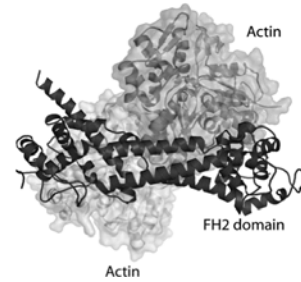


**W0340**

**Structural Basis of Actin Filament Nucleation and Processive Capping by a Formin Homology 2 Domain.** Machius, M., Otomo, T., Tomchick, D.R., Otomo, C., Panchal, S.C., Rosen, M.K., Univ. of Texas Southwestern Medical Center at Dallas, Dallas, TX 75390.

The conserved formin homology 2 (FH2) domain nucleates actin filaments and remains bound to the barbed end of the growing filament. Here we report the crystal structure of the yeast Bni1p FH2 domain in complex with tetramethylrhodamine-actin. This structure represents the first structure of a protein bound to two actin monomers. Each of the two structural units in the FH2 dimer binds two actins in an orientation similar to that in an actin filament, indicating that this structure could function as a filament nucleus. Biochemical properties of heterodimeric FH2 mutants suggest that the wild-type protein equilibrates between two bound states at the barbed end: one permitting monomer binding and the other permitting monomer dissociation. Interconversion between these states allows processive barbed-end polymerization and depolymerization in the presence of bound FH2 domain. Using the structural information combined with the observation of kinetic and/or thermodynamic differences in the conformational and binding equilibria, we have derived a model for actin polymerization that can explain the variable activity of different FH2 domains as well as the effects of the actin-binding protein profilin on FH2 function.



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