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Introduction

The Trypanosomatidae: Amazing Organisms

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Trypanosomatidae, hemoflagellated protists belonging to the order Kinetoplastida, continue to present us peculiar aspects of their biochemistry and molecular biology. In 1985 I reviewed a number of these peculiarities, such as the kinetoplast DNA, the mitochondrial respiratory chain, the glycosomes, and mitochondrial protein synthesis (Opperdoes, 1985), but since that time several new and exciting aspects have been added to the list of oddities characterizing these protists.

The Kinetoplastida must be considered to be representatives of very early eukaryotes. Based on phylogenetic analyses of genes coding for the small subunit ribosomal RNA (Sogin *et al.*, 1986) they represent, together with the Euglenoida, the earliest eukaryotic lineage with both mitochondria and microbodies. This early separation is often seen as the explanation for the fact that these organisms combine so many properties that are unique in nature.

This issue is intended to highlight some of the more striking aspects of the Trypanosomatidae related to energy metabolism and the functioning and biogenesis of the organelles involved therein, such as the mitochondrion and the glycosome. A complete coverage of all peculiar aspects of these intriguing organisms would be impossible and also would be largely outside the scope of *Bioenergetics and Biomembranes*. Therefore a number of reviews have been selected that, at the same time, may give an insight into the exciting world of trypanosome research and present the state of the art of the bioenergetics of this group of organisms.

The order Kinetoplastida comprises the biflagellated Bodonidae and the monoflagellated Trypanosomatidae. The Bodonidae can either be free-living or parasitic, while the known members of the family Trypanosomatidae are all parasitic without exception. The Trypanosomatidae often display complex life cycles involving either one single arthropod host, or both an arthropod and a vertebrate or plant host. They are capable of infecting a variety of organisms including birds, mammals, fish, frogs, insects, and plants. Many of these parasites are of medical and veterinary importance since they infect man and his livestock. Parasites infecting man all belong to two trypanosomatid genera: *Trypanosoma* and *Leishmania*. In sub-Saharan Africa, organisms belonging to the *Trypanosoma brucei* complex (*T. b. brucei, T. b. gambiense* and *T. b. rhodesiense*) and *T. vivax* and *T. congolense* are responsible for nagana in cattle and *T. gambiense* and *T. rhodesiense* cause human sleeping sickness, while *T. cruzi* causes Chagas' disease in humans in Latin America. Leishmaniasis is known in various manifestations such as kala azar, oriental sore, and espundia, and is caused by various species of the genus *Leishmania*. The biochemical peculiarities of the Trypanosomatidae have attracted scientists from many disciplines, not only because a better understanding of the differences between parasite and host may lead to an improved control of these diseases, but also because their study may help elucidate fundamental biological phenomena. For this reason especially the African trypanosome *T. brucei* has now become the "*Escherichia coli*" of biochemical parasitology.

The Trypanosomatidae are characterized by an extreme flexibility of their energy metabolism. This flexibility is imposed upon the organisms by the highly variable environments to which different members of the family and even different stages of the life cycle of one organism had to adapt because of the parasitic life style. The organisms of the *T. brucei* complex are extracellular at all times. They

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survive as epimastigotes and trypomastigotes in the tsetse fly and as trypomastigotes in the bloodstream and tissue fluids of a mammalian host. *Leishmania* spp. survive as promatigotes in the intestinal tract and the proboscis of the sand fly, and as amastigotes in the lysosomal compartment of mammalian macrophages. *T. cruzi* lives as epimastigote in the intestinal tract of triatomine bugs and as amastigote survives and divides in the cytosol of many mammalian cell types. The diversity and adaptability of their energy and intermediary metabolism have been studied in detail and is discussed in this issue in two contributions dealing with respectively, *T. brucei*, *Leishmania*, and *T. cruzi*.

A recent development in the study of the energy metabolism of trypanosmatids is the characterization of proteins involved in metabolite transport in *T. brucei* and in *Leishmania* spp. Such studies are of great importance for the better understanding of how these organisms adapt to the widely varying environmental conditions such as the acidic lysosomal compartment and the mammalian tissue fluids and the mechanisms that provide them access to essential nutrients. Despite the fact that glucose-transporter genes have already been cloned and expressed in heterologous systems, our understanding of the role played by various transporters in the organisms during their different life-cycle stages is still very incomplete. Moreover, a controversy exists as to the presence of active glucose transport in parasites that dwell in the insect gut. A pyruvate transporter, unique to the bloodstream stage of *T. brucei*, and facilitating the very high rate of efflux of this end-product of metabolism without energy conservation, has recently been described. One contribution deals with all of these issues.

The Trypanosomatidae have a single mitochondrion at all stages of their life and cell cycle, whose contribution to the overall ATP generation varies significantly from one member of the trypanosomatid family to another and from one life-cycle stage to another. As a consequence, the contribution of carbohydrate catabolism to the overall energy generation is also highly variable. An extreme situation is encountered in the bloodstream forms of the African trypanosome *T. brucei* where cytochromes and tricarboxylic-acid cycle enzymes are absent altogether. In *T. brucei* glucose serves as the predominant carbon and energy source and metabolic ATP is only obtained via a modified form of the Embden–Meyerhoff–Parnass pathway. The suppression and derepression of mitochondrial metabolism and the regulation of expression of mitochondrial enzymes in the insect and vertebrate stages of *T. brucei* is a fascinating area of research and has led to the discovery of the editing of RNA. Mitochondrial biogenesis, new results in the fascinating area of RNA editing and the properties of the trypanosome F_0F_1-ATPase, are also covered in this volume.

As a consequence of the absence of mitochondrial energy generation in *T. brucei* this organism has a very active glycolytic pathway. In all Trypanosomatidae studied the early enzymes of this pathway are sequestered inside a subcellular organelle. At present the order Kinetoplastida is the only known group of organisms where compartmentation of the glycolytic pathway has been found. This organelle, for which the name "glycosome" has been coined (Opperdoes and Borst, 1977), is a member of the family of microbodies, to which also belong the peroxisomes, present in other eukaryotic cells, and the glyoxysomes, typical of germinating plants. Glycosomes have been found in all members of the Kinetoplastida studied thus far and therefore represent a very primitive trait of these organisms. The high degree of specialization of glycolysis as found in *T. brucei* is considered a late adaptation to a parasitic life style in the mammalian bloodstream. Our present knowledge about the structure and functioning of the glycosome, its biogenesis, and the evolutionary aspects related to the presence of this unique type of organelle are being discussed in two reviews. Also some new and challenging ideas related to the question as to why the Kinetoplastida have chosen compartmentation of the glycolytic pathway inside a separate cellular organelle, while other eukaryotes have chosen another solution, are presented.

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