Health Care Current Reviews 2018, Volume 6
DOI: 10.4172/2375-4273-C7-057

New opportunities in hematologic malignancy treatment: Therapeutic application of PI3K inhibitors

Davood Bashash
Shahid Beheshti University of Medical Sciences, Iran

Field of Research: Targeted therapy in cancer

Statement of the Problem: Among signaling pathways involved in the pathogenesis of hematologic malignancies, constitutive activation of phosphatidylinositol 3-kinase (PI3K) has been observed in a high proportion of patients, largely as a result of genetic mutation. Here, we have evaluated and compared the effects of two different classes of PI3K inhibitors, which are currently being tested in clinical trials.

Methodology: To define the effect of the isoform-specific PI3Kδ inhibitor CAL-101 and pan-PI3K inhibitor BKM120 in different types of hematologic malignancies, a panel of cell lines consists of multiple myeloma, acute lymphoblastic leukemia, and acute myeloblastic leukemia were chosen. Cell viability, apoptosis and caspase-3 activity were determined during incubation with either the inhibitors. The molecular mechanism was also evaluated by RQ-PCR and western blot analysis.

Findings: Our results showed that both BKM120 and CAL-101 effectively reduced the cell viability of all malignant cells, independent of the mutational status of PTEN and p53, by causing cell cycle arrest and promoting ROS-mediated apoptosis. Despite favorable cytotoxic effects, we found remarkable differences in the ability of CAL-101 and BKM120. As compared to CAL-101, lower concentrations of BKM120 blocked Akt phosphorylation and caused a more pronounced apoptosis through both p53- and NF-κB-dependent pathways; suggesting that probably complete inhibition of class I PI3K isoforms more effectively abrogates leukemic cell proliferation and survival.

Conclusion & Significance: Our data indicate a potential application for PI3K inhibitors in the treatment of hematologic malignancies, irrespective of the adverse prognostic markers, and support the clinical application of these inhibitors for patients.

d.bashash@sbmu.ac.ir