P21-activated kinase is required for mitotic progression and regulates Plk1.

Abstract:
P21-activated kinases (Paks), a family of serine/threonine kinases, are effectors of the Rho GTPases Cdc42 and Rac1. Mammalian Pak1 and Pak homologs in simple eukaryotes are implicated in controlling G(2)/M transition and/or mitosis. Another serine/threonine kinase, polo-like kinase 1 (Plk1), is an important regulator of mitotic events, such as centrosome maturation, mitotic entry, spindle formation, sister chromatid cohesion and cytokinesis. Plk1 phosphorylation is thought to be one of the critical regulatory events leading to these Plk1-mediated functions. We show here that Pak1 is required for cell proliferation, mitotic progression and Plk1 activity in HeLa cells. Gain or loss of Pak function directly impacted phosphorylation and activity of Plk1. Phosphorylation of Plk1 on Ser 49 is important for metaphase-associated events. Inhibition of Pak activity leads to delay in G(2)/M progression and abnormal spindle formation, mirroring some attributes of Plk1 deregulation. Our results reveal a role for Pak in regulating Plk1 activity and mitotic progression, and connect Pak to the complex protein interaction network enabling cell division.