Available online at www.sciencedirect.com
ScienceDirect
Parasitology International 56 (2007) 161–170
www.elsevier.com/locate/parint

Review

Macro, micro and nano domains in the membrane of parasitic protozoa

Wanderley de Souza *

Laboratório de Ultraestrutura Celular Hertha Meyer, Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, 21941-900, Rio de Janeiro, RJ, Brazil

Received 20 November 2006; received in revised form 30 January 2007; accepted 1 February 2007
Available online 8 February 2007

Abstract

The structural organization of the plasma membrane of eukaryotic cells is briefly revised taking into consideration the organization of proteins and lipids and the concept of microdomains, lipid rafts and detergent resistant membranes. The biochemical data available concerning the presence of microdomains in parasitic protozoa is reviewed and emphasis is given on the identification of special domains recognized by morphological approaches, especially with the use of the freeze–fracture technique.

Keywords: Parasitic protozoa; Microdomain; Lipid raft; Detergent-resistant membrane; Freeze–fracture; Electron microscopy

Contents

1. Introduction

For several decades the idea that biological membranes were formed by a lipid bilayer and layers of protein-containing material, both on the outer and the inner faces predominated. Subsequently, several studies led Singer and Nicholson [1] to propose the fluid mosaic model, which considered that the proteins were immersed, in variable degrees, in the lipid bilayer in a dispersed state and at low concentrations. Also the lipid bilayer could be seen as a sea in which mainly monomeric proteins float un-embedded. For the following years these ideas constituted the basic framework for the explanation of data obtained as well as for the planning of new experiments. However, during this period several new observations point to the idea that the membranes are patchy, with the presence of specialized regions or domains, where proteins or lipids are aggregated and even segregated [2]. On the other hand, biochemical studies have shown the existence of small domains, called microdomains or lipid rafts, which are rich in sterols and sphingolipids, visualized with the use of filipin, a sterol binding fluorescent antibiotic or cholera toxin, which binds to the

* Tel./fax: +55 21 22602364.
E-mail address: wsouza@biof.ufrj.br.

1383-5769/$ - see front matter © 2007 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.parint.2007.02.001

ganglioside GM1. They have been envisioned as liquid-ordered (I_0) membrane phases whereas surrounding non-raft regions are in a liquid-disordered (I_d) phase [3–7].

These regions are also resistant to solubilization in cold non-ionic detergents, especially Triton X-100 at 4 °C [8], thus explaining their description as detergent resistant membranes (DRMs) and are also characterized by the concentration of glycosylphosphatidylinositol (GPI)-anchored proteins. Although there is still some controversy concerning the actual existence of a lipid raft [7,9], if it exists, it has been considered to be small (around 25–100 nm) and transient.

2. Identification of microdomains (raft-like membrane domains)

Using a biochemical approach raft-like membrane domains have been identified in some protozoa. This has been done based on (a) the use of fluorescent lipid analogues that specifically partition into raft and non-raft regions of the membrane, (b) disruption of raft-like domains by cholesterol-binding agents such as filipin and methyl-β-cyclodextrin, (c) localization of binding sites to β cholera toxin, which bind to the ganglioside GM1 and (d) localization of glycosylphosphatidylinositol (GPI)-anchored proteins such as caveolins and flotilins.

There are few studies on the characterization of raft-like membrane domains in parasitic protozoa. Initial studies carried out with bloodstream forms of *Trypanosoma brucei* showed that a surface alanine-rich protein was located in detergent-resistant membranes (DRMs). Immunofluorescence microscopy showed that this protein is located on the parasite surface, appearing as small discrete spots [10]. GPI-anchored glycoconjugates such as lipophosphoglycans (LPG) and a 63 kDa glycoprotein (GP63) are localized in the DRMs of *Leishmania*. However, other proteins, such as the dual acylated surface protein are not enriched in the DRMs [11]. In the case of *Leishmania* there have been the suggestions that (a) a significant proportion of glycosylinositolphosholipids (GIPLs) are localized in detergent-resistant membranes (DRMs) of the

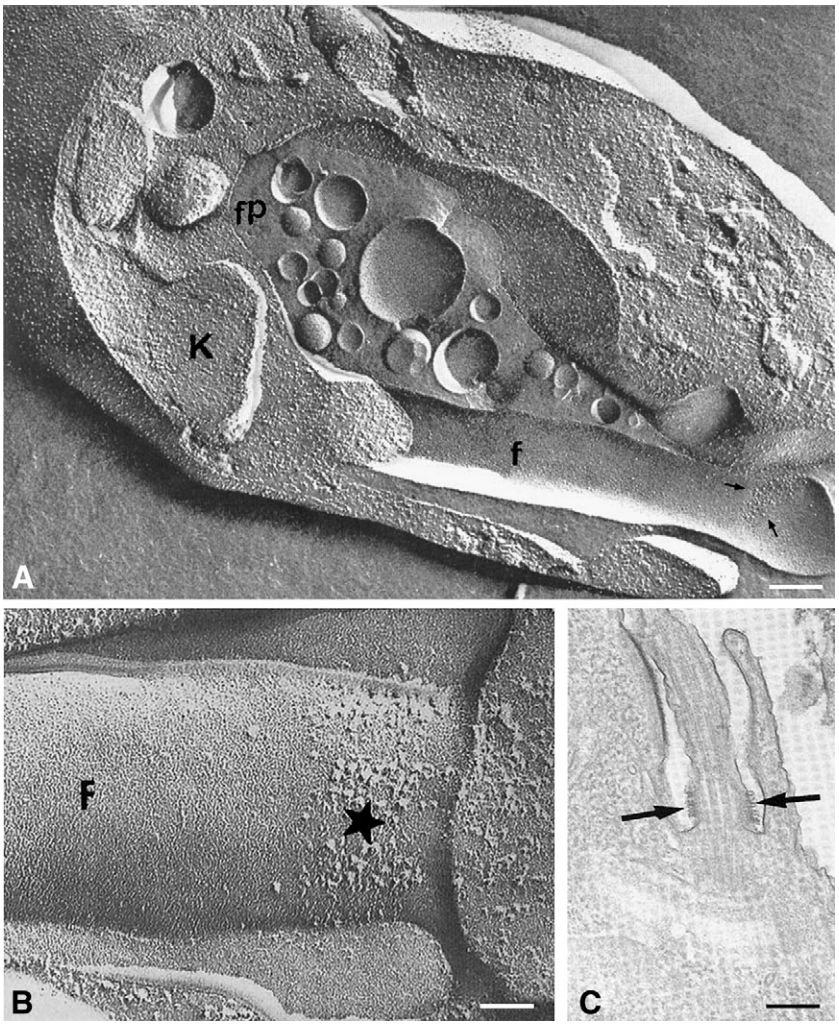

Fig. 1. A. General view of the anterior regions of *Herpetomonas samuelpessoai* as seen in a freeze–fracture replica. The Kinetoplast (K), the flagellum (F) and a large flagellar pocket (FP) are seen. Several vesicles are seen within the flagellar pocket. Short arrows show an aggregation of particles at the region of contact of the flagellum with the cell body. Bar, 250 nm. After De Souza et al. [27] B and C. The base of the flagellum (F) of *Trypanosoma cruzi*, as seen in a freeze–fracture replica and in a thin section of a cell labeled with ruthenium red. The flagellar necklace appears as a special domain containing several intramembranous particles (asterisk) and thin surface projections (arrows). Bars, 100 and 200 nm, respectively. After De Souza et al. [25].