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Novel pan PI3K inhibitor-induced apoptosis in APL cells correlates with suppression of telomerase: an emerging mechanism of action of BKM120

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Abstract

The intertwining between cancer pathogenesis and perturbation of multitude signaling pathways ushered the cancer therapeutic approaches into an unbounded route of targeted therapies. For the nonce and among the plethora of promising inhibitors, intense interest has focused on small molecules targeting different component of PI3K axis. Intrigued by the constant activation of PI3K in leukemia, this study aimed to investigate the effects of BKM120, as the excelled member of pan PI3K inhibitors, in a panel of hematologic malignant cell lines. The resulting data showed that BKM120 exerted a concentration-dependent growth suppressive effect; however, IC_{50} values varied among the tested cells. Our results outlined that the blockage of PI3K in NB4, as the most sensitive cell line, resulted in a caspase-3-dependent apoptosis probably through NFκB-mediated suppression of c-Myc and hTERT. As far we are aware, to date, there have been no reports of BKM120 effect on enzymatic repression of telomerase, and this study