Cortactin: An Effector of Cell Propulsion

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Cortactin is involved in invadopodia and podosome formation, and persistent lamellipodia protrusion. Here, we use a biomimetic *in vitro* model system to study the mechanism of cortactin-mediated regulation of actin polymerization-driven motility. We add cortactin to a system that comprises a "motility medium" (actin, Arp2/3 complex, cofilin, profilin and capping proteins) and beads covered with the constitutively active domain of WASP (VCA). Our findings show that cortactin primarily localizes, and distributes homogenously, at the bead surface. We demonstrate that cortactin distribution is affected primarily by VCA and not by the actin network. We also find that cortactin significantly enhances the bead velocity non-monotonously in a concentration dependent manner. Using a simple theoretical analysis we show that the increase in velocity can be explained using a model that consider the reduction in VCA/Actin network binding time by cortactin. In addition, we find that cortactin changes the morphology of the comet tail, apparently by interfering with the cofilin-mediated actin network disassembly. Overall, our data show that even though cortactin alone cannot promote Arp2/3-driven motility, it could strongly augment it, working in concert with VCA at the site where new actin branches are formed, probably by reducing the binding time of VCA and the newly formed branches. This line of reasoning would explain the involvement of cortactin in Arp2/3-dependent actin polymerization processes *in vivo* (as in lamellipodia, invadopodia, and around the vesicles), controlled by WASP and WAVE.