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Nomenclature of fatty acid-binding proteins

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Summary

A variety of designations is currently being used to refer to cellular fatty acid-binding proteins (FABPs). Besides from the use of other general names (e.g. Z protein), confusion mostly arises from the application of various abbreviations and symbols to denote the tissue(s) of origin and cellular localization (cytoplasm, plasma membrane) of a specific FABP. In order to minimize confusion a more unified and rational nomenclature is proposed, which is based on application of the formula X-FABP$_Y$. The prefix X is a capital letter indicating the tissue of greatest abundance, the suffix Y similarly denotes the (sub)cellular localization of the protein. The general and functional name 'fatty acid-binding protein' (FABP) is preferred for the cellular proteins with the property to bind fatty acids, unless future research reveals that the binding of fatty acids is not the primary biological property or physiological role of (some of) these proteins

Introduction

In 1972 Ockner and coworkers [1] discovered a class of mammalian cytoplasmic proteins by their ability to bind *in vitro* long-chain fatty acids, and designated these accordingly as fatty acid-binding proteins (FABP). Subsequent research in several laboratories revealed FABP to be identical to a cytoplasmic anion-binding protein previously identified in liver and called protein A by Ketterer *et al.* [2] and Z protein by Levi *et al.* [3]. In addition, more recently it was established that FABP from liver cytoplasm is identical to heme binding protein [4] and to the mitosis-associated p14 protein [5]. (The identity with sterol and squalene carrier protein (SCP) isolated by Dempsey and coworkers has been discussed elsewhere; see ref. 6.) Conversely, an ileal cytoplasmic protein initially called gastrotropin now appears a distinct fatty acid-binding protein [7]. Although these proteins are currently referred to mostly as FABP, the other above-mentioned names are still also widely used. (The term Z-protein is especially confusing as it also refers to a tetrameric (55 kDa subunits) Z-line component found in chicken striated muscle [8].)

The number of designations used to describe this protein did further increase when the existence of tissue-specific types of FABP and of isoforms of one type became apparent [9]. Moreover, another fatty acid-binding protein, distinct from cytoplasmic FABP, was recently found to be associated with the plasma membrane [10]. The FABPs are generally named after their tissues of greatest abundance, a custom which in itself has hardly caused confusion. However, since the tissues are referred to in different manners, a host of abbreviations and symbols has appeared. For example, the designation H-FABP (or h-FABP) has been used to denote the FABPs both from heart cytoplasm and from liver (hepatic) cytoplasm, as well as from liver plasma membrane. Another common abbreviation for plasma membrane FABP is M-FABP which, however, may also stand for (heart) muscle FABP from cytoplasmic origin.

The existence of this multitude of designations clearly calls for the need of a uniform and prefer-

ably rational nomenclature, especially with respect to abbreviations and symbols used. On the occasion of the First International Workshop on Fatty Acid-Binding Proteins, held in Maastricht, the Netherlands, in September 1989, the problems outlined above were discussed and provisonal agreement was reached on a recommended nomenclature for FABPs.

Subclasses of fatty acid-binding proteins

Each protein that exhibits affinity for the non-covalent binding of long-chain fatty acids can be designated as a fatty acid-binding protein. The best known representative of this class of proteins is serum albumin (68 kDa), which derives its trivial name from a physical appearance similar to that of the earlier known water-soluble proteins found in egg-white and milk (now called ovalbumin and lactalbumin, respectively) (cf. albus, white; albumen, white of egg). The other presently known examples, being those proteins isolated from plasma membranes (40 kDa) and those from cytoplasm (13–15 kDa), have not (yet) been given a trivial name and hence are referred to each as fatty acid-binding protein, thus disclosing their putative main physiological function. For the cytoplasmic FABP other trivial names have been suggested, e.g. lipmodulin [11], but general preference is given to an abbreviated form of a name that expresses the main biological property of the protein. Since the latter is not yet known in much detail [9], the term 'fatty acid-binding protein' is recommended for continued use. However, as soon as more knowledge is obtained on its biological role(s), a revision of the names should be considered. To this end several proposals have already be made, e.g. fatty acyl-L-carnitine binding protein (also abbreviated as FABP) [12], fatty acid-transfer protein (FATP), fatty acid translocase (FAT), and the more general term (cellular) lipid binding protein (LBP) [13]. Similarly, the plasmalemmal FABP is recommended to be renamed (into e.g. fatty acid receptor or fatty acid translocator) only when given rise to by new insights into its nature and physiological significance.

Types and isoforms of cytoplasmic fatty acid-binding proteins

Several cytoplasmic FABP types have now been identified [9, 14] and each is named after the tissue of greatest abundance. Being the product of a separate gene, each FABP type has a distinct amino acid sequence and length (within the range of 120 to 134 residues). FABPs found in the same tissue and differing in only a few amino acid residues are referred to as isoforms within a type [14]. Note that FABPs with identical polypeptide chains but differing in amount and/or type of bound ligands are designated as apo- and holoforms (not isoform) of the protein (with the apo-form being the ligand-free protein).

Suggested nomenclature

To unambiguously indicate the subclass and type of a particular FABP or to give its full biological origin in case of a FABP not earlier described, it is recommended to apply the following formula:

$$X\text{-}FABP_Y$$

in which the prefix X denotes the tissue of origin or of greatest abundance, to be indicated by the first (capital) letter of the regular English name of that tissue, and in which the suffix Y denotes the (sub) cellular localization of the protein (C for cytoplasmic, PM for plasma membrane, MI for mitochondrial, N for nuclear etc.). In practice, a consequent use of these suffixes will be necessary only in texts dealing with more than one subcellular FABP. Capital letters are preferred (i) for analogy, e.g. with the tissue related nomination of creatine kinase isozymes, and (ii) since lower-case letters already have several other meanings for example in cDNA, mRNA, rRNA, cAMP.

In Table 1 the recommended abbreviations are given for the distinct proteins now identified, together with some of the most common other designations used in literature. It should be noted that for the time being heart muscle $FABP_C$ should be abbreviated as $H\text{-}FABP_C$, so that the term M-

$FABP_C$ is reserved for the protein from skeletal muscle. In case the two FABPs appear to be identical the term M(uscle)-$FABP_C$ may be adopted. Gastrotropin could be included in this system, by virtue of its presence in the ileum, as I(leal)-$FABP_C$, but this would require the well-characterized I(ntestinal)-$FABP_C$ to be renamed, e.g. into J(ejunal)-$FABP_C$.

It has also been suggested to include in the above formula a one-letter symbol to indicate the species origin of the protein. However, bearing in mind that clarity and unambiguity are more important than brevity [15], the addition of more symbols should be avoided. Thus, it is recommended to give the full species name preceding the formula.

Since the existence of specific isoforms has not (yet) been found to be a common feature of FABP types, for these no recommendations for terminology are given (cf. ref 14).

Related terminology

The 13–15 kDa FABPs are currently called either cytosolic (or (cyto)soluble) proteins, or cytoplasmic proteins. However, the non-identity of these terms should be kept in mind [16]. The biochemical term 'cytosol' refers to the soluble phase (105,000 × g supernatant) of cell extracts, which contains essentially components of the aqueous cytoplasm (i.e. the interorganelle cytoplasm) of intact cells, but may also contain compounds easily released from other subcellular compartments as well as interstitial components. Above all, 'cytosol' cannot be taken as a subcellular compartment. Therefore, the biological term '(aqueous) cytoplasm' may be recommended for general use, as it can well be applied in most cases, whereas the term 'cytosol' can be applied in a strictly biochemical context only.

Since many of the papers on FABPs deal with studies on their binding properties for fatty acids and derivatives, the reader's attention is also drawn to a proper use of fatty acid nomenclature [17, 18].

Concluding remarks

The existence of at least six (but probably more) distinct types of cytoplasmic FABP (Table 1) makes this subclass of proteins rather unique, but at the same time presents us with the problem of plainly nominating each of them. Analogous issues from related areas of research are scarce. Perhaps the best example is the family of phospholipid transfer proteins, in which individual members ex-

Table 1. Nomenclature of 'fatty acid-binding proteins'[1]

FABP subclass and type[2]	Recommended abbreviation	Other common designations
Cytoplasmic FABP	$FABP_C$	
Liver	L-$FABP_C$	Z, h-FABP
Intestinal mucosa[3]	I-$FABP_C$	g-FABP, i-FABP
Heart muscle	H-$FABP_C$	c-FABP, h-FABP
Adipose tissue	A-$FABP_C$	p422, aP2, a-FABP, ALBP[4]
Brain	B-$FABP_C$	b-FABP
Kidney	K-$FABP_C$	r-FABP
Skeletal muscle[5]	M-$FABP_C$	
Plasma membrane FABP	$FABP_{PM}$	M-FABP, PM-FABP
Liver[5]	L-$FABP_{PM}$	L-FABP, LPM-FABP
Heart[5]	H-$FABP_{PM}$	h-$FABP_{PM}$

[1] Note the hyphen, recommended to facilitate literature searches.
[2] Type denotes the tissue of greatest abundance.
[3] Excluding gastrotropin (see text).
[4] Adipose lipid binding protein.
[5] Identification as a distinct type neither established nor excluded.

hibit a unique preference for specific phospholipids so that the acquired nomenclature is based on this property, e.g. PC-TP stands for phosphatidylcholine-specific transfer protein [19].

The presence of one type of cytoplasmic FABP in more than one tissue, as was found for L-$FABP_C$ and H-$FABP_C$, might make the use of a prefix denoting to a tissue rather irrational. However, since in these two cases the prefix still indicates the tissue of greatest abundance, this custom has met general approval. Hence, for lack of other useful criteria, the distinction on the basis of tissue occurrence was hold on in the formulation of the presently recommended nomenclature. For the same reason, the FABPs associated with mitochondria and nuclei should, for clarity, be designated as $FABP_{MI}$ and $FABP_N$, respectively, unless their presumed identity with $FABP_C$ [14] is confirmed, so that the latter designation may replace these terms.

Recently it was established that L-$FABP_C$ is identical to heme binding protein (HBP) [4] and to the mitosis-associated p14 protein [5]. In addition, functioning of L-$FABP_{PM}$ as a glutamic oxaloacetic transaminase has been suggested [20]. These new findings illustrate that it is not excluded that the principal function of a certain FABP may ultimately appear to be different, whereby its fatty acid-binding property should be regarded as a secondary phenomenon. Obviously, such development would then implicate a change of nomenclature for that particular FABP.

In summary, in this report a recommended nomenclature for fatty acid-binding proteins is presented, which agrees to a large extent with the currently applied terminology (cf. notes on nomenclature in refs. 6, 21 and 22), but in which confusing issues, especially with regard to the use of prefixes and suffixes to denote the origin of the protein, are eliminated. Because of our as yet limited knowledge on the physiological significance of FABPs options for other recommendations are kept open. It is hoped that on an interim basis this more uniform nomenclature may help to minimize confusion and thus to facilitate the exchange of knowledge on this intriguing family of proteins.

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