

# Uncapping the mystery behind the mechanism of cap removal from actin filaments

July 6 2010

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In this study, Shuichi Takeda at Nagoya University and colleagues present the X-ray crystal structures of the actin capping protein (CP) complexed with its inhibitors, V-1 and CARMIL, and demonstrate that the two regulators modulate the filament capping activity in very different manners. These findings will be published next week in the online, open access journal *PLoS Biology*.

Dynamic rearrangement of actin cytoskeleton structure is fundamental to many cellular processes, such as neuronal development, [immune response](#), and cancer metastasis. CP is a key regulator of actin, capping tightly to the dynamic end of the [filament](#) (the barbed end) to limit elongation. V-1 completely inhibits free CP from interacting with actin, whereas CARMIL acts on the barbed end-bound CP and uncaps the filament. However, the molecular mechanisms by which the two inhibitors modulate the capping activity remain poorly understood.

The new structures clearly indicate that while V-1 directly blocks the actin-binding site of CP preventing filament capping, CARMIL does not. So how does CARMIL uncap the filament? A clue was provided by a structural comparison analysis: CP has two stable domains that are continuously twisting relative to each other. Since CARMIL binds CP across the two domains like a chain, the authors concluded that CARMIL inhibits CP by suppressing the twisting movement required for tight-barbed end capping.

According to the authors, "CP is not a constitutively active inhibitor of barbed-end [elongation](#); rather, the capping activity of CP is fine-tuned for the highly orchestrated assembly of the cellular actin machinery, and the conformational flexibility of CP provides the structural basis for the regulation." The new findings will pave the way for understanding the regulating mechanisms of actin dynamics that drives cell movement.

**More information:** Takeda S, Minakata S, Koike R, Kawahata I, Narita A, et al. (2010) Two Distinct Mechanisms for Actin Capping Protein Regulation-Steric and Allosteric Inhibition. PLoS Biol 8(7): e1000416. [doi:10.1371/journal.pbio.1000416](https://doi.org/10.1371/journal.pbio.1000416)

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