Abstract

Polo-like kinases are important regulators of cell cycle progression and mitosis. They constitute a family of conserved serine/threonine kinases which are highly related in their catalytic domains and contain polo boxes involved in protein-protein interactions and subcellular localization. In mammals, five Plks (Plk 1-5) encompass diverse roles in centrosome dynamics, spindle formation, intra S-phase and G2/M checkpoints and DNA damage response. Plk1 is a key positive regulator of mitosis and is overexpressed in various types of cancers. Plk4 is a divergent member of the Plk family, with essential functions in centriole duplication. Homozygous disruption of Plk1 or Plk4 in mice is lethal in embryos. Two Plk members SmPlk1 and SmSak, homologous to Plk1 and Plk4 respectively, are present in the parasitic platyhelminth Schistosoma mansoni. Structural and functional analyses of SmPlk1 have demonstrated its conserved function in the regulation of cell cycle G2/M transition in Xenopus oocytes. The anti-cancer drug BI 2536 (the most potent and selective Plk1 inhibitor) inhibits specifically the catalytic activity of SmPlk1 and induced profound alterations in schistosome gonads, indicating a role of SmPlk1 in parasite gametogenesis and its potential as a novel chemotherapeutic target against schistosomiasis. Functions of SmSak in cell cycle regulation and schistosome gonad development are currently investigated.

Keywords

Cell cycle, Polo-like kinases, reproduction, Schistosoma mansoni.