Short Communication

iMedPub Journals
http://www.imedpub.com

Archives of Clinical Microbiology
ISSN 1989-8436

2021
Vol. 12 No. 6:181

Cholesterol Crystals in Reservosomes: An Unsolved Mystery

Miria G. Pereira*

Lab Ultraestrutura Celular Hertha Meyer, Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

*Corresponding author: Miria G. Pereira,

Lab Ultraestrutura Celular Hertha Meyer, Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

miriagpereira@gmail.com

Citation: Pereria MG (2021) Cholesterol Crystals in Reservosomes: An Unsolved Mystery. Arch Clin Microbiol Vol.12 No.6: 181.

Received: November 16, 2021; **Accepted:** November 30, 2021; **Published:** December 07, 2021

Introduction

In higher eukaryotes, the major sterol described in membranes is cholesterol. Plasma membrane contains around 65%-85% cholesterol. Endosomes, lysosomes and recycling vesicles also present high amounts of cholesterol and cholesteryl esters as a consequence of uptaking of lipoproteins. Cholesterol leaves endolysosomal system into endoplasmic reticulum by the orquestration of a set of proteins recruited to the contact site stablished between both compartiments. In this scenario, NPC1, NPC2, Rab7, ORP1L, STARD3, STARD3NL among others interact with proteins from endoplasmic reticulum, such as ORP5, VAP e RILP to ensure that cholesterol is trafficked to other compartiments or storaged in lipid droplets [1]. The imbalance of this route impairs lipid metabolism resulting in formation of foam cells and progression of atherosclerosis or even congenital consequences for human health, as the neurodegenerative Niemann Pick type C disease, Wolman disease leading to a state of cellular starvation [2]. These conditions create a favorable environment to cholesterol crystalization, from a bidimensional crystal to a packed rectangular or flatten crystal structure [3]. Cholesterol crystals are associated with many cellular responses, for example, activation of NLRP3 inflammasomes, NETosis, atherosclerotic plaque erosion, thrombosis, renal embolism [4].

Although cholesterol physiology has been studied for a long time in mammals, general awareness in protozoan parasites is fairly limited. It is well accepted that parasites depend on exogenous sterols to proliferate, synthesize and remmodel membranes. In *Trypanosoma cruzi*, etilogical agent of Chagas disease, cholesterol is acquired during insect stage phase or in intracelular stage in mammals. One intriguing point that parasitologists have to solve is how parasites keep the equilibrium of ergosterol and cholesterol rates. Our group has been studied lipid endocytosis in proliferative forms of *T. cruzi.* Cholesterol gains intracelular environment after LDL endocytosis and is stored temporarily in reservosomes (lysosome like organelles) and lipid droplets [5]. Round, needle or rectangular shaped lipid inclusions are frequently observed in ultrathin sections [6]. However, high serum concentration triggers profound alterations in parasite morphology, resulting in skewed reservosomes, fulfilled by large and abundant cholesterol crystals as well as several lipid droplets and crystals along parasite body [7,8]. Moreover, the parasite ability to mould and dissolve these crystalline arrangements does not culminate in extensive effects on viability, survival or proliferation. So, many questions emerge to understand this puzzle:

- Under which conditions does cholesterol crystallize? What triggers crystallization?
- Do cholesterol crystals in resrvosomes show the same three-dimensional pattern as those described in mammals?
- Is the disassembly of crystals associated to physicalchemical environment of the reservosomes?
- Which targets do some enzymatic inhibitors present in order to avoid cholesterol exit and consequent accumulation in reservosomes?
- High amounts of cholesterol crystals do interfere on metacyclogenesis?
- Why parasite does not succumb to several cholesterol crystals?

Conclusion

These and others questions arise gradually according to parasitologists try to comprehend the mysterious mechanisms of *T. cruzi* survival and the challenges to adaptate in distinct hosts. Probably, in the digestive tract of insect vector, *T. cruzi* epimastigotes do not have abundant lipid sources as in axenic cultures. More importantly is to determine the molecular mechanisms behind crystal dismantling and cholesterol utilization by parasite.

References

1. Raiborg C, Wenzel EM, Stenmark H (2015) ER-endosome contact sites: Molecular compositions and functions. EMBO J 34: 1848-58.
2. Schulze H, Sandhoff K (2011) Lysosomal lipid storage diseases. Cold Spring Harb Perspect Biol. 3: a004804.
3. Varsano N, Fargion I, Wolf SG, Leiserowitz L, Addadi L (2015) Formation of 3D cholesterol crystals from 2D nucleation sites in lipid bilayer membranes: Implications for atherosclerosis. J Am Chem Soc 137: 1601-1607.
4. Tall AR, Westerterp M (2019) Inflammasomes, neutrophil extracellular traps and cholesterol. J Lipid Res 60: 721-727.
5. Pereira MG, Visbal G, Costa TFR, Frases S, de Souza W, et al. (2018) *Trypanosoma cruzi* epimastigotes store cholesteryl esters in lipid droplets after cholesterol endocytosis. Mol Biochem Parasitol 224:6-16.
6. Sant'Anna C, Pereira MG, Lemgruber L, de Souza W, Silva CNL (2008) New insights into the morphology of *Trypanosoma cruzi* reservosome. Microsc Res Tech 71: 599-605.
7. Pereira MG, Nakayasu ES, Sant'Anna C, De Cicco NN, Atella GC, et al. (2011) *Trypanosoma cruzi* epimastigotes are able to store and mobilize high amounts of cholesterol in reservosome lipid inclusions. PLoS One 6: e22359.
8. Sangenito LS, Pereira MG, Souto-Padron T, Branquinha MH, Santos ALS (2021) Lopinavir and nelfinavir induce the accumulation of crystalloid lipid inclusions within the reservosomes of *Trypanosoma cruzi* and inhibit both aspartyl-type peptidase and cruzipain activities detected in these crucial organelles. Trop Med Infect Dis. 6: 120.