BIOCHEMICAL LETTERS

A role for repeated 18-amino-acid stretches in the sequence of synapsin I in tubulin binding?

The amino acid sequences of two microtubule associated proteins, MAP2 and τ , have recently been deduced from the analysis of cDNA clones [1,2]. They reveal three repeated stretches in each protein of 18 amino-acid residues. These sequences are not completely identical, but show strong preferences for particular types of amino acid at each position. Synthetic peptides based on these structures bind tubulin and will co-cycle with microtubules through hot/cold cycles [1]. These sequences therefore represent microtubule binding motifs.

The amino acid sequence of another microtubule binding protein, synapsin I, has also recently been published [3]. Synapsin I is a multifunctional protein with binding activities having been reported for spectrin [4], actin [5], intermediate filaments [6] and synaptic vesicles [7] in addition to tubulin [6,8]. Sequence similarities with regions of the spectrin-binding protein 4.1 [9], and the actin-binding proteins villin and profilin [3] have previously been detected. Synapsin I is thought to be responsible for regulating the availability of synaptic vesicles for exocytosis at the nerve ending, and is controlled by multisite phosphorylation: in this context it is of interest to identify active domains in the protein and examine their interplay. In contrast to MAP2 and τ , synapsin will not promote microtubule polymerization, but *in vitro* will induce the formation of microtubule bundles [8]. There are apparently two tubulin-binding sites, one in a globular head domain and the other in an elongated tail [10]. In analysing the cDNA for synapsin, McCaffery & De Genarro [3] found three stretches of the predicted protein sequence in the tail region which

appeared to repeat. The lengths of these repeats appears similar to the microtubule-binding motif of MAP2 and τ . The repeats are shown in Fig. 1. Aligning the sequences reveals some interesting similarities.

In examining these sequences it is immediately apparent that the degree of similarity is very limited, and that identical residues are infrequent. However, in synapsin repeat I, for example, residues at positions 2, 6, 17 and 18 are identical to residues found in MAP2 and/or τ . Allowing conservative substitutions, 8/18, 8/18 and 4/18 are found in repeats I, II and III respectively. The level of similarity is not conclusive, but makes a provocative basis for future experiments.

These similarities between the sequences of synapsin I and MAP2/ τ are intriguing and may point to the convergent evolution of microtubule-binding activities. It will be of interest to produce synthetic peptides based on the synapsin I repeats and investigate whether they do represent true tubulin-binding domains. Do the differences in the 18-amino-acid motif in MAP2/ τ /synapsin account for differences in their activities towards tubulin?

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Position	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	
I	V	R	S	K	I	G	S	T	E	N	L	K	H	Q	P	G	G	G	τ 187–204
II	V	T	S	K	C	G	S	L	G	N	I	H	H	K	P	G	G	G	218–231
III	V	Q	S	K	I	G	S	L	D	N	I	T	H	V	P	G	G	G	250–267
I	V	K	S	K	I	G	S	T	D	N	I	K	Y	Q	P	K	G	G	MAP2 1674–1691
II	V	T	S	K	C	G	S	L	K	N	I	R	H	R	P	G	G	G	1705–1722
III	A	Q	A	K	V	G	S	L	D	N	A	H	H	V	P	G	G	G	1727–1754
I	S	Q	Q	P	A	G	P	P	A	Q	Q	D	P	P	P	Q	G	G	Syn 434–452
II	G	P	Q	R	Q	G	P	P	L	Q	Q	R	P	P	P	Q	G	Q	458–476
III	K	P	Q	L	A	Q	K	P	S	Q	D	V	P	P	P	I	I	A	618–636

Fig. 1. Similarities between the repeating stretches in MAP2, τ and synapsin I (Syn)

Sequence data are taken from [1,2,3]. Identical residues in synapsin I and the MAPs are marked in bold lines, conservative substitutions in fine lines.

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