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PIN1 Provides Dynamic Control of MYC in Response to Extrinsic Signals

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Abstract

PIN1 is a phosphorylation-directed member of the peptidyl-prolyl cis/trans isomerase family that facilitates conformational changes in phosphorylated targets such as c-MYC (MYC). Following signaling events that mediate phosphorylation of MYC at Serine 62, PIN1 establishes structurally distinct pools of MYC through its trans-cis and cis-trans isomerization activity at Proline 63. Through these isomerization steps, PIN1 functionally regulates MYC's stability, the molecular timing of its DNA binding and transcriptional activity, and its subnuclear localization. Recently, our group showed that Serine 62 phosphorylated MYC can associate with the inner basket of the nuclear pore (NP) in a PIN1-dependent manner. The poised euchromatin at the NP basket enables rapid cellular response to environmental signals and cell stress, and PIN1-mediated trafficking of MYC calibrates this response. In my presentation, I will describe the molecular aspects of PIN1 target recognition and PIN1's function in the context of its temporal and spatial regulation of MYC.