Atomic insights into the genesis of cellular filaments by globular proteins

Michael R. Sawaya[1], Laura McPartland[2], Danielle M. Heller[2], David S. Eisenberg[1], Ann Hochschild[2]

[1]Molecular Biology Institute, Los Angeles, CA 90095, United States of America.

[2]Department of Microbiology and Immunobiology, Harvard Medical School, Boston, MA, United States of America.

Self-assembly of proteins into filaments, such as filaments formed by actin and tubulin, underlies essential cellular processes in all three domains of life. The early emergence of filaments in evolutionary history suggests that filament genesis might be a robust process. Here we describe the fortuitous construction of a GFP fusion protein that self-assembles as fluorescent polar filaments in bacterial cells. Filament formation is achieved by appending as few as 12 residues. Multiple crystal structures reveal a consensus view of the protofilament; each protomer donates an alpha-helical appendage (donor domain) to complement a groove between two successive protomers along the protofilament (acceptor domain). Importantly, this energetically favorable complementation between donor and acceptor domains is unattainable in isolated monomers; it requires the appended helices to assemble into a protofilament. Ample evidence of this "domain coupling" mechanism in nature suggests it could facilitate the evolutionary pathway from globular protein to polar filament, requiring a minimal extension of protein sequence and no significant refolding.