

Chk2 (checkpoint kinase 2), a regulatory protein of the cell cycle checkpoints, is coded by CHEK2 gene. Chk2 belongs to serine/threonine kinase family and its dominant activity is in regulation and signal distribution of intracellular response to DNA damage. The upstream regulator of Chk2 protein is the ATM kinase that activates Chk2 by its phosphorylation on Thr68 localized in FHA domain. This in turn leads to the conformation change inducing homodimerization of Chk2 protomers and their activating phosphorylation within their kinase domains. Upon phosphorylation, catalytically active Chk2 protomers dissociate and phosphorylate various intracellular proteins (incl. p53, E2F-1, BRCA1, Cdc25A a C, BRCA2 a PLK3). By regulation of these proteins, Chk2 contributes to the cell cycle arrest, regulation of DNA repair and apoptosis. Germline mutations in CHEK2 gene were identified with the increased frequency in many human cancers, including breast and colorectal cancer. Hence, the failure of Chk2 intracellular activity contributes to the process of malignant transformation.