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

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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.