Molecular architecture of the Spire-actin nucleus and its implication for actin filament assembly

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The Spire protein is a multifunctional regulator of actin assembly. We studied the structures and properties of Spire-actin complexes by X-ray scattering (SAXS), X-ray crystallography, total internal reflection fluorescence (TIRF) microscopy, and actin polymerization assays. We show that Spire/actin complexes in solution assume a unique, longitudinal-like shape, in which Spire WH2 repeats, in an extended configuration, line-up actins along the long axis of the core of the Spire-actin particle. In the complex, the KIND domain is positioned at the side of the first N-terminal Spire/actin module. In addition, we find that pre-formed, isolated Spire/actin complexes are very efficient nucleators of polymerization and afterwards dissociate from the growing filament. However, under certain conditions, all Spire constructs - even a single WH2 repeat - sequester actin and disrupt existing filaments. This molecular and structural mechanism of actin polymerization by Spire should apply to other actin-binding proteins that contain WH2 domains in tandem.

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