A state-of-the-Arp structure

As a major component of the cell motility machinery and one of the most abundant proteins in the eukaryotic cell, actin plays an important role in a number of processes, including locomotion, phagocytosis, cell division and axon extension. Actin filaments allow cells to change shape and move about through polymerization of ATP-bound actin at the leading (barbed) end of the filament.

For everything to go smoothly, new barbed ends must be continually generated. This is accomplished through the Arp2/3 complex, a protein assembly containing actin related proteins 2 and 3 along with five other subunits, which nucleates branches on the sides of actin filaments and is responsible in large part for pushing the leading edge forward. The importance of this complex is well established; in addition to its role in cell motility, it is also responsible for the movement of bacterial pathogens such as *Listeria monocytogenes*, which recruit the Arp2/3 complex to help push them around the host cytoplasm. Despite the apparent importance of this complex, the exact mechanism by which it nucleates actin filaments is not completely understood.

As published recently in *Science* (Robinson, R.C., Turbedsky, K. *et al. Science* **294**, 1697–1684; 2001), Thomas D. Pollard and colleagues have solved the 2.0 Å crystal structure of the bovine Arp2/3 complex (left). In addition to confirming the predicted actin-like folds of Arp2 and Arp3 (middle), the structure also provides a detailed picture of the five associated subunits, four of which have novel folds, and the arrangement of all the components within the complex.

The Arp2/3 complex is not active in its isolated state; it requires actin filaments, ATP and certain activating proteins, such as WASps (Wiscott-Aldrich Syndrome proteins), to initiate a new filament. A comparison between the orientation of Arp2 and Arp3 in the structure from Robinson, Turbedsky *et al.* (middle) with that of adjacent actin monomers in a filament (right) suggests why the complex is not active. Although the two Arps are thought to form the first two subunits of the new branch, in the structure they are not oriented in the same way as subunits in an actin filament. In addition, the central cleft in each of the Arps is open, as opposed to in actin where the cleft binds an ATP molecule. The authors propose that ATP binding closes these clefts and that a rigid-body rotation of Arp2 and three other subunits brings the Arps together in an orientation compatible with polymerization. They suggest that other activators of the Arp2/3 complex would also favor this conformation, explaining the coupling between different activation mechanisms.

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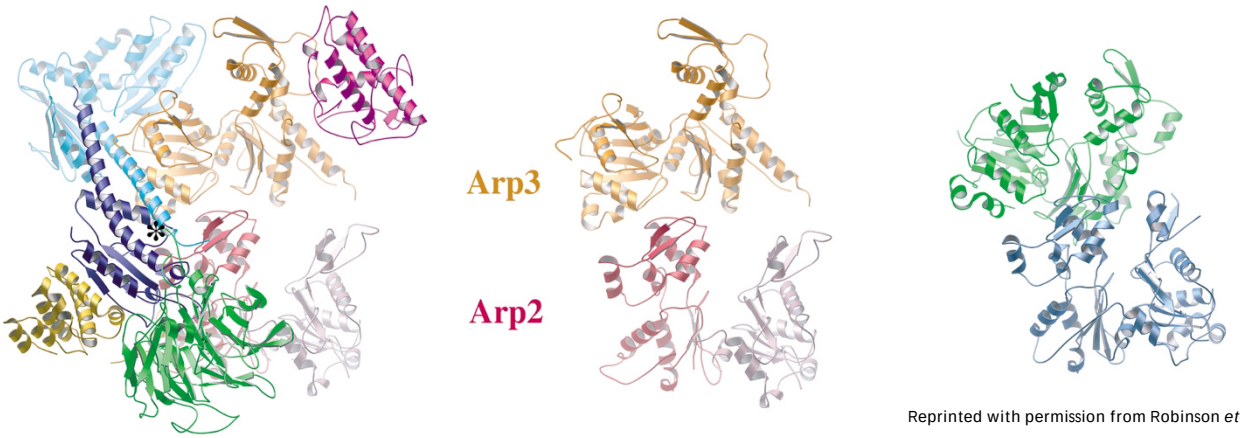

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