Watching Actin Grow to Help Understand Cancer Metastasis

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Abstract: The actin-associated human protein palladin plays a pivotal role in cytoskeletal organization in normal and cancerous cells. In pancreatic and breast cancer cell lines, palladin expression levels have been shown to correlate with metastatic potential. Previous work established that palladin contributes to actin dynamics by promoting nucleation of actin, crosslink formation, and filament stabilization. Actin polymerization assays have revealed that the Ig3 domain of palladin is involved in the nucleation step of actin polymerization. Bulk fluorescence assays were used to demonstrate that palladin Ig3 increased the polymerization rate of actin; however, the morphology of the filaments and mechanism remain unclear. It should also be noted that bulk assays cannot distinguish between increased nucleation, branching, or elongation. We have turned to total internal reflection fluorescence microscopy (TIRFm) to image individual actin filaments under different conditions to monitor actin polymerization dynamics and topology. This delves into areas of research that have previously been limited in bulk assay experiments and allows for tracking of actin polymerization in different phases: nucleation, early-stage polymerization, and late-stage polymerization. Up to this point, analysis of TIRFm images has been performed manually. Actin polymerized in the presence of palladin results in more crosslinking and suggests that the network morphology of the bundles may also be altered which we will detect and quantify using this technique. Recent work has shown that perturbations to actin polymerization rates can dramatically alter the architecture of crosslinked F-actin networks which could influence the metastatic motility of cancer cells.

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