Targeting of actin barbed ends by actin regulators.

Many proteins target barbed ends (see figure below) by inserting a short amphipathic α-helix at the hydrophobic cleft exposed at the barbed face of terminal actin subunits\(^1,\ 2\). This structural motif is present in barbed-end cappers gelsolin, Capping Protein and Eps8, as well as in assembly promoters formin FH2 domain and in WH2 domains. WH2 domains exhibit versatile functions \textit{in vitro}, by binding both G-actin and terminal subunits at barbed ends\(^3\). \textit{In vivo} the strong competition of profilin for G-actin restricts the binding of WH2 domains to filament barbed ends. Spire thus caps barbed ends\(^4,\ 5\), while Ena/VASP\(^6\), BimA\(^7\) and VopF\(^8\) are polymerases that use their WH2 domains to track barbed ends. All members of the WASP protein family also possess one (sometimes two in tandem) WH2 domain (called V) immediately N-terminally adjacent to the Arp2/3 binding CA region in the C-terminal VCA domain, which catalytically branches filaments. The variability of WH2 domains of WASP proteins in number and sequence\(^9,\ 10\) may modulate the strength of their interaction with actin\(^11,\ 12\) and the rate of detachment of the WASP molecule from the branch junction, a key step in the branching cycle\(^13\). Establishing a graded competition between different WASP-Arp2/3 complexes and Capping Proteins, formins, other WH2 domains like VASP, and profilin (Figure 3A, B), provides a specific regulation of branching density in dendritic arrays mediating trafficking, adhesion, or protrusion. Finally profilin also binds barbed ends (see figure below).
References

