Structural Basis of Actin Filament Nucleation and Processive Capping by a Formin Homology 2 Domain

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The conserved Formin Homology 2 (FH2) domain nucleates actin filaments and caps the filament barbed end in a manner that allows actin monomer addition and loss. Here we report the crystal structure of the Bni1p FH2 domain in complex with tetramethylrhodamine-actin. Each half of the FH2 dimer binds two actins in an orientation that approximates a short-pitch actin dimer, suggesting this structure could function as a template for growth of a new filament. Biochemical properties of heterodimeric FH2 mutants suggest the wild type protein equilibrates between two bound states at the filament barbed end that differentially permit monomer binding and dissociation. Interconversion between these states allows barbed end polymerization and depolymerization in the presence of bound FH2 domain. Kinetic and/or thermodynamic differences in the conformational and binding equilibria can explain the variable activity of different FH2 domains, and the effects of profilin-mediated recruitment of actin on FH2 function.

Keywords: actin filament nucleation, actin binding protein, binding equilibria