Biochimica et Biophysica Acta 829 (1985) 377–386
Elsevier

BBA 32232

Molecular size heterogeneity of ferritin in mouse liver

William H. Massover

Department of Anatomy, University of Medicine and Dentistry of New Jersey (UMDNJ)- New Jersey Medical School, 100 Bergen Street, Newark, NJ 07103 (U.S.A.)

(Received November 12th, 1984)

Key words: Ferritin; Isoferritin; Iron metabolism; Heterogeneity; (Mouse liver)

As much as 4% of the total protein in pure liver ferritin from mice with short-term parenteral iron overload produces a minor band migrating anodally to the major (alpha) band of holoferritin with non-denaturing polyacrylamide gel electrophoresis. The components in this minor band and the alpha band have been isolated to purity by preparative electrophoretic fractionation. The protein in the minor band is ferritin, since it contains ferric iron and fulfills defining criteria at the level of biochemistry, immunology and ultrastructure. Native polyacrylamide electrophoresis with pore-size-gradient gels shows that the ferritin molecules in the minor band have a slightly smaller diameter than the holoferritin in the alpha band. Isoelectric focusing reveals that the smaller ferritin has an identical number and range of charge isomers (p*I* 4.9–5.3) as the larger ferritin, but the relative amount of each size class within some isoferritin bands differs. The smaller ferritin molecules are structurally intact and are made from polypeptide subunits with M_r 18000; the larger ferritin molecules have subunits with M_r 22000. The minor species of hepatic ferritin thus has a smaller molecular size because it is made mainly from smaller subunits. No minor electrophoretic band can be detected in liver ferritin obtained from mice with normal iron levels. These results demonstrate that siderosis induces the formation of molecular size polymorphism (macroheterogeneity) in mouse liver ferritin. The new smaller hepatic ferritin could serve to redistribute excess iron into the main storage organs during the early response to iron overload, since it appears to be identical to one of the two types of serum ferritin molecules present in these siderotic mice.

Introduction

The major iron-storage protein, ferritin, plays a key role in iron metabolism by maintaining a reserve supply of this essential metal inside cells [1,2]. Iron is stored in ferritin as a microcrystalline hydrated ferric oxide [3,4]; the mineralized iron is surrounded by an outer protein shell representing a polymerized complex of 24 polypeptide subunits (external diameter = 130 Å) [1,2]. This unique molecular architecture keeps the iron in a soluble and non-toxic state. When confronted with parenteral iron overload (siderosis), the existing population of molecules sequesters increased amounts of iron, and cells are induced to rapidly synthesize and assemble new apoferritin [5,6]. With siderosis, some ferritin is also processed by lysosomes to form the insoluble secondary iron-storage protein, hemosiderin [7].

All unfractionated populations of pure ferritin show a prominent protein heterogeneity, particularly with regard to molecular charge [1,8–10]. Numerous isomeric forms (isoferritins) are normally present in different tissues [8–11], and even within some single types of cells [12,13]. The many charge isomers of ferritin all seem to be heteropolymers made from characteristic proportions of two classes of polypeptide subunits: H-type (M_r 21000), which is prominent in heart ferritin, and L-type (M_r 19000), which is enriched in ferritin