

## Actin-related Protein Nomenclature and Classification

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**R**ECENTLY several laboratories have discovered genes or cDNAs encoding proteins that are 35–55% identical to conventional actin isoforms. The initial discoveries, largely serendipitous, were unexpected, as for some time it had been thought that actin was a unique protein. These actin-related proteins apparently play profound roles in cells. Those discovered to date have been shown to be essential or important in yeasts (Lees-Miller et al., 1992a; Schwob and Martin, 1992; Muhua et al., 1994; Clark and Meyer, 1994; Harata et al., 1994), and one is known to copolymerize with actin in vivo (Schafer et al., 1994) to form a short, discrete microfilament. The emerging consensus is that there are only a few such proteins, and that they are highly conserved in all eukaryotes, from protozoa to yeasts to mammals.

Functional studies of the actin-related proteins are proceeding rapidly. It was suspected from the time of their initial discovery that actin-related proteins would have distinct cellular roles, for while their similarities to actins are striking, the novel proteins are much less abundant, and in many instances have peptide insertions never found within actin isoforms. Indeed, the best characterized actin-related protein, referred to by various authors as actin-RPV, centractin, *Saccharomyces cerevisiae* Act5 protein, and *S. cerevisiae* Act3 protein (Lees-Miller et al., 1992b; Clark and Meyer, 1992, 1994; Muhua et al., 1994), has been found in vertebrates to form a short filament that facilitates movements of vesicles on microtubules by cytoplasmic dynein (Lees-Miller et al., 1992b; Paschal et al., 1993; Schafer et al., 1994), and in yeast and filamentous fungi to implement mitotic spindle orientation and nuclear migration (Muhua et al., 1994; Clark and Meyer, 1994; Plamann et al., 1994). In *Acanthamoeba*, two different actin-related proteins are found in a complex, four members of which bind to profilin-Sepharose (Machesky et al., 1994). The importance of these actin relatives now seems well established, but much remains to be learned.

In the course of analyzing primary sequences of actin-related proteins from several sources we have noted that

three families are widely distributed. As might be expected, very similar, and in some cases identical, proteins have been given a variety of names. Both the random naming and the fact that actin-related proteins are not designated so as to differentiate them from conventional actins have created confusion within the literature. Therefore, we feel that it is essential to devise a more unifying nomenclature for actin-related proteins, and also to point out the apparent subsets of equivalent proteins defined by us independently using phylogenetic tree analysis programs, such as CLUSTAL V.

We propose designating actin-related proteins with the Arp (actin-related protein) prefix. Of the currently known families, the one that is most similar to conventional actin (~47–56% amino acid identity, small peptide insertions or deletions near threonine 229 of actin) is named Arp1, the next most similar (~47% identity, one peptide insertion near actin alanine 321) would be named Arp2, and the least similar (~35% identity, four peptide insertions near actin histidine 40, glycine 146, valine 247, and alanine 321) Arp3. In the summary below we group the various proteins according to this classification scheme. Identical superscripts designate identical proteins.

Arp1: vertebrate actin-RPV\* (Lees-Miller et al., 1992b), vertebrate centractin\* (Clark and Meyer, 1992), vertebrate  $\beta$ -centractin (Clark et al., 1994), *Drosophila* Arp87C (Fyrberg et al., 1994), *Neurospora* Arp1 (Plamann et al., 1994) *Pneumocystis* Arp1 (Christopher et al., 1994), *Saccharomyces* Act3p\*\* (Clark and Meyer, 1994), *Saccharomyces* Act5p\*\* (Muhua et al., 1994), and *Caenorhabditis* ActB (Waterston, R., D. Helfman, personal communication).

Arp2: *Saccharomyces* Act2p (Schwob and Martin, 1992), *Drosophila* Arp14D (Fyrberg et al., 1994), *Acanthamoeba* 43 kD (Machesky et al., 1994), *Caenorhabditis* ActC (Waterston R., D. Helfman, personal communication), *Dictyostelium* 44 kD (Atkinson, S. J., R. Insall, P. N. Devreotes, and T. Pollard. 1993. *Mol. Biol. Cell.* 4:36a).

Arp3: *Schizosaccharomyces act2*<sup>+</sup> protein (Lees-Miller et al., 1992a), Bovine actin-like protein; actin 2 (Tanaka et al., 1992), *Drosophila* Arp66B (Fyrberg et al., 1994), *Acanthamoeba* 49 kD (Machesky et al., 1994), *Caenorhabditis* ActD (Waterston, R., D. Helfman, personal communication), *Dictyostelium* 44 kD (Atkinson, S. J., R. Insall, P. N. Devreotes, and T. Pollard, 1993. *Mol. Biol. Cell.* 4:36a).

Genes that encode three additional actin-related proteins,

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none of which fit into this classification, have been discovered. Two of them, *Drosophila* Arp13E (Frankel et al., 1994), and a second *Saccharomyces* Act3p (Harata et al., 1994), are more distant relatives of actin, while one of them, *Drosophila* Arp53D (Fyrberg et al., 1994), is more like actins than Arp1-3. Until more is known about the distribution of these three proteins in various organisms, it seems premature to classify them. However, our proposed nomenclature system can accommodate the hypothetical families represented by these proteins as Arp4, 5, 6, etc. Isoforms of family members would be designated as Arp1 $\alpha$ , Arp1 $\beta$ , etc. (Clark et al., 1994).

Finally, we point out that while the Hsc70 protein family and sugar kinases are closely related to actin structurally (Flaherty et al., 1991; Bork et al., 1992), we do not designate members as actin-related proteins because of their limited primary sequence similarity.

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