World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:16, No:05, 2022

Mechanism of Modeling the Level of Bcr-Abl Oncoprotein by Ubiquitin-Proteasome System in Chronic Myeloid Leukemia

Authors : Svitlana Antonenko, Gennady Telegeev

Abstract : Introductive statement: The development of chronic myeloid leukemia (CML) is caused by Bcr-Abl oncoprotein. Modern treatments with tyrosine kinase inhibitors are greatly complicated by the mutational variability of the Bcr-Abl oncoprotein, which causes drug resistance. Therefore, there is an urgent need to develop new approaches to the treatment of the disease, which will allow modeling the level of Bcr-Abl oncoprotein in the cell. Promising in this direction is the identification of proteases that can selectively promote cellular proteolysis of oncoproteins. The aim of the study was to study the effect of the interaction of Bcr-Abl with deubiquitinase USP1 on the level of oncoprotein in CML cells. Methodology: K562 cells were selected for the experiment. Cells were incubated with ML323 inhibitor for 24 hours. Precipitation of endogenous proteins from K562 cell lysate was performed using anti-Bcr-Abl antibodies. Cell lysates and precipitation results were studied by Western blot. Subcellular localization of proteins was studied by immunofluorescence analysis followed by confocal microscopy. The results were analyzed quantitatively and statistically. Major findings: The Bcr-Abl/USP1 protein complex was detected in CML cells, and it was found that inhibition of USP1 deubiquitinating activity by the compound ML323 leads to disruption of this protein complex and a decrease in the level of Bcr-Abl oncoprotein in cells. The interaction of Bcr-Abl with USP1 may result in deubiquitination of the oncoprotein, which disrupts its proteasomal degradation and leads to the accumulation of CML in cells. Conclusion: We believe that the interaction of oncoprotein with USP1 may be one of the prerequisites that contribute to malignant cell transformation due to the deubiquitination of oncoprotein, which leads to its accumulation and disease progression. A correlation was found between the deubiquitinating activity of USP1 and the level of oncoprotein in CML cells. Thus, we identify deubiquitinase USP1 as a promising therapeutic target for the development of a new strategy for the treatment of CML by modulating the level of Bcr-Abl in the cell.

Keywords : chronic myeloid leukemia, Bcr-Abl, USP1, deubiquitination Bcr-Abl, K562 cell
Conference Title : ICLIBC 2022 : International Conference on Leukemia, Immunology and Blood Cells
Conference Location : Istanbul, Türkiye
Conference Dates : May 05-06, 2022