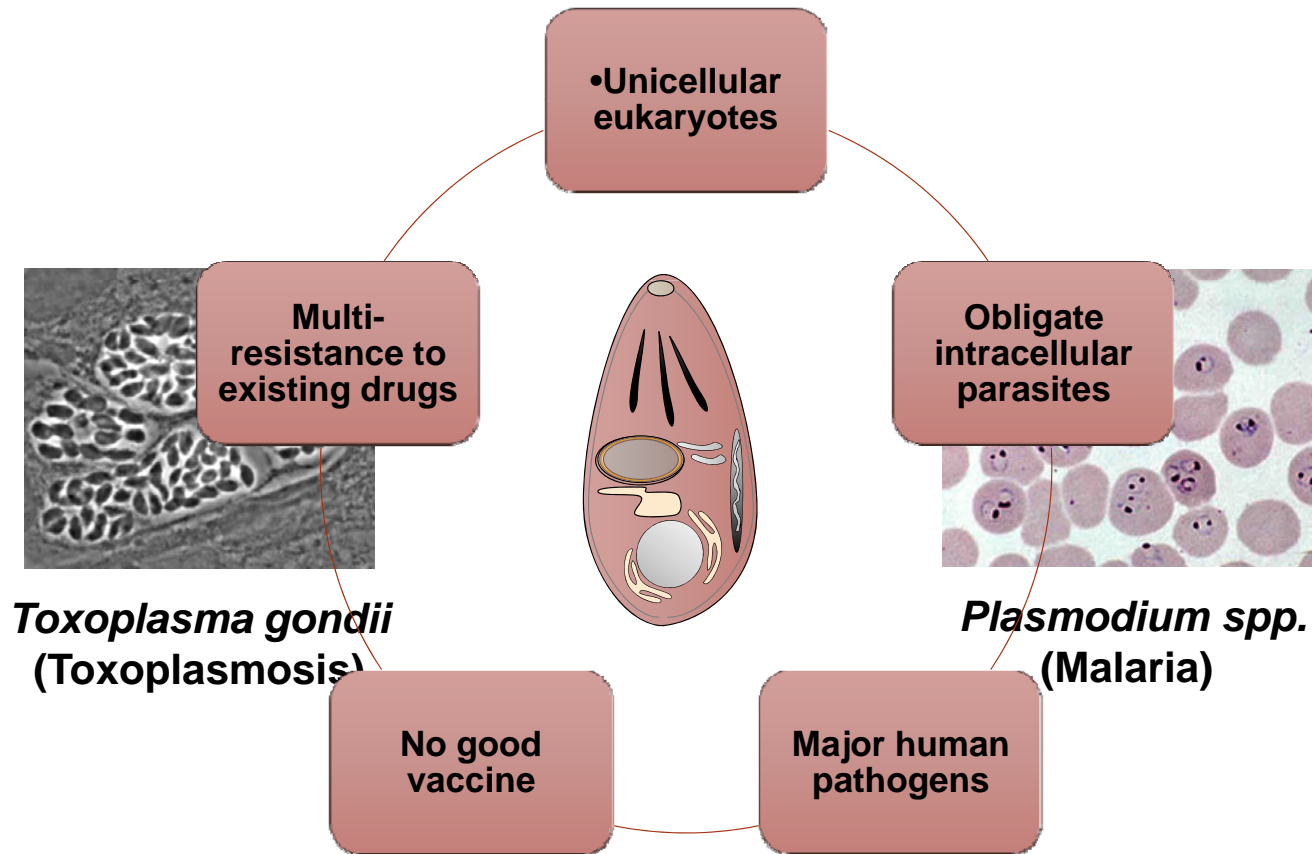


The role of AcylCoA binding proteins (ACBPs) and lysophospholipases (LPLs) in lipid recycling and trafficking for membrane biogenesis, and remodelling in Apicomplexa parasites and their host cell

Serena Shunmugam, Yoshiki Yamaro-Botté and Cyrille Botté
ApicoLipid Group

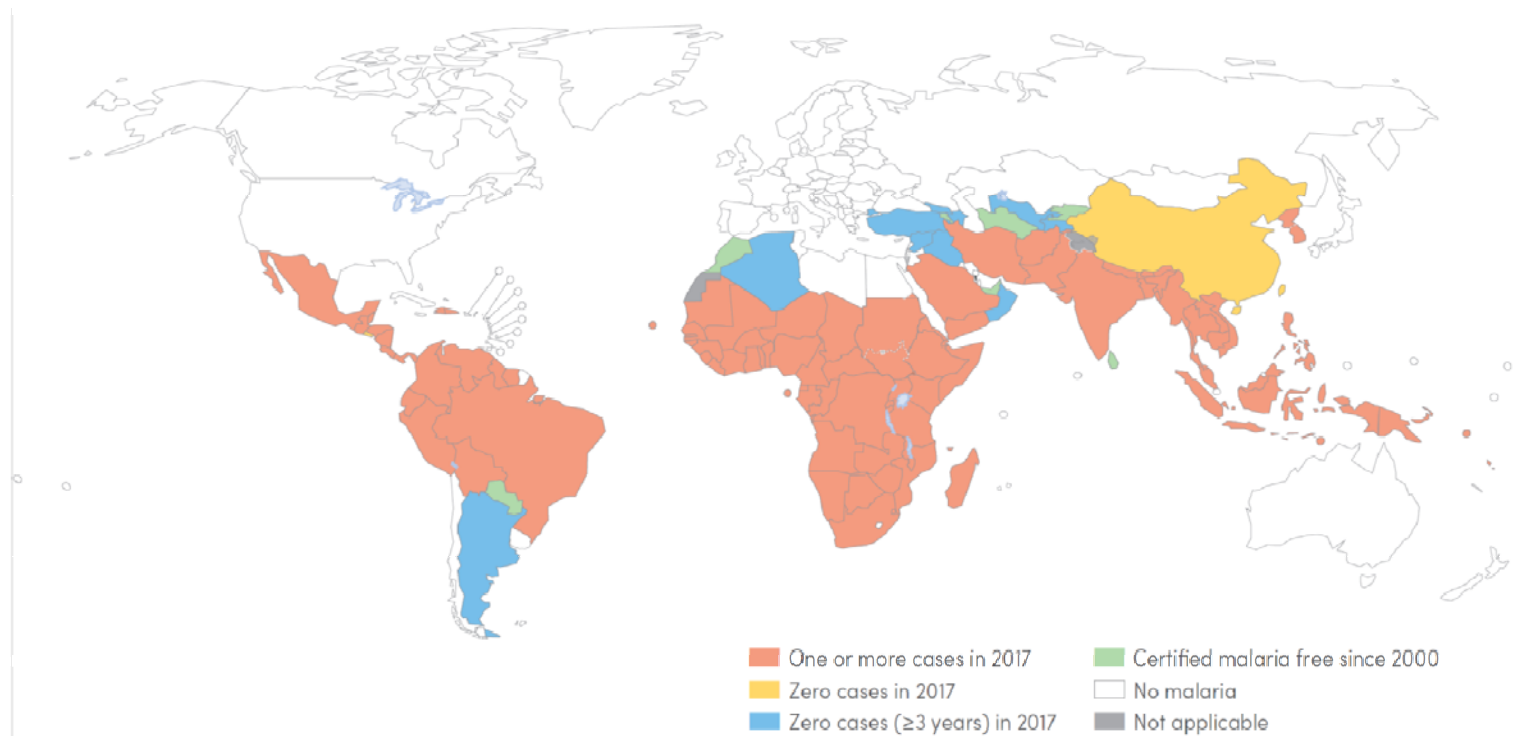
Institute for Advanced Bioscience, Université Grenoble Alpes
Indo-French Centre for the Promotion of Advanced Research

The apicomplexan model



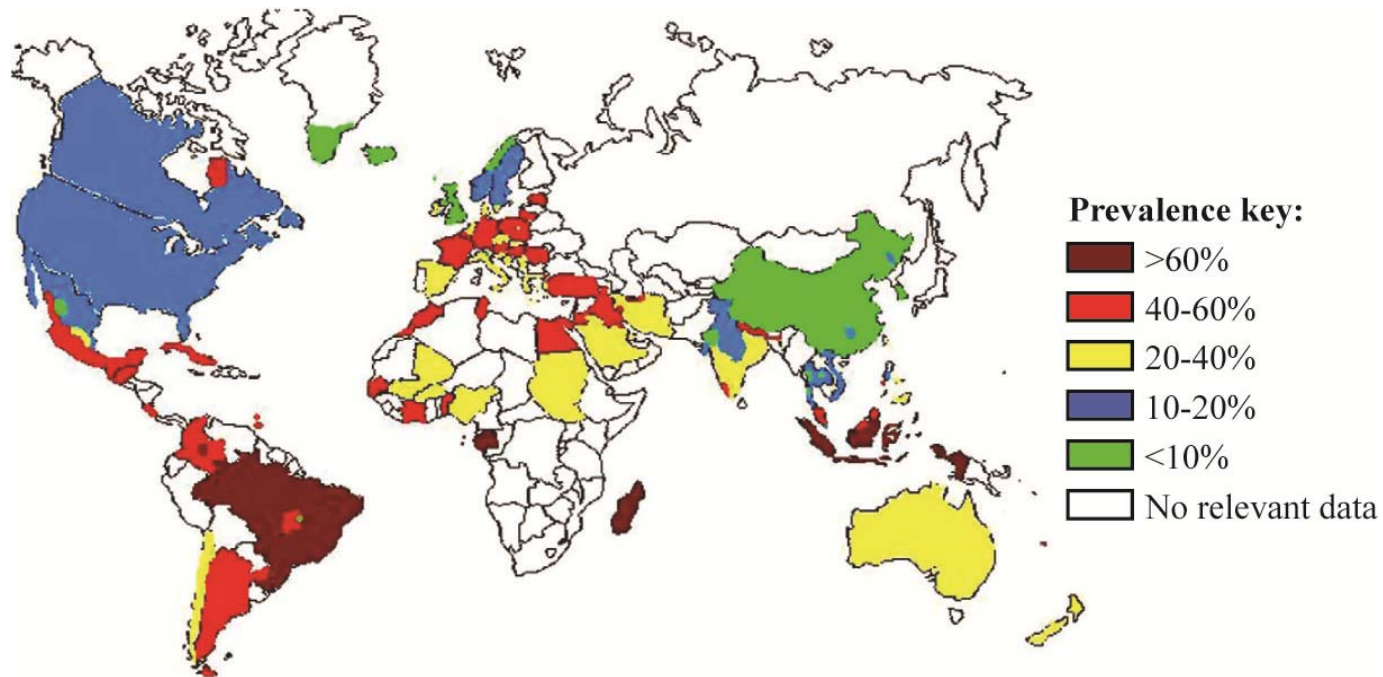
The Malaria endemic

Countries endemic for malaria:

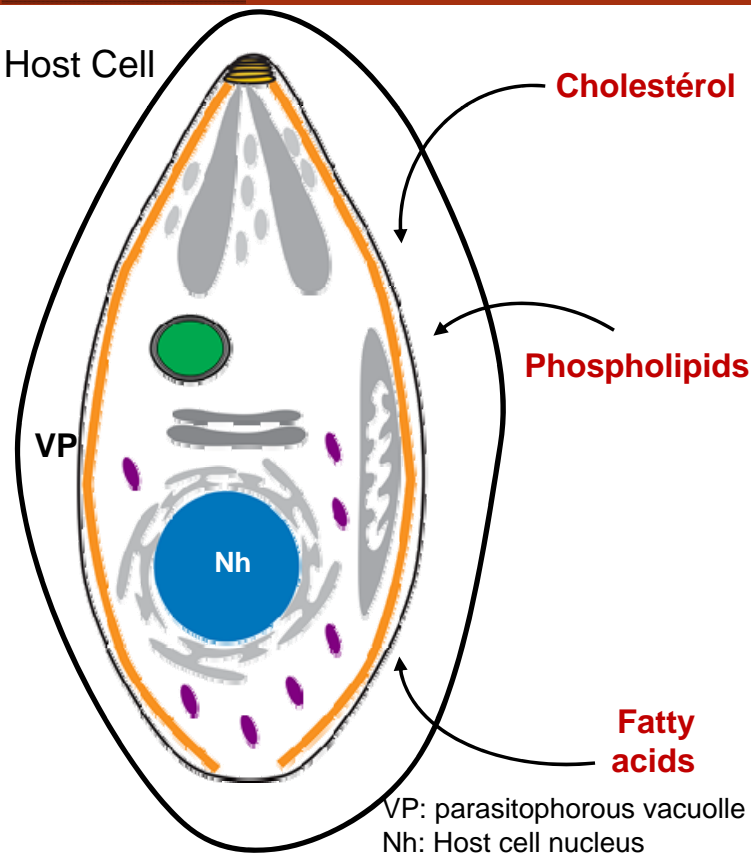


Toxoplasmosis prevalence

Global prevalence of Toxoplasmosis:



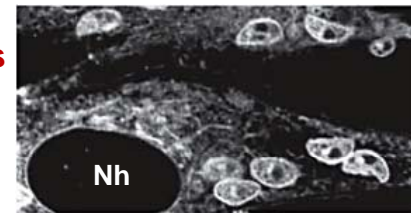
Survival of apicomplexan: Lipids



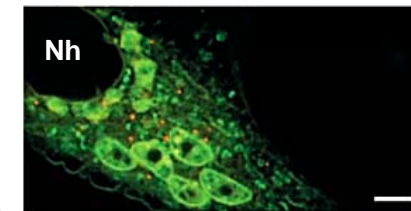
Fluorescent lipids



Charron and Sibley J. Cell Sci. (2002)



Charron and Sibley J. Cell Sci. (2002)
Bisanz *et al.* Biochem. J (2006)



Quittnat *et al.* Mol. Biochem. Parasito. (2004)
Ramakrishnan *et al.* JBC (2012)

Lipid acquisition:

- Scavenging from host cell
- Intense flux recycling-reshuffling
- Assembly in parasitic compartments
- *De novo* synthesis in the APICOPLAST

The Apicoplast: an essential 'algae inside' the parasites

the apicoplast is **vital**
FA synthesis

(McFadden et al. 1996, He et al. 2001)

Secondary endosymbiosis

plant-like drug target

Green lineage

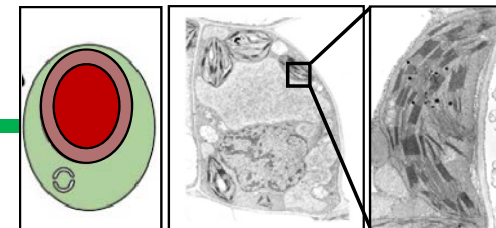
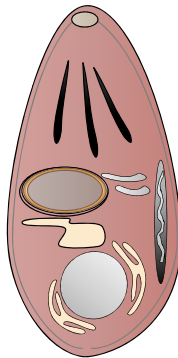
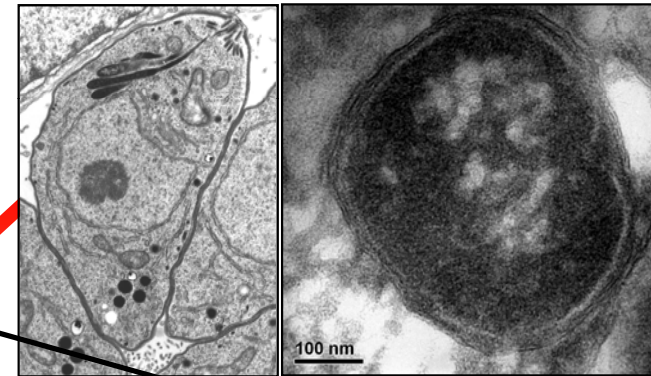
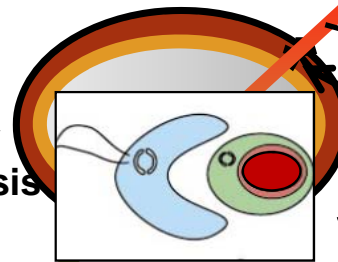
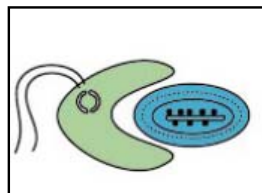
Red lineage

Apicomplexa
(*Plasmodium*,
Toxoplasma)

Loss of photosynthesis



Cyanobacteria

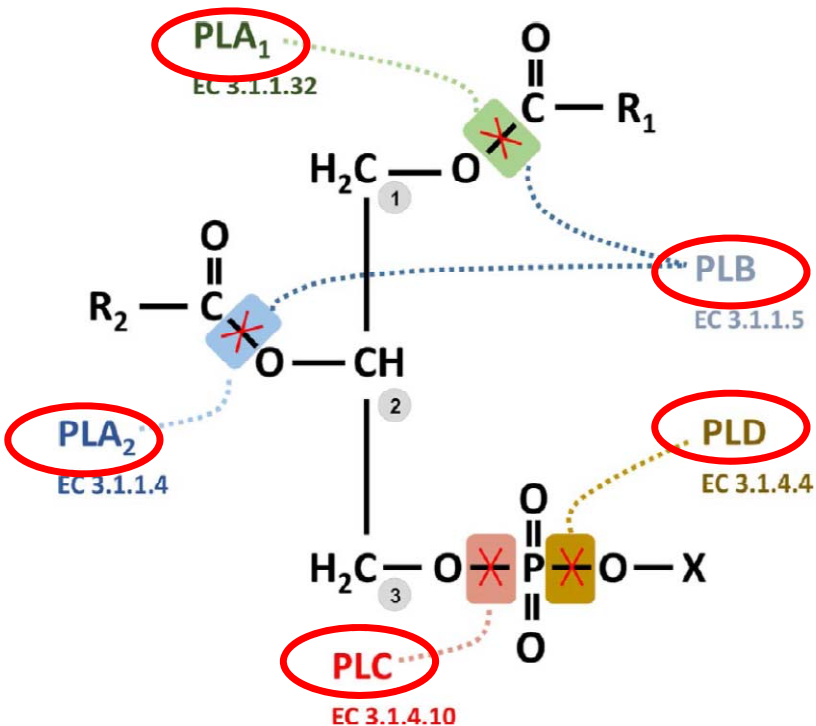


Lipid processing pathway for membrane lipid biogenesis in parasites

- Multiple processes for parasite membrane biogenesis

Molecular Microbiology (2017) 105(1), 158–174 ■

doi:10.1111/mmi.13694
First published online 3 May 2017



TgPL2, a patatin-like phospholipase domain-containing protein, is involved in the maintenance of apicoplast lipids homeostasis in *Toxoplasma*

Maude F. Lévêque,^{1†} Laurence Berry,¹
Yoshiaki Yamaryo-Botté,² Hoa Mai Nguyen,¹
Marine Galera,² Cyrille Y. Botté² and
Sébastien Besteiro ^{1*}

¹DIMNP – UMR5235, CNRS, Université de Montpellier, Montpellier, France.
²Apicolipid Team, Institute for Advanced Biosciences, UMR5309 CNRS, Inserm U1209, Université Grenoble Alpes, Grenoble, France.

Plasmodial Phospholipases (Flammersfeld et al. 2017)

Lipid processing pathway in this study

- Important in this study:
 - ACBPs: AcylCoA binding proteins
 - Responsible for lipid trafficking to targeted membranes



Comprehensive Characterization of *Toxoplasma* Acyl Coenzyme A-Binding Protein TgACBP2 and Its Critical Role in Parasite Cardiolipin Metabolism

Yong Fu,^{a,b} Xia Cui,^c Sai Fan,^d Jing Liu,^{a,b} Xiao Zhang,^{a,b} Yihan Wu,^{a,b} Qun Liu^{a,b}



cellular
microbiology

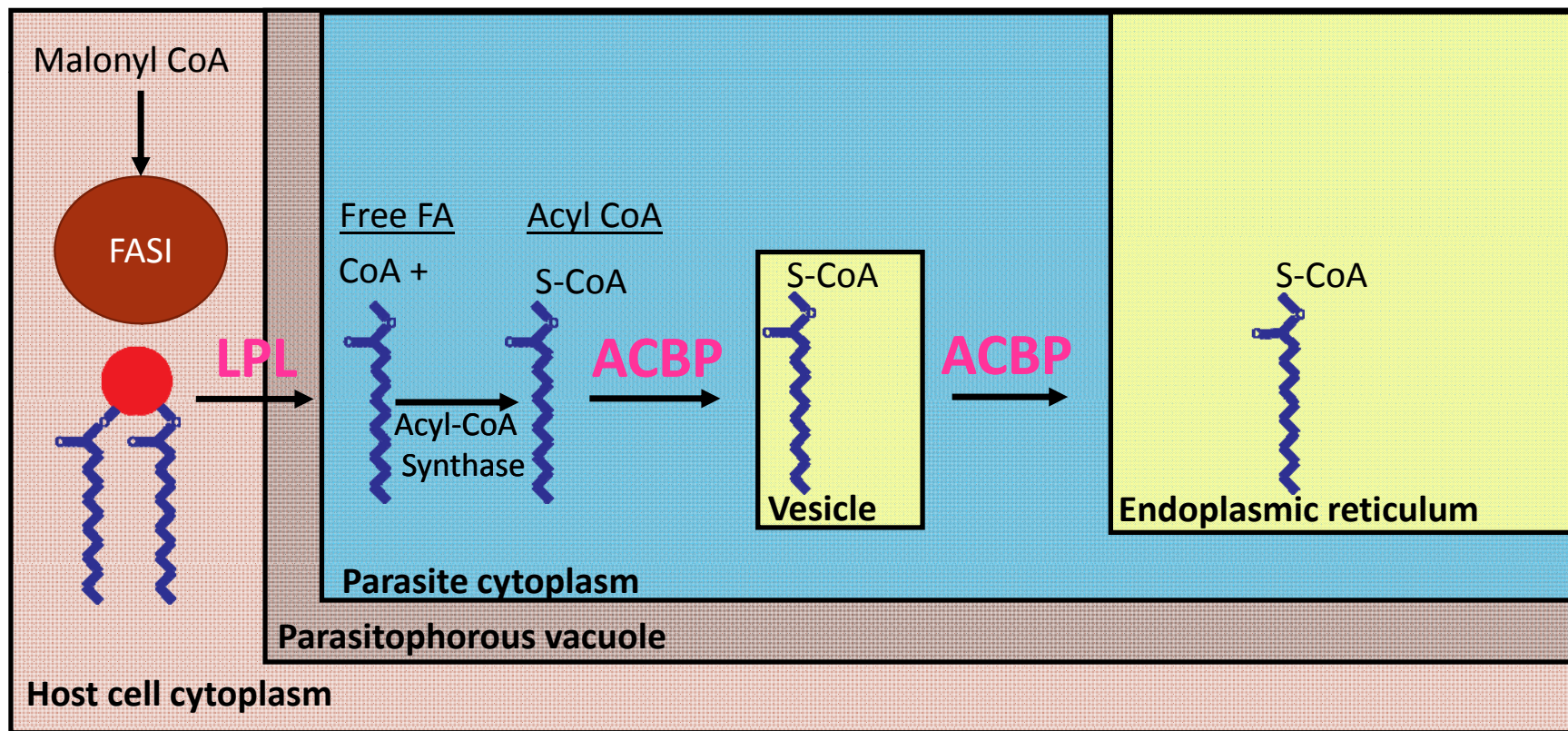
RESEARCH ARTICLE

Synergistic roles of acyl-CoA binding protein (ACBP1) and sterol carrier protein 2 (SCP2) in *Toxoplasma* lipid metabolism

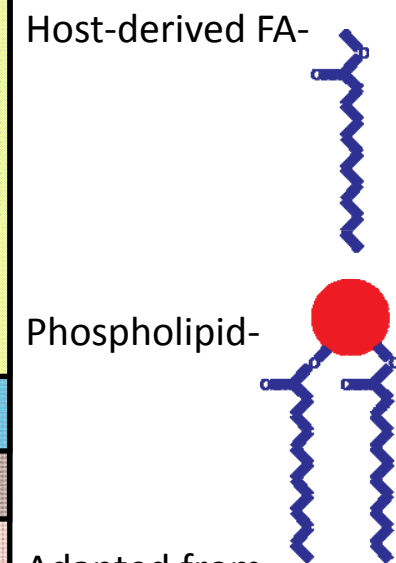
Yong Fu, Xia Cui, Jing Liu, Xiao Zhang, Heng Zhang, Congshan Yang, Qun Liu ✉

First published: 26 October 2018 | <https://doi.org/10.1111/cmi.12970>

Host lipid processing

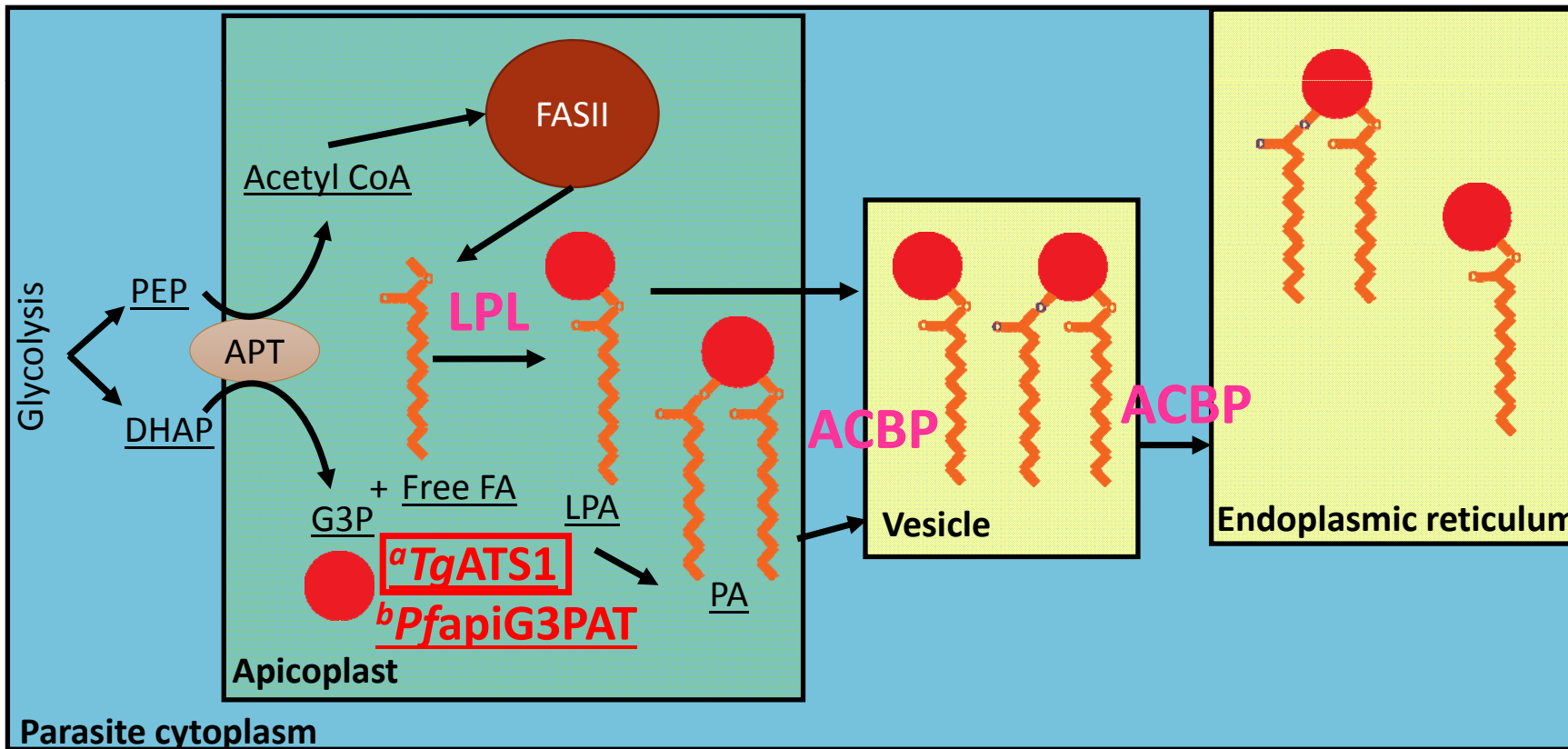


Key:
LPL-lysophospholipases
ACBP- AcylCoA binding protein



Adapted from
Amiar et al. (2016)

Parasite lipid processing

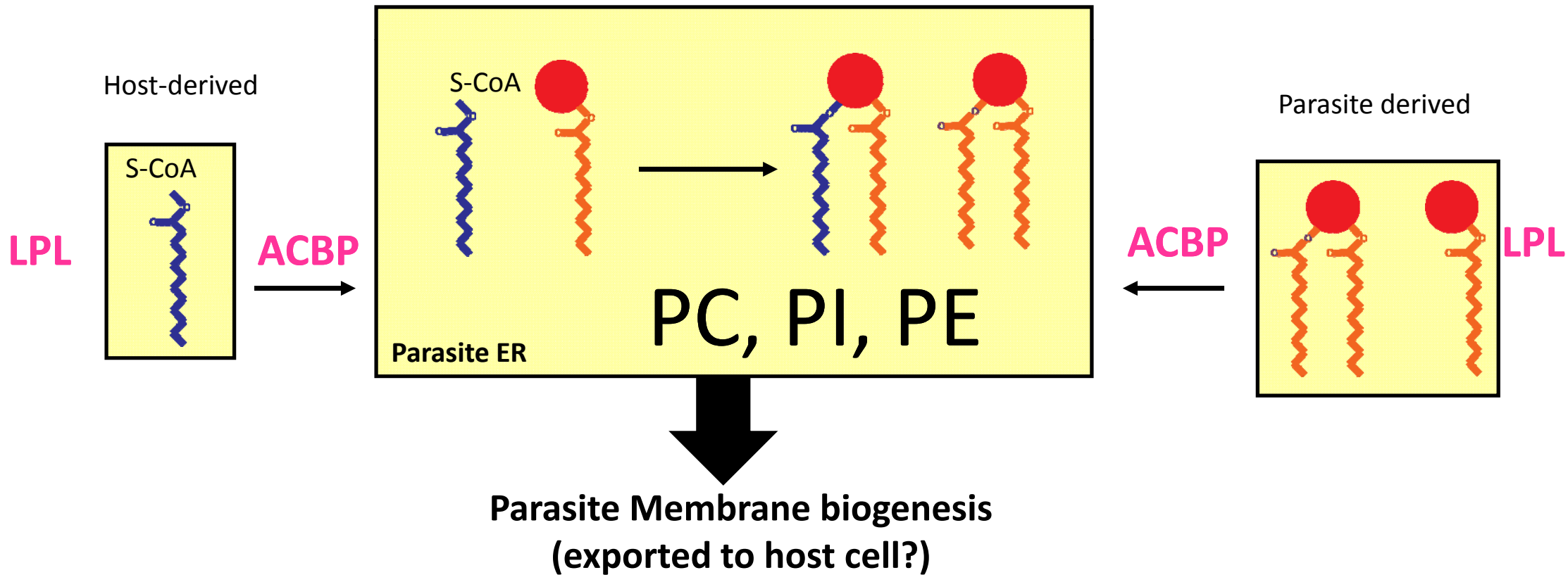


Key:

- PEP- phosphoenol pyruvate
- DHAP- Dihydroxyacetone phosphate
- APT- Apicoplast phosphate transporter
- G3P- Glyceraldehyde 3-phosphate
- LPA- lysophosphatidic acid
- PA- phosphatidic acid
- Parasite-derived FA-

Adapted from
^aAmiar *et al.* (2016)
^bShears *et al.* (2017)

Final lipid assembly: 'Patchwork model'



Aim and objectives

- Elucidate the roles of ACBPs and LPLs in Apicomplexa
 - Generate molecular tools
 - In progress- CRISPR JITMM workshop 2017 provided gRNA
 - Assess cellular context of proteins
 - Microscopy, viability assays, binding studies
 - Function of the ACBPs/LPLs at the parasite lipid synthesis level
 - In-house Lipidomic facility

Are they viable drug targets?

Acknowledgments

Apicolipid Team, Institute for Advanced Biosciences, University Grenoble Alpes



The Apicos 2018:

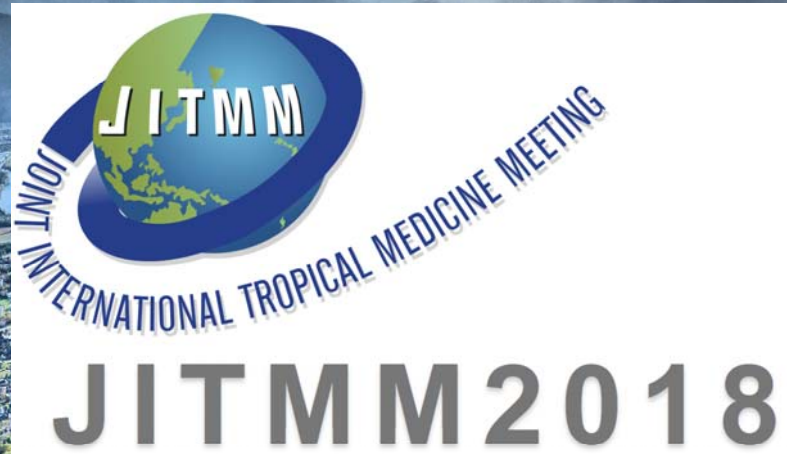
- Cyrille Botté, Group leader (CNRS)
- Yoshiki Yamaro-Botté, Research Fellow (UGA)
- Nick Katris, Postdoctoral fellow (Parafrap CNRS)
- Sheena Dass, PhD (Parafrap CNRS)
- Serena Shunmugam (PhD CEFIPRA, UGA)
- Christophe Sebastien Arnold (M2, UGA)



PC3 cell culture facility for infectious agents: *P. falciparum* blood stages, *T. gondii*, *Leishmania*



Metabolomic platform dedicated to lipidomics and fluxomics



Serena Shunmugam

JITMM 2018: Free Paper Malaria