Localisation of a 3-Hydroxy-3-methylglutaryl-Coenzyme A Reductase in the Mitochondrial Matrix of *Trypanosoma brucei* Procyclics

Norton Heise[§] and Fred R. Opperdoes*

Research Unit for Tropical Diseases, Christian de Duve Institute of Cellular Pathology (ICP), and Laboratory of Biochemistry, Catholic University of Louvain, Av. Hippocrate 74, B-1200 Brussels, Belgium. Fax: +32/2/7626853. E-mail: Opperdoes@trop.ucl.ac.be

* Author for correspondence and reprint requests

Z. Naturforsch. **55 c,** 473–477 (2000); received February 14/March 23, 2000

Trypanosoma brucei, Glycosomes, Mitochondrion, 3-Hydroxy-3-methylglutaryl-coenzyme A Reductase

Contrary to *Leishmania* spp. and *Trypanosoma cruzi*, *Trypanosoma brucei* bloodstream forms do not synthesise their own sterols but take these compounds in the form of cholesterol directly from the mammalian host. However, procyclic insect stages synthesise ergosterol rather than cholesterol. Here the sub-cellular localisation of the first committed enzyme of this pathway of isoprenoid synthesis 3-hydroxy-3-methylglutaryl-coenzyme A reductase in *T. brucei* procyclics (0.9 nmol. min^{-1}. mg^{-1} protein) was carried out using both cell-fractionation by isopycnic centrifugation and digitonin-titration experiments. The majority of the $NADP^+$-linked 3-hydroxy-3-methylglutaryl-coenzyme A reductase is a soluble enzyme present in the mitochondrial matrix with some additional membrane-associated activity in glycosomes and possibly in the endoplasmic reticulum. It is suggested that the active metabolism of threonine and/or leucine as preferred 2-carbon source for the incorporation of acetyl units into lipids and/or sterols in the mitochondrion of *T. brucei* procyclics is the explanation for a high 3-hydroxy-3-methylglutaryl-coenzyme A reductase activity in these protozoan organelles.