

THE ROLE OF PALLADIN IN METASTATIC CANCER AS IT AFFECTS ACTIN BINDING, BUNDLING, AND POLYMERIZATION

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The phosphorylation of palladin, a recently discovered actin binding protein, has been shown to play a role in the regulation of cancerous cell motility. The initial discovery of palladin came when it was seen to be upregulated in invasive metastatic cancer cells. Upon isolation of the protein, the C-terminal immunoglobulin (Ig) domains of palladin proved to be those directly involved in its interaction with filamentous actin (F-actin). In the past two years, research has indicated that palladin is regulated by the kinase Akt1, which is involved in inhibiting apoptosis and promoting tumor initiation. Akt1 phosphorylates palladin at a linker region between domains Ig3 and Ig4. Cell-based assays suggest that this phosphorylation event increases the F-actin crosslinking or bundling activity of palladin. The work presented here quantifies this difference between phosphorylated and non-phosphorylated domains through the in vitro assays of F-actin bundling and binding co-sedimentation as well as fluorescence microscopy. Initial work indicates that no difference exists between the wild type and mutants abilities to bind actin. However, our results indicate a detectable difference between the bundling abilities of wild type and phosphorylated Ig34 at low concentrations. These initial results corroborate earlier cell-based findings. Furthermore, studies done under non-polymerizing conditions show that the Ig domains of palladin also induce polymerization of monomeric actin, which is verified by fluorescence microscopy and kinetic assays. This work allows for further understanding of the dynamic actin structure and the role palladin plays, phosphorylated or not, in its regulation within healthy and cancerous cells.