Exploring the Role of Linker Region and Ig4 on the Activity of Palladin Ig34 Tandem Domain

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The protein palladin is a known regulator of the actin cytoskeleton and acts as an actin scaffold due to its ability to bind multiple actin-binding proteins. This grants palladin a key role in regulating actin rearrangement—a key step in cancer metastasis. While the Ig3 domain of palladin confers its actin-binding activity, previous studies have shown that the tandem Ig34 domain has increased actin binding and bundling activity compared to Ig3 alone. While Ig3's activity is known, there is little information on the role of the 34linker region and Ig4 on this enhanced activity. Since other sarcomeric proteins' function have been linked with their linker region length, we created several Ig34 constructs with shortened 34 linker sequences. We also made mutants where the Ig34 linker region or the Ig4 domain was replaced with the Ig45 linker region or Ig5 domain, respectively, to probe the function of both. Our results show that shortening the 34linker region decreases the binding affinity to actin but improves its bundling activity. Also, preliminary results show that replacing the Ig4 domain with Ig5 severely depleted Ig3's ability to bind actin. We hypothesize that Ig5 binds to Ig3 and blocks its actin-binding function, which we hope to prove in future assays. These results will improve our understanding of the role of palladin in actin cytoskeleton dynamics and eventually lead into developing inhibitors of this key step in cancer metastasis.