expression in the gut, so this is not simply a case of the effects of a tissue-specific enhancer.

The analysis of *cis*-acting elements required for the tissue and temporal specificity of gene expression is in its early days. Yet it would be safe to predict that it will be a topic that will dominate discussions at the next Kolymbari meeting, that will take place in 1986. □

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Cell biology

Actin-binding protein evolution

from Thomas D. Pollard

READERS of *Nature* must find the seemingly endless proliferation of actin-binding proteins a bit overwhelming. They might well ask when will it end and how does the paper on page 424 by Maruta *et al.*[1], describing the possible evolutionary origin of *Physarum* capping proteins, fit into the story?

Let us consider first where the field stands and where it might be headed. With some rare exceptions, actin is present in the cytoplasm at concentrations up to several hundred micromolar, higher than that of any other protein. Such concentrations of purified actin would polymerize very rapidly, leaving less than one per cent in monomeric form at physiological salt concentrations. In cells, only part of the actin is polymerized and a repertoire of regulatory proteins appear to govern the time, place and extent of polymerization and to organize the filaments into higher-order structures (see Table). Specific regulatory proteins probably exist for each step in the assembly process, including nucleation, growth at the two ends of the polymer and fragmentation of polymers.

Although more than 60 such actin-binding proteins have been described from various tissues, each passing month makes it clearer that they will eventually all fit into a limited number of families. (The problem, as one wag has put it, is that scientists would rather use each others' toothbrushes than their nomenclature, hence there is usually more than one name for similar proteins.) More importantly, I now feel it is safe to predict that representatives of at least most, and perhaps all, of these families are present in all non-muscle cells. Consequently, information about a new actin-binding protein isolated from *Acanthamoeba*, *Dictyostelium* or *Physarum* (the three favourite 'primitive' cells for such studies) is likely to be informative about homologous proteins in vertebrate cells.

With this in mind, what have we learned from the new work of Maruta *et al.* on *Physarum* capping proteins? The proteins in question are part of a family of Ca^{2+}-sensitive proteins that can both fragment actin filaments and block their 'barbed' (fast-growing) end. (There are three other families of these proteins that bind to the ends of actin filaments; see the Table.) Intriguingly, Maruta *et al.* have found that three actin filament-capping proteins — fragmin[2], Cap 42(a) and Cap 42(b)[3] — share some features with actin itself: all four proteins bind ATP; there is partial cross-reactivity among antibodies to the four proteins; and pairs of the proteins have similar peptide maps. There are equally clear differences: actin and Cap 42(b) bind to DNase I but fragmin and Cap 42(a) do not; there are kinases specific for subsets of these proteins; and nucleotide-binding properties of the proteins differ. The main difference, of course, is that actin polymerizes whereas the capping proteins interfere with this process by blocking the fast-growing end.

The fascinating suggestion of this work is that at least one class of actin-binding proteins has evolved by duplication and modification of the actin gene itself. This idea will have to be substantiated by examining the primary structure of the proteins and their genes but, if true, argues for a clever economy in the evolutionary processes. Perhaps the actin gene has been modified selectively, so that the resulting capping protein has retained the sites used by actin to bind to the end of the filament but has lost (or modified) the sites used by actin to bind the next subunit in the polymer. Such a modified actin would be ideal for capping the end of the polymer.

Have other actin-binding proteins evolved by modification of an actin gene? Although not conclusive, most evidence suggests that they are not related to actin. For example, the sequence information available on profilin[4] and gelsolin[5] reveal no similarity to actin. Fingerprints of profilin, actophorin, capping protein and actin from *Acanthamoeba*[6] are clearly different. Finally, I know of no other case where an antibody to actin-binding proteins cross-reacts with actin; in fact, with the exception of some antibodies to spectrin[7], most antibodies to actin-binding proteins show no reactivity with proteins outside their own class.

The organization of the actin system will be understood only when the catalogue of components is completed and the mechanism of action of each protein has been elucidated in detail. Current work suggests that these mechanisms will be complex. But this will only be the begining, because the actin-binding proteins form a highly interactive regulatory system. Consequently, direct tests at the cellular level will be necessary to assign physiological function. □

Distribution of actin-binding proteins

Class	Families	Subunit MW	Protozoa	Other lower eukaryotes	Vertebrates
Bind actin monomers	**Profilin**	**12–15K**	+	+	+
	Depactin/actophorin	**16–20K**	+	+	+
Bind end of actin filaments	Capping protein	29K + 31K	+	+	+
	Fragmin/severin	40–45K	0	+	+
	Accumentin	65K	0	0	+
	Gelsolin/villin	90–95K	0	0	+
Bind along actin filaments	**Tropomyosin**	**30–40K**	**0**	**0**	+
Cross-link actin filaments to each other	Gelactins	23–38K	+	0	0
	Fascin/fimbrin	55–70K	0	+	+
	α-Actinin	90–100K	+	+	+
	Actin-binding protein/filamin	250K	0	0	+
Cross-link actin filaments to other structures	**Brush border 110K**	**110K**	**0**	**0**	+
	Spectrin	**220–260K**	+	+	+
	Microtubule-associated protein 2	**~260K**	**0**	**0**	+
Myosins	Myosin/myosin-II	175–220K	+	+	+
	Myosin-I	125–130K	+	0	0

Actin-binding proteins are grouped into classes by their established properties and subdivided into families according to physical properties and presumed mechanisms of action. This classification is arbitrary and will probably be modified as more data become available. +, the protein has been identified in these cells; 0, the protein has not yet been identified in these cells (or rarely, for example in the case of tropomyosin in protozoa, the protein has been sought but not found). MW, molecular weight.

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