Sialoglycoconjugates in *Trypanosoma cruzi*-Host Cell Interaction: Possible Biological Model – a Review

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A number of glycoconjugates, including glycolipids and glycoproteins, participate in the process of host-cell invasion by Trypanosoma cruzi *and one of the most important carbohydrates involved on this interaction is sialic acid. It is known that parasite trans-sialidase participates with sialic acid in a coordinated fashion in the initial stages of invasion. Given the importance of these sialoglycoconjugates, this review sets out various possible biological models for the interaction between the parasite and mammalian cells that possess a sialylated receptor/ligand system.*

Key words: sialoglycoconjugates – *Trypanosoma cruzi*-host cell – sialic acid – neuraminidase/trans-sialidase – biologicals models

The infection of mammalian cells by *Trypanosoma cruzi* – a process which is of fundamental importance to the life cycle and pathogenicity of this parasite involves interaction between the plasma membranes of both the pathogen and the host cell (Nogueira & Cohn 1976, Alcantara & Brener 1980, Andrews & Colli 1981, Villalta & Kierszenbaum 1985, Boschetti et al. 1987, Capron & Dessaint 1989, De Souza 1989).

This interaction has been studied in several different *in vitro* cell culture systems, using macrophages, fibroblasts, established cell lines and primary culture muscle cells (Dvorak & Hyde 1973, Nogueira & Cohn 1976, Alcantara & Brener 1980, Bertelli & Brener 1980, Henriquez et al. 1981, Zingales et al. 1982, Piras et al. 1983, 1987, Meirelles et al. 1984a, 1986, Zingales & Colli 1985, Araújo-Jorge 1989, Barbosa & Meirelles 1992, Araujo-Jorge et al. 1993). Some of these reports have demonstrated that certain parasite and host cell glycoconjugates, such as glycolipids and glycoproteins, participate in the process of host cell invasion and that the carbohydrate moiety of these molecules is the most likely candidate in this type of interaction (Andrews & Colli 1981, Crane & Dvorak 1982, Zenian & Kierszenbaum 1983, Meirelles et al. 1983, Colli 1984, Villalta & Kierszenbaum 1983, 1984, Araújo Jorge & De Souza 1984, 1986, Zingales & Colli 1985, Barbosa & Meirelles 1992, Vermelho et al. 1992a).

Theoretically, carbohydrates are well suited for specific recognition processes, since monosaccharides possess many hydroxyl groups that can be O-glycosidically linked in both branched and linear arrays (Springer & Lasky 1991).

One of the most important carbohydrates involved in *T. cruzi*-host cell interaction is sialic acid, although the exact nature of the relevant receptor and ligand molecules, both on *T. cruzi* and on the host target cell, has yet to be fully established (Schauer et al. 1983, Souto Padron & De Souza 1985, Pereira, 1990, Couto et al. 1990, Schenkman et al. 1991). The possible role of sialic acid in the interactive process first began to attract investigative attention following the detection of this carbohydrate on the surface of the parasite (Schauer et al. 1983). The known biological functions of sialic acid appeared to make it a leading candidate for involvement in parasite-host cell interaction, and – in general – it was already thought to play a dual role, either masking antigens or acting as a receptor in relation to physiological and pathological agents (Jeanloz & Codington 1975). The role of sialic acid was further clarified by studies that: (a) detected neuraminidase activity in *T. cruzi* (Pereira 1983) and (b) investigated the effects of treatment with neuraminidase and of sialic acid blockage using lectins, on parasite-host cell interactions (Kipnis et al. 1981, Zenian & Kierszenbaum 1983, Meirelles et al. 1984b, Araújo-Jorge & De Souza 1986, 1988, Pereira 1990, Soeiro et al. 1992).

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More recently, it has been shown that a number of molecules involved in the invasion of the target cell by *T. cruzi,* such as the glycoprotein Tc-85 (Couto et al. 1987) and the antigen-Ssp-3 are sialylated (Schenkman et al. 1991).

Given that sialoglycoconjugates have thus been shown to participate in the invasion process, this review sets out various possible biological models for the interaction between the parasite and mammalian cells that possess a sialylated receptor/ligand system.

INVOLVEMENT OF GLYCOCONJUGATES IN *T. CRUZI*-HOST CELL INTERACTION

The majority of the studies on the role played by glycoconjugates in *T. cruzi*-host cell interaction have used indirect carbohydrate detection methods. These procedures include treatment with glycosidases (Villalta & Kierszenbaum 1983, 1984) or lectins (Meirelles et al. 1983, Araújo-Jorge & De Souza 1986, Stiles & Kierszembaum 1986), oxidation with metaperiodate (Araújo-Jorge & De Souza 1984, Pereira 1990), incubation of both cells with monosaccharides or oligosaccharides, or addition of these compounds to the culture medium during interaction (Crane & Dvorak 1982, Araújo-Jorge & De Souza 1984), and inhibition of the glycosylation process using agents such as tunicamycin (Piras et al. 1983, Zingales et al. 1985).

At the ultrastructural level, meanwhile, the involvement of glycoconjugates in the invasion of heart muscle cells by *T. cruzi* has recently been demonstrated by cytochemical studies using both the Thièry technique and other methods that employ colloidal gold and ferritin-lectin complexes (Barbosa & Meirelles 1992, 1993).

The above experiments have shown that a number of carbohydrates – such as galactose, N-acetyl galactosamine, mannose, N-acetyl glucosamine, and the sialic acid component of glycoproteins and glycolipids present on the surface of both the parasite and/or the host cell may participate in the interaction process.

As yet, only a few glycoconjugates have been purified from the parasite, chemically characterized and then tested for their effect on *T. cruzi*-host cell interaction. Preliminary studies have shown that lipopeptidophosphoglycan isolated from epimastigotes (Lederkremer et al. 1976, Previato et al. 1990) has an inhibitory effect on the invasion of macrophages by *T. cruzi* Y strain (Araújo-Jorge & De Souza 1988). In addition, previous incubation of this strain with a glycosphingolipid isolated from epimastigotes (Barreto-Bergter et al. 1985, 1992) has been shown to lead to 80% reduction in the penetration of the parasite into heart muscle cells. Conversely, when administered to *T. cruzi* clone Dm28c, the same treatment induces an increase of 170% in the level of heart muscle cell infection (Vermelho et al. 1992b).

An immunogenic 83 kDa glycoprotein (Gp 83) has been detected on the membrane of *T. cruzi* trypomastigote and has been found to be capable of binding to rat myoblasts (Lima & Villalta 1988, 1989). Addition of Gp 83 to heart myoblast monolayers and treatment of trypomastigotes with anti-Gp 83 monoclonal antibody (MAb4A4) has been shown to inhibit attachment of trypomastigotes to myoblasts (Villalta et al. 1990, 1992). Other glycoproteins with a similar molecular mass (Tc-85) have also been detected (Alves et al. 1986, Boschetti et al. 1987), and these, likewise, have been shown to be involved in parasite adhesion (Abuin et al. 1989). They may, in addition, act as fibronectin receptors (Ouaissi et al. 1984, 1986, Ouaissi 1988, Pereira 1990). Fibronectin (Fn) is a glycoprotein that has been implicated in a wide variety of cellular processes, including cell adhesion (Hynes & Yamada 1982, Ouaissi 1985). This molecule binds to culture and bloodstream *T. cruzi* trypomastigotes and may play a role in parasite-host cell interaction, given that anti-Fn antibodies inhibit internalization of *T. cruzi* (Ouaissi et al. 1986, Peyrol et al. 1987, Pereira 1990).

SIALIC ACID

Indications that sialic acid might be present in *T. cruzi* first came from experiments involving, variously, the use of colloidal iron hydroxide particles, treatment with neuraminidase (Martinez-Palomo et al. 1976) and agglutination induced by lectins (Alves & Colli 1974, Pereira et al. 1980). Following these early studies, N-acetyl and N-glycolil neuraminic acid were detected in *T. cruzi* Y, V, and CL strains by chemical analysis (Schauer et al. 1983).

Subsequently, direct measurement of electrophoretic mobility showed that the parasite surface carries a net negative charge that is altered by treatment with neuraminidase and trypsin and also by the addition of inhibitors of protein synthesis, indicating that sialoglycoproteins and sialoglycolipids are present on the surface of *T. cruzi* (Souto-Padron et al. 1984, Souto-Padron & De Souza 1985, Soeiro et al. 1992).

At the ultrastructural level, moreover, cytochemical studies using cationized ferritin particles capable of binding to anionic sites suggested that sialic acid may participate in the interaction between *T. cruzi* and various types

of host cells such as macrophages and heart muscle cells (Meirelles et al. 1982, 1984a,b, 1986, Soeiro et al. 1991).

Although sialic acid is present on the surface of *T. cruzi*, a number of studies have demonstrated that the parasite is unable to synthesize this carbohydrate: (1) after incubation of the parasite with either [^{3}H] acetate or N-acetyl [^{3}H]-mannosamine, no radioactivity is detectable, indicating that the parasite cannot synthesize sialic acid from these precursors (Schauer et al. 1983); (2) neuraminidase-treated epimastigotes incorporate sialic acid from sialylated compounds such as [^{3}H]-fetuin or sialyllactose in sialoglycoconjugates, but do not incorporate free sialic acid. On the basis of this evidence, the authors suggested that the parasite may possess a surface sialyl transferase, which would explain the transfer of sialyl residues from exogenous donors to *T. cruzi* epimastigotes (Previato et al. 1985); (3) trypomastigotes incubated with [^{3}H]-fetuin produce labeled sialoglycolipids. No radiolabeled sialoglycolipids are detectable after incubation with [^{3}H]-sialic acid (Zingales et al. 1987); (4) it has been shown that a *T. cruzi* trans-sialidase does not utilize cytidine 5'-monophosphate-N-acetyl neuraminic acid as a donor substrate (Schenkman et al. 1991).

The presence of sialic acid in compounds belonging to several classes of glycoconjugates, such as glycolipids and glycoproteins, has now been well established. In *T. cruzi*, sialoglycolipids were detected – following metabolic labeling with [^{3}H] palmitate and tritiated sodium borohydrate – on the surface both of epimastigotes and trypomastigotes (Confalonieri et al. 1983, Couto et al. 1985, Zingales et al. 1987). In addition, two sialoglycoproteins involved in parasite-host cell interaction have been described. One of them is the trypomastigote-specific surface antigen (Ssp-3), whose chemical structure remains unknown although the presence of a sialyl a (2→3) β galactose structure has been established by enzymatic and immunochemical studies (Andrews et al. 1987, Schenkman et al. 1991). The other is Tc-85, a putative fibronectin receptor (Pereira 1990) that contains sialic acid, galactose, mannose, glucose and hexosamine (Couto et al. 1987, 1990).

NEURAMINIDASE/TRANS-SIALIDASE

A number of different studies have detected neuraminidase activity in *T. cruzi*. The enzyme is present in trypomastigote and (at a level that is approximately ten times lower) in epimastigotes, but it is not detectable in amastigotes (Pereira 1983, Harth et al. 1987). The enzyme is anchored to the cell surface by a glycosylphosphatidyl inositol linkage and can be released into culture medium (Rosenberg et al. 1991a). In addition, neuraminidase has been implicated in the pathogenesis of Chagas' disease (Pereira 1983) and has been associated with myotropism of different parasite strains of *T. cruzi*. (Pereira & Hoff 1986).

Chagas' disease is a common cause of congestive heart failure and sudden death. The majority of patients (90-95%) survive the acute phase of the illness and enter the latent phase, in which there are no clinical symptoms. Most patients then progress to the chronic phase, manifested by cardiovascular, digestive and autonomic nervous system disorders. One of the most important cardiovascular diagnostic indicators is palpitation caused by arrhythmia (Rosenbaum & Alvarez 1955, Laranja et al. 1956, Mott & Hagstrom 1965, Iosa et al. 1991).

A number of studies have lent support to the idea of neurogenic pathogenesis in cardioneuropathy and suggest that it is a natural human model of intrinsic denervation of neuronal pathways in the heart (Koberle 1956, Vieira 1968, Oliveira et al. 1985). Sialoglycolipids found in the host cell plasma membrane may be the targets of parasitic neuraminidase activity. These glycoconjugates play important roles in membrane function, particularly in the cardiac conduction system. Iosa et al. (1991) found that cronassial (mixed sialoglycolipids), which has been shown both *in vitro* and *in vivo* to stimulate reinnervation in neuropathies of varying etiologies, significantly reduced arrythmia in chronic patients.

Furthermore, it has been shown that neuraminidase cleaves sialic acid units from mammalian erythrocytes, rat myocardial cells, human endothelial cells and serum glycoproteins (Pereira 1983, Libby et al. 1986, Piras et al. 1987, Previato et al. 1985). These neuraminidase-treated erythrocytes mimic the ageing erythrocytes and are rapidly cleared by the liver and spleen (Csete et al. 1985). In view of these findings, it has been hypothesized that the desialylation of erythrocytes, platelets and lymphocytes may be the cause of the anemia, thrombocytopenia and leukopenia observed in *T. cruzi*-infected mice (Cardoso & Brener 1980, Pereira 1983). In endothelial cells, neuraminidase treatment causes platelet adhesion to the endothelial surface, since it is sialic acid that normally prevents platelet adhesion to the normal vascular endothelium (Libby et al. 1986).

In addition, it has been demonstrated that in myocardial cells, which are highly sialylated,

neuraminidase treatment causes aberrant electrical activity (Woods et al. 1982). In rat myocardial cells, the enzyme also induces an increase in the absortion of calcium (Ca^{++}) into these cells (Frank et al. 1977). Treatment of trypomastigotes with neuraminidase renders them susceptible to complement-mediated lysis, suggesting that the presence of sialic acid on the parasite surface may normally confer resistance to lysis (Kipnis et al. 1981). An 87-93 kDa glycoprotein from m888 and Y strain trypomastigotes exhibits a function analogous to that of a mammalian complement regulatory protein called decay accelerating factor (DAF) (Hall & Joiner 1993).

A number of other possible functions have been associated with neuraminidase. The enzyme may alter parasite-host cell interaction by cleaving sialic acid and decreasing the negative charge in both cells (Springer & Lasky 1991, Katzin et al. 1991, Soeiro et al. 1992), or equally by cleaving sialic acid from glycoproteins and/or glycolipids, it may alter the susceptibility of infected cells to immune functions and other external effectors (Khan et al. 1991).

Treatment of mouse peritoneal macrophages with serum from acutely *T. cruzi*-infected mice has been shown to induce an increase in the capacity of these cells to internalize bloodstream trypomastigotes (Titto & Araújo 1987). Similar results have been obtained following treatment of macrophages with *Clostridium perfringens* neuraminidase (Araújo-Jorge & De Souza 1984) and following treatment of heart muscle cells with *Vibrio cholerae* neuraminidase (Soeiro et al. 1992).

Antibodies against *T. cruzi* neuraminidase (Na) have been used to established two parasite subsets: Na^+ parasites (20-30%) that express neuraminidase and are more infective, and Na^- parasites (70-80%) that do not express this enzyme (Cavallesco & Pereira 1988). Recently, in the light of the biological activities displayed by these antibodies, it has been possible to identify the amino acid sequence within *T. cruzi* neuraminidase that is recognized by them (Prioli et al. 1992). It has also been demonstrated that during exiting from the host cell, trypomastigotes remain Na^+. However, when free in the extracellular environment, the proportion of Na^+ parasites declines to about 20%. These results indicate that neuraminidase is expressed at the time of transformation of amastigotes into trypomastigotes, and, since the majority of the trypomastigotes become Na^- in the extracellular medium, the authors propose that *T. cruzi* neuraminidase could also play a role in the exiting of the parasite from the infected cell (Rosenberg et al. 1991b).

Plasma from uninfected humans has been shown to contain an inhibitor of the neuraminidase expressed by the infective form of *T. cruzi*, namely high density lipoprotein (HDL). When first observed, this lipoprotein was identified as cruzin (Prioli et al. 1987a,b). The specific binding of HDL to the parasite neuraminidase may be used by the parasite to obtain cholesterol in humans and in other mammals (Pereira 1990).

Sialyl-transferase activity in *T. cruzi* was first described by Previato et al. (1985), who reported the occurrence of a transglycosylase reaction leading to the incorporation of sialic acid into epimastigote glycoconjugates, with exogenous sialoglycoconjugates acting as sialic acid donors. Zingales et al. (1987) reported that trypomastigotes possess a similar enzyme, capable of transferring sialic acid from fetuin to parasite glycolipids and to bovine brain gangliosides. Subsequently, a cell surface trans-sialidase which specifically transfers α (2→3) linked sialic acid from host-derived macromolecules to parasites, leading to the formation of Ssp-3 epitope, was also detected (Schenkman et al. 1991, for review see Schenkman & Eichinger 1993).

Recently, Schenkman et al. (1992) reported that there is a structural relationship between the trans-sialidase and the neuraminidase detected in trypomastigotes, and that their activities are coupled. The authors suggest that a single enzyme can catalyze the transfer of sialic acid residues to, or their removal (by hydrolysis) from appropriate oligosaccharide acceptors. The hypothesized reaction starts with the binding of a sialic acid donor, such as siallylactose, fetuin or glycolipid to the enzyme to form an intermediate, followed by one of two alternative pathways: (a) the bound sialic acid may be transferred to an appropriate acceptor, such as lactose; or (b) it may be transferred to water in a hydrolysis reaction (Schenkman et al. 1992, Schenkman & Eichinger 1993, Scudder et al. 1993). Apparently contradictory results have been obtained with respect to the molecular weight of neuraminidase/trans-sialidase. One group of investigators reported molecules ranging in size from 121-220 kDa (Prioli et al. 1990). However, Harth et al. (1987) reported a molecular mass of 69 kDa, and Khan et al. (1991) showed that the 85 kDa surface antigen of *T. cruzi* belongs to a family of sialidases. The enzyme is a member of a gene family named shed acute phase protein (SAPA), that encodes 85 kDa surface antigens specific to the mammalian phase of the *T. cruzi* life cycle. Parodi et al.

(1992) showed that SAPA has neuraminidase and trans-sialidase activity. Schenkman & Carvalho (1992) suggest that neuraminidase/trans-sialidase may belong to a family of *T. cruzi* proteins that contains two antigenically distinct groups: one migrating in sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) as 85 kDa, and the other between 120-220 kDa.

Although most studies on the role of neuraminidase suggest that this enzyme performs an extracellular function, the enzyme has also been associated with the release of intracellular trypomastigotes from the parasitophorous vacuole into the cytoplasm. *T. cruzi* enters host cells via the formation of an acidic vacuole which is subsequently disrupted. In an acidic environment, release of parasite neuraminidase is enhanced and the enzyme is capable of desialylating parasitophorus constituents such as the lysosomal membrane glycoprotein (lgp). The removal of the terminal sialic acid (which contributes to maintaining lysosomal integrity), by parasite neuraminidase, enhances the activity of *T. cruzi* hemolysin (TC Tox). (Hall et al. 1992, Hall & Joiner 1993).

SIALOGLYCOCONJUGATES IN *TRYPANOSOMA CRUZI*- HOST CELL INTERACTION: PROPOSED MODELS

The literature on *T. cruzi*-host cell interaction involves a variety of experimental conditions. It is important to note that the use of different strains, host cells and culture media makes any direct comparison of the results difficult. In spite of this, however, a number of biological models of interaction have been proposed.

One proposed mechanism of interaction is similar to that observed with the influenza virion (Csete et al. 1985). The influenza virus surface is composed of two major glycoproteins: one is an enzyme (neuraminidase) and the other, a lectin (hemagglutinin). Hemagglutinin recognizes host cell sialic acid and adsorbs to the host cell via this receptor, while viral neuraminidase is thought to remove sialic acid from the host prior to its transfer to the virus. *T.cruzi,* like the virus, contains a neuraminidase that could contribute to the pathogenesis of Chagas' disease (see neuraminidase/trans-sialidase section). Given the findings of Crane and Dvorak (1982), pointing to the existence of a receptor on the host cell containing N-acetyl glucosamine, it has been hypothesized that parasite-host cell interaction may be mediated by a parasite lectin-like molecule which binds to this carbohydrate (Katzin & Colli 1983).

In the light of these studies carried out using lectins, enzymes and inhibitors (Zenian & Kierszenbaum 1983, Villalta & Kierzenbaum 1984, Araújo-Jorge & De Souza 1984, 1986, 1988) it has been suggested that when parasite neuraminidase cleaves sialic acid residues, it may expose N-acetyl galactosamine and or galactose receptors on the surface of macrophages (Lee et al. 1988, Kelm & Schauer 1988). Given that *T. cruzi* also possess a sialyltransferase (Previato et al. 1985, Zingales et al. 1987), the parasite itself may be able to sialylate and desialylate its own surface molecules, modulating the exposure of galactose and or N-acetyl galactosamine and consequently its own penetration of the target cell. This theory is compatible with the model shown in Fig. 1. Galactosyl residues on the surface of heart muscle cells (HMC) traced with ferritin-labelled RCA, have been found to migrate to the region of parasite adhesion, and subsequently become internalized along with the parasite. Since galactose binding molecules have been found on the surface of trypomastigotes (Degett et al. 1990), it has recently been proposed that galactosyl residues of HMC may be important components of a putative receptor to which a *T. cruzi* lectin-like molecule(s) and/or soluble multivalent lectin with galactosyl specificity binds prior to the parasite-induced phagocytosis by the host cell (Barbosa & Meirelles 1992, 1993).

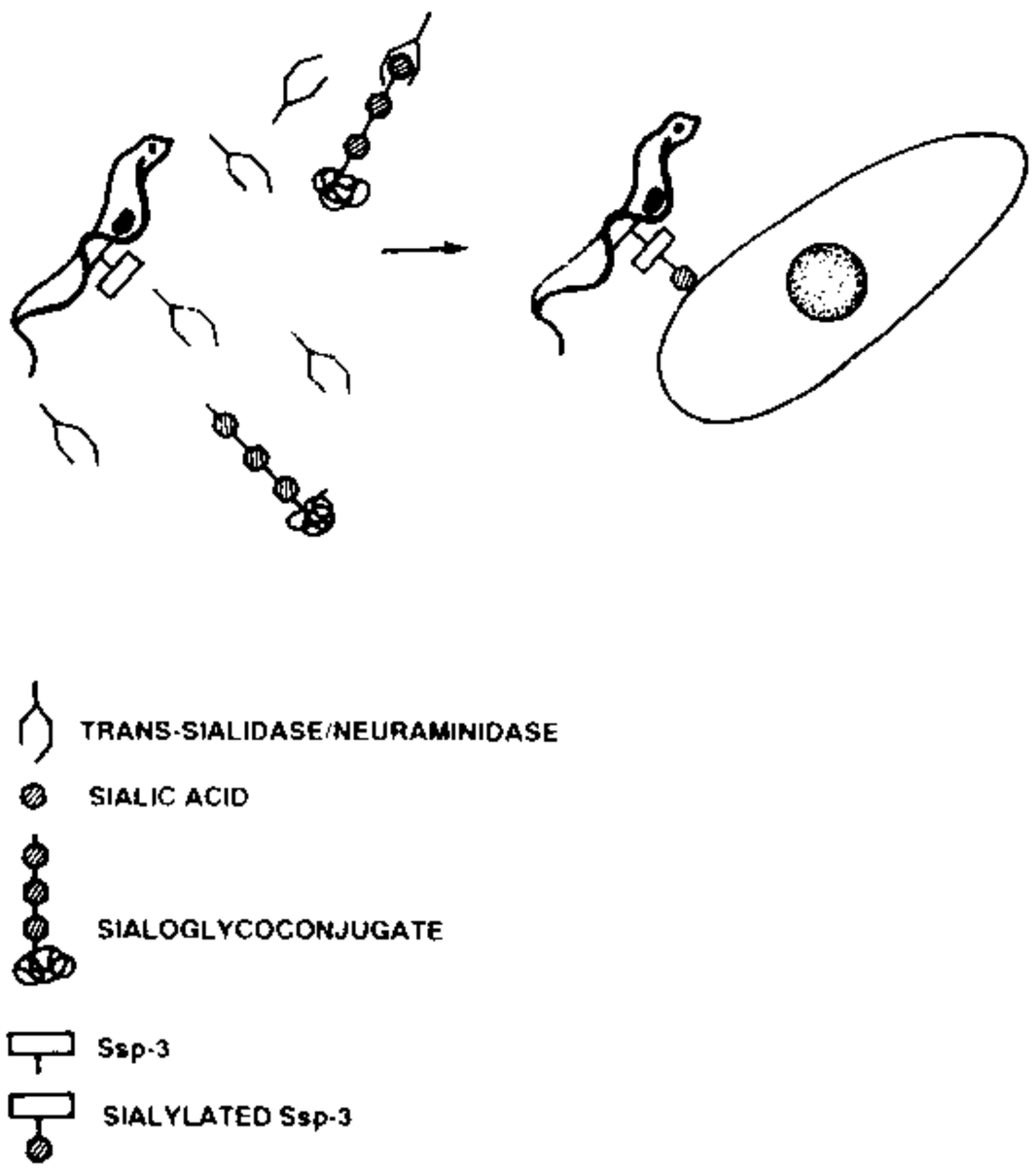

Fig. 1: model of *Trypanosoma cruzi* penetration into mammalian cells mediated by sialylation and desialylation of T. cruzi glycoconjugates. Neuraminidase removes sialic acid from the parasite surface allowing the binding to a galactose acceptor on the host cell.

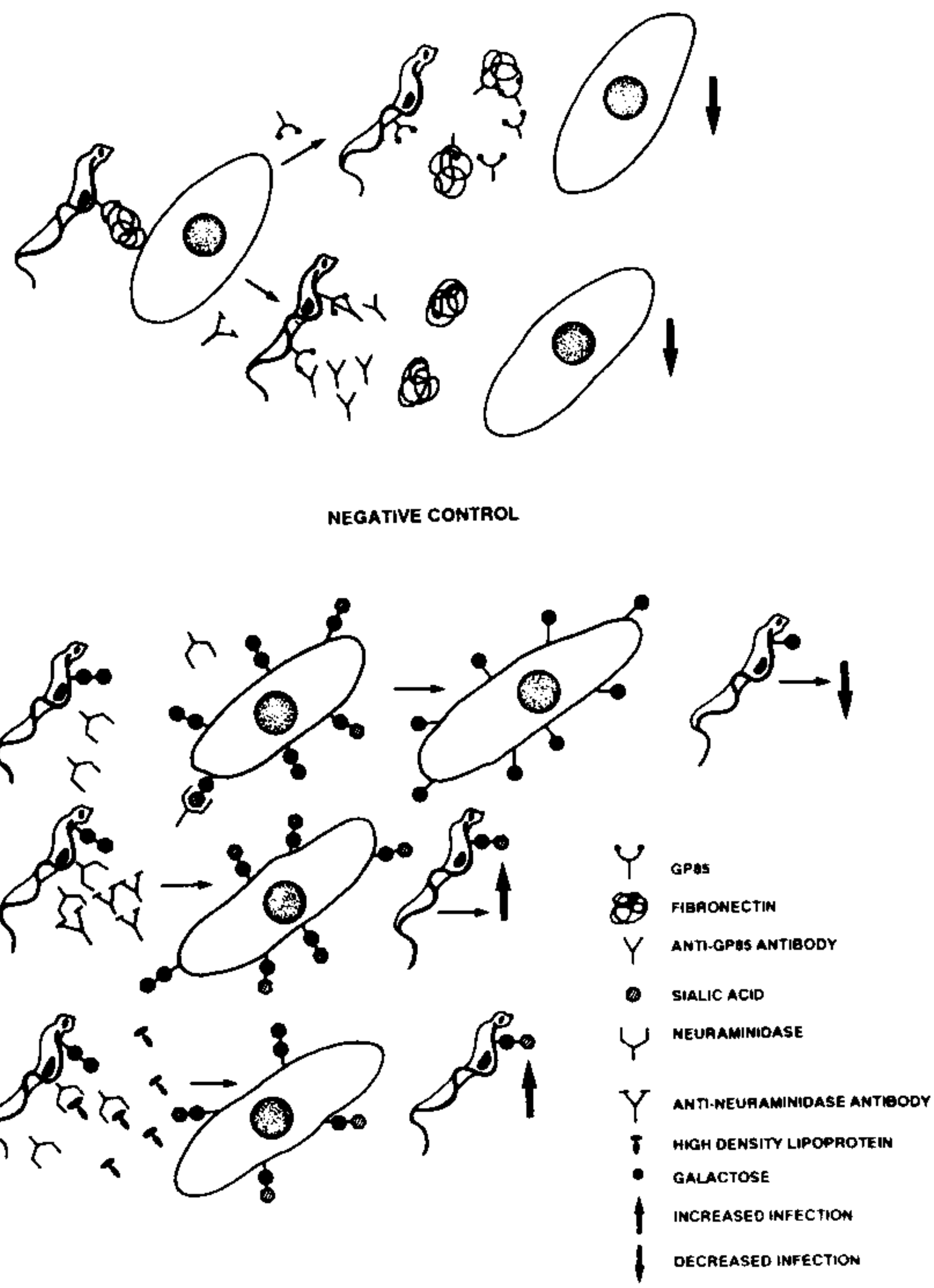

Fig. 2: model of host cell invasion by *Trypanosoma cruzi* modulated by positive and negative controls. The positive control is the sialoglycoprotein Gp85. The binding of the fibronectin to Gp85 allows the attachment of the parasite to the host cell. Neuraminidase acts as a negative control, promoting the desialylation and decreasing the level of infection.

A second model suggested by Pereira (1988, 1990), proposes that the infection process may be modulated by positive and negative control mechanisms (Fig. 2). The positive control mechanism could involve Gp-85 or another possible fibronectin receptor, acting as a ligand when the pathogen binds to the host, thereby promoting infection. Treatment with anti-Gp85 antibodies, or with the purified glycoprotein itself, decreases the level of infection (see the section on involvement of glycoconjugates in *T.cruzi*-host cell interaction). Another possible positive control mechanism involves trans-sialidase activity (Previato et al. 1985, Zingales et al. 1987, Schenkman et al. 1991). This enzyme transfers sialic acid units from sialoglycoconjugates contained in serum to the surface of the parasite, thereby increasing the level of parasite attachment to Vero cells (Piras et al. 1987, Pereira 1990).

There is evidence that neuraminidase may act as a negative control, decreasing the level of infection. Sialic acid, whether on the parasite or on the host cell surface, exhibits a positive effect (Pereira, 1990). Using the chinese ovary cell mutant, lec 2 (which expresses much less

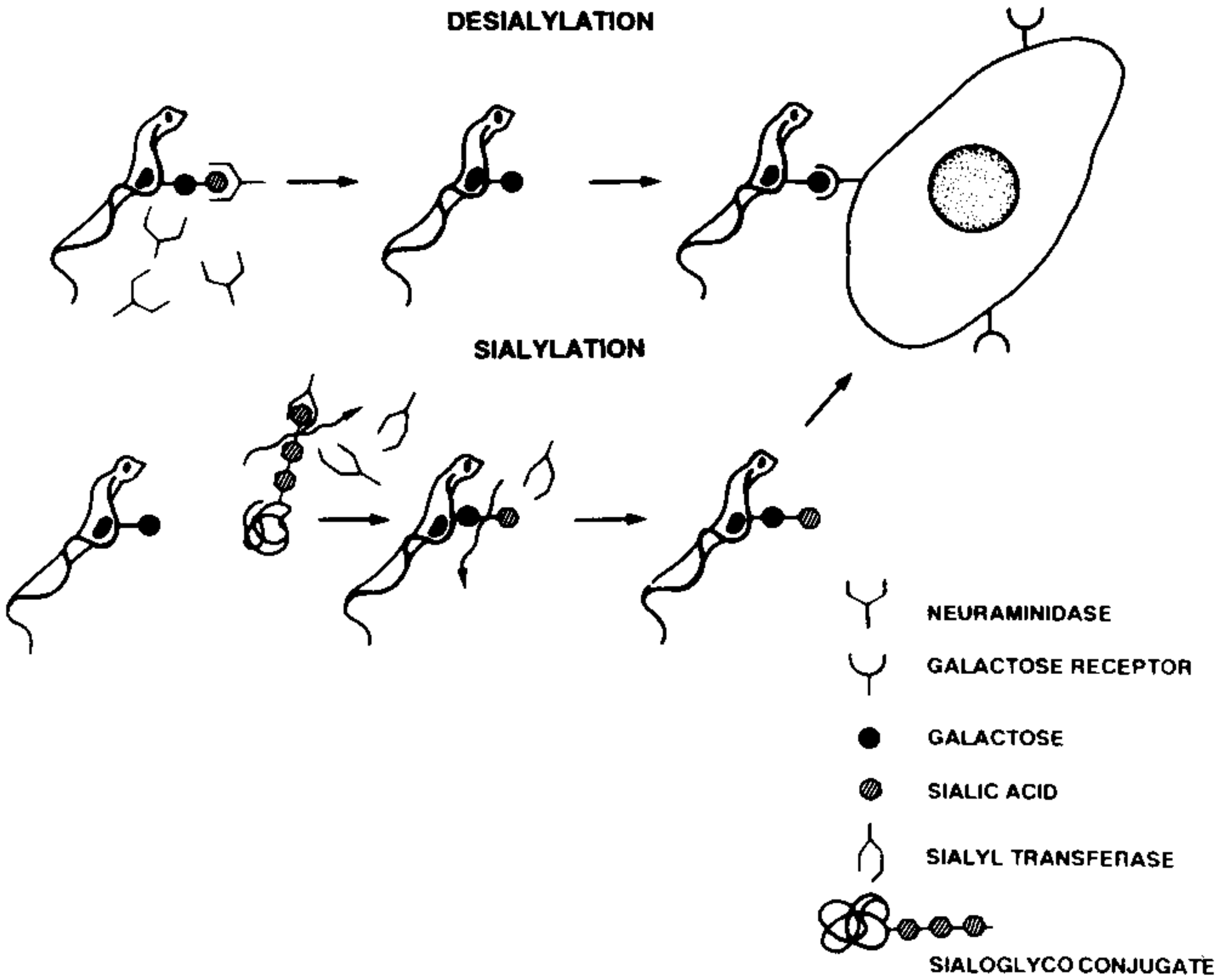

Fig. 3: the sialylation of Ssp3 antigen is associated with the attachment of the *Trypanosoma cruzi* trypomastigotes to host cells and represents an essential step in the process of parasite penetration.

sialic acid than the wild cell type, Pro5) as a target cell for *T.cruzi* invasion, Schenkman et al. (1993a) observed a decrease in parasite invasion. Resialylation of the mutant cells with trans-sialidase and sialyllactose restored invasion to normal levels, suggesting the participation of host cell sialic acid in this process. Similar results were obtained by Ming et al. (1993). Rabbit antibodies against *T.cruzi* neuraminidase when administred at concentrations that inhibit enzyme activity, have been found to promote infection of fibroblasts and smooth muscle cells *in vitro* (Cavallesco & Pereira 1988). The neuraminidase activity is specifically inhibited by high density lipoprotein (HDL). *In vitro,* the addition of HDL to a defined medium augments the ability of the parasite to infect tissue cultures (Prioli et al. 1987, 1990).

Recent studies have shown that when trypomastigotes enter the boodstream, they express a surface trans-sialidase which specifically transfers $\alpha(2\rightarrow3)$-linked sialic acid from host-derived macromolecules to the parasite, leading to the formation of Ssp3, a trypomastigote-specific antigen (Andrews et al. 1987, Schenkman et al. 1991). This antigen appears to be associated with the attachment of trypomastigotes to host cells, since monoclonal antibodies that recognize the sialic acid component of this antigen inhibit the binding of the parasite to the host cell (Schenkman et al. 1991, 1992). These studies have concluded that sialylation of Ssp-3 antigen is an essential step in the process of parasite penetration. Metacyclic trypomastigote do not express the Ssp-3 epitope. The major acceptor of sialic acid in these forms are mucin-like proteins (35-50 kDa). These molecules are linked to the membrane of the parasite by a glycosylphosphatidylinositol anchor (Schenkman et al. 1993b). This model is shown in Fig. 3. Recently, it has been proposed a model of cell invasion of *T. cruzi* into mammalian cells involving sialoadhesins and trans-sialidase (Ortega-Barria & Pereira 1992, Schenkman & Eichinger 1993).

CONCLUDING REMARKS

Trypanosoma cruzi is the causative agent of one of South Americas most important endemic public health problems, Chagas' disease, in which parasite-induced destruction of heart muscle cells leads to heart failure, cardiac blocks and

arrhythmia. Several molecules have been implicated in the invasion of host cells by *T. cruzi* and these molecules participate singly or in concert in various processes that allow the parasite to penetrate and survive in host cells. There is now a general consensus that these molecules can function together in a coordinated series of events that weaken host defense mechanisms. Sialoglycoconjugates, present both in the parasite and in the host cells, may significantly modulate this interactive process and they should therefore be targetted in subsequent research. Since the biochemical basis of these cellular recognition mechanisms is still poorly understood, there is an urgent need for an investigative strategy aimed at identifying and analysing sialoglycoconjugates isolated both from the parasite and from its host cells.

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