α -hubs as an example of the utility of hub categorization in signaling research

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Video Byte

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Abstract

The fidelity of cellular signaling is largely dependent upon “hubs” of protein-protein interaction that integrate signals across large intersecting signaling webs. Hub proteins tend to have a high degree of intrinsic disorder, which allows them to interact with an array of differently structured proteins. However, in some cases the hub is structured and interacts with disordered ligands instead. One example is a recently described group of folded hubs, the $\alpha\alpha$ -hubs, which are connected by a shared structural foundation. The $\alpha\alpha$ -hubs are small α -helical domains found in large modular proteins that interact with disordered ligands such as transcription factors. A recent commentary suggests that the harmonin-homology-domain (HHD) belongs to the $\alpha\alpha$ -hub group based on structural analysis. The inclusion of HHD adds several functions to the group, such as telomere regulation and neurovascular integrity. Connecting the $\alpha\alpha$ -hubs as a group allows for greater insight not achievable through single hub analysis. Including HHD as an $\alpha\alpha$ -hub uncovers new features of the group as a whole and highlights how discoveries about one member can aid in the discovery in others.