
Disrupting P21 activated Kinase 1 and its Substrate Specific Interaction : a Strategy for Drug Design in Cancers

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Abstract

It is widely accepted that signalling kinases play a vital role in Oncogenesis. Kinase Interacting Substrate Screening (KISS) approach is the combination of in vitro protein–protein interaction and mass spectrometry-based phosphoproteomics technology. We utilised this technique to decipher the interacting substrates of a Serine/Threonine kinase - Pak1 (P21 activated kinase 1). Pak1 substrates specific to different subtypes of breast cancers were identified using this novel approach. In this approach, PAK1 knockout cell lysates were used for the pull-down of substrates along with exogenous GST active PAK1 with and without ATP and phosphoproteomics method was used to identify PAK1 specific substrates. Similarly, Co-immunoprecipitation of PAK1 with protein lysates obtained from various types of breast cancer tissues were subjected to phosphoproteomics. These results were further validated with in vitro kinase assay to unearth novel substrates that are cancer specific and we explored disrupting P21 activated Kinase 1 and its Substrate Specific Interaction as a novel strategy for Drug Design in solid tumors.