A Review on the Role of Lipid in Selected Apicomplexan, Anaerobic, Kinetoplastid and Intestinal Parasitic Infections

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ABSTRACT

Lipids are a diverse class of biomolecules that play a major role as energy source, membrane components and cellular signaling molecules. Because of the variation in modes of life, different parasites can partly or fully utilized significant amount lipids during infection. The aims of this paper were to provide an overview to the role of lipids in selected apicomplexan, anaerobic, kinetoplastid and intestinal parasitic infections. Lipid particles are fundamentally engaged in host-pathogen interactions like cell signaling and immunity. As a source of eicosanoid production, they are involved in different aspects of innate signaling and antigen presentation for the host organism. For the pathogen, lipid droplets also employed to facilitate attachment, empowering pathogenesis and used to subvert host metabolism as ways of immune evasion. The apicomplexan parasites utilized lipid particles for various purpose including changing permeability and fragility of host cells, support the insertion of parasite into the host cell membrane, and promote growth, invasion and optimal replication of the organism. In anaerobic groups of parasites, the lipid plays a considerable role as growth promoter, increasing virulence, facilitate encystation and vesicle formation as well as initiation of immune system and maturation of dendritic cells. Kinetoplastid also engaged in the uptake of essential lipid particles to produce more complex lipids, develop protective mechanisms against host innate and adaptive immunity and support pathogen survival. The lipid bodies also utilized by the intestinal parasites for disease pathogenesis, differentiation and survival of larvae in the host tissue. This review showed that the different in vivo and in vitro studies indicated that lipids have different role in different stage of the parasites infection. The associations between parasites and the lipids were observed during the attachment, invasion and other stages of parasitic infection. So far, evidences in lipid profile alteration related to different parasitic infection suggested that parasites are able to remodel/metabolize host lipids during the overall pathogenesis of parasitic infection.

Key words: Infection, Lipid, Parasitic, Role

INTRODUCTION

The burden of parasitic disease is enormous. It accounts 1 million deaths per year and 3 billion infections per year experienced worldwide (GBD, 2017). These parasite are residing in various organ and tissue like intestine, blood, liver, lungs, brain, muscles and lymphatic tissues and causing great impact on their habitants (Beaver et al., 2006).

Pathogenic microbes have evolved myriad strategies to evade the host cells and secure a protected environment within their hosts. Some avoid ingestion by the phagocytic cells designed to degrade them and some others promote their uptake and reside within safe compartments inside host cells. It is becoming increasingly apparent that the mechanism by which microbes enter cells can impact their intracellular survival (Shin and Gao, 2000). Their nutritional requirements and means of obtaining and utilizing the nutrients required for growth, motility and reproduction are also varied. Lipid is required for internalization of eukaryotic pathogens under such variable circumstances. It is present in tissues and plasma lipoprotein either as free cholesterol or combined with a long-chain fatty acid, as cholesteryl ester. It is synthesized in many tissues from acetyl-CoA and is ultimately eliminated from the body in the bile as cholesterol or bile salts (Maxfield, 2008).

Lipids are a diverse class of biomolecules that play a major role not only as membrane components, but also as cellular signaling molecules (Aswin et al., 2018). Chemically, lipids can be classified on basis of their head group (choline, ethanolamine, inositol and serine), their backbone (glycerol or sphingosine) or on basis of their lipid anchors (acyl and alkyl) (Zufferey and Mamoun, 2005). Lipid micro domains, including rafts and caveolae, have an important role in the organization of membrane proteins, in cell–cell contact and in numerous signaling processes. They are increasingly being implicated in the interactions between macrophages and parasites. Host cell lipid rafts and other lipid microdomains also serve as targets for disrupting host cell function and indeed, act as a portal of parasite entry (Rodriguez et al., 2006).

The lipid raft of these micro domains are small, highly dynamic and enriched in cholesterol, glycosphingolipids and signaling phospholipids, which compartmentalize cellular processes (Beaver et al., 2006). These lipid rafts engaged in various activities and played considerable role in organism attachment, engulfing process and signal transduction of disease pathogenesis. During infection, many pathogens utilized host membrane micro domain dependent mechanisms to evade the host immune system (Rodriguez et al., 2006).

Lipid has a vital role in the overall invasion of pathogens. The interactions between lipid-raft and endosomal system is detrimental to pathogens residing within the cells compartment, avoiding of host's defense mechanism and for antimicrobial arsenal. The requirement of lipids in pathogens under such variable circumstances is poorly understood. Thus, the present review highlights the role of lipids and their metabolic products in certain parasitic infections.

General overview

Lipid rafts appear to have many functions, although their complete roles are not well understood. These functions included diverse processes as polarized secretion, membrane transport, transcytosis across epithelial monolayers and the generation of cell polarity (Vallochi et al., 2018). The importance of lipid rafts in signal transduction is highlighted by their enrichment for many signaling molecules such as receptor tyrosine kinases, mitogen-activated protein kinases, adenylyl cyclase and lipid signaling intermediates (Toledo et al., 2016). Although lipid rafts comprise only a small percentage of the cell surface area, their high concentration of signaling molecules makes them a natural target for microbes to communicate with the host cell. Lipid rafts are also known to undergo fission from the plasma membrane mediating a form of endocytosis (Parton et al., 2004). Microbial agents might favor interaction with lipid rafts as a potential way to enter host cells. While utilizing caveolae and other lipid micro domains as sites for microbial action, the biological consequence of this interaction is important for both hosts and pathogens (Rodriguez et al., 2006). The role of lipid rafts in different cell types has been numerous and their physiological significance for cell biology has recently become clear. These membrane regions play an important role in a variety of cellular functions including polarization, signal transduction, endocytosis, secretion, cell–cell and cell–pathogen adhesion (Jacobson, 2007). One of the most widely appreciated roles of lipid rafts is the recruitment and concentration of molecules involved in cellular signaling. The formation of a molecular cluster and their signal transduction machinery in membrane rafts leads to enhanced signaling efficiency (Triantafilou et al., 2002).

An interesting manner that allows pathogens to evade the immune system is through membrane microdomains (Borges et al., 2016). As signaling for the innate and adaptive immune responses initiated in rafts, some pathogens have evolved mechanisms to subvert this signaling by co-opting raft-associated pathways (Melo et al., 2006). Different pathogens can use the host-cell lipid rafts to secure their entrance and maintenance inside the target cells. The benefit provided by interaction with lipid rafts can vary from one pathogen to another (Borges et al., 2016). Parasites interacted with lipid rafts during the disease pathogenesis is indicated by parasitophorous vacuole membranes that contain host raft lipids and proteins. Furthermore, Glycosyl Pphosphatidyl Inositol (GPI)-anchored proteins, such as cluster of Differentiation 55 (CD55) and CD59 which are major inhibitors of membrane complements progressively depleted from the infected cell surface (Nolan et al., 2017).

Lipid role in certain parasitic infestation

Apicomplexan parasites

The presence of hypercholesterolemia and hypertriglyceridemia observed in both uncomplicated and complicated malaria indicated the interaction between lipid molecule and the pathogen (Sabrina et al., 2006; Ross et al., 2009). The amount of octadecenoic fatty acids and cholesterol in the host erythrocyte plasma membrane are highly linked with the lipid metabolism of the parasites to change permeability and fragility of the cells (Bansal et al., 2005).

The difference in concentration of serum High Density Lipoprotein (HDL) indicated reverse effect to the culture of *Plasmodium falciparum*. The low concentration of HDL promote the growth of whereas high concentration was found to be toxic to the organism (Vielemeyer et al., 2004). The plasmodium genome contains genes encoding enzymes for phospholipids metabolism allowing de novo synthesis of phosphatidylcholine via the Kennedy pathway and necessitating the uptake of the small choline molecule (Imrie et al., 2004). During malaria invasion, the host cell membrane rapidly expands around the parasite to form the Parasitophorous Vacuole Membrane (PVM) that support the insertion of parasite lipids into the host cell membrane (Wein.et al., 2018). In this phenomena, relative depletion of intra-membranous particles in the outer leaflet of the PVM is observed in malaria infection (Ross et al., 2009). Host cell cholesterol also implicated during the entry and replication of toxoplasma pathogens. The PVM surrounding *Toxoplasma gondii* utilized cholesterol during entry and invasion through a caveolae independent mechanism (Johnston et al., 2016). This parasite attachment and entrance is greatly impaired when the host cell plasma membrane cholesterol content is depleted (Nolan et al., 2017). *Toxoplasma gondii also* exploits host low density lipoprotein receptor-mediated by endocytosis for cholesterol acquisition and acyl-CoA, cholesterol acyl transferase and cholesterol esters to the optimal

replication of the organism (Coppens et al., 2008). The successful replication of *T. gondii* within the Parasitophorous Vacoul (PV) requires considerable amounts of selected lipids for membrane biogenesis (Charron and Sibley, 2004). Eventhough *T. gondii* has the ability to synthesize phospholipids, it takes precursors of these lipids from the environment to construct more complex lipids (Gupta et al., 2005). In *Cryptosporidium*, the parasite is unable to de novo synthesize cholesterol, it relies on host cell-derived cholesterol. It is auxotroph for plasma Low Density Lipoprotein (LDL) and derives its cholesterol from the host cells. Moreover, the cholesterol incorporated by *Cryptosporidium* did not only originate from de novo synthesis of the host cell but also from micelles imported via transporter into the cell (Ehrenman et al., 2013).

Anaerobic parasites

In vitro study, the finding indicated that the cholesterol is a growth promoter for *Entamoeba histolytica* and the avirulent strain can be revived by adding cholesterol to culture media (Vallochi et al., 2018). Moreover, replacing bovine serum with a lipoprotein cholesterol solution and bovine serum albumin in pre-encystation and excystation media stimulates *Giardia lamblia* encystations and vesicle formation. This suggests that the parasites utilize cholesterol for their growth from infected individuals (Bansal et al., 2012). In *Entamoeba*, the disruption of cholesterol rich raft like membrane with the cholesterol binding agent (fillipin and methyl-β-cyclodextrin) inhibit several important virulence functions, fluid phase pinocytosis and adhesion to host cell monolayers (Laughlin et al., 2004). In Giardia, membrane biogenesis requires cholesterol. Because *Giardia* is unable to synthesize cholesterol, it obtains this from upper small intestine, which is rich in biliary and dietary cholesterol (Kaneda and Goutsu, 2013). In vitro, the addition of lipoprotein cholesterol solution in pre-encystation and excystation media of *G.1amblia* promote encystation of specific secretory vesicles formation. Cholesterol also regulate the receptor dependent signaling responsible encystations process (Kaul et al., 2011). The HDL in *Trichomonas* have important roles in parasite biology and disease pathogenesis (Gilbert et al., 2009). The addition of purified Lipophosphoglycan (LPG) mediated the adhesion of *Trichomonas* parasites to human vaginal epithelial cells in a dose-dependent manner. The Interleukin 8 (IL-8) is also triggered by LPG to promote inflammatory cell that initiate immune system and maturation of dendritic cell (Raina et al., 2006). Giardia possessing a limited capacity to synthesize lipid molecules depends on host lipids for its growth and differentiation. It has been suggested that most lipids and fatty acids are taken up by endocytic and non-endocytic pathways and used by for energy production and membrane/organelle biosynthesis of the organism (Yichoy et al., 2011).

Kinetoplastid parasite

Among kinetoplastid parasites, *Trypanosomes* bind and take up plasma LDL from host lipids. They require lipoproteins to multiply under axenic culture conditions (Johndrow et al., 2014). The other cholesterol like HDL, LDL, and *Trypanosome* Lytic Factor (TLF) were bound and taken up by a lipoprotein scavenger receptor as the parasite's major pathway mediating the uptake of essential lipids. The role of HDL, LDL and TLF1 also involved for attaching to the surface receptors of Trypanosomes (Green et al., 2003). The lipid particles as sites of prostaglandin E2 synthesis during chagas disease has grate role to the escape mechanism of the parasite against host immunity (Almeida et al., 2018). Lipid bodies (LBs) in *Trypanosoma cruzi* also act as dynamic organelles to respond to host interaction and a potent immune-modulatory that hinder innate and adaptive immunity and support the pathogen survival in its host (Toledo et al., 2016). Microscopic investigation on *Trypanosoma cruzi* indicated the brown fat tissue where lipid bodies are higher in number and smaller in size is the preferred localization to the organism. The parasites disrupt adipokines synthesis in this tissue and used as a site of reservoir (Comb et al., 2005). *Trypanosoma cruzi* parasite present in the adipose tissue biopsy of chronically infected human patients have further confirmed the finding that adipose tissue is the reservoir of chronic *T. cruzi* infection (Matos et al., 2011). In *Leishmania* infection the plasma membrane cholesterol is required for efficient attachment and internalization of the parasite in to macrophages (Rodriguez et al. 2017). Stage-specific binding of different lectins to distinct forms of the *Leishmania* parasite during its cell cycle demonstrates molecular changes in the glycocalyx. Changes in the major component of the promastigote glycocalyx such as in the glycosyl-phosphatidylinositol anchored Lipophosphoglycan (LPG), are important in the defense against lytic activities of the mammalian host. LPG also protects the procyclic promastigote against hydrolases in the midgut of the insect vector (Wilson and Pearson, 2004). Increased infectivity of the metacyclic promastigote is mediated by increased number free fatty acids, cholesterol, sphingomyelin and phosphatidylserine (Hana et al., 2017). In *Leishmania amazonensis* the proliferation of the parasite during cultivated in dilapidated fetal calf serum influenced by the presence or absence of LDL. The media supplemented with LDL cholesterol showed enhanced and sustainable parasite growth (Nuccia et al., 2012).

Intestinal worms

The cestode parasites utilized greater amount total lipid and phospholipid whereas the nematode takes more of neutral lipid and glycolipid by absorbing them from the intestinal fluids (Mondal et al., 2016). The trematode also

engaged *in* taking up the lipid requirements from host rumen fluid which is required for their reproductive strategy (Ghosh and Misra, 2014). A low level of HDL cholesterol in hookworm, strongyloides and trichuris infected patients evidenced the involvement of lipid particles by the parasites to disease pathogenesis and larvae survive in the host tissue (Wiedermann et al., 2011). The decreased in total cholesterol, HDL and triglycerides observed in guinea pig affected by Ascaris evidenced the utilization of lipid by the parasite. The lipid particles are involving in enhancing larval survival, yield and growth of L4 stage of *Ascaris* (Biadun, 2005). The Phospholipid/cholesterol ratio in liver of golden hamsters infected with *Ancylostoma ceylanicum* showed significantly reduction due to structural and functional disturbance of the membrane by utilization of these biomolecules by the parasite and its hepatotoxic effects (Srivastava, 2004).

CONCLUSION

Lipids are a diverse class of biomolecules that play a major role as energy source, membrane components and cellular signaling molecules. Pathogenic microbes have evolved myriad strategies to evade the host cells to secure a protected environment and reside within safe compartments inside host cells. The interaction between parasites and the lipid contents were observed during penetration, invasion and at various developmental stage of parasitic infestation. The uptake of the lipid particles by the parasites employed for production of more complex lipids, developing protective mechanisms against host innate and adaptive immunity, support pathogen survival, differentiation of larvae stage and promote growth, invasion and optimal replication of the organism. But the mechanism of such interaction remains elusive. A comprehensive lipidomic analysis will be needed for identification and characterization of lipid molecules and enzymes involved in pathways for the proper understanding of the interaction between parasites and lipid molecules. Recent technologies in molecular biology and parasite genome have also be applied to identify the genes and enzymes in lipid metabolic pathways during parasitic infection.

DECLARATIONS

Competing interests
The authors declared that they have no competing interests.

Author contributions
All authors equally involved in searching literature review, write up the paper and critically analyze the core idea of the paper and reviewed the manuscript. Finally, all authors read and approved the final version of the manuscript.

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REFERENCES

Almeida PE, Toledo DAM, Rodrigues GSC and D'Avila H (2018). Lipid bodies as sites of prostaglandin E2 synthesis during chagas disease: impact in the parasite escape mechanism. Front Microbiology, 9:499. Doi:10.3389/fmicb.2018.00499.

Aswin T, Srivatsav MM and Shobhna K (2018). Small-Molecule Modulation of Lipid-Dependent Cellular Processes against Cancer: Fats on the Gunpoint. Biomedical Research International, 2018(1):1-17. Article ID 6437371, 17 pages, Doi:https://doi.org/ 10.1155/2018/6437371.

Bansal D, Bhat HS and Sehgal R (2005). Role of lipid in parasitic infection. Biomedical central, 4(10):342-349.

Bansal D, Bhatti HS and Sehgal R (2012). Altered lipid parameters in patients infected with Entamoeba histolytica, Entamoeba dispar and Giardia lamblia. British Journal of Biomedical Science, 5:13-15.

Beaver P, Jung R and Cupp E (1984). Clinical Parasitology, 9th edition. Lea and Febiger, Philadelphia, pp. 515-526.

Biadun W (2005). Studies of serum lipids in guinea pigs with larval Ascariasis. Wiad Parazytol, 36:15-26.

Borges TK, Alves ÉA, Vasconcelos HA, Carneiro FP, Nicola AM and Magalhães KG (2017). Differences in the modulation of reactive species, lipid bodies, cyclooxygenase-2, 5-lipoxygenase and PPAR-γ in cerebral malaria-susceptible and resistant mice. Immunobiology, 222:604–19. doi: 10.1016/j.imbio.2016.11.010.

Charron AJ and Sibley LD (2004). Molecular partitioning during host cell penetration by Toxoplasma gondii. Traffic, 5:855-867.

Combs TB, Mukherjee S and De Almeida CJ (2005). The adipocyte as an important target cell for Trypanosoma cruzi infection. Journal of Biological Chemistry, 280(25):4085-4094.

Coppens I, Baudhuin P, Opperdoes FR and Courtoy PJ (2008). Receptors for the Host Low Density Lipoproteins on the Hemoflagellate Trypanosoma brucei: Purification and Involvement in the Growth of the Parasite. Proceedings of the National Academy of Sciences of the United States of America, 85:753-757.

Ehrenman K, Wanyiri JW, Bhat N, Ward HD, and Coppens I (2013). Cryptosporidium parvum scavenges LDL-derived cholesterol and micellar cholesterol internalized into enterocytes. Cellular Microbiology, 15: 1182-1197.

Ghosh D and Misra KK (2014). Comparison of fatty acid contents of the neutral and phospholipids of the trematode *Paramphistomum cervi* and liver of its host, *Capra hircus*. Journal of Parasitic Diseases, 38:223–232. doi: 10.1007/s12639-012-0229-6.

Gilbert RO, Elia DH, Beach S, Klaessig H and Singh BN (2009). Cytopathogenic effect of Trichomonas vaginalis on human vaginal epithelial cells cultured in vitro. Infection and Immunity, 68:4200-4206.

Global Burden Diseases (GBD) (2017). Measuring progress from 1990 to 2017 and projecting attainment to 2030 of the health-related Sustainable Development Goals for 195 countries and territories: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet, 8 Nov 2018: 392.

Green HP, Del Pilar MPM, St Jean EN, Lugli EB and Raper J (2003). Evidence for a Trypanosoma brucei lipoprotein scavenger receptor. Journal of Biological Chemistry, 278:422-426.

Gupta N, Zahn MM, Coppens I, Joiner KA, and Voelker DR (2005). Selective disruption of phosphatidylcholine metabolism of the intracellular parasite Toxoplasma gondii arrests its growth. Journal of Biology and Chemistry, 280:1645-1653.

Hana B, Marion G, Philippe L, Isabelle D and Samira A (2017). Changes in Lipid and Fatty Acid Composition during Intramacrophagic Transformation of Leishmania donovani Complex Promastigotes into Amastigotes. Lipids, 52: 433-441.

Imrie H, Ferguson DJP, Carter M, Drain J, Schiflett A and Hajdur SL (2004). Light and electron microscopical observations of the effects of high-density lipoprotein on growth of Plasmodium falciparum in vitro. Parasitology, 128:577-584.

Jacobson K, Mouritsen OG and Anderson RG (2007). Lipid rafts: at a crossroad between cell biology and physics. Natural Cell Biology, 9:7-14.

Johndrow C, Nelson R, Tanowitz H, Weiss LM and Nagajyothi F (2014). Trypanosoma cruzi infection results in an increase in intracellular cholesterol. Microbes and Infection, 16:337–344. doi: 10.1016/j.micinf.2014.01.001.

Johnston AC, Piro A, Clough B, Siew M, Virreira Winter S, Coers J, and Frickel EM (2016). Human GBP1 does not localize to pathogen vacuoles but restricts Toxoplasma gondii. Cellular Microbiology, 18(8):1056–1064. doi:10.1111/cmi.12579

Kaneda Y and Goutsu T (2013). Lipid analysis of Giardia lamblia and its culture medium. Annals of Tropical Medicine and Parasitology, 82:83-90.

Laughlin RC, McGuan GC, Powell RR, Welter BH and Temesvari LA (2004). Involvement of raft-like plasma memebrane domains of Entamoeba histolytica in pinocytosis and adhesion. Infection and Immunity, 72:5349-5357.

Matos AV, Segatto M and Menezes Z (2011). Evidence for Trypanosoma cruzi in adipose tissue in human chronic Chagas disease. Microbes and Infection, 13 (12):1002-1005.

Maxfield F (2008). Plasma membrane microdomains. Current Opinion in Cell Biology, 14:483-487.

Melo RCN, Fabrino DL, Dias FF and Parreira GG (2006). Lipid bodies: structural markers of inflammatory macrophages in innate immunity. Inflammation Research, 55(8):342–8. doi:10.1007/s00011-006-5205-0

Mondal M, Kundu JK and Misra KK (2016). Variation in lipid and fatty acid uptake among nematode and cestode parasites and their host, domestic fowl: host-parasite interaction. Journal of parasitic diseases. official organ of the Indian Society for Parasitology, 40(4), 1494–1518. doi:10.1007/s12639-015-0718-5

Nolan SJ, Romano JD and Coppens I (2017). Host lipid droplets: an important source of lipids salvaged by the intracellular parasite Toxoplasma gondii. PLoS Pathogenis, 13: e1006362. doi: 10.1371/journal.ppat.1006362

Nuccia NT, Miria G, Jose R, Correa VV, Felipe B and Saraiva C (2012). LDL uptake by Leishmania amazonensis: Involvement of membrane lipid microdomains. Experimental Parasitology, 130:330-340.

Parton RG, Joggerst B and Simons K (2004). Regulated internalization of caveolae. Journal of Cell Biology, 128:1199-1215.

Raina NF, Radiana TT, Robert OG, Catherine EC, Gary RH and John J (2006). Trichomonas vaginalis Lipophosphoglycan triggers a selective upregulation of cytokines by human female reproductive tract epithelial cells. Infection and Community, 74 (10):5773-5779.

Rodriguez NE, Gaur UA and Wilson ME (2006). Role of caveolae in Leishmania Chagasi phagocytosis and intracellular survival in macrophages. Cell Microbiology, 8:1106-1120.

Rodríguez NE, Lockard RD, Turcotte EA, Araújo-Santos T, Bozza PT and Borges VM (2017). Lipid bodies accumulation in Leishmania infantum -infected C57BL/6 macrophages. Parasite Immunology, 39: e12443. doi:10.1111/pim.12443

Ross BM, Markus K, Kaylan S, Wadwat PS, and Rupert SU (2009). The role of lipids in Plasmodium falciparum invasion of erythrocytes: A coordinated biochemical and microscopic analysis. Journal of Cell Science, 102:527-532.

Sabrina S and Adrian BH (2006). Lipid biology of Apicomplexa: perspectives for new drug targets. Trends in Parasitology, 22:41-47.

Shin J, Gao Z and Abraham S. (2000). Involvement of cellular caveolae in bacterial entry into mast cells. Science, 289: 785-788.

Srivastava SC (2004). Liver plasma membrane-bound enzymes and lipids in golden hamsters infected with Ancylostoma ceylanicum. International Journal of Parasitology, 24:249-51.

Toledo DA, D'Avila H and Melo RC (2016). Host lipid bodies as platforms for intracellular survival of protozoan parasites. Front Immunology, 7:174. doi:10.3389/fimmu.2016.00174.

Toledo DAM, Roque NR, Teixeira L, MilánGarcés EA, Carneiro AB and Almeida MR, (2016). Lipid Body Organelles within the Parasite Trypanosoma cruzi: A Role for Intracellular Arachidonic Acid Metabolism. PLoS ONE, 11(8): e0160433. doi: 10.1371/journal.pone. 0160433.

Triantafilou M, Miyake K, Golenbock DTK and Triantafilou K (2002). Mediators of innate immune recognition of bacteria concentrate in lipid rafts and facilitate lipopolysaccharide induced cell activation. Journal of Cell Science, 115:2603-2611.

Vallochi AL, Teixeira L, Oliveira K, Maya-Monteiro CM and Bozza PT (2018). Lipid Droplet, a Key Player in Host-Parasite Interactions. Frontiers in immunology, 9, 1022. doi:10.3389/fimmu.2018.01022

Vielemeyer O, McIntosh MT, Joiner KA and Coppens I (2004). Neutral lipid synthesis and storage in the intraerythrocytic stages of Plasmodium falciparum. Molecular and Biochemical Parasitology, 135:197–209. doi:10.1016.

Wein S, Ghezal S, Bure C, Maynadier M, Perigaud C, Vial HJ, Lefebvre-Tournier I, Wengelnik K and Cerdan R (2018). Contribution of the precursors and interplay of the pathways in the phospholipid metabolism of the malaria parasite. Journal of Lipid Research 59, 1461- 1471

Wiedermann U, Stemberger H, Unfried E, Widhalm K, Kundli M and Altenriederer M (2011). Intestinal worm burden and serum cholesterol or lipid concentration in a Shipibo population (Peru). International Journal of Medical Microbiology, 275:279-286.

Wilson ME and Pearson RD (2004). Stage-Specific Variations in Lectin Binding to Leishmania donovani. Microbiology, 46:128-134.

Yichoy M, Durate TT, Deachatterjee A, Mendez TL, Aguilera KY and Roy D (2011). Lipid metabolism in Giardia: a post-genomic perspective. Parasitology, 38 (3) 267-78.

Zufferey R and Mamoun CB (2005). The initial step of glycerolipid metabolism in Leishmania major promastigotes involves a single glycerol-3-phosphate acyltransferase enzyme important for the synthesis of triacylglycerol but not essential for virulence. Molecular microbiology, 56:800-810.