題名:Tubulozole-induced G2/M cell cycle arrest in human colon cancer cells through formation of microtubule polymerization mediated by ERK1/2 and Chk1 kinase activation

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摘要:Our studies demonstrated that human colon cancer cells (COLO 205), with higher expression level of check point kinase 1 (Chk1),
were more sensitive to microtubule damage agent Tubulozole (TUBU) induced G2/M phase arrest than normal human colon epithelial
(CRL) cells. TUBU (10 lM, for 3 h) treatment resulted in rapid and sustained phosphorylation of Cdc25C (Ser-216) leading to increased
14-3-3b binding. This resulted in increased nuclear translocation. In addition, TUBU induced phosphorylation of the Cdc25C (Ser-216)
and Bad (Ser-155) proteins were blocked by Chk1 SiRNA-transfection. Surprisingly, cellular apotosis was observed in cells treated with
TUBU after Chk1 SiRNA inhibition. We further demonstrated that extracellular signal-regulated kinase (ERK) activation by TUBU
was needed for Chk1 kinase activation and microtubule formation as shown by the attenuation of these responses by the ERK1/2 specific
inhibitor PD98059. However, TUBU induced ERK1/2 phosphorylation was not blocked in the Chk1 SiRNA-transfected COLO 205
cells. These results imply that ERK1/2 mediated Chk1 activation may be play an important role in determining TUBU induced

G2/M arrest or apoptosis in COLO 205 cells.