Biogenesis of Glycosomes (Microbodies) in the Trypanosomatidae

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ABSTRACT

Glycosomes, the microbodies of Trypanosomatid haemoflagellates, contain several enzymes involved in glucose and glycerol metabolism. Enzymes such as glyceraldehyde-phosphate dehydrogenase, aldolase and glycerol-3-phosphate dehydrogenase are synthesized in the cytosol on free polyribosomes as polypeptides of mature size. They remain in the cytosol with a half-life of 3 min, while in the glycosome the three enzymes turn over with a half-life of less than 1 h. Most glycosomal enzymes have an apparent M_r which is 1 - 5 kDa larger than their homologous counterparts from the cytosol or from other organisms and are highly basic proteins. It is proposed that the topogenic signal responsible for import into the glycosome is integral and consists of unique insertions in the polypeptide chain which give rise to an additional positive charge to the protein.

INTRODUCTION

Glycosomes are the microbodies typical of the members of the family of Trypanosomatidae, protozoan haemoflagellates, parasitic to man and animals[1-3]. Although glycosomes are highly specialised in glycolysis and in general lack any trace of catalase activity they are considered microbodies since they resemble the peroxisomes of other eukaryotic organisms in several respects. They are round or ellipsoid in shape with a diameter of 0.3 µm, they are surrounded by a single membrane, contain an electron-dense matrix and occasionally a crystalloid core[3]. In the highly glucose-dependent bloodstream-form of the African trypanosome Trypanosoma brucei these organelles

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are abundantly present. Two to three hundred glycosomes per cell represent together approximately 4% of the total cellular volume and an equal or even higher percentage of the total protein[3,4]. The nine glycosomal enzymes involved in the conversion of glucose and glycerol into phosphoglycerate represent together more than 90% of the organellar protein[4,5]. In addition to the enzymes of glycolysis and glycerol metabolism[1] enzymes involved in purine salvage[6], pyrimidine biosynthesis[7], carbon-dioxide fixation[8], ether-lipid biosynthesis[9] and beta-oxidation of fatty acids[10] have also been found in glycosomes. No evidence has been found for the presence of DNA in glycosomes[3].

STRUCTURE AND ORGANISATION OF GENES CODING FOR GLYCOLYTIC ENZYMES

Glycolytic enzymes are a class of proteins which are highly conserved throughout evolution. This allowed the identification of the genes coding for several of these enzymes in T. brucei using heterologous probes originating from yeast and mammals. The genes for aldolase, glyceraldehyde-phosphate dehydrogenase (GAPDH), triosephosphate isomerase (TIM) and phosphoglycerate kinase (PGK) have all been identified in the nuclear genome and have each been localised on a different chromosome[11]. Two tandemly linked completely identical genes have been found for the glycosomal GAPDH[12] and aldolase (Michels PAM, unpublished), while for TIM only one gene is present[13]. In the case of PGK three tandemly linked, related but not identical, genes have been described of which two code for the cytosolic (cPGK) and glycosomal (gPGK) isoenzymes, respectively[14]. The function of the third gene is unknown.

SITE OF SYNTHESIS OF GLYCOSOMAL ENZYMES.

Pulse-chase experiments with [^{35}S] methionine, using alive procyclic trypomastigotes of T. brucei followed by subcellular fractionation, has allowed us to study the sequence of events involved in the synthesis of glycosomal enzymes and their subsequent