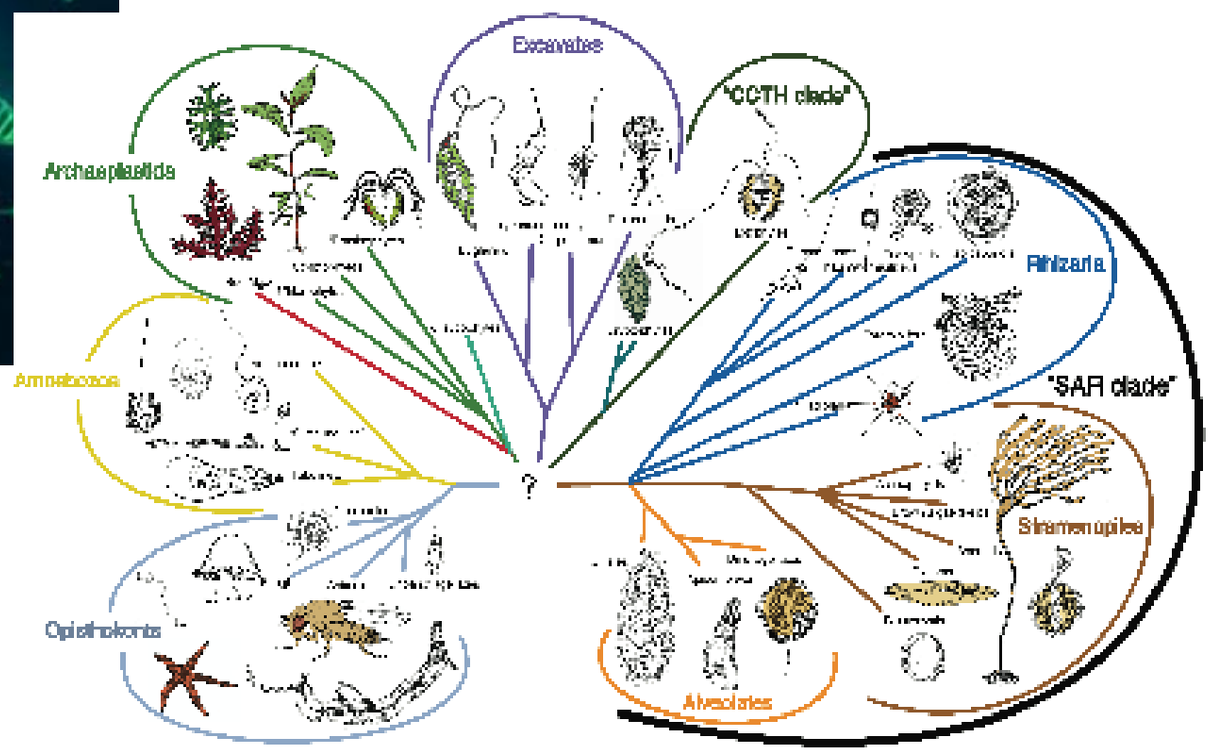
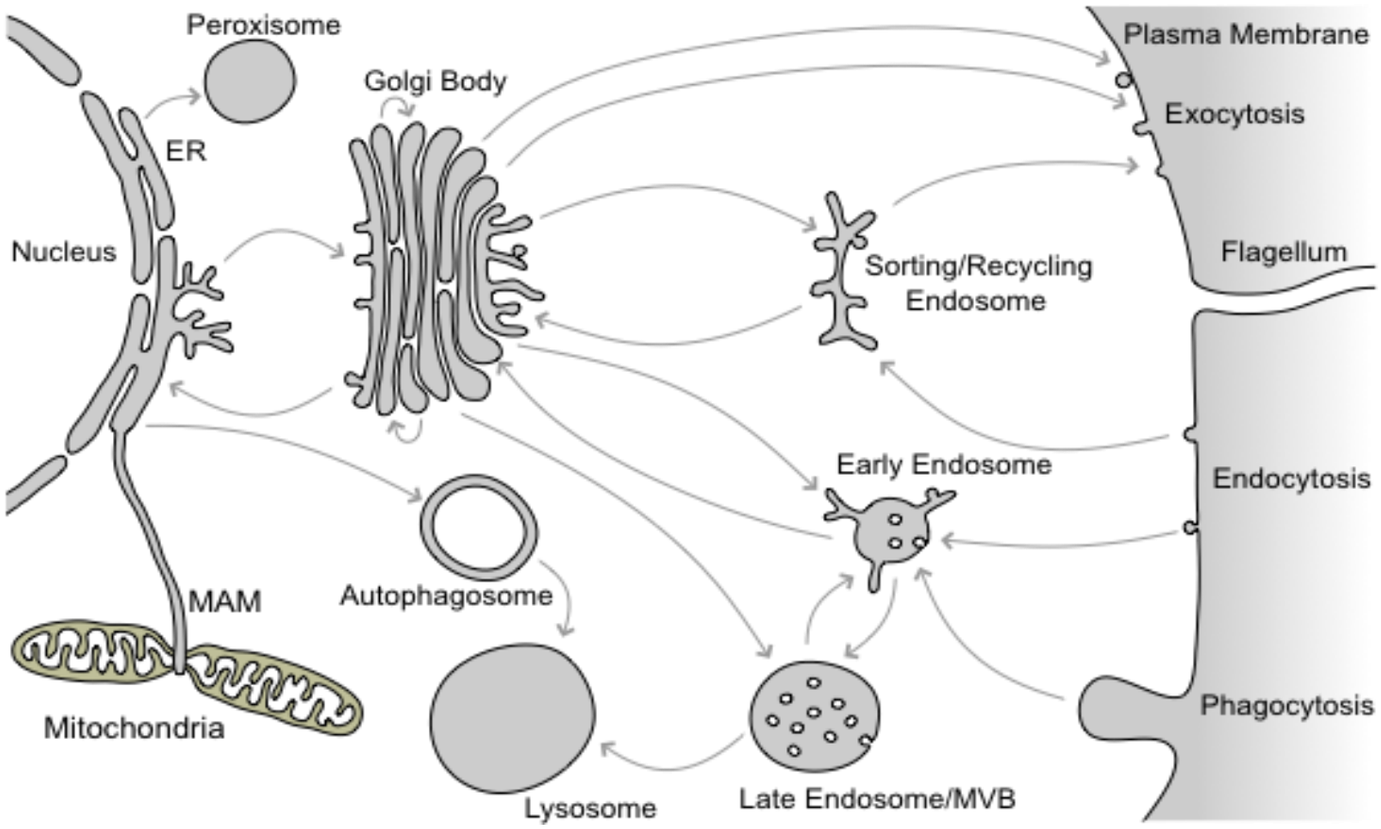
Evolution of the Endomembrane System

Joel Dacks, Univ. Alberta





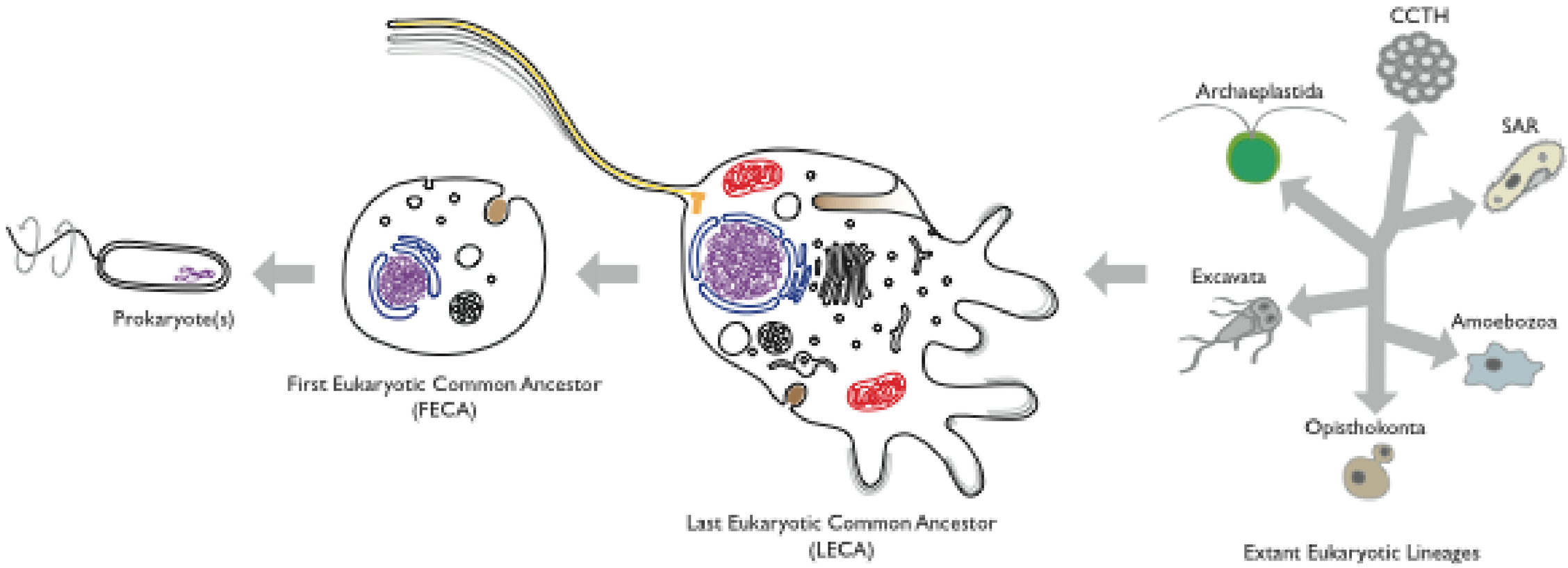
http://ismh.s3.amazonaws.com/2012-12-13-five-flavors.jpg
http://cdn.slashgear.com/wp-content/uploads/2015/08/genome.jpg

KITP Evocell15, Aug 18, 2015

Questions

- What diversity exists in eukaryotic membrane-trafficking: organismal biology
- In what way does the model as derived in animal and yeast apply to eukaryotic cells in general?
- When and how did the eukaryotic membrane-trafficking machinery evolve?

Talk Outline



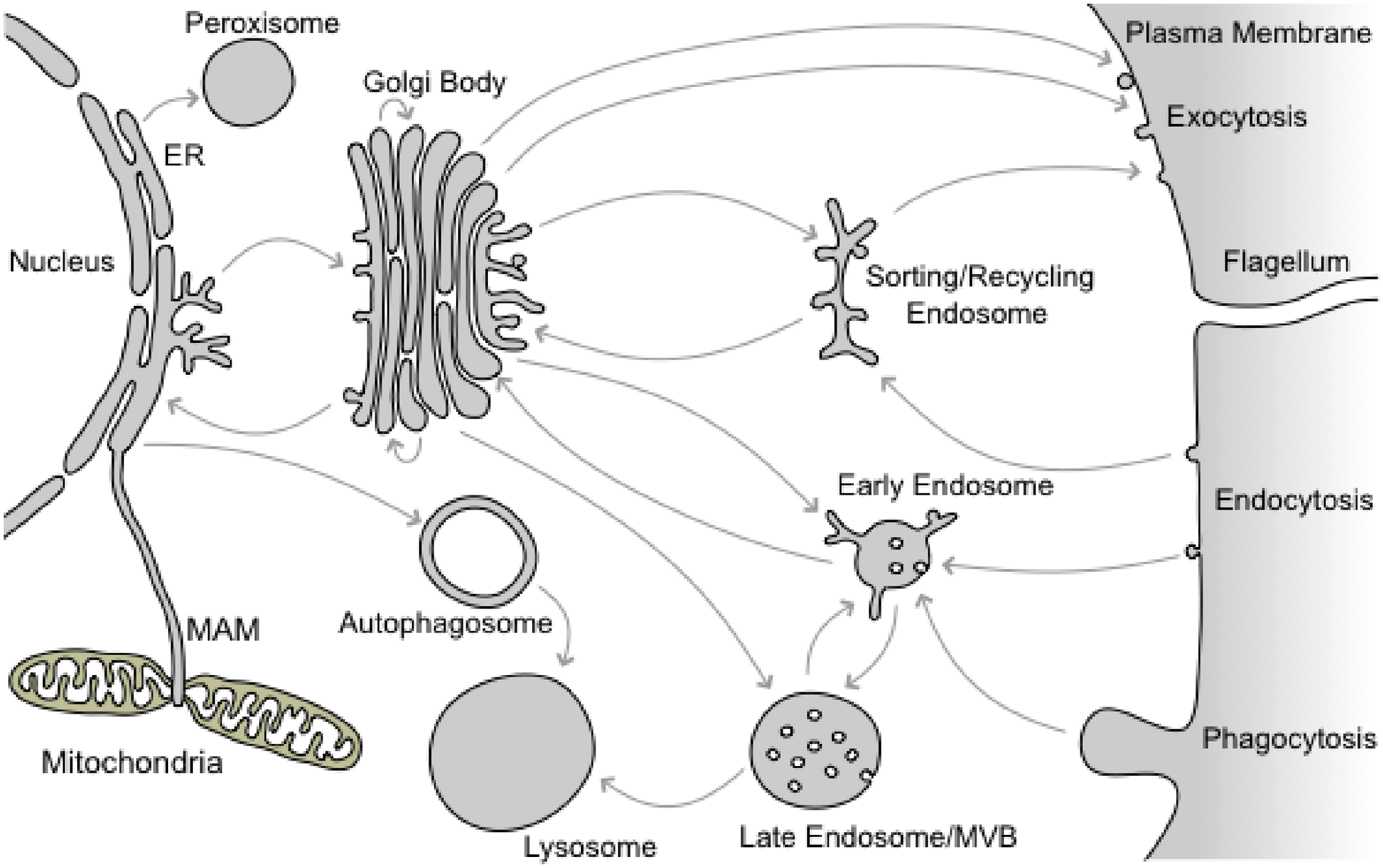
- How can an evolutionary approach be useful to cell b

Eukaryotes are more than

Colpodellids
Apicomplexa
Dinoflagellates
Chromerids
Perkinsids
Ellobiopsids
Labyrinthulids
Bicosoecids
Sloomycetes
Stramenochromes
Slopalinids
Placidids
Ciliates
Endomyxa
Filosa
Foraminifera
Radiozoa
Haptophytes
Picobiliphytes
Cryptomonads
Kathablepharids
Centrohelids
Telonemids
Glaucophytes
Cyanidiophytes
Rhodophytes
Streptophytes
Chlorophytes
Flabellinida/Discosea
Tubulinea
Pelobionts
Acanthamoebae
Cochliopodids
Dictyostelids
Archamoebae
Myxogastrids
Thecamoebae
Protostelids
Entamoebae
Breviates
Jakobids
Malawimonads
Oxymonads
Trimastix
Heterolobosea
Euglenozoa
Parabasalids
Carpediemonads
Retortamonads
Diplomonads + Enteromonads
Apusozoa
Metazoa
Choanoflagellates
Capsaspora owczarzaki
Ichthyosporids
Corallochytrium
Blastocladiomycetes
Rozellids
Ascomycetes
Basidiomycetes
Glomeromycetes
Zygomycetes
Nephridiophagids
Microsporidia
Chytridiomycetes
Fonticulids
Nucleariids

Walker, Dorrell, Schlacht and Dacks 2011

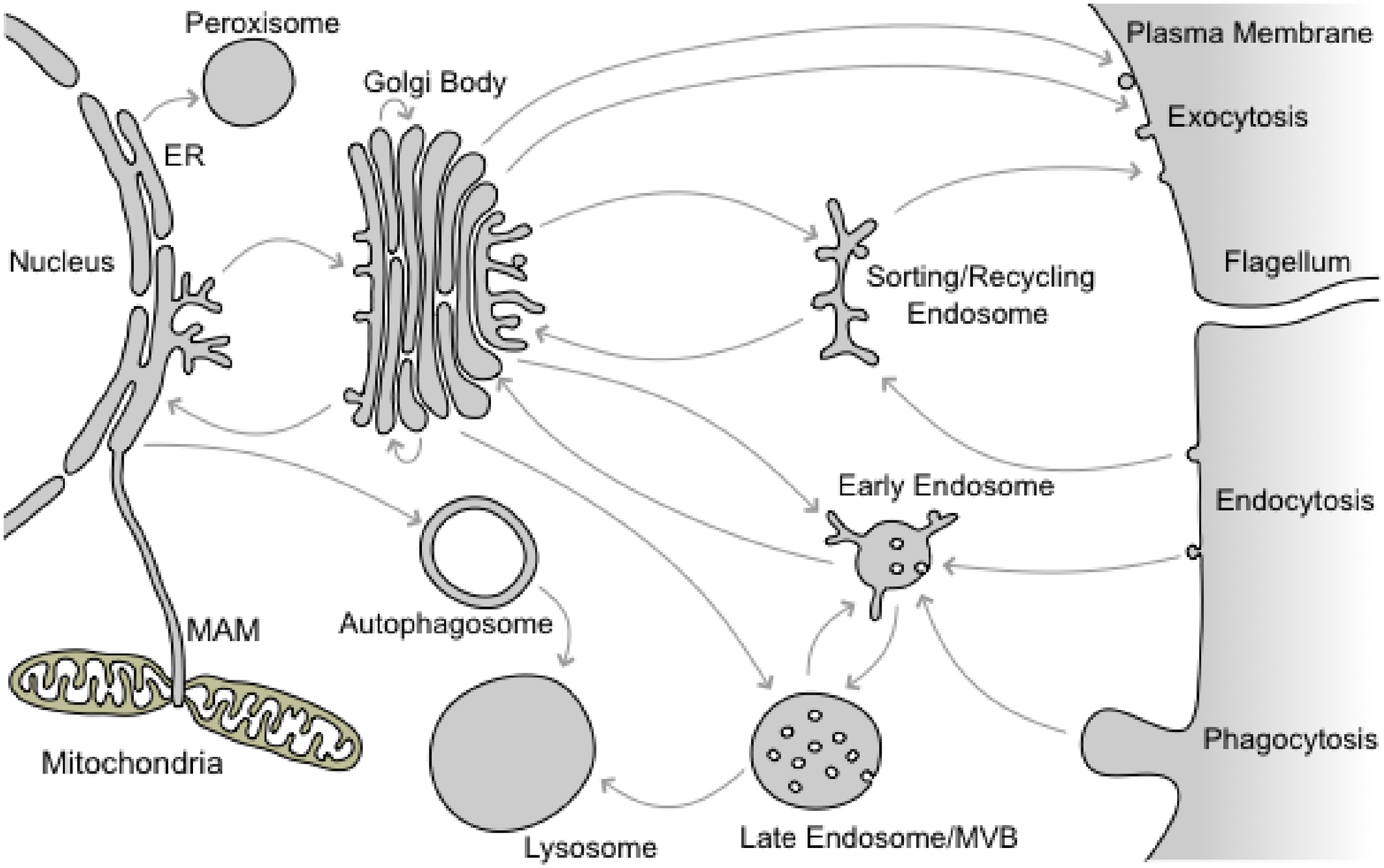
Eukaryotic Membrane Trafficking System



In modern eukaryotes enables:

- Uptake from the environment
- Export to the environment
- Cell surface remodelling
- Intracellular targeting
- Compartmentalization

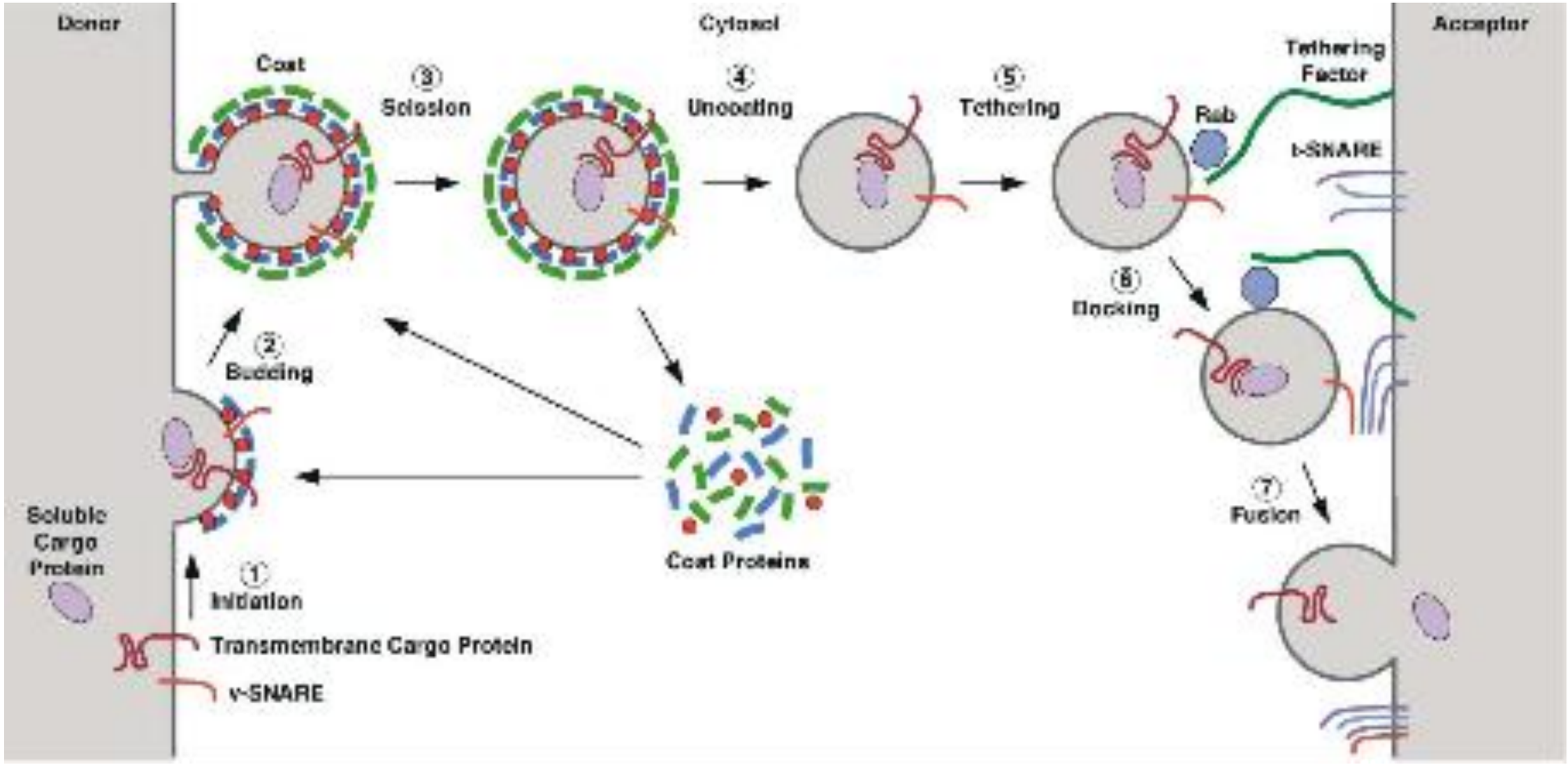
Eukaryotic Membrane Trafficking System



For the earliest eukaryotes

- Environmental sensing
- Population communication
- Communication with MROs
- Sequestration (introns, enzymes)
- Nutrient acquisition

Protein machinery in Membrane Trafficking

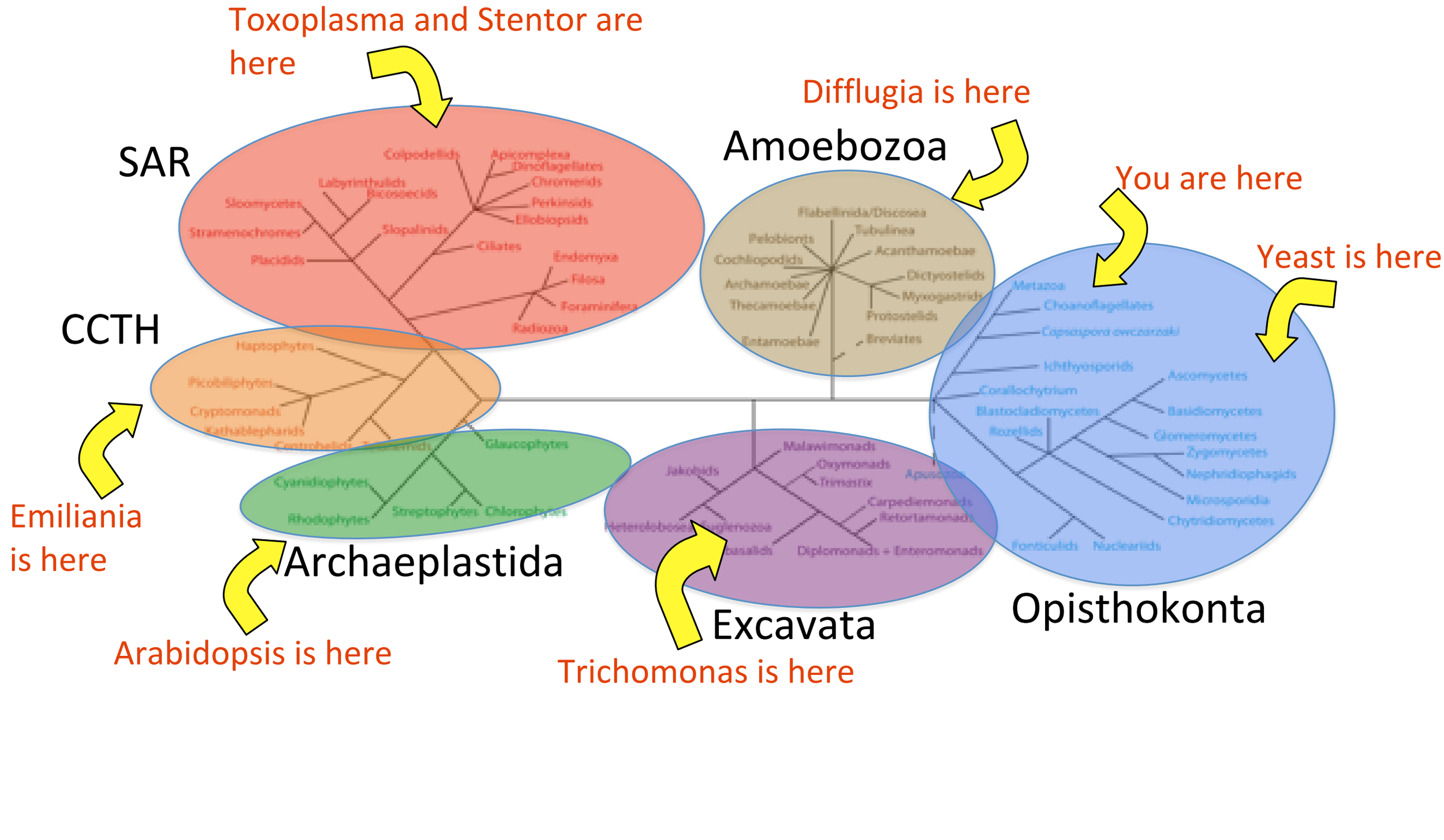


Bonifacino & Glick, *Cell*, 2004

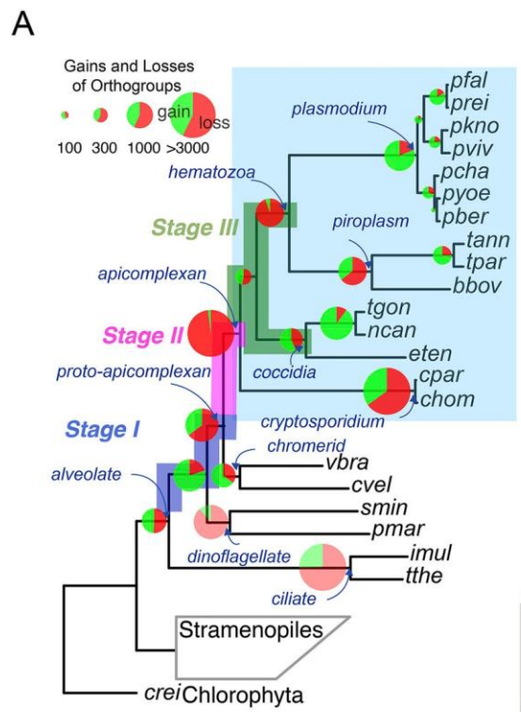
Methodology

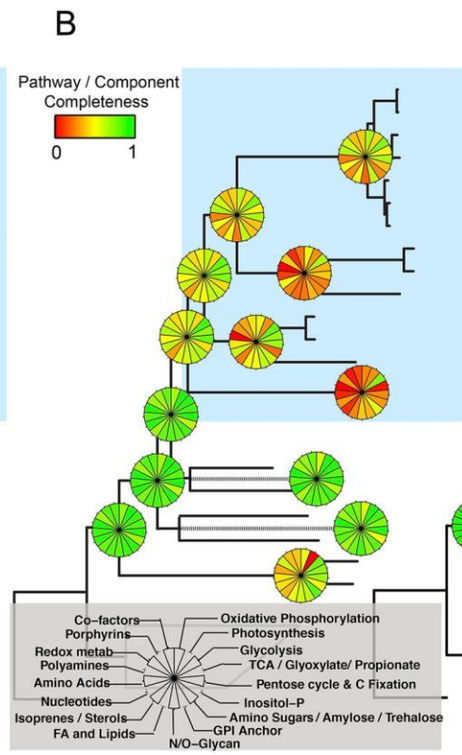
- Use of publicly available data
- Genome sequence analysis, collaboration with genome sequencing centres (JGI, TIGR) or with a few labs
- Homology searching (BLAST, HMMer, RBH,domains)
- Phylogenetic analyses (MB, PhyloBayes, RAxML)
- Molecular cell biology in collab with relevant labs

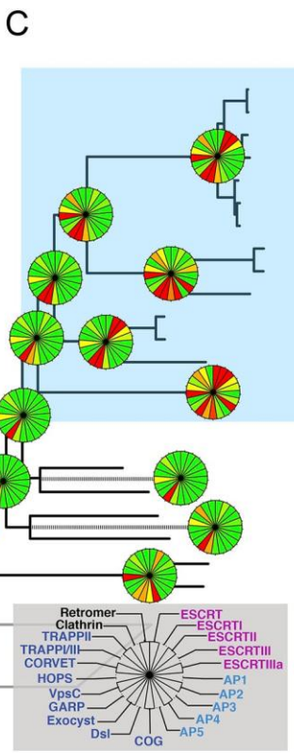
The diversity of Eukaryotes

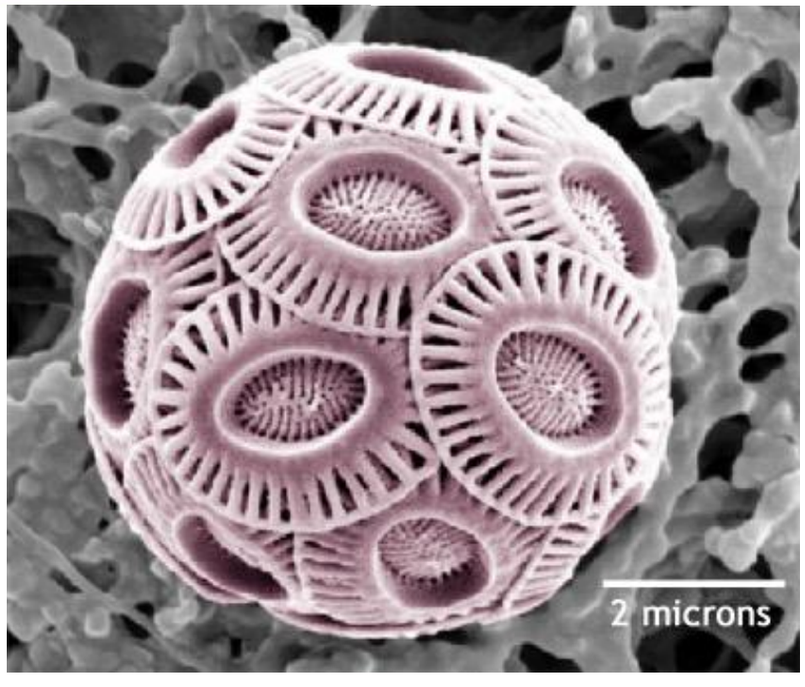


Use genome information to understand trafficking in these organisms







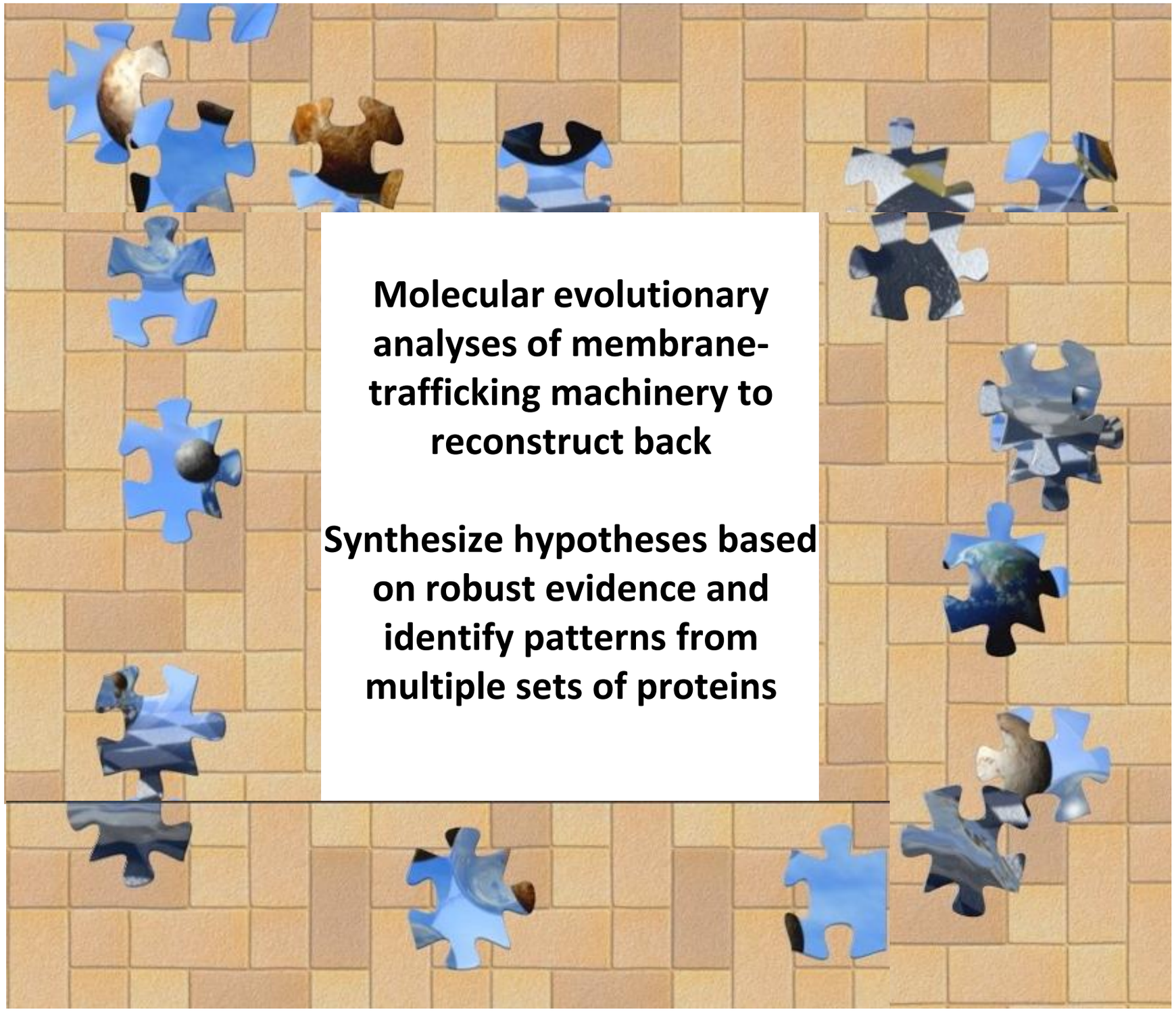


Carlton et al. 2007, Read et al. 2013, Woo et al. 2015

A theory for the evolution of the endomembrane system

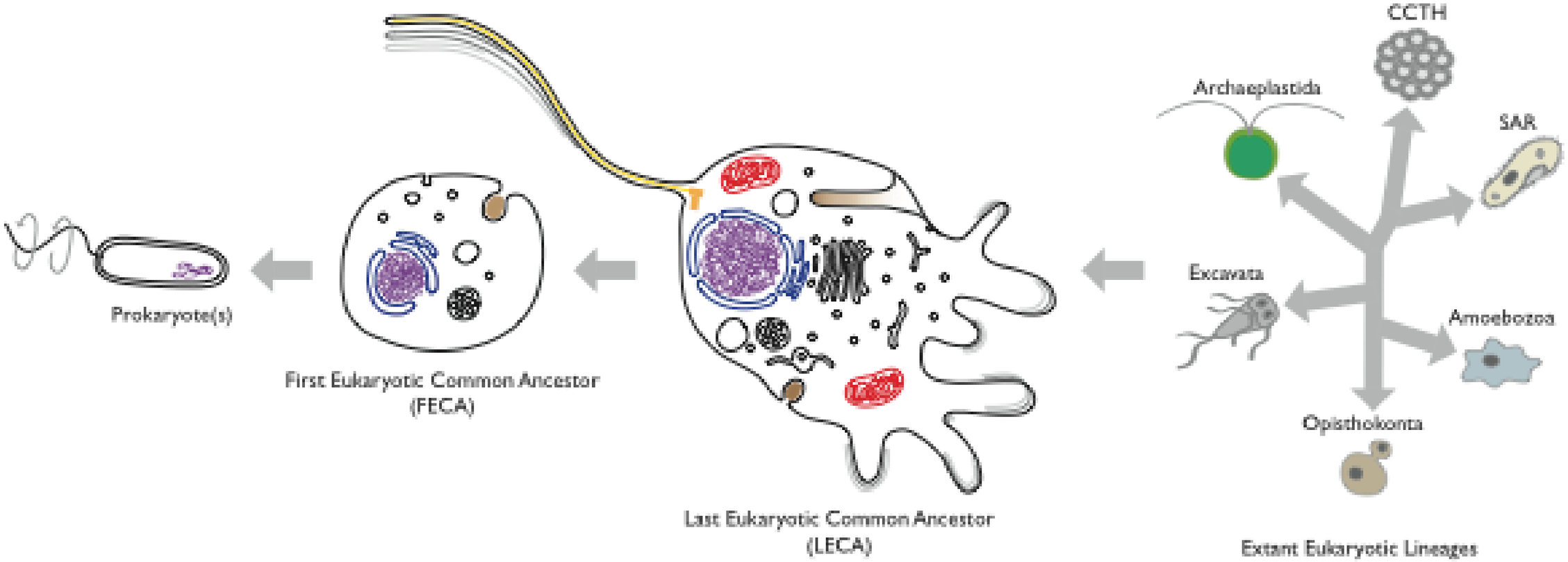
http://www.gaiadreamcreation.com/games/gaia-pc-jigsaw-puzzle/

Understanding the pieces of the puzzle

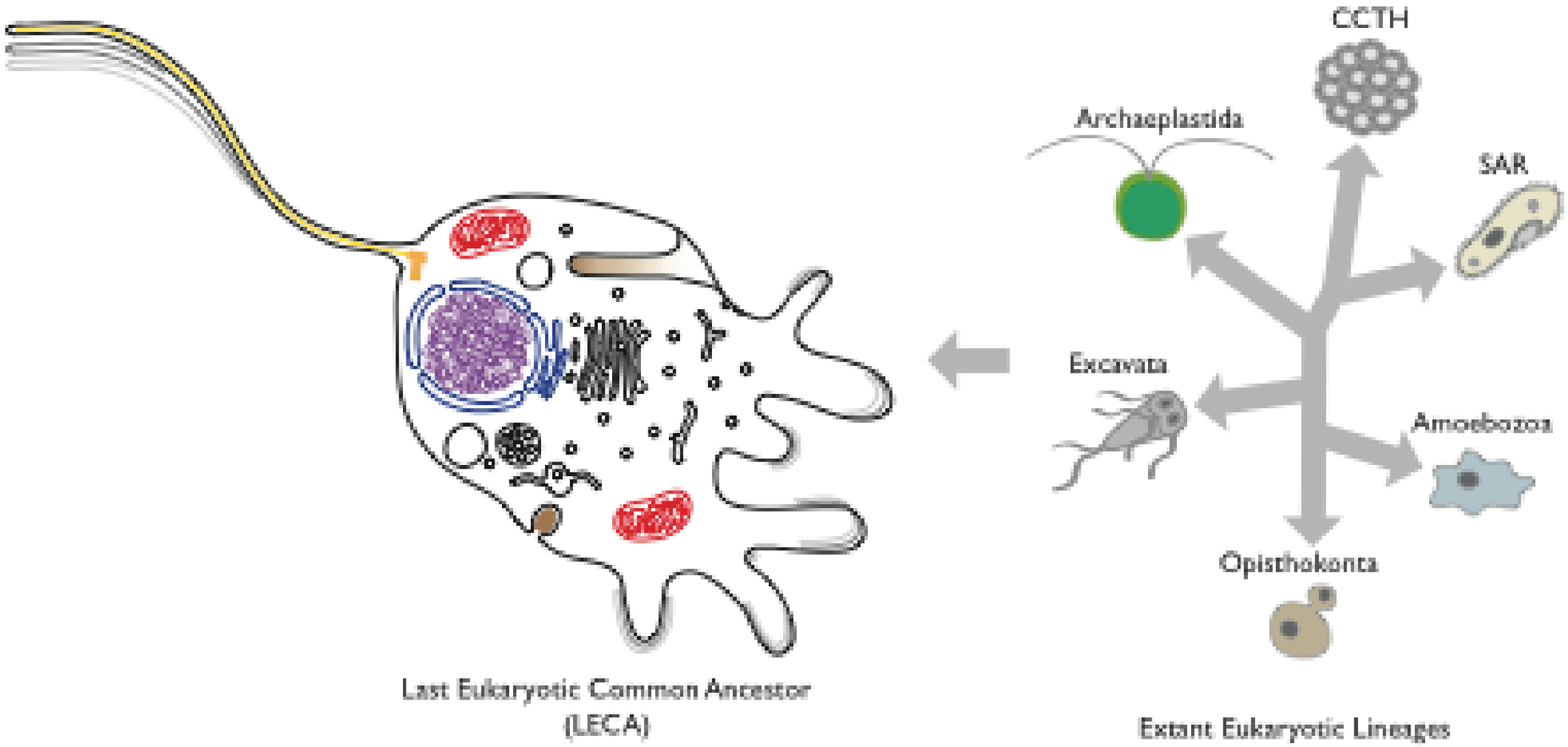


Can they be put together?

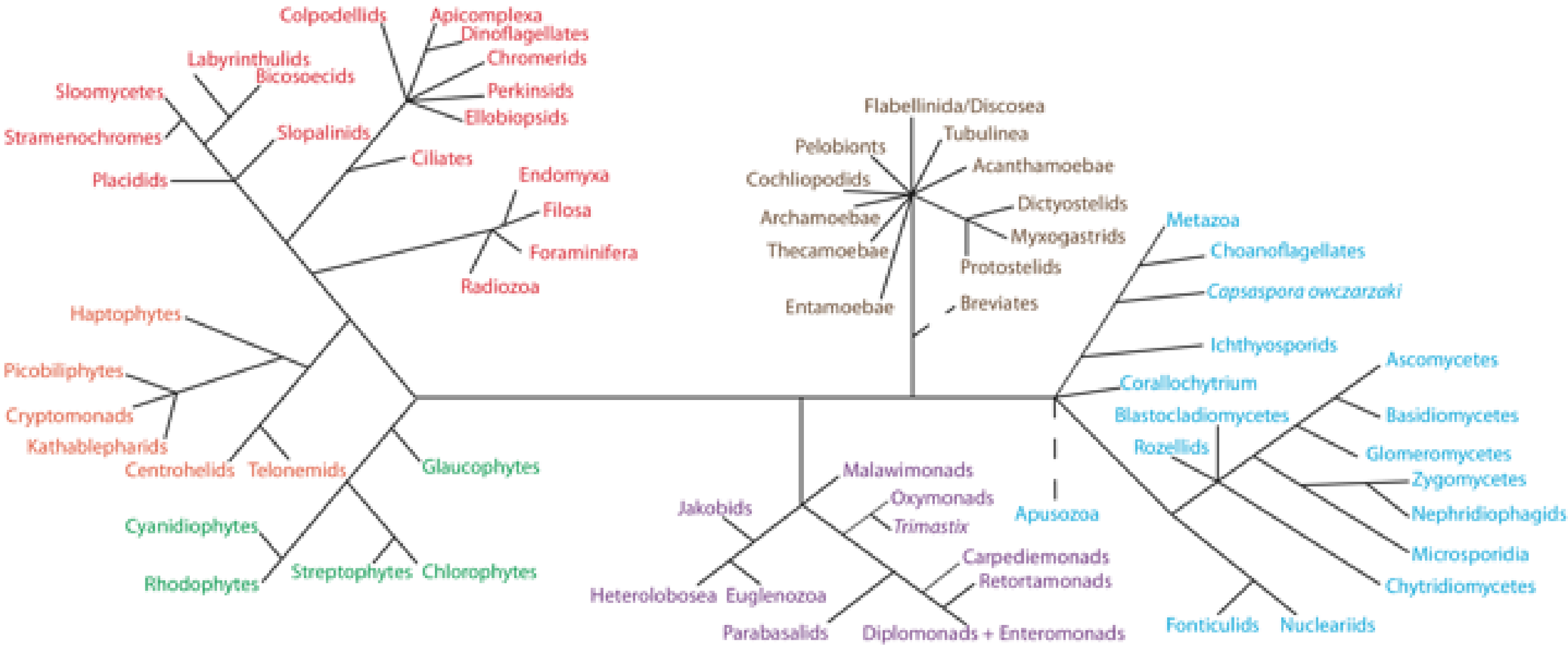
Reconstruct back



LECA is a tractable reconstruction point

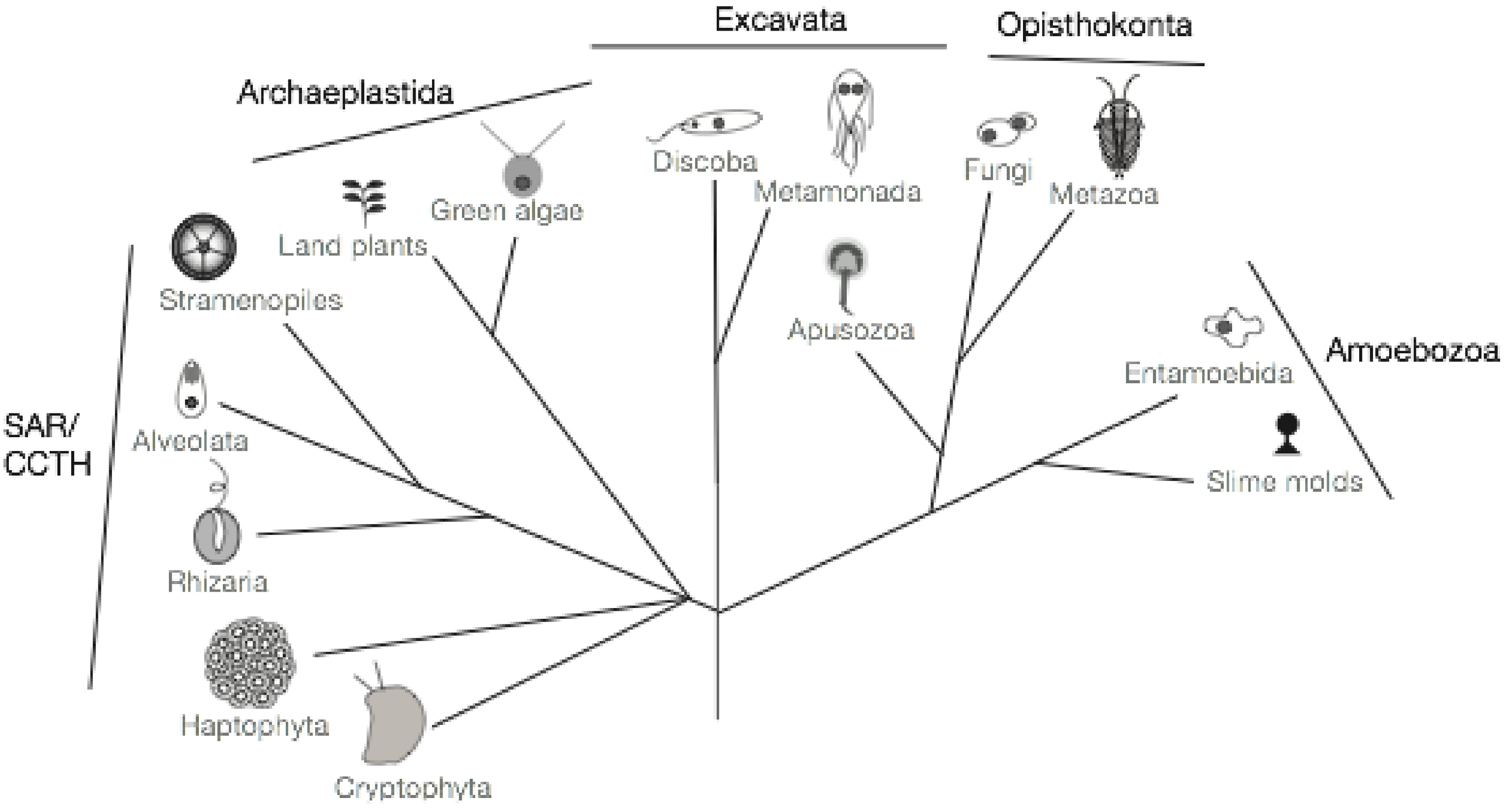


Eukaryotic diversity

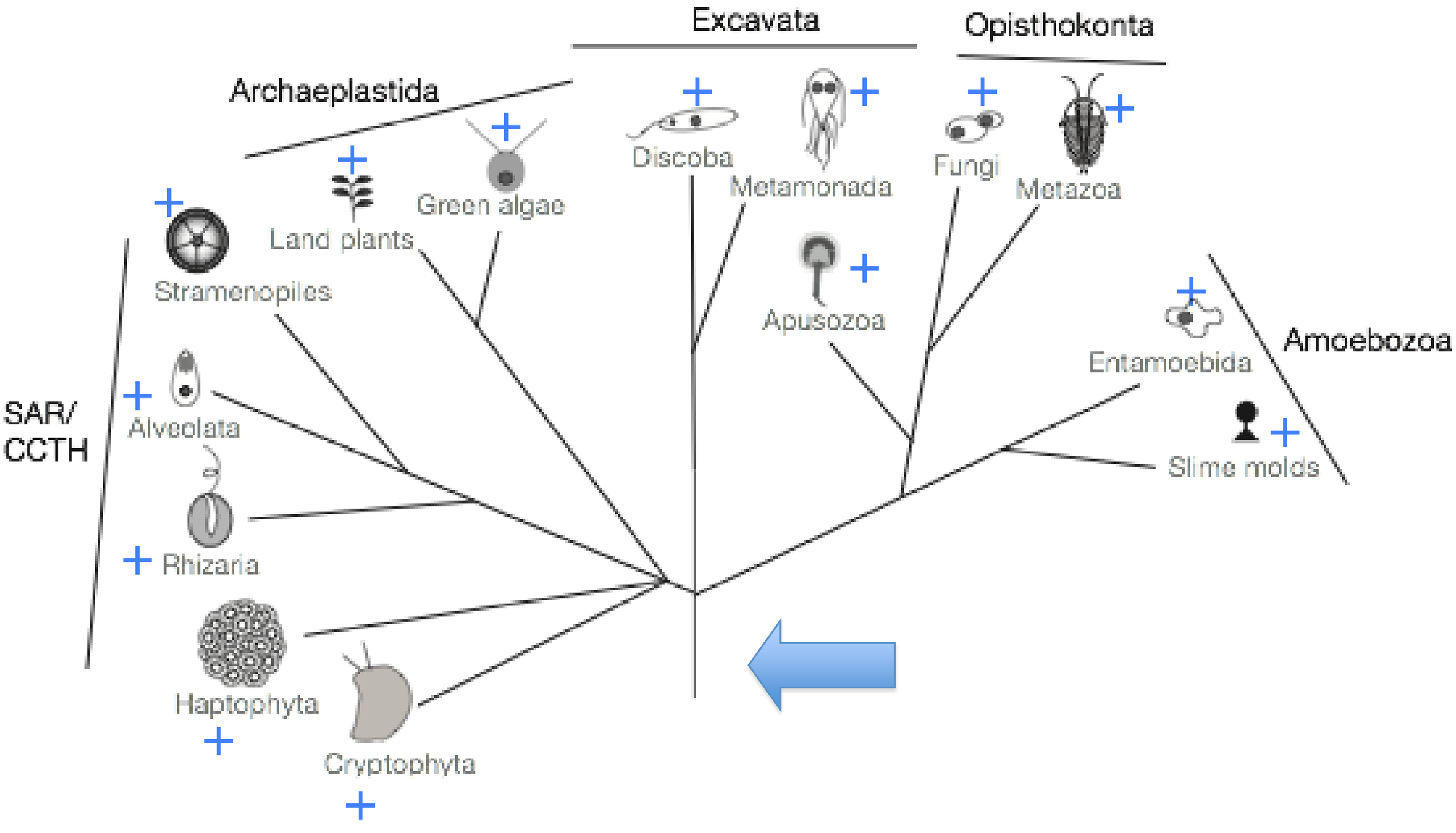


Walker, Dorrell, Schlacht and Dacks 2011

Simplified view of Eukaryotic diversity



Distribution indicates history and essentiality



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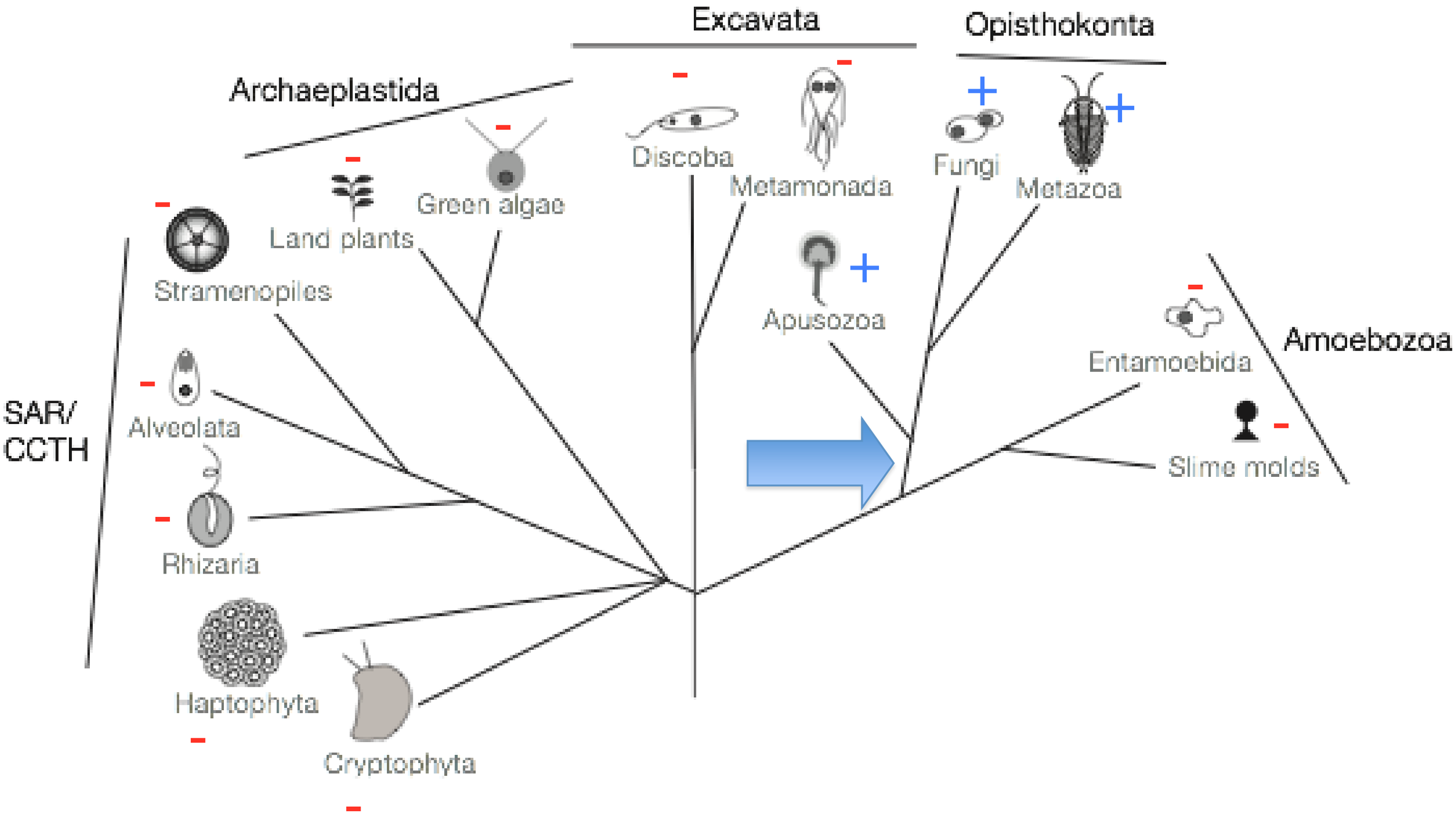
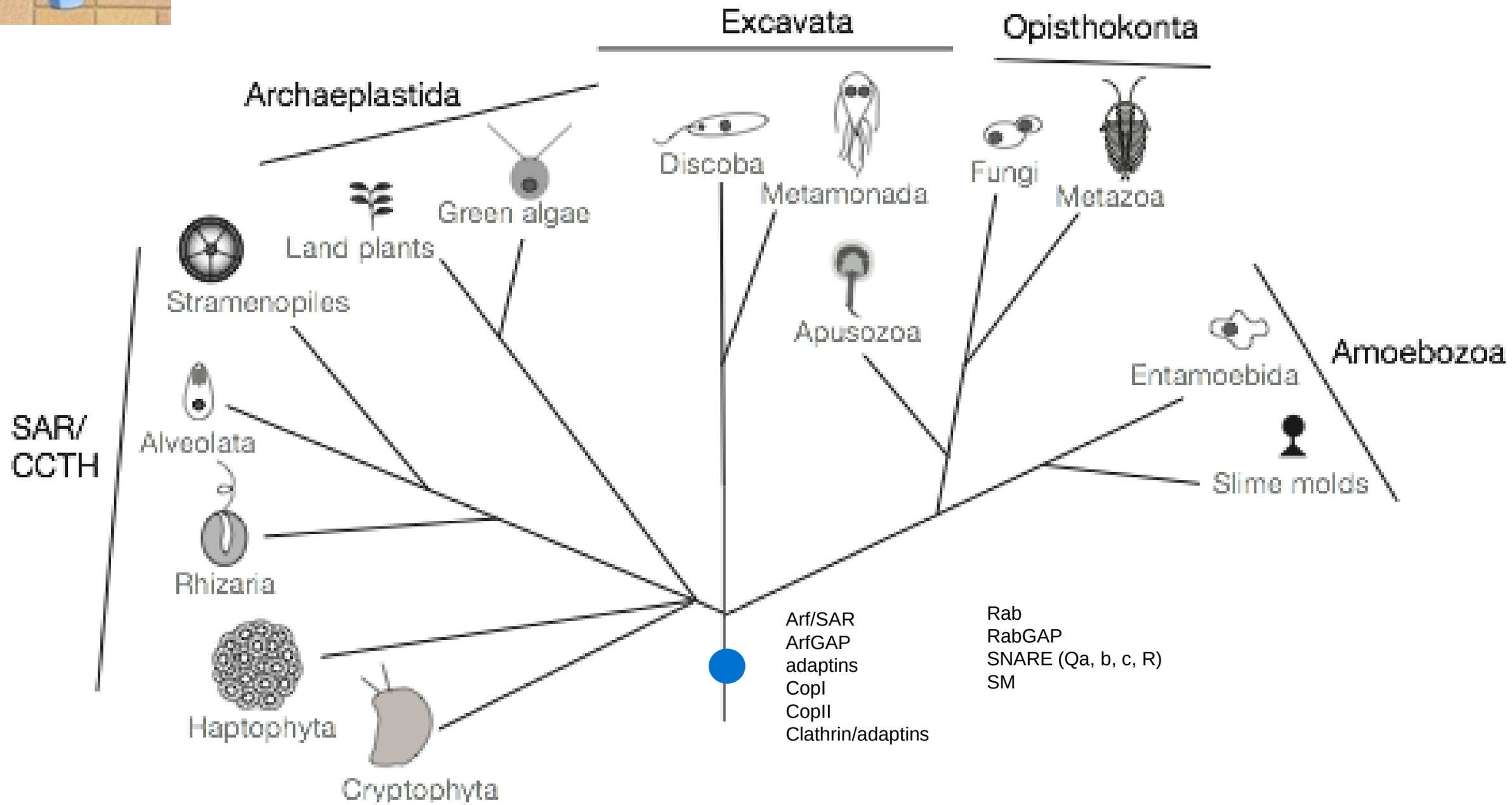
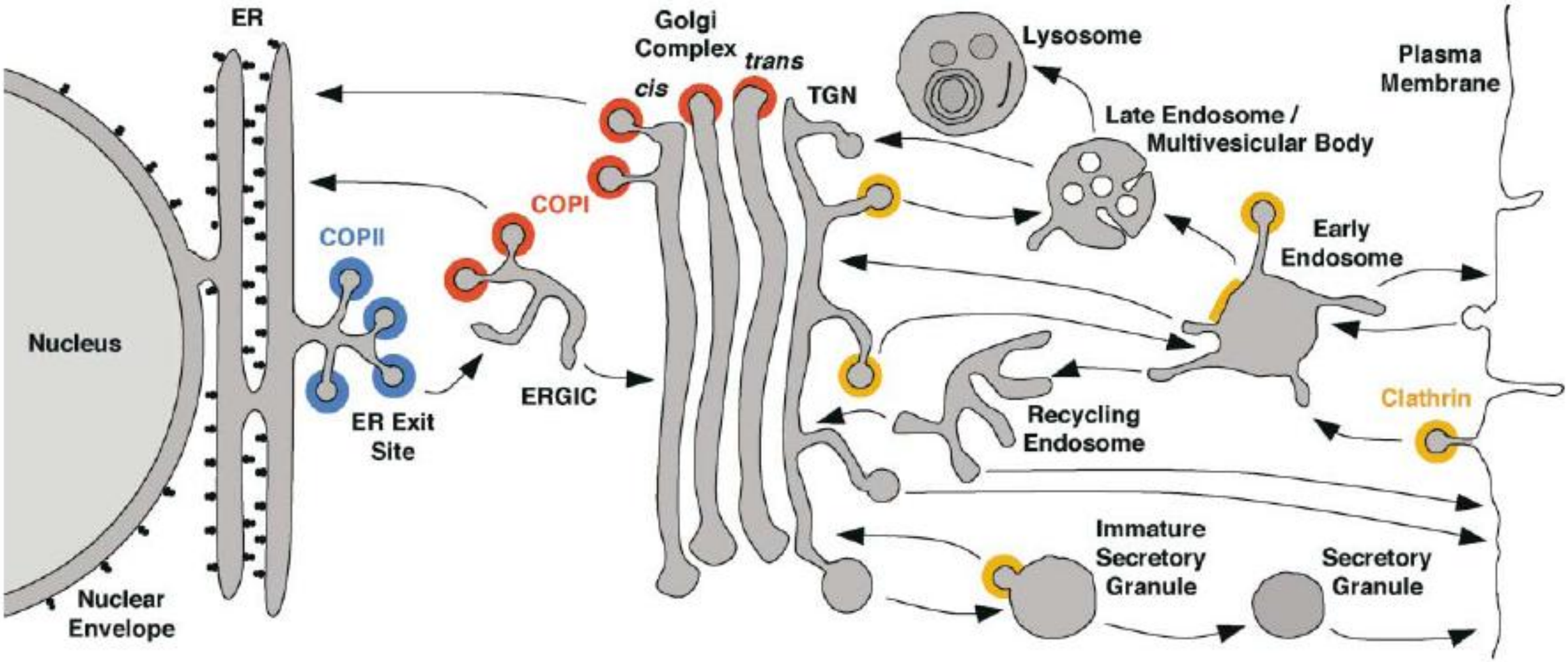


A sophisticated complement in the LECA



Comparative genomics from taxa across the span of eukaryotic diversity showed the major families of trafficking proteins present in the LECA

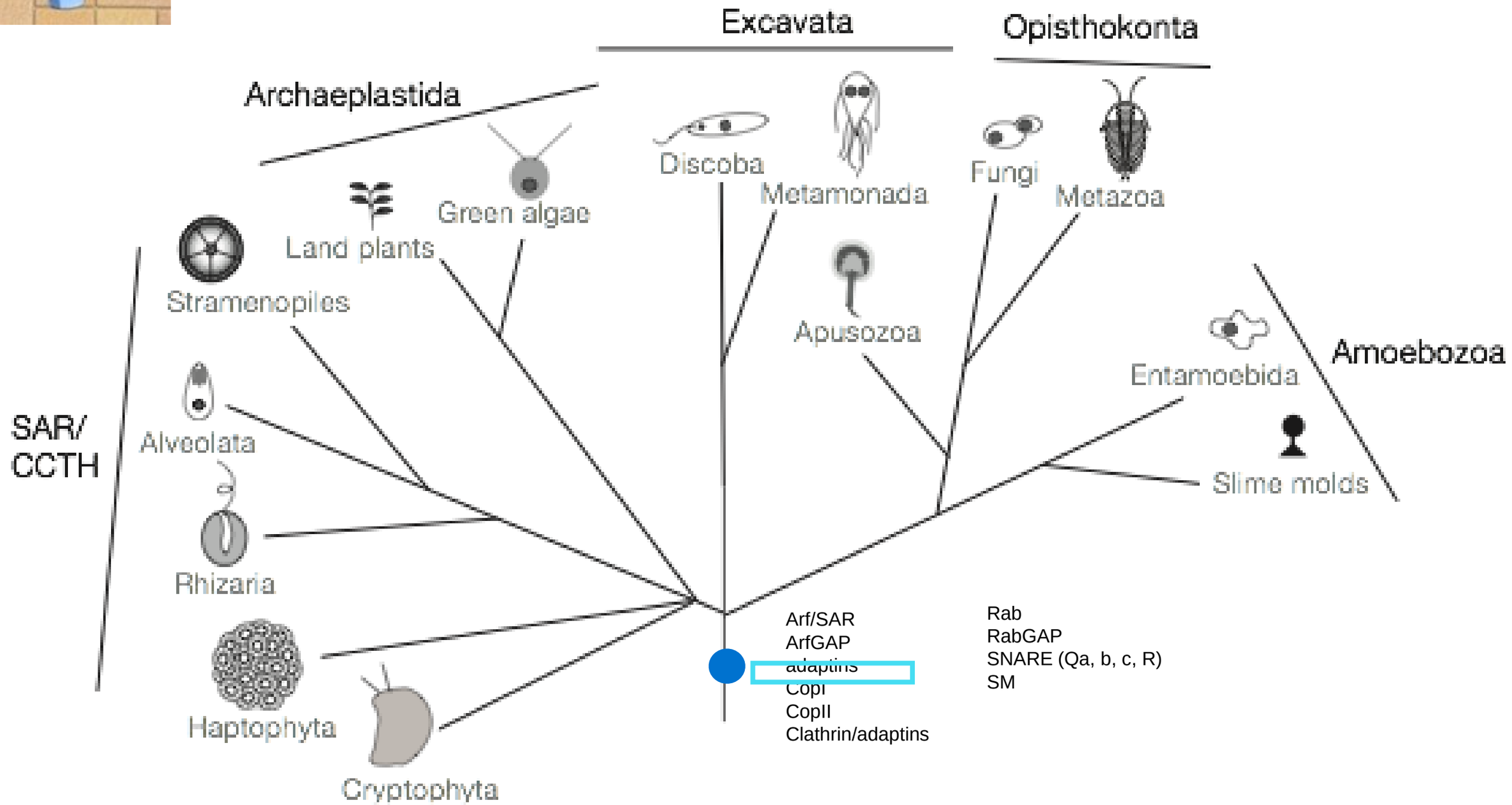
Organelle or pathway-specific machinery



Understanding the history of the organelle-specific proteins:
Understand the history of the organelles

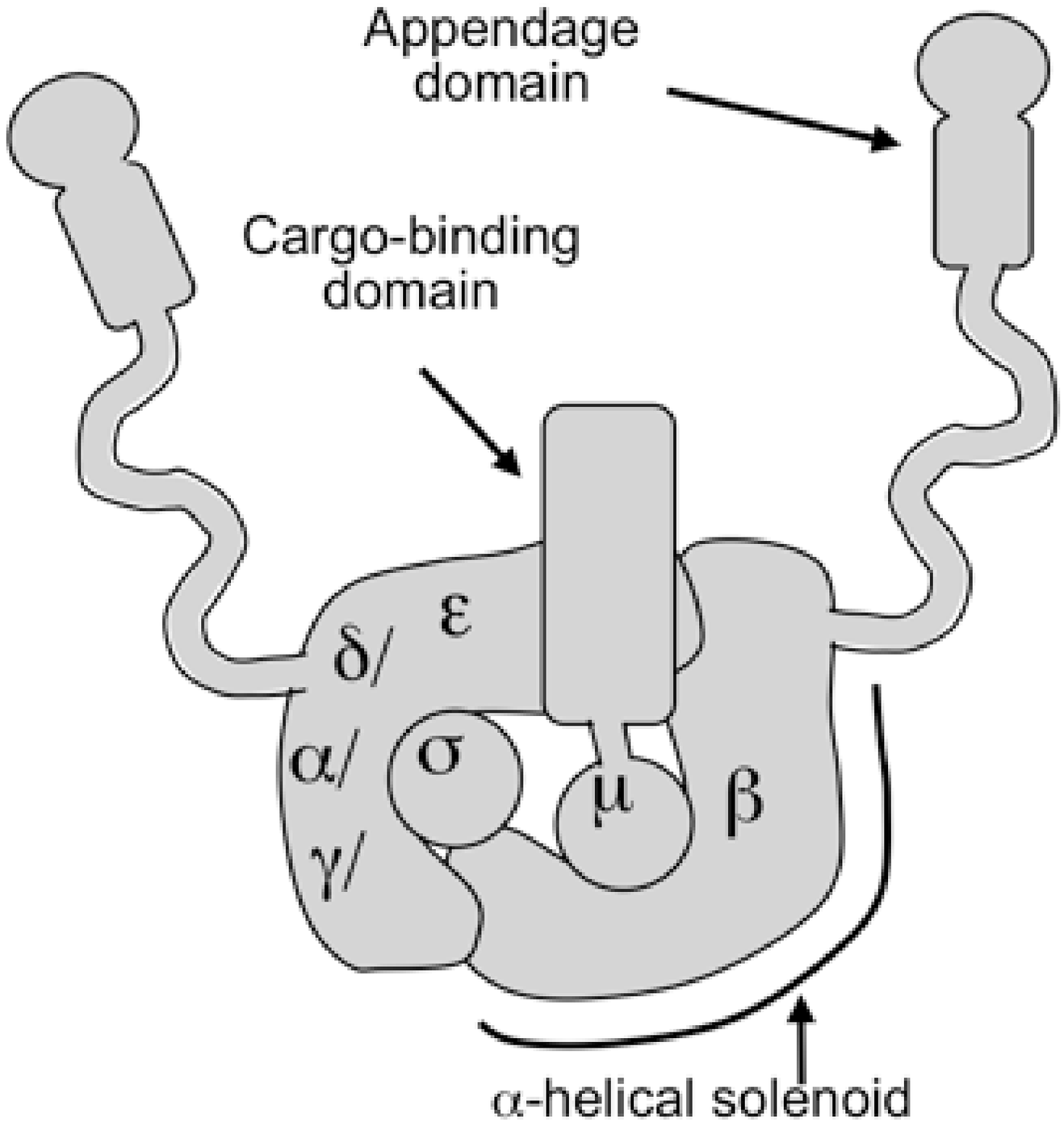
Bonifacino & Glick, *Cell*, 2004

A sophisticated complement in the LECA



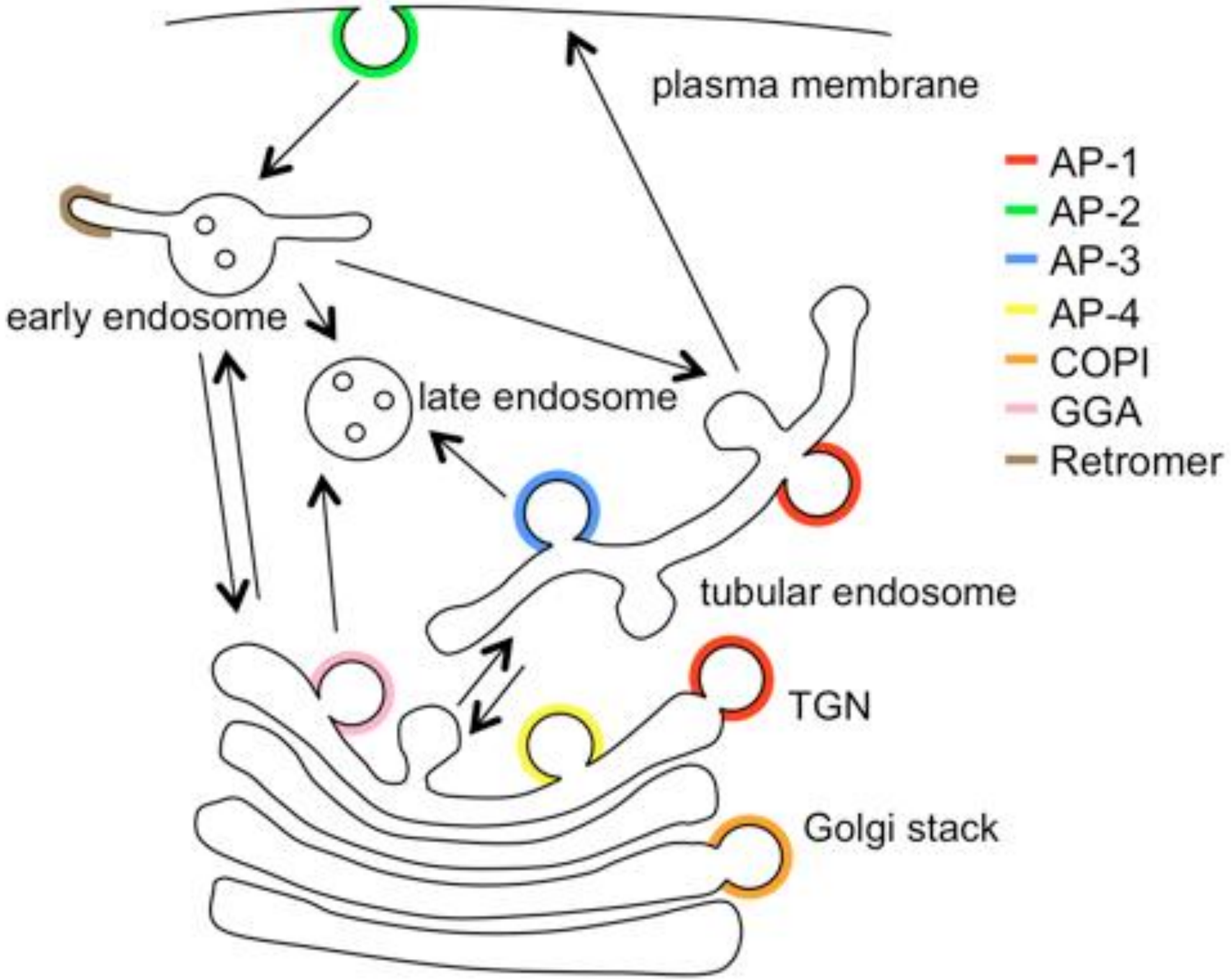
When did the organelle/pathway-specific subfamilies arise?

Adaptins



Hirst, Barlow, et al. 2011

Adaptins



Hirst, Barlow, et al. 2011

Questions

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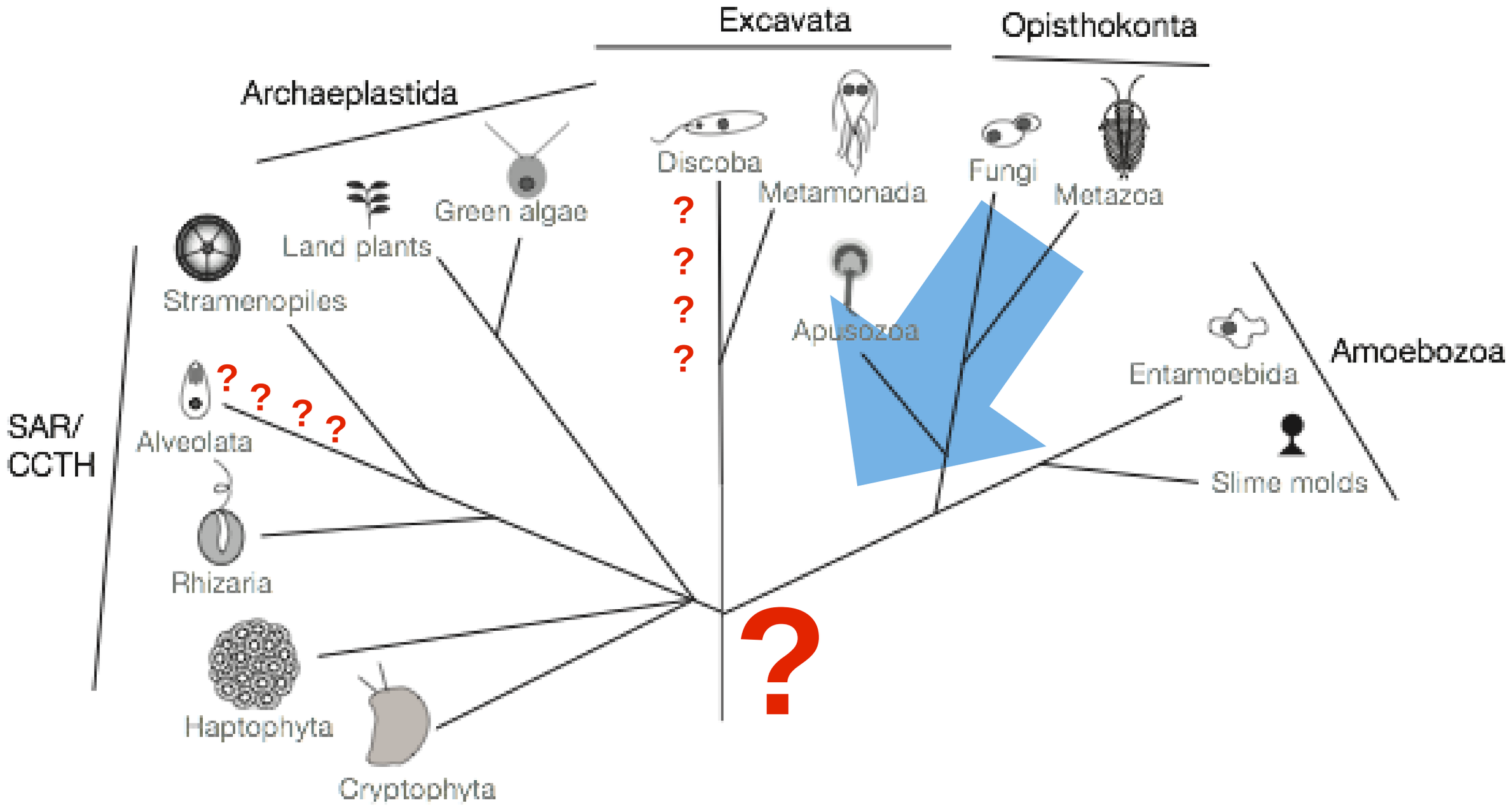
- **How can an evolutionary approach be useful to cell biologists?**

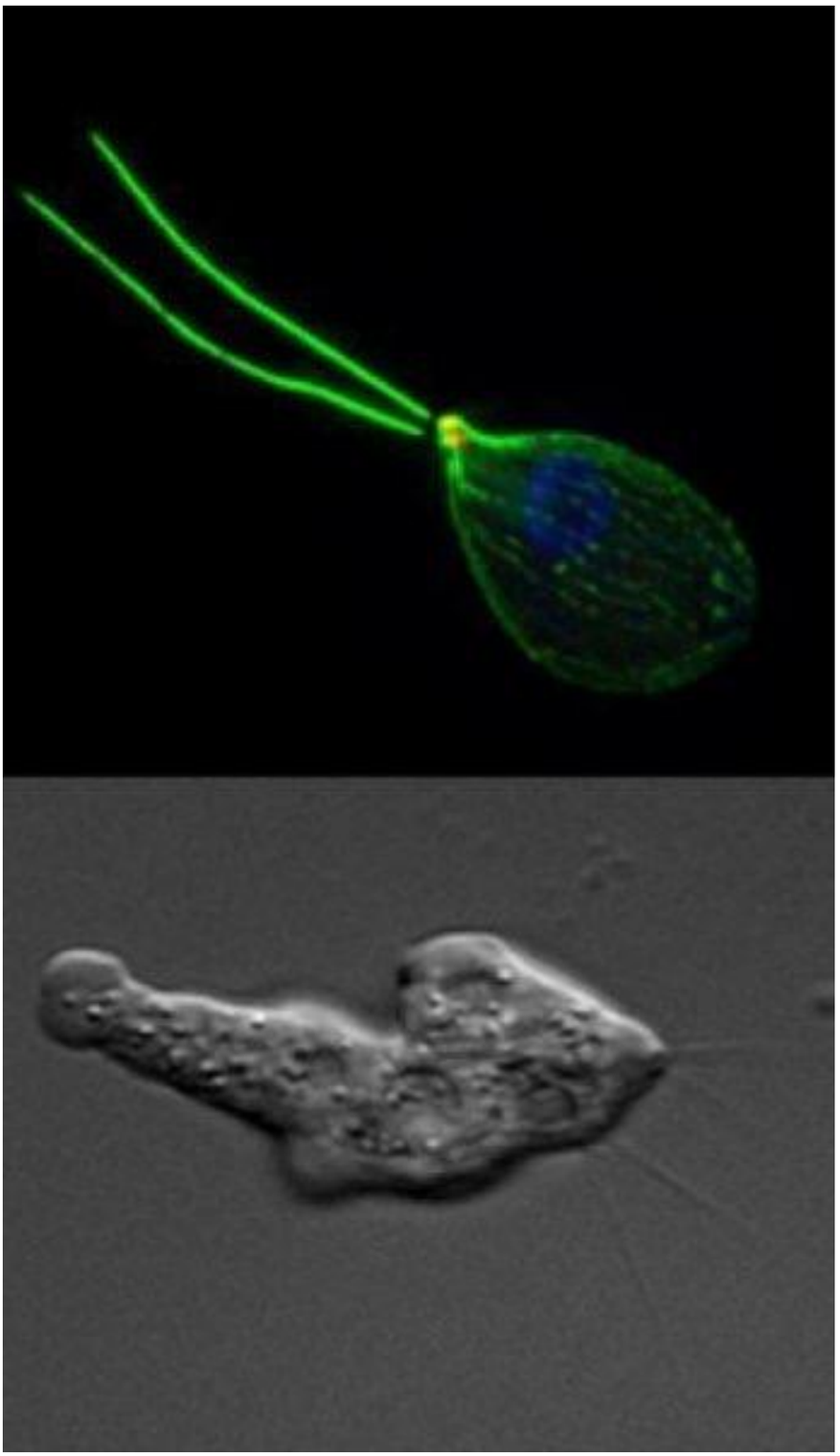
Questions

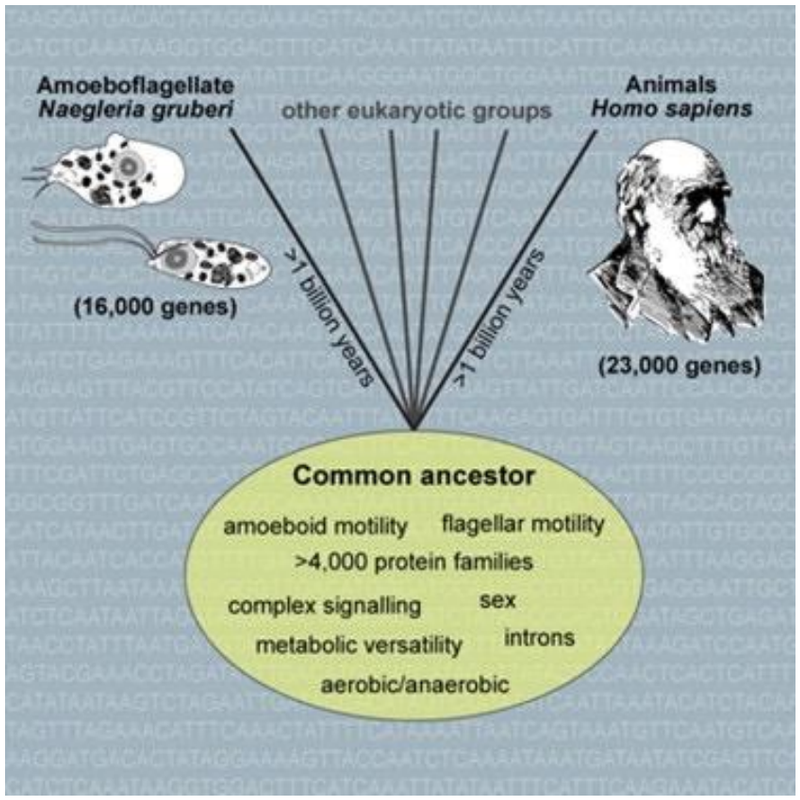
- In what way does the model as derived in animal and yeast apply to eukaryotic cells in general?
- When and how did the eukaryotic membrane-trafficking machinery evolve?
- What diversity exists in eukaryotic membrane-trafficking: organismal biology
- **Are there pieces that we have been missing or ignoring due to the emphasis on our model cell biological systems (asymmetry?)**

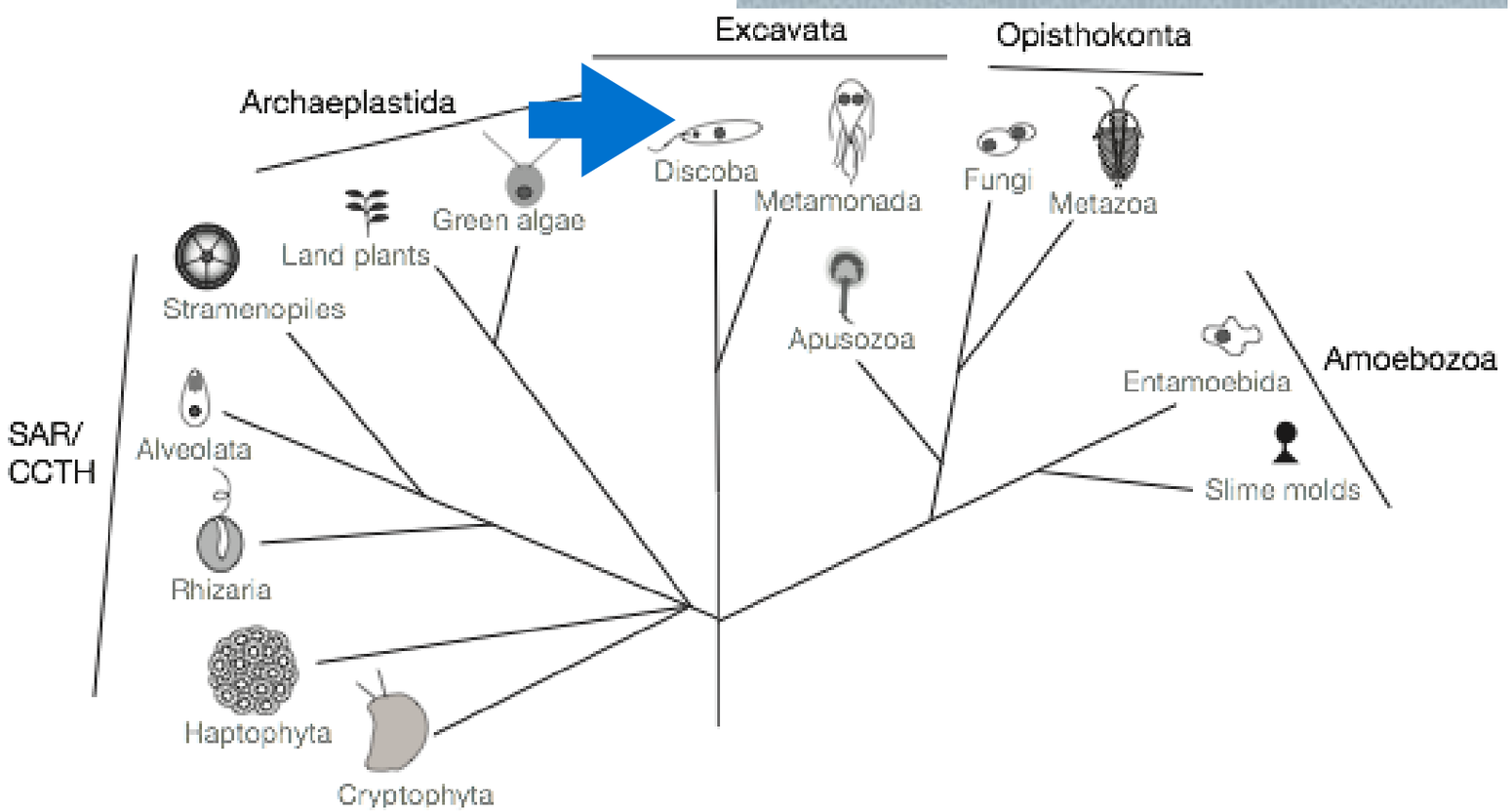
The asymmetry problem



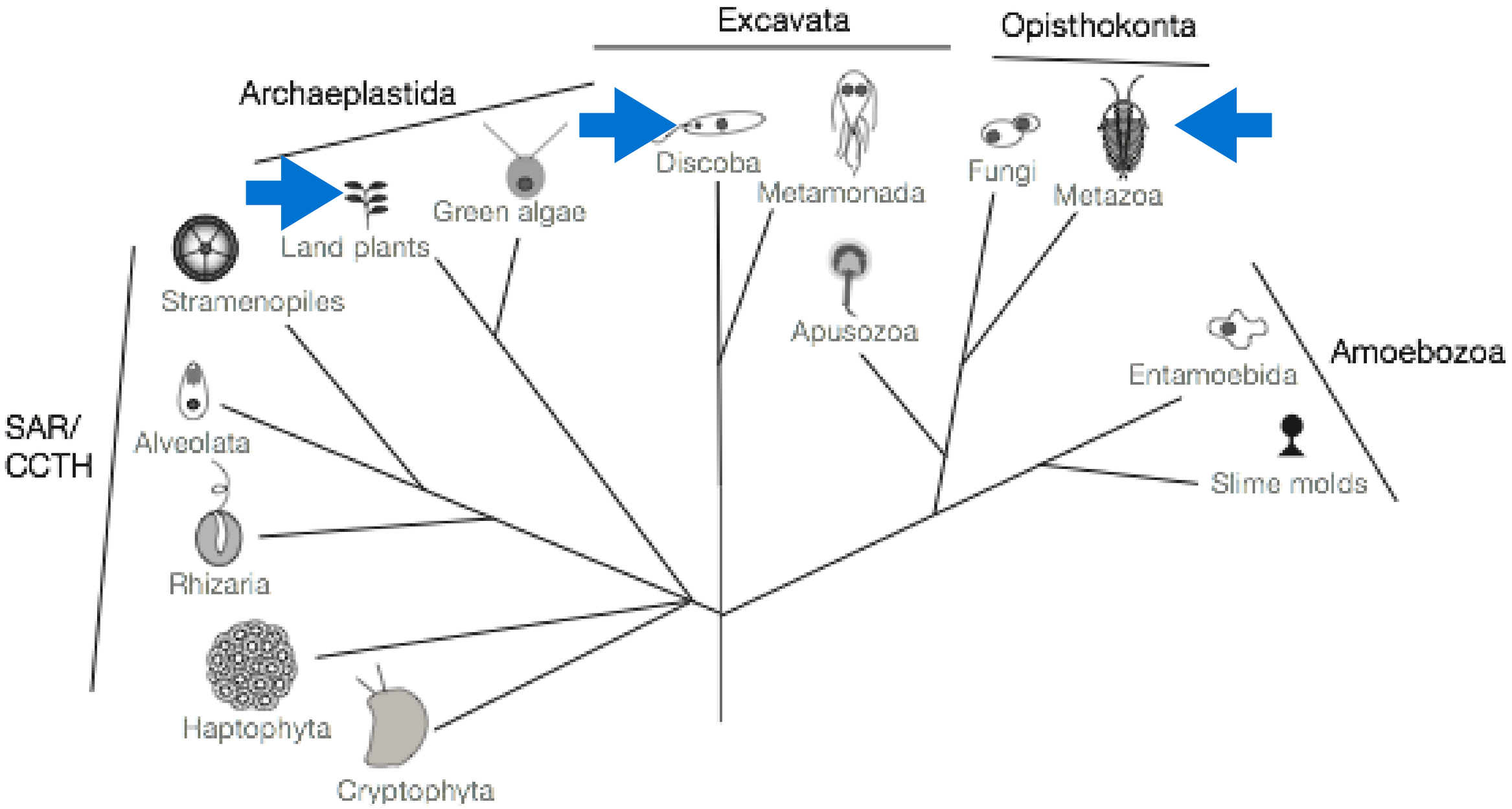
Use genome information to understand trafficking in these organisms





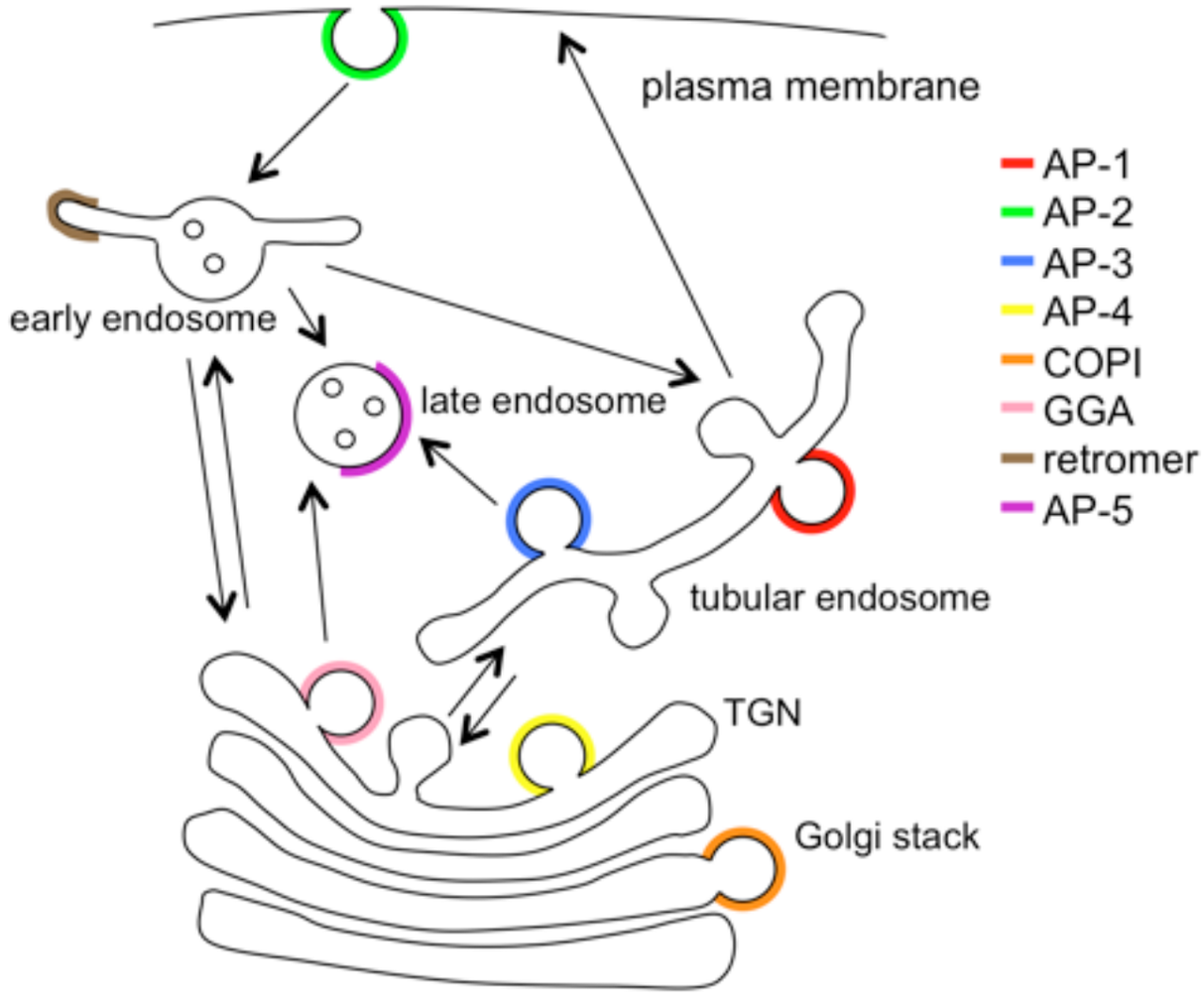


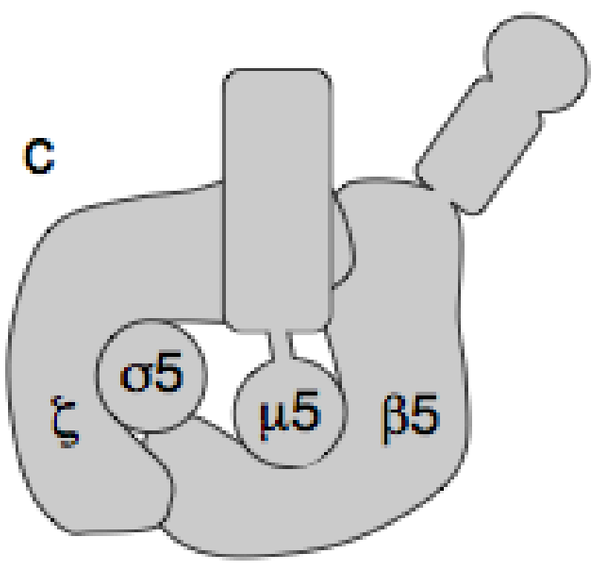
An extra clade of Adaptins?



AP5-A novel endosomal AP

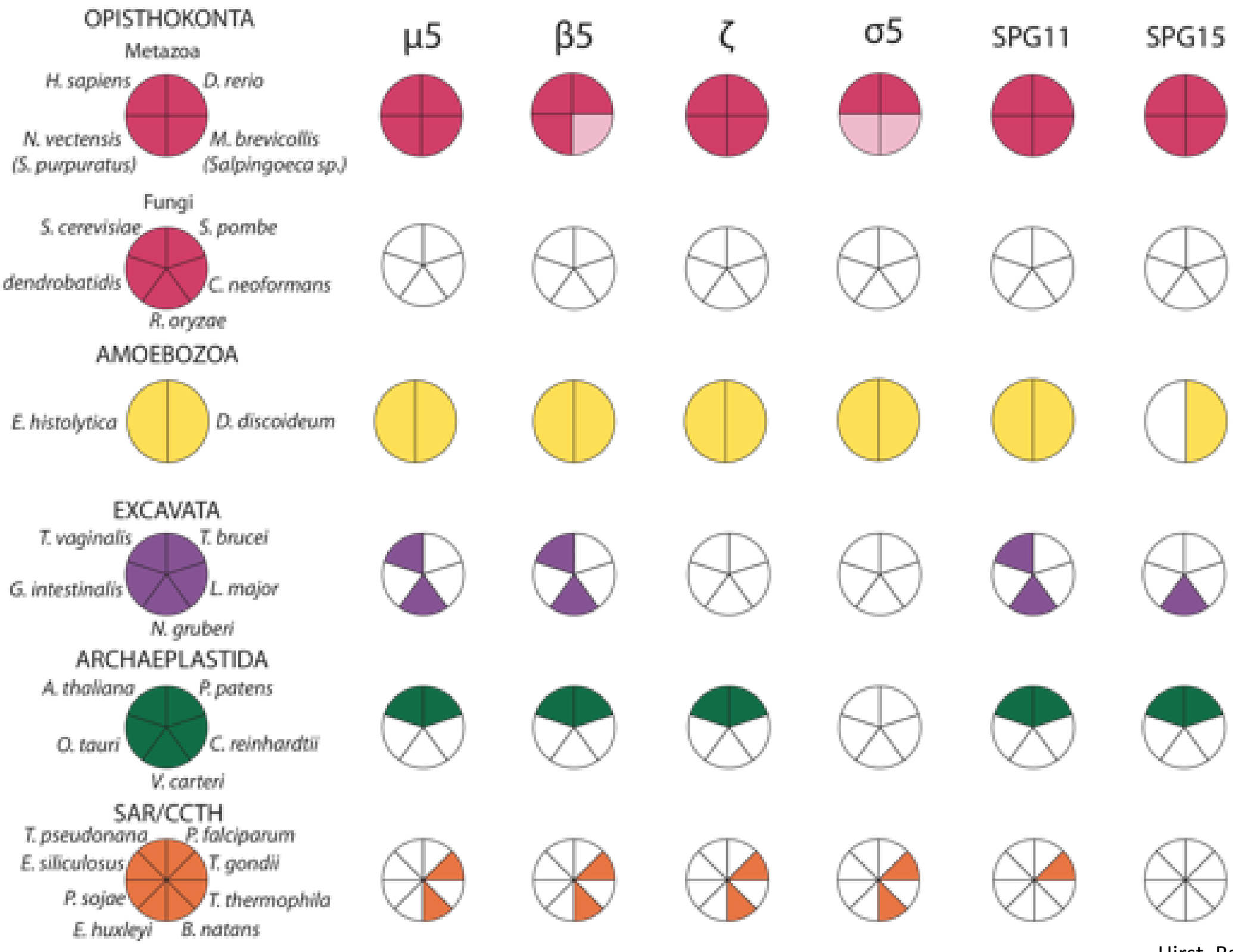
- Characterized in Hela cells
- Localizes to LAMP1-positive endosomes
- Affects CIMPR trafficking
- NOT clathrin associated, not brefeldin sensitive





μ5 = C14orf108
β5 = DKFZp761E198
ζ = KIAA0415/SPG48
σ5 = C20orf29

All components have similar distribution: ancient but patchy



Hirst, Barlow, et al. 2011

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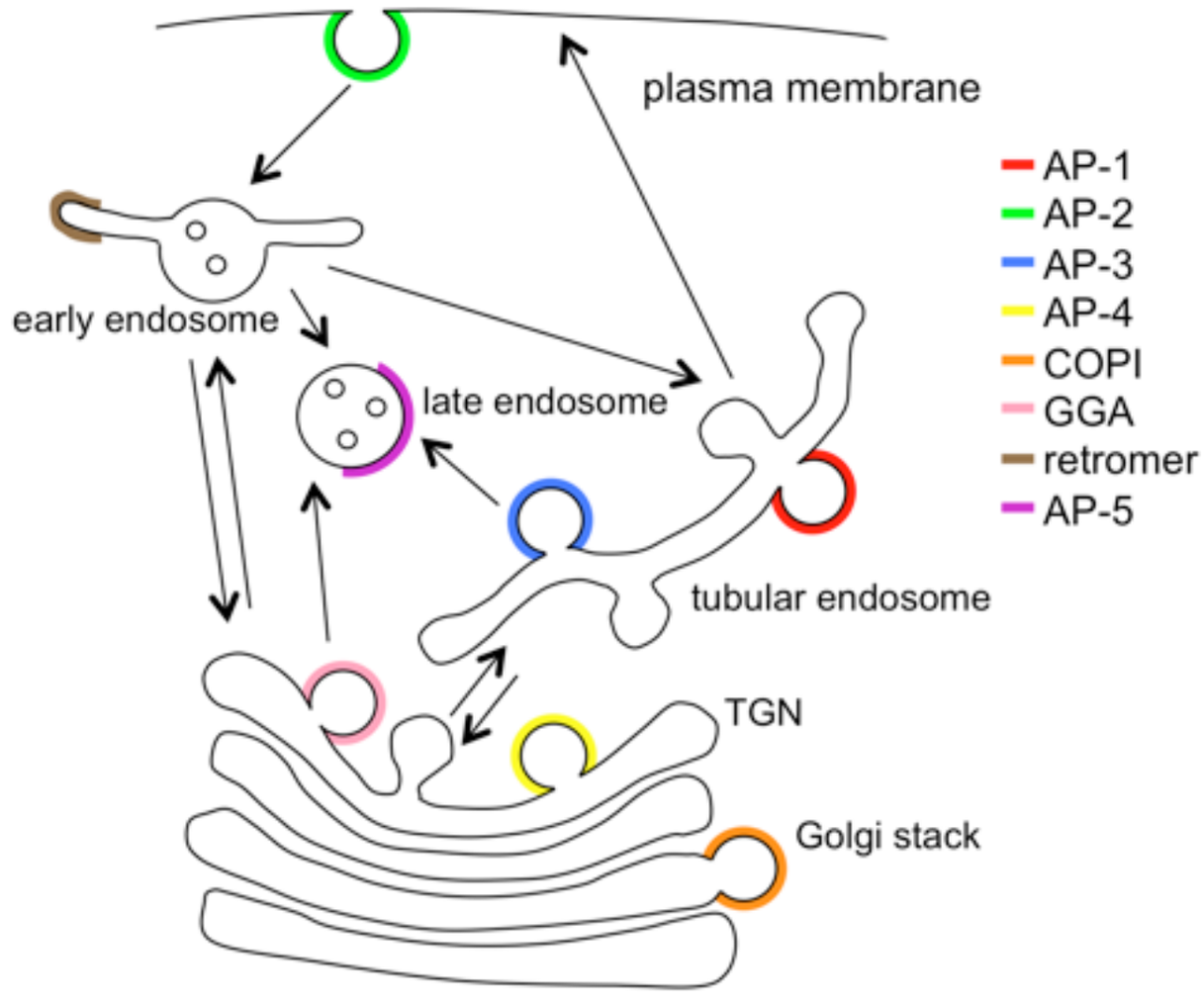

- **Found in high-throughput screen for Hereditary Spastic Paraplegia!**

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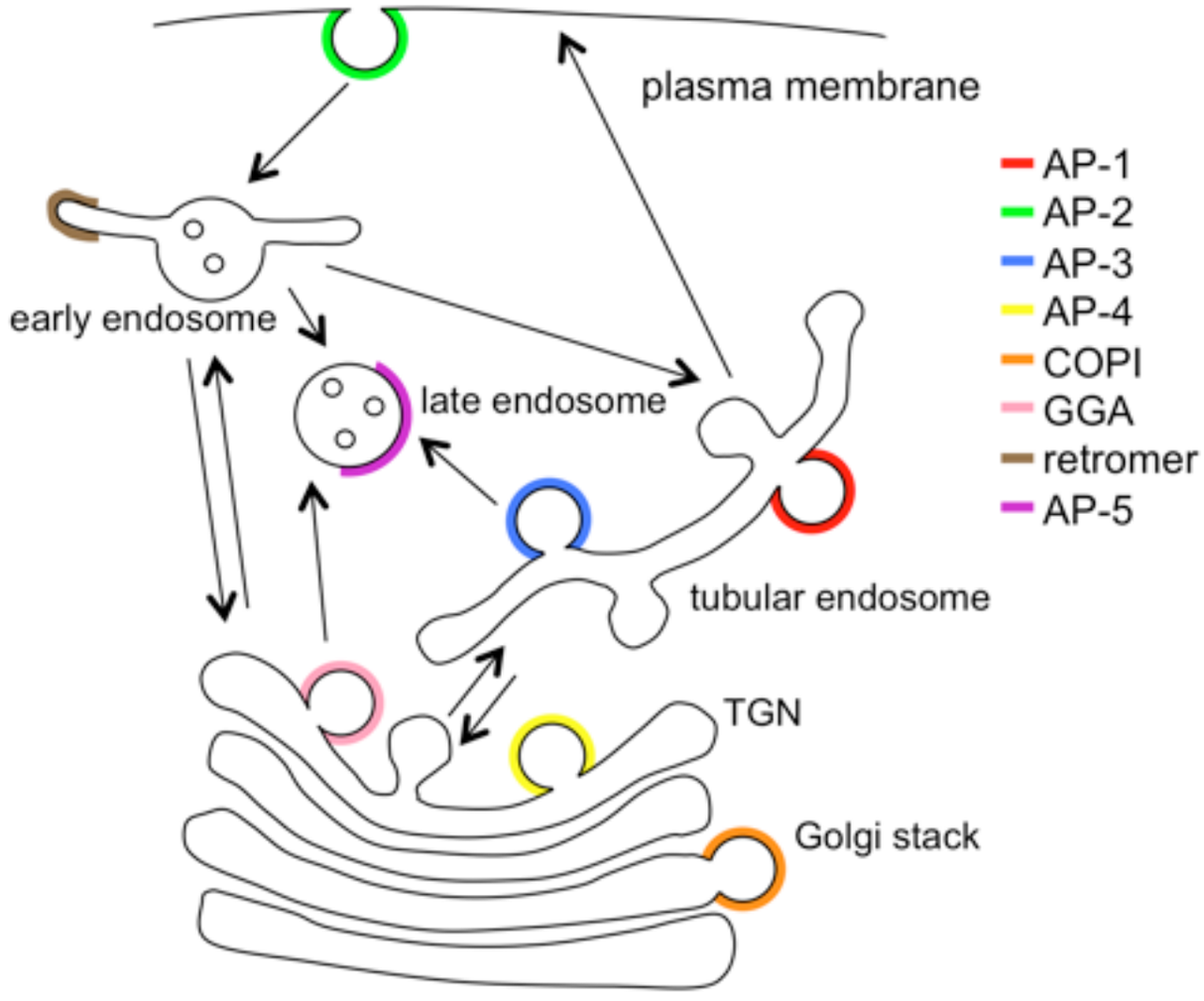

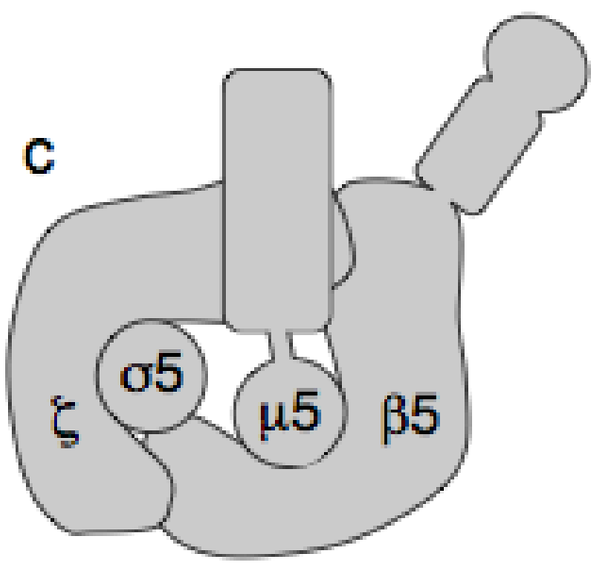

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β5 = DKFZp761E198
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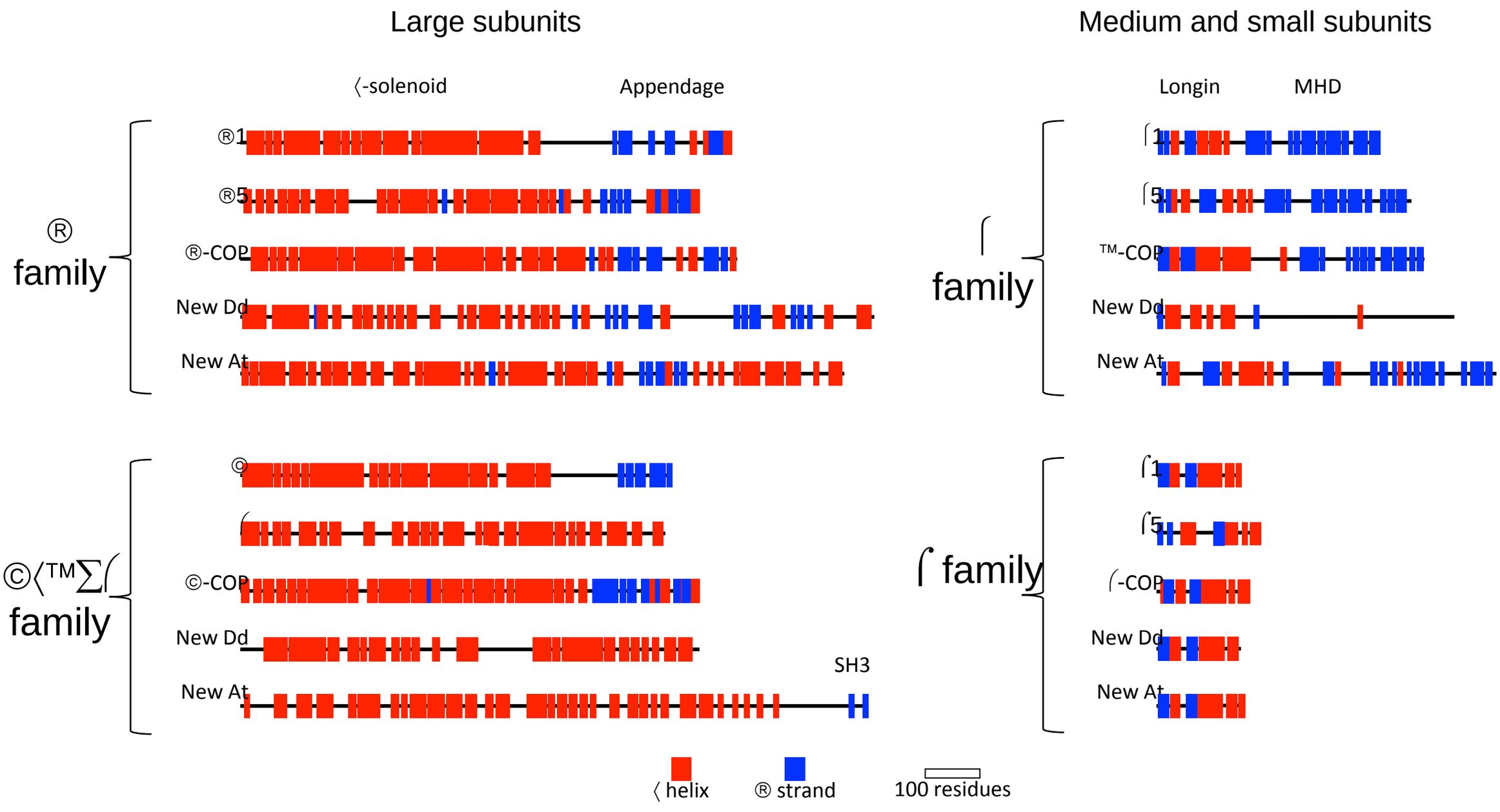
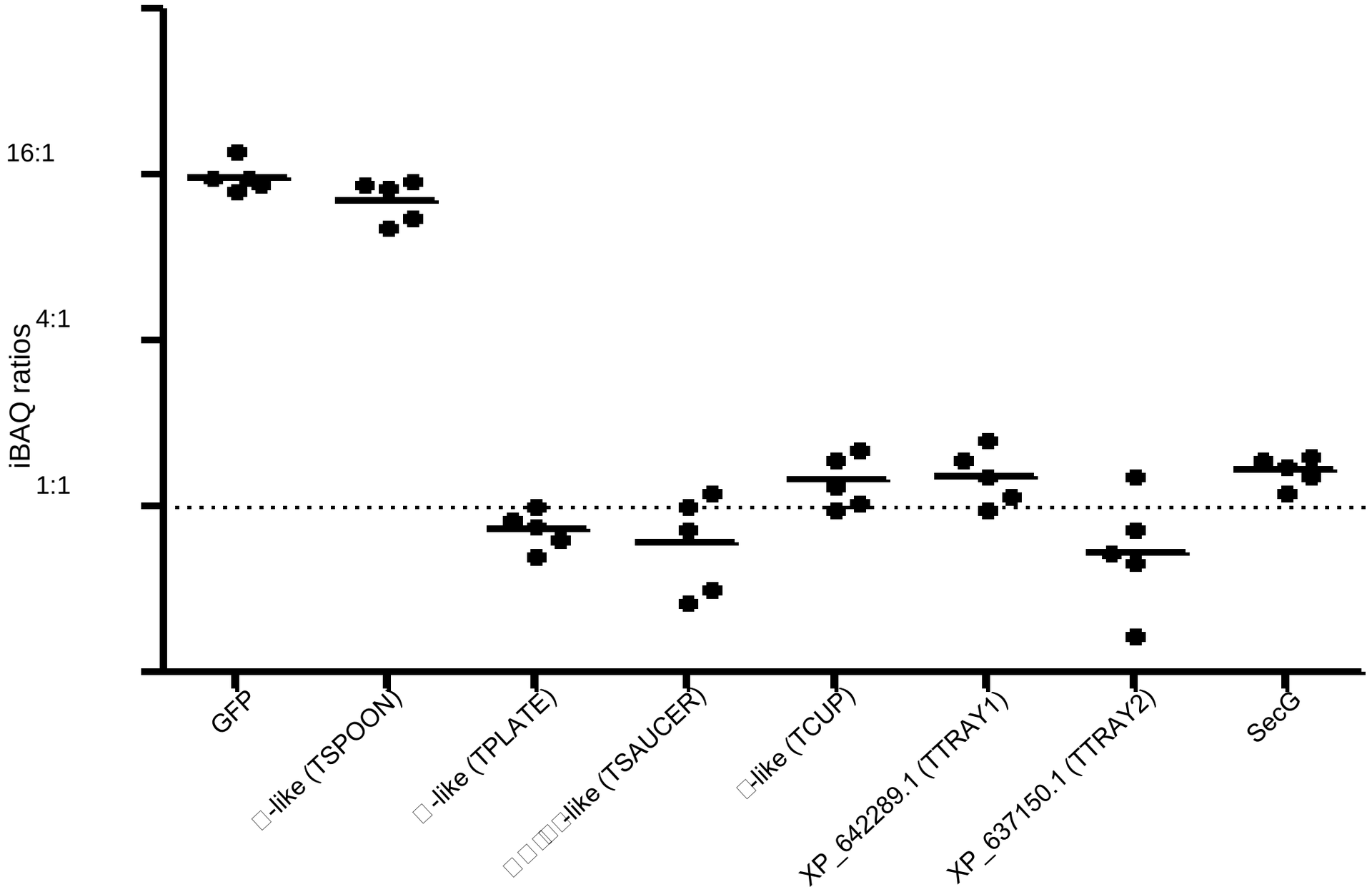
Are there others?

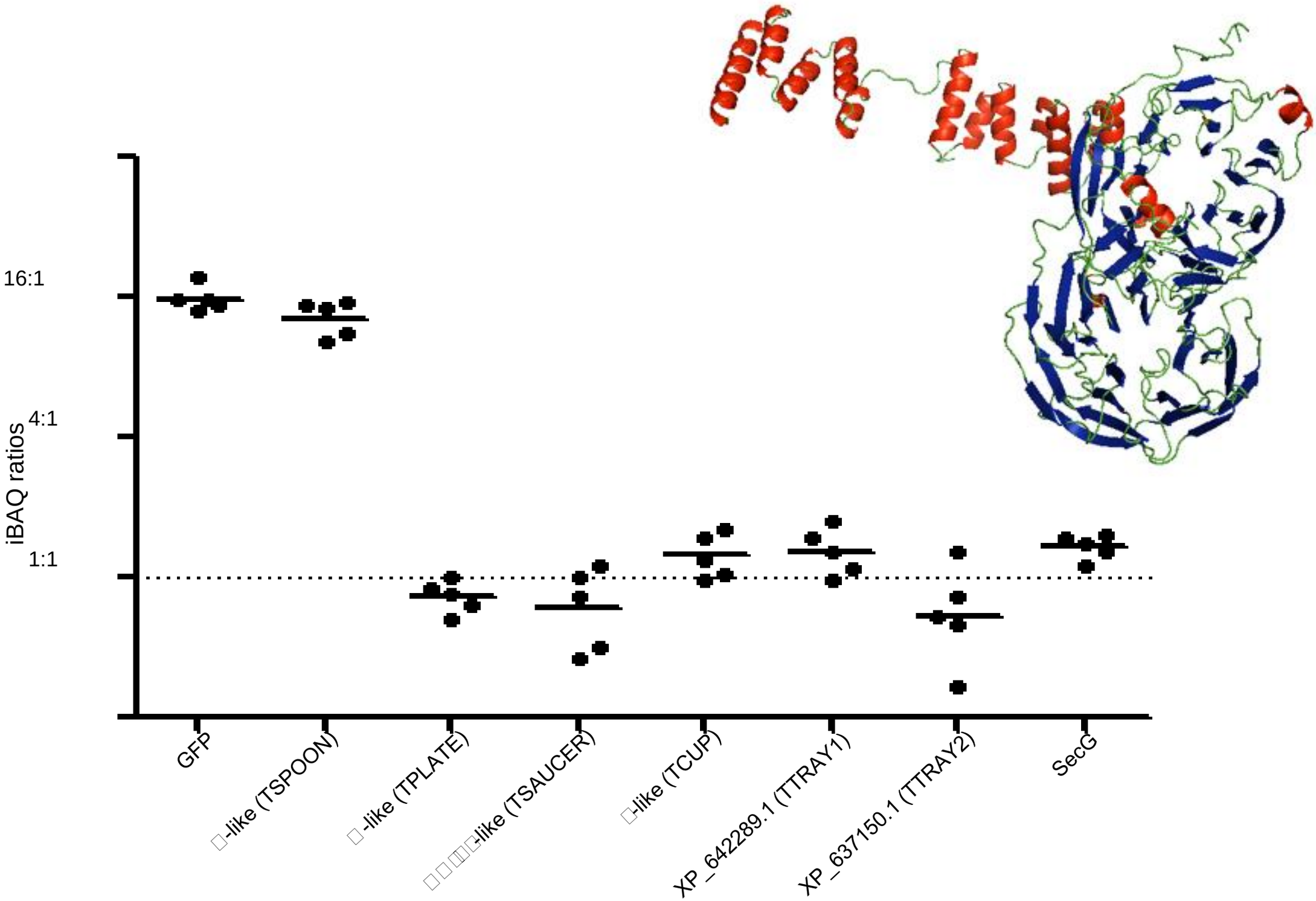
4 proteins resembling APs



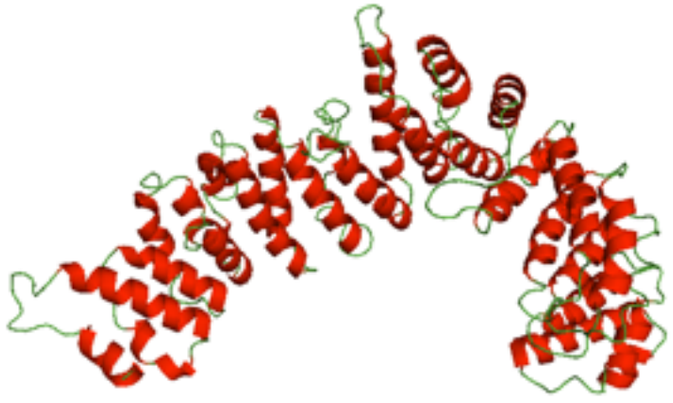
4 proteins forms a complex



Identified “coat” proteins

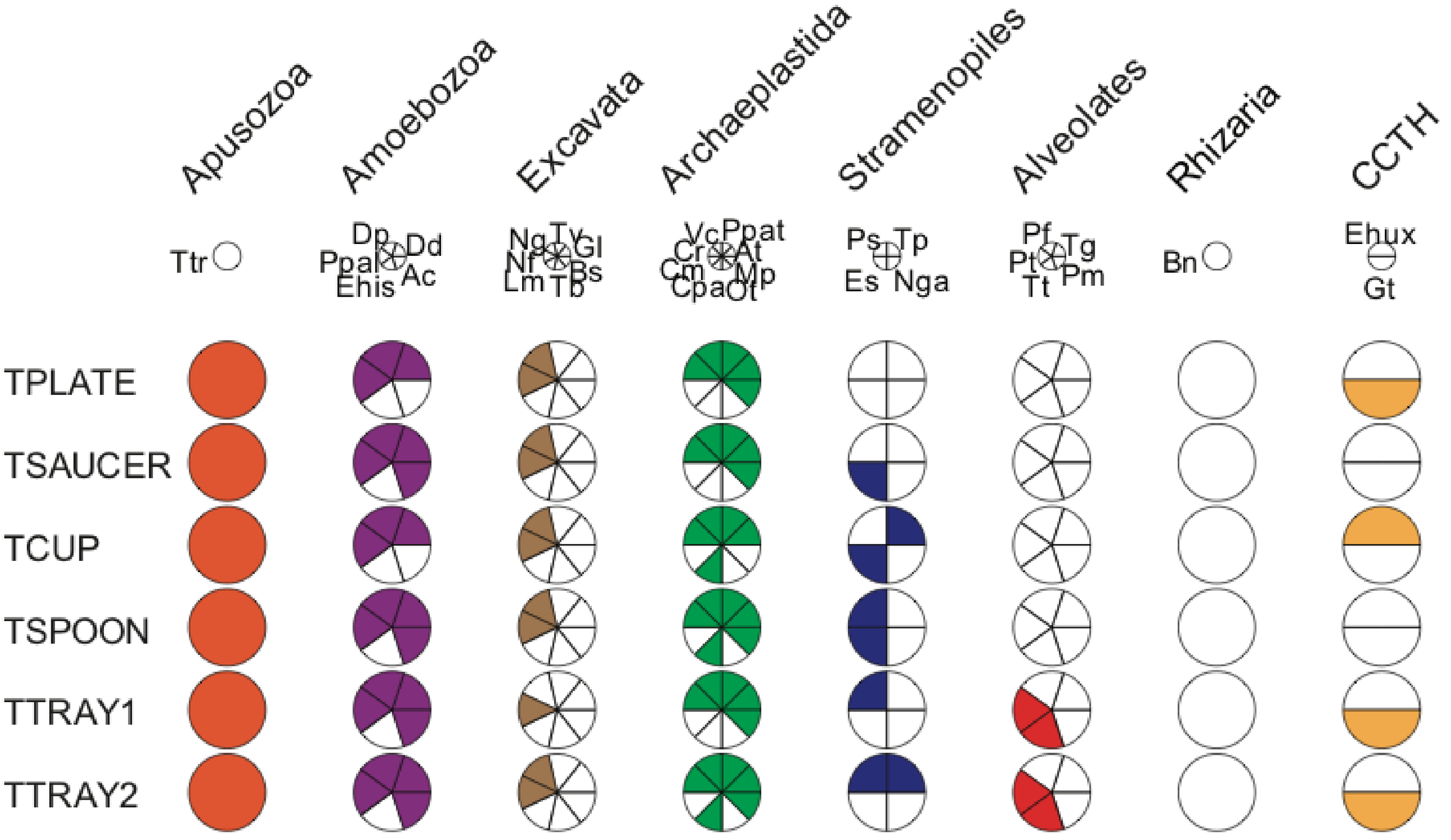


Predicted Secondary Structures of *D. discoideum* proteins

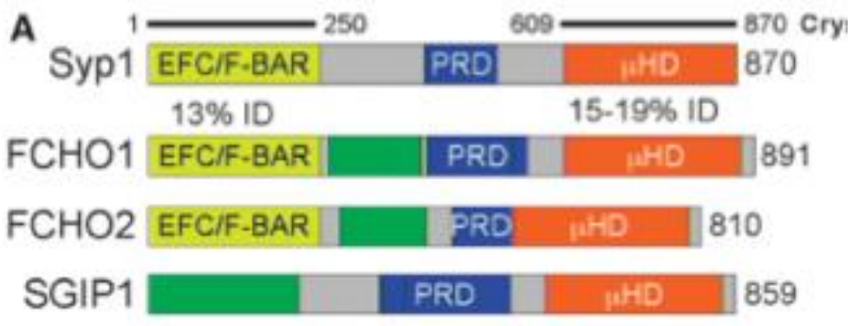


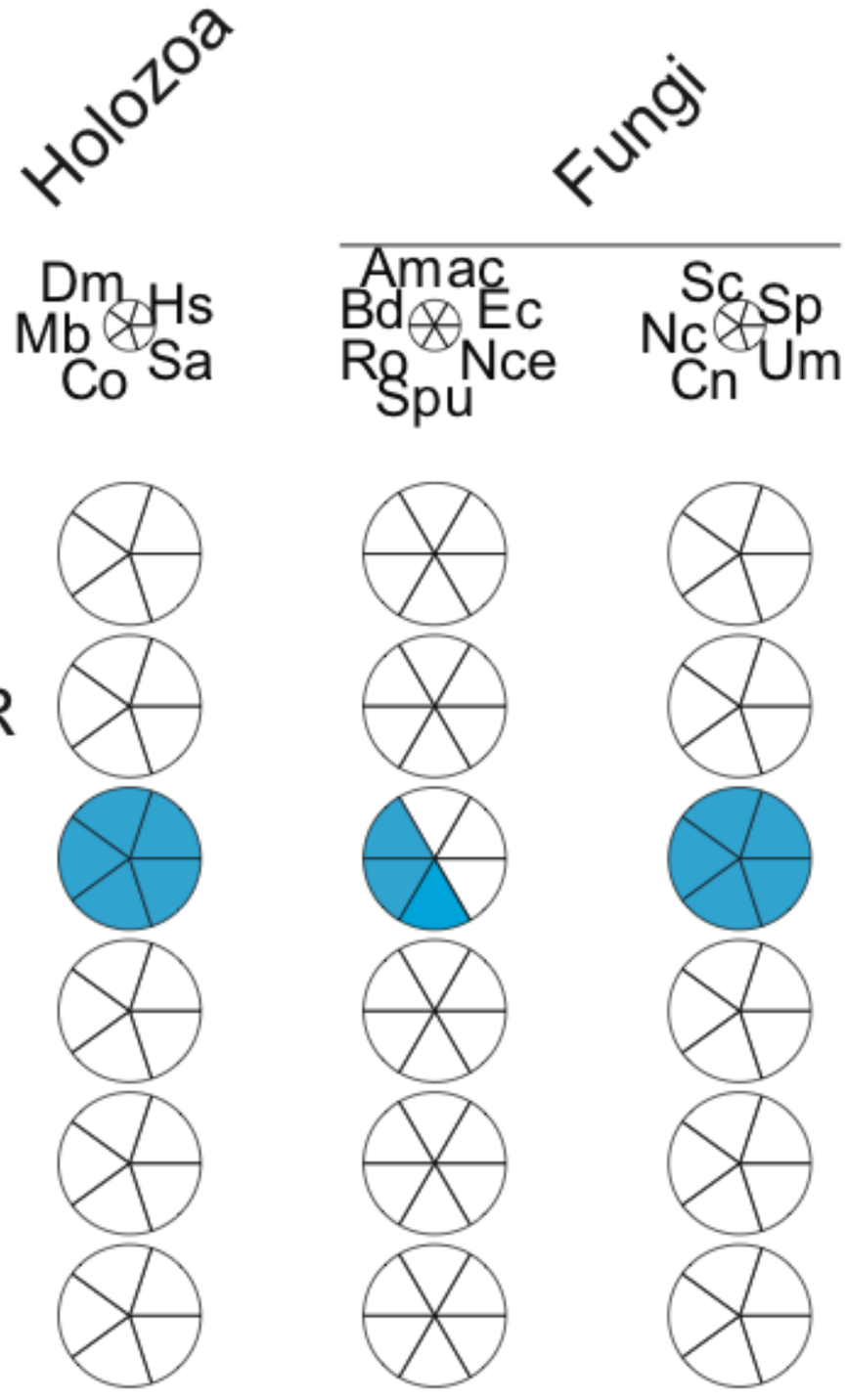
TPLATE

TSET is Widely Distributed

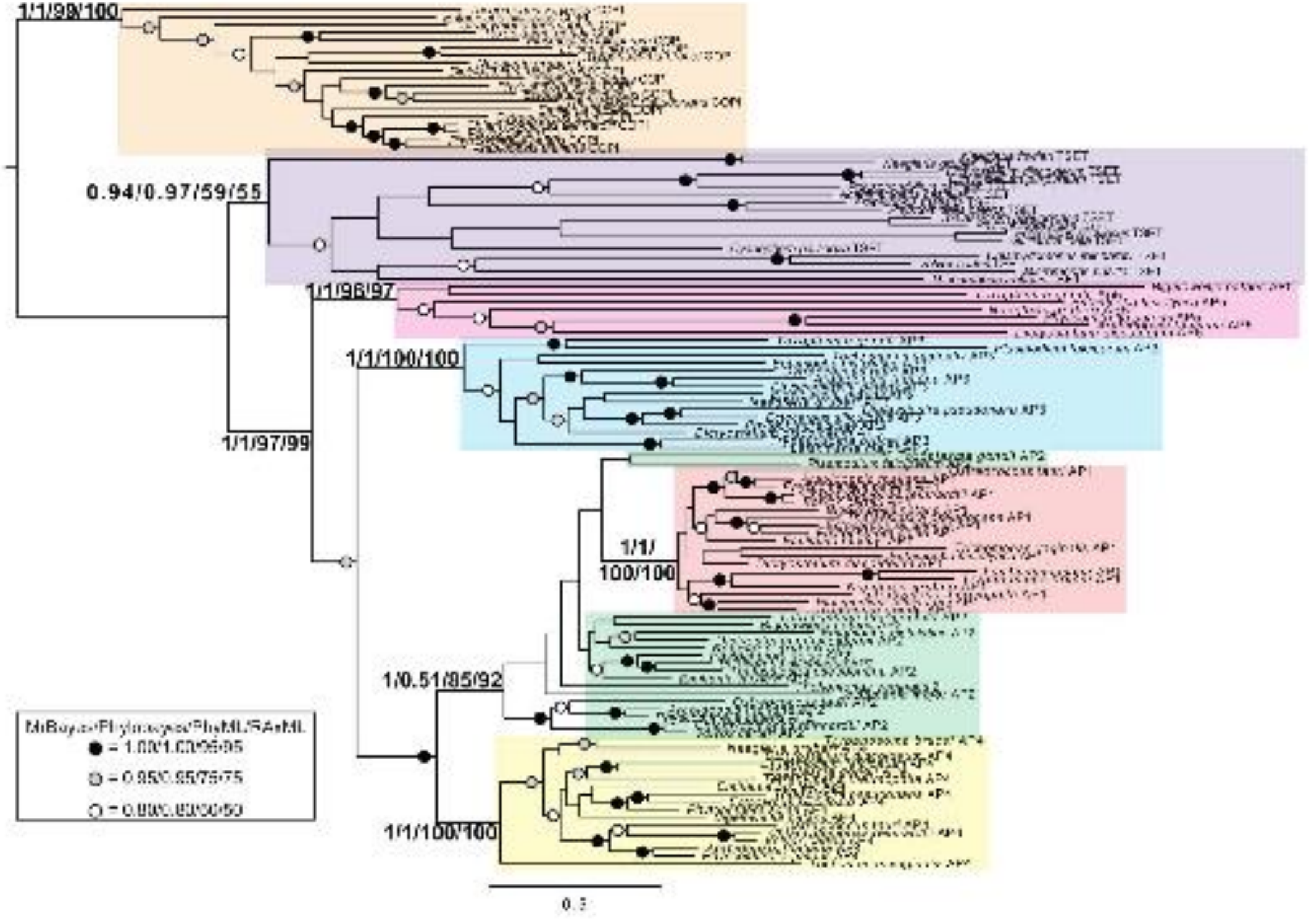


FCHo/Syp1 proteins regulate clathrin
Remnants of TSET in Opisthokonts





Phylogeny of organelle-paralogues-HTACs

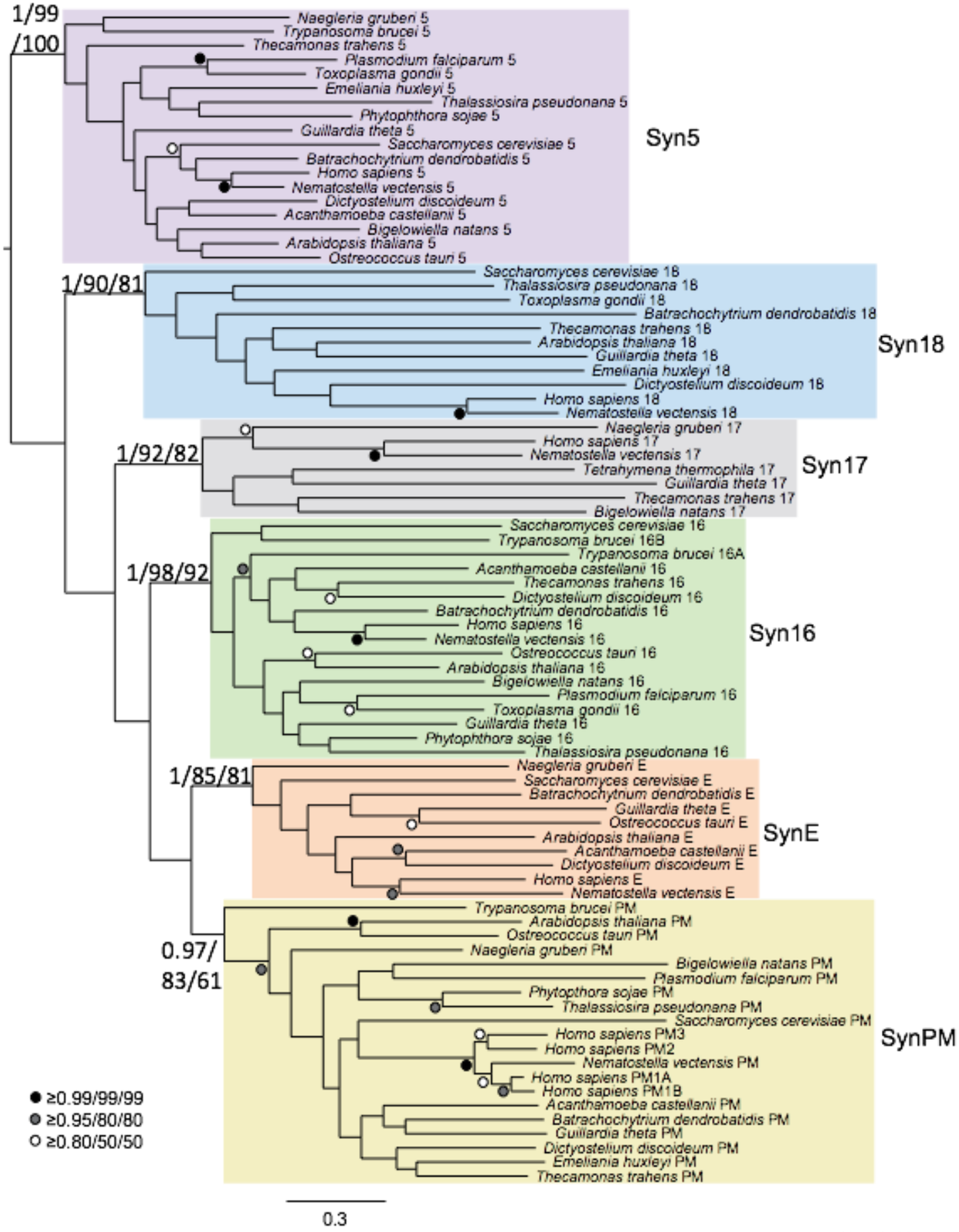


TSET, AP1-5, CopI: all pre-LECA

Hirst, Schlacht et al. 2014

Phylogeny of organelle-paralogues: Qa-SNAREs

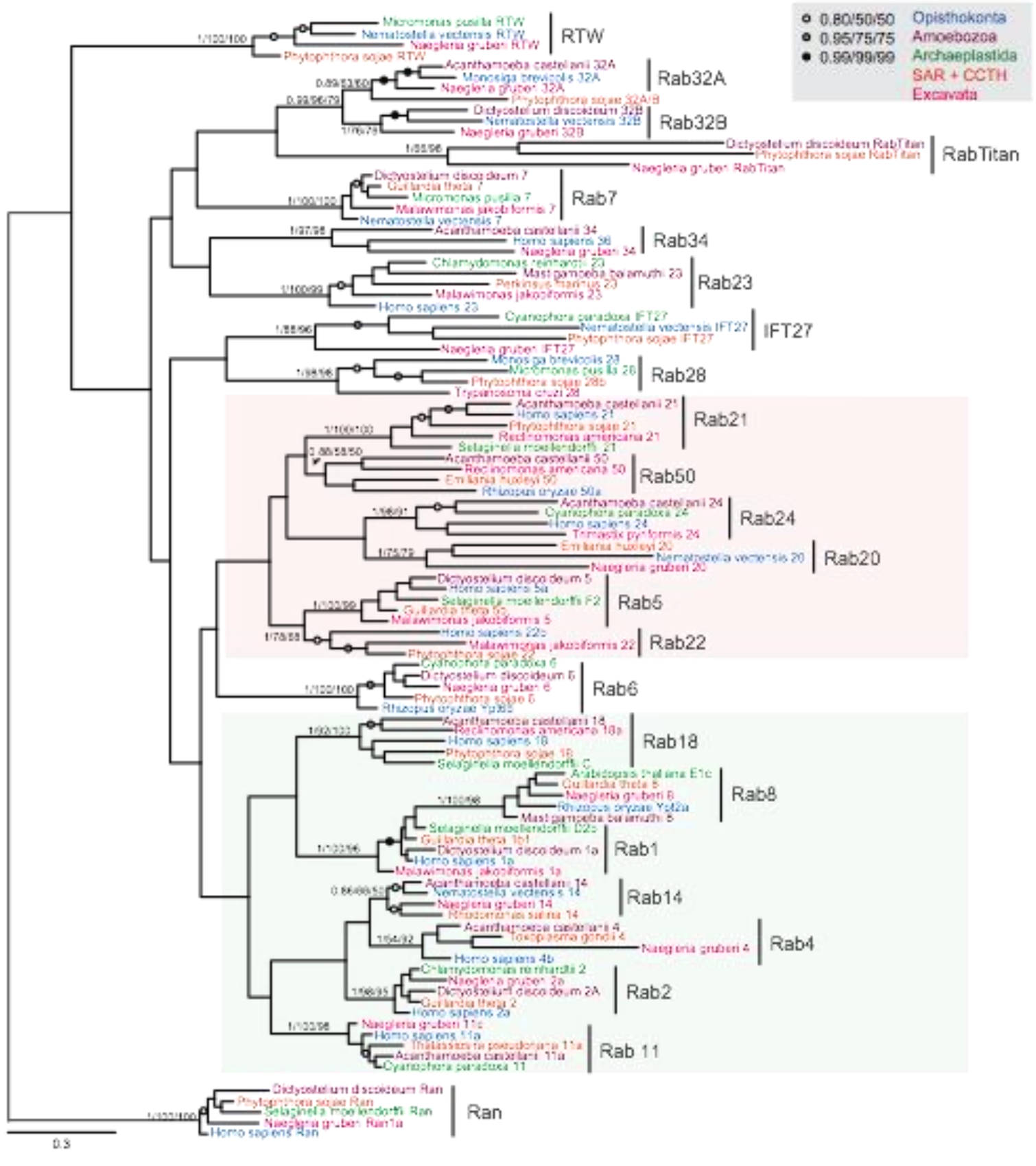
Syn5(Golgi), Syn18 (ER), SynPM, SynE, Syn16 (TGN-Endosomes), and Syn 17(MAM/ER/autophagosome)



Arasaki et al. 2015

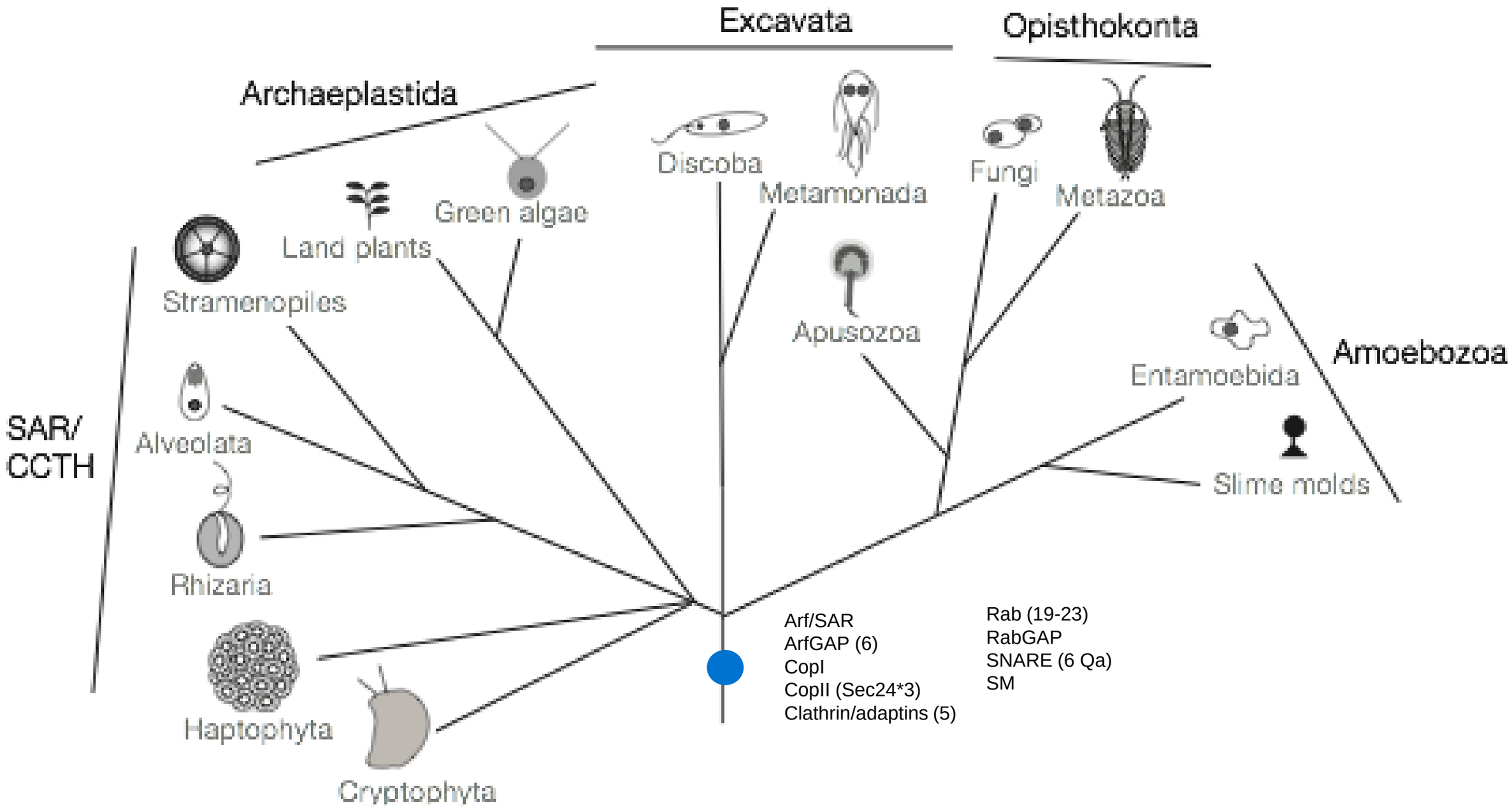
Phylogeny of organelle-paralogues: Rabs

19-23 LECA Rab clades, covering all MTS organelles, including Ran (NPC), IFT27 (Flagella) and RabTitan



Elias et al. 2012

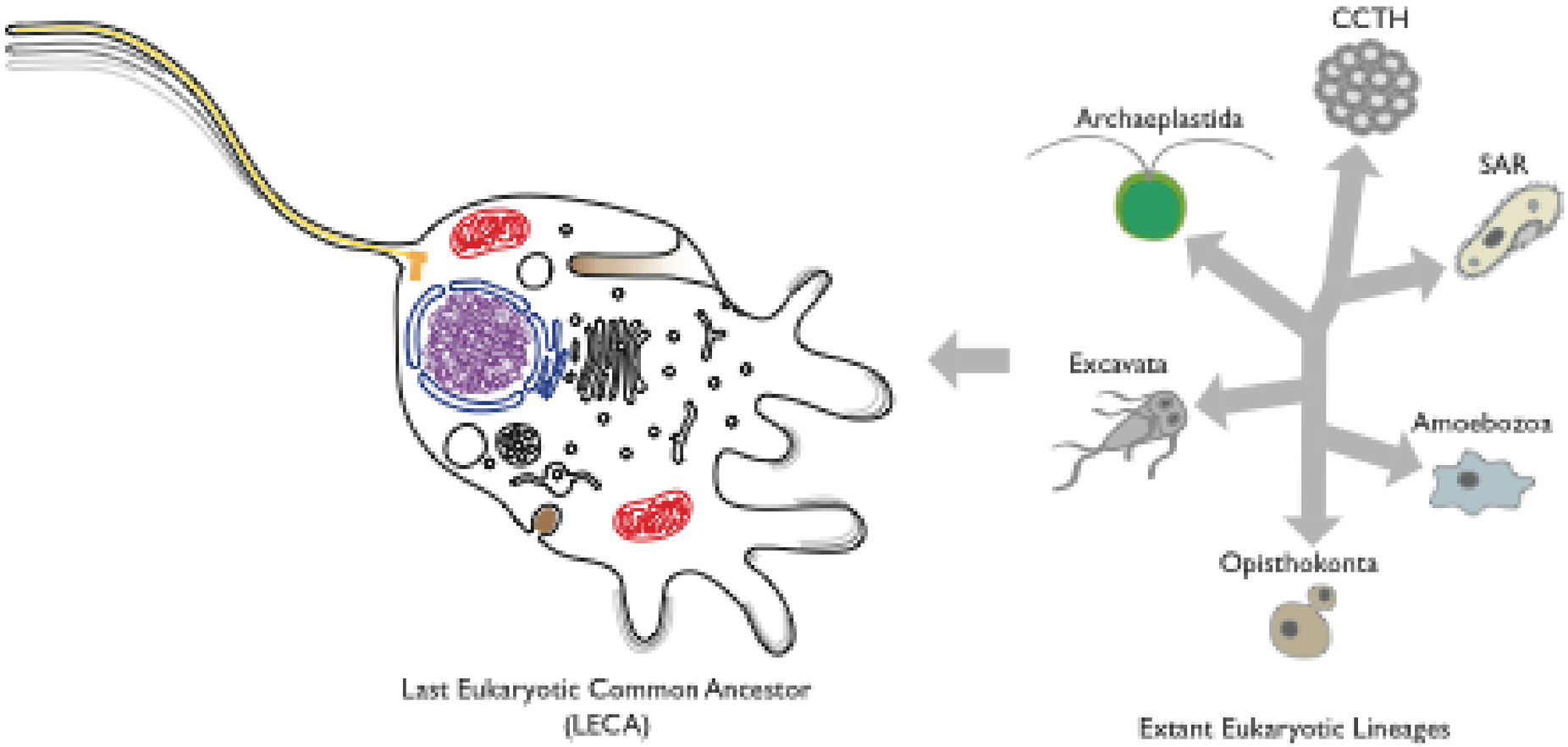
Organelle-specific paralogues present in the LECA



Reconstruction of sophisticated trafficking machinery in the LECA

Also instances of unheralded trafficking machinery (TSET, AP5, ArfGAP_C2...)

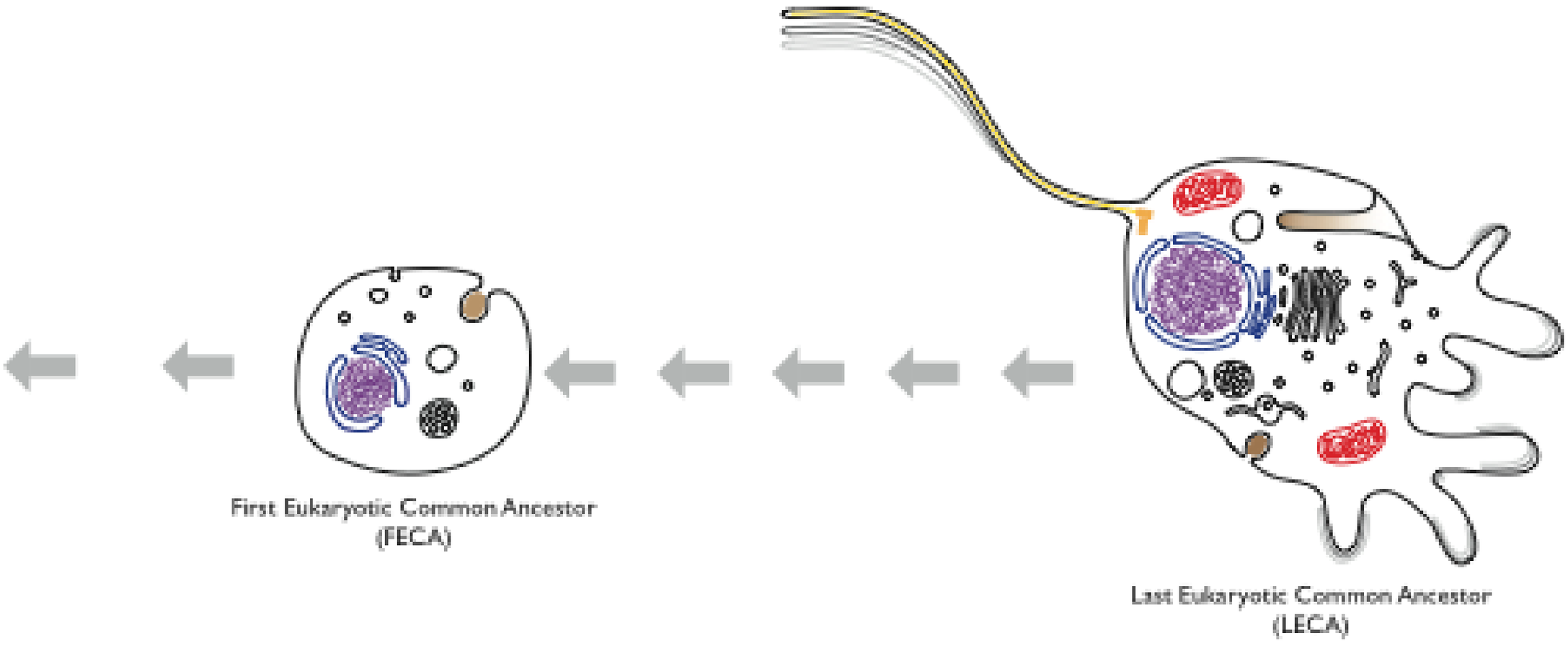
LECA and complexity



Last Eukaryotic Common Ancestor
(LECA)

Extant Eukaryotic Lineages

Back beyond the LECA to the step from the FECA



First Eukaryotic Common Ancestor
(FECA)

Last Eukaryotic Common Ancestor
(LECA)

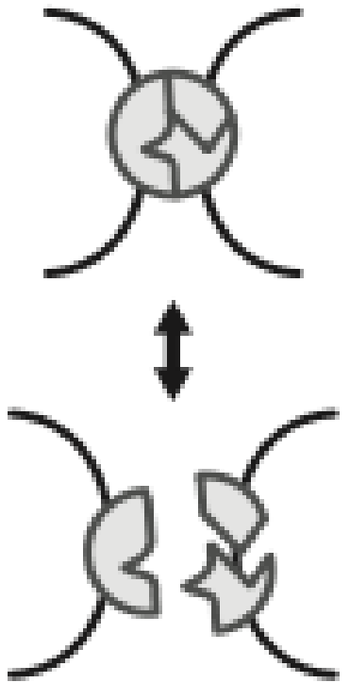
Many phylogenies show similar patterns

- SM proteins- Koumandou, Dacks, Coulson and Field, 2007
- Syntaxins- Dacks and Doolittle, 2002, 2004
- Coats (Clathrin, COPI, COPII…NPC) - Schledzewski et al. 1999, Singh and Gupta, 2004, …Devos et al. 2004
- R-SNAREs- Yoshizawa et al. 2006, Kloepper et al, 2007,Vedovato 2009
- Rabs- Pereira-Leal and Seabra, 2001, Pereira-Leal 2007, Diekmann 2011

- **Elaborate machinery early on…**

Model of autogenous organelle evolution

Organelle Paralogy Hypothesis: A mechanism for non-endosymbiotic organelle evolution



Specificity is encoded in the combinatorial interactions

Gene duplication and co-evolution specificity machinery

Schlacht et al. 2014

Conclusions-I

Evolutionary cell biological studies of membrane trafficking machinery shows a sophisticated complement early in eukaryotic evolution

Not only protein families but also organelle-specific paralogues- Most recently Syntaxin 17

These have lead to discoveries of novel proteins (Rabtitan, ArfGAP_C2), complexes (TSET) and trafficking pathways (AP5) or have shed light on the origins of ‘orphan’ proteins in model cell biological systems

Neither could have been anticipated in an application targeted for commercialization=BASIC RESEARCH

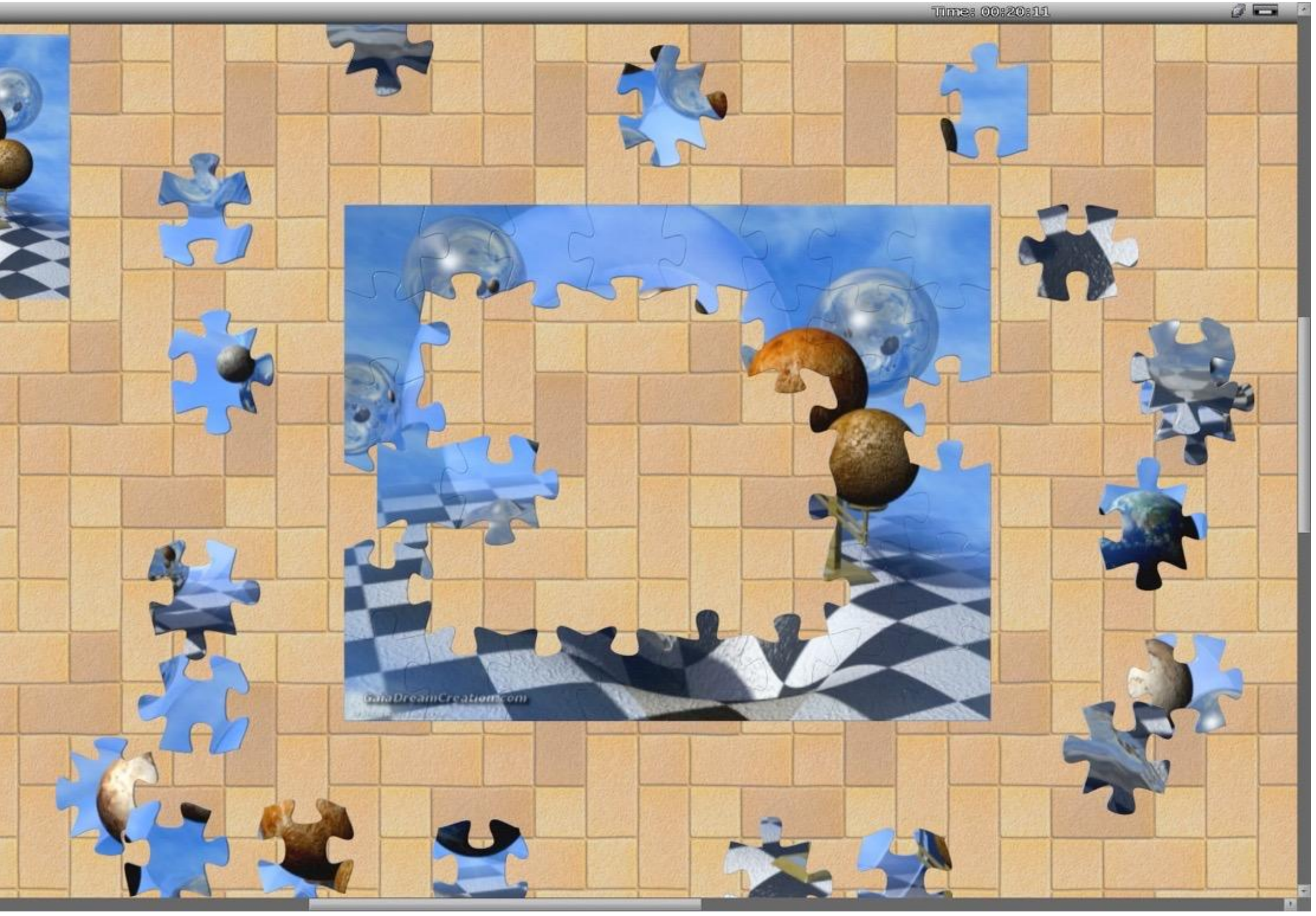
Conclusions-II

Larger patterns of protein conservation show the mechanisms driving complexity in the LECA-OPH, PC, Neutral

Mechanisms of non-endosymbiotic organelle evolution combined with improved phylogenetic resolution are allowing for speculative, but hopefully testable models of how the membrane trafficking system arose.

New microbial diversity is allowing for new insights into the constituent contributions of cellular systems

Evolutionary cell biology is a fruitful way of discovering aspects of how cells work today, in a complementary way to focused work in model systems, and yields information about our cellular past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