CHAPTER 4

Role of the gp85/Trans-Sialidase Superfamily of Glycoproteins in the Interaction of Trypanosoma cruzi with Host Structures

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Abstract

Invasion of mammalian cells by T. cruzi trypomastigotes is a multi-step and complex process involving several adhesion molecules, signaling events and proteolytic activities. From the blood to the cell target in different tissues the parasite has to interact with different cells and the extracellular matrix (ECM). The review focus on the role of the gp85/trans-sialidase superfamily members in the interaction of the parasite with the host cell, particularly with ECM components, with emphasis on the significant variability among the ligands and receptors involved. Use of the SELEX technique to evolve nuclease-resistant RNA aptamers for receptor identification is briefly discussed.

Introduction

The protozoan Trypanosoma cruzi is the etiological agent of Chagas’ disease of major medical significance throughout South to Central America. Chagas’ disease was discovered by Carlos Chagas almost 100 years ago. In 1909, the Brazilian physician described the parasite (Trypanosoma cruzi) in the gut of a bug belonging to the Reduviidae family. Due to the bloodsucking habits of the insect, he hypothesized and demonstrated that the parasite infected different experimental mammals and searched for cases of infection among local inhabitants and their domestic animals. Chagas described the infectivity of the parasite for different mammals, its life cycle in the insect and vertebrate hosts, demonstrated the presence of the parasite in acute cases of the disease and, finally, described the symptoms for the acute and chronic phase of the disease in humans.1 With some modifications, the complex dixenic life cycle (Fig. 1) of the parasite is basically the same as originally described. Some observations on the parasite’s life cycle that have been misinterpreted led Chagas to propose a change of genus to Schyzotrypanum. However, independent experiments conducted by him and others showed that the parasite should indeed belong to the genus Trypanosoma.2 This is one of the few examples in the literature where the parasite and the insect vector were first described, followed by the description of the disease in humans.

The parasite has a complex life cycle characterized by several developmental forms present in vertebrate and invertebrate hosts.3 Based mainly on morphological criteria, such as the spindle shape of the parasite, as well as the position of the kinetoplast (mitochondrial DNA, kDNA)
Trypanosoma cruzi life cycle. Insect vector releases epimastigotes and metacyclic trypomastigotes with feces and urine infecting mammalian hosts through a skin wound or mucosae. After adhesion to the host cell membrane followed by cell invasion, the parasite escapes from the parasitophorous vacuole and replicates in the cytoplasm as amastigotes. Intracellular differentiation from amastigotes to trypomastigotes occurs through intermediate forms, including a characteristic intracellular epimastigote that precedes the differentiation to trypomastigotes. Trypomastigotes that are released into the bloodstream infect new cells or are taken up by the insect vector during a blood meal. In the digestive tract, trypomastigotes differentiate to epimastigotes that replicate and differentiate to metacyclic trypomastigotes at the end of the digestive tract. Intermediate forms are also found in the digestive tract.

Relative to the nucleus and the flagellar emergency region, three forms are classically described: (i) amastigotes (greek, \(a\) = without; mastis = whip for flagellum) which are dividing round cells with 2.4—6.5 \(\mu\)m in diameter with a very short flagellum found in the cytoplasm of the vertebrate host cell; (ii) trypomastigotes (trypo = to drill, referring to a property of this cell to attach to glass by one point while making rotatory movements), an infective, flagellated and nondividing form present in vertebrate (blood trypomastigotes) and invertebrate (metacyclic trypomastigotes) hosts; trypomastigotes are spindle-shaped, approximately 18 \(\mu\)m in length (including a 6 \(\mu\)m free flagellum) and 2-3 \(\mu\)m in breadth; (iii) epimastigotes (epi = anterior, from above), an extracellular flagellated, 20-40 \(\mu\)m long and 2-5 \(\mu\)m large, noninfective and dividing stage present typically in the invertebrate host intestine. Trypomastigotes appear in the rectum of the insect as a differentiation product of the epimastigotes. When the insect bites the vertebrate host and initiates blood sucking it concomitantly eliminates in feces and urine the trypomastigotes—in that case called metacyclic trypomastigotes—which are mechanically carried into the wound by the host. Metacyclic means “beyond the cycle” because parasitologists believed that this form was terminal and could not transform into the other forms in