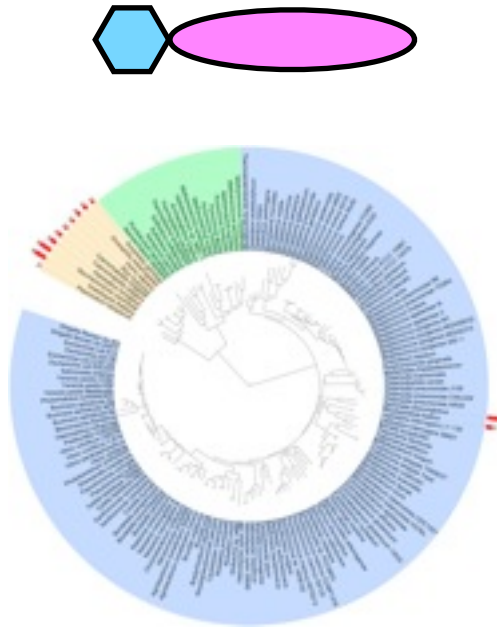
Bud membrane

# Complex bacterial endomembrane system

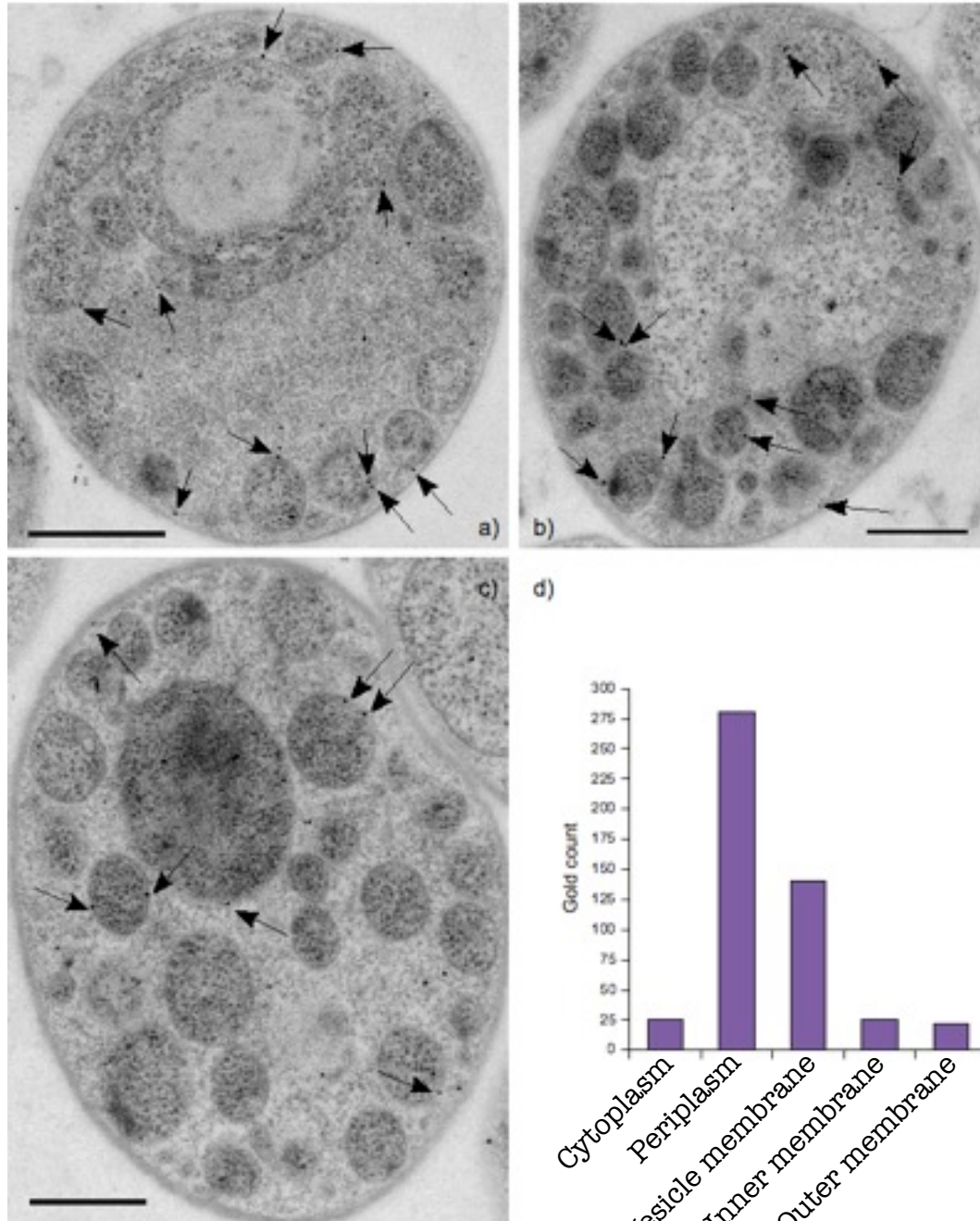


Santarella et al., PLoS Biology 2010

# Complex bacterial endomembrane system



Bacterial endomembrane system  
unlike any other bacterial one  
sustain by eukaryotic-like membrane coats



Santarella et al., PLoS Biology 2010

# Homologous?

Lack of sequence similarity

(doesn't imply lack of homology MreB/Actin & FtsZ/Tubulin)

HGT (too complex)

Convergence

Similarity of features (tertiary structure and function)



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The bacterial PVC superphylum might have lain on the path of the origin of the eukaryotic endomembrane

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The bacterial PVC superphylum might have lain on the path of the origin of the eukaryotic endomembrane

Might the bacterial PVC superphylum have lain on the path of the origin of other eukaryotic or archaeal characters?

# Euk/Arch characteristics in the PVC superphylum

PVC Superphylum		
Features	Specific to	Found in
Compartmentalized cell plan (20)	Eu	Pl, Ve
DNA surrounded by membrane (21)	Eu	Pl
Condensed DNA (22)	Eu	Pl
Division by budding (24)***	Eu	Pl
Membrane coats (11)	Eu	Pl
Sterol (25)	Eu	Pl, Ch
Peptidoglycan loss (26)	Eu, Ar*	Pl, Ch
Proteic cell wall (27)	Eu	Pl
Ester and ether lipids (28)	Ar	Pl
FtsZ loss (7)	Eu, Ar**	Pl, Ch
Tubulin (8, 9)	Eu	Ve
C1 transfer (29, 30)	Ar	Pl
Endocytosis (15)	Eu	Pl

Eukaryotes (Eu),  
 Planctomycetes (Pl),  
 Gemmata obscuriglobus (Ge),  
 Annamox (An),  
 Verrucomicrobia (Ve),  
 Chlamydiae (Ch),  
 Archaea (Ar),  
 Crenoarchaeota (Cr).

# Euk/Arch characteristics in the PVC superphylum

- No other prokaryote display so many euk or arch features.
- There is no other prokaryote that combines all those similarities into a single group.
- In some cases, PVC one is the most similar to the eukaryotic equivalent or to the primitive feature (endomembranes/sterol).

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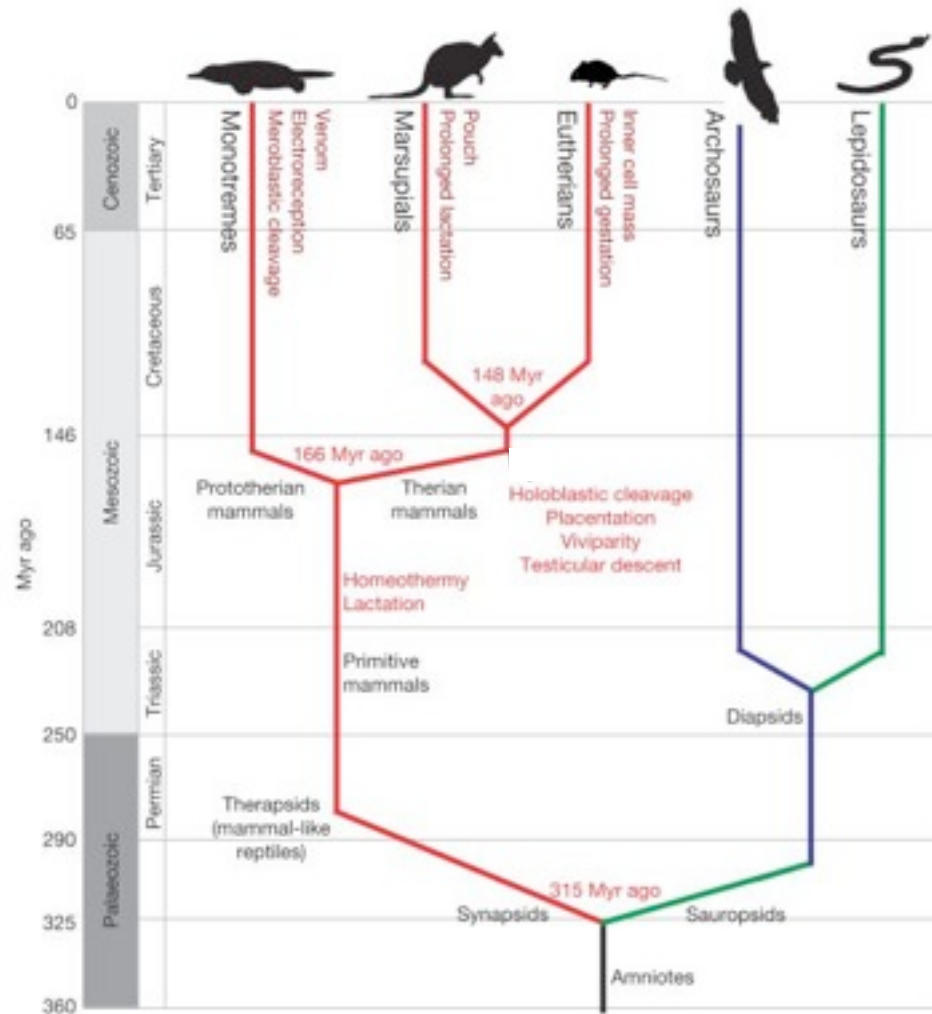
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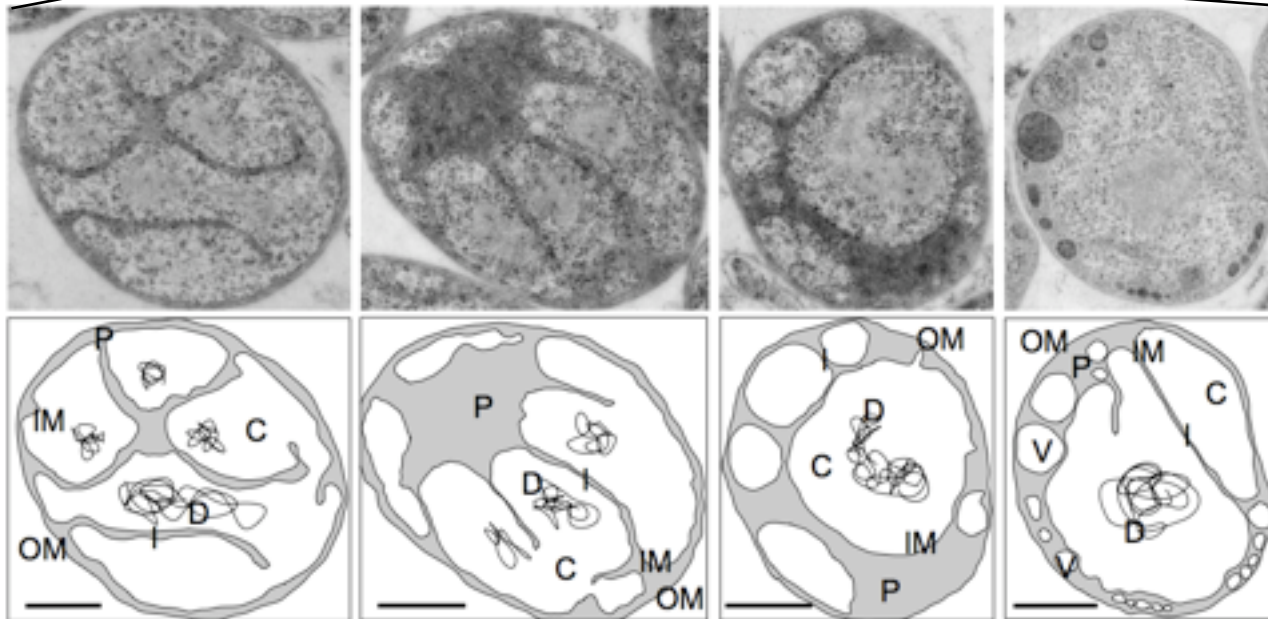
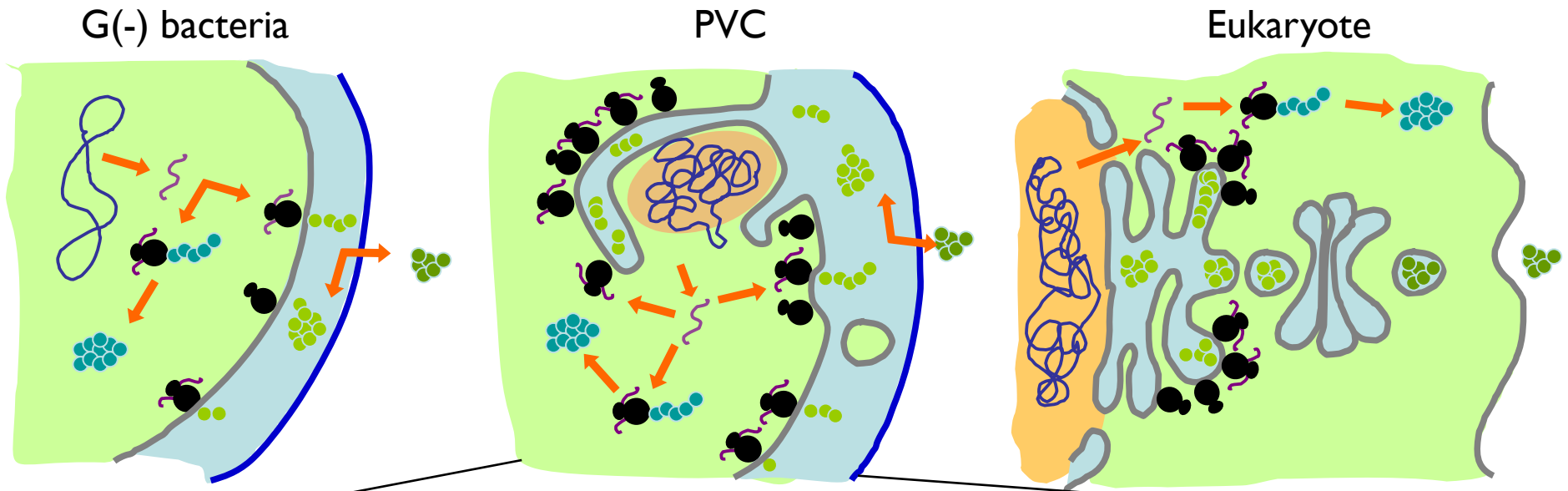
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# Microbiology's platypus



Similar to the platypus that exhibits a combination of characteristics that are a legacy of the common ancestor shared between birds, reptiles and mammals, the archaeal and eukaryotic features found in PVC members might reflect a common ancestor between bacteria and the LAECA

# Internalization of the bacterial periplasm at the origin of the eukaryotic endoplasm



Devos & Reynaud, *Science* 2010; Reynad & Devos *Proc R Soc B* 2011





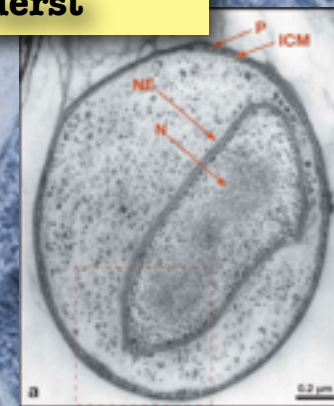
Thanks to

**Andrej Sali**

Frank Alber  
Maya Topf  
Fred Davis  
and the Sali Group

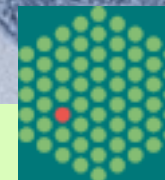
**Queensland Uni,  
Australia**

**John Fuerst**



**UCD, Ireland**

**Emmanuel Reynaud**



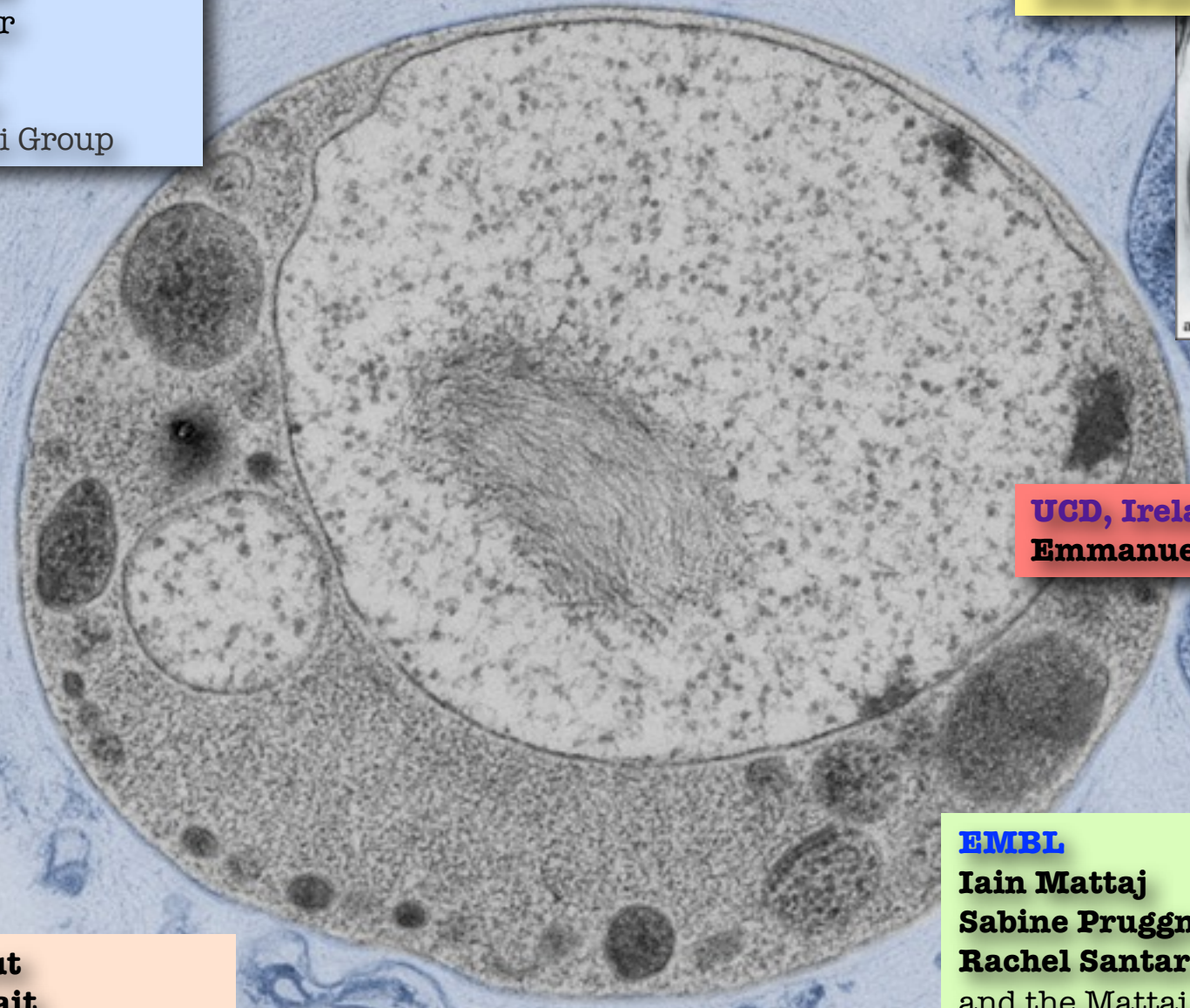
**EMBL**

**Iain Mattaj**  
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**Rachel Santarella**  
and the Mattaj group



**Mike Rout**  
**Brian Chait**

Josef Franke  
Svetlana Dokudovskaya  
Rosemary Williams







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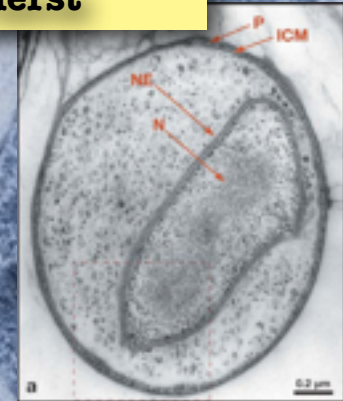
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**Queensland Uni,  
Australia**  
**John Fuerst**

**Center for  
Organismal  
Studies (COS)  
Heidelberg Univ.**

**Now hiring!**

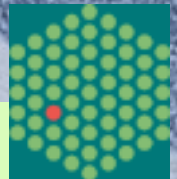


**UCD, Ireland**  
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