PAK

p21 activated kinases

PAKs (p21-activated kinases) are a family of six serine/threonine kinases that act as key effectors of RHO family GTPases in mammalian cells. PAKs are subdivided into two groups: group I (PAK1, PAK2, and PAK3) and group II (PAK4, PAK5, and PAK6), based on their domain architecture and regulation. Group I PAKs are activated by GTPases such as Cdc42, Rac, TC10, CHP, and Wrch-1, as well as in a GTPase-independent manner. Group II PAKs are generally not activated by Cdc42/Rac binding. PAK plays important roles in cytoskeletal organization, cellular morphogenesis, and survival, and members of this family have been implicated in many diseases including cancer, infectious diseases, and neurological disorders.

PAKs participate in various signaling networks. PAKs activate the MAPK pathway by phosphorylating Raf1 in addition to NF-κB. PAKs also phosphorylate a number of regulators of the cytoskeleton such as MLCK, LIMK, filamin A, ILK, merlin, and Arpc1b. In addition, PAKs regulate survival and apoptotic pathways through phosphorylation of its effectors such as DLC1 and BimL. On translocation to the nucleus, PAKs directly affect gene transcription. Several transcription factors and transcriptional co-regulators such as FKHR, SHARP, CTBP1 and SNAI1 are substrates to PAK1. PAKs also regulate cell cycle progression through phosphorylation of histone H3, Aurora A and PlK1.