International Conference on "Novel Approaches in Agro-ecology, Forestry, Horticulture, Aquaculture, Animal Biology and Food Sciences for Sustainable Community Development"
(Agro-tech-2017)

Discovery of New Natural Product G9a Inhibitor IN00595 and its Role Autophagy

Suraya Jan[1], Mohd. Ishaq Dar[1] and Syed Sajad Hussain[1]

Indian institute of integrative medicine (IIIM)-CSIR, Jammu

Abstract—*Posttranslational modifications of histones are important in maintaining and regulating genome organization. These modifications include Acetylation, Methylation, Sumolyation and Ubiqutination. These modifications usually occur at lysine residues. Any aberration in these modifications can lead to serious diseases like cancer due to change in 3D genome organization. Targeting of methyltransferases by inhibitors has proved useful for controlling various abnormal states resulting from aberrant methylations. This study was carried out to find an inhibitor against G9a, a methyltransferase. Institutional natural product library comprising 600 compounds was screened by using Enzyme based assay. Seven hits were identified and their IC50 was determined, ranging from 0.4-8µM. Among them, one inhibitor, IN00595 with IC50 of 2.035 µM, impairs the G9a HMTase activity resulting in the reduction of H3K9me2 in cell based assays. Moreover, we showed that inhibition of G9a leads G2/M arrest and autophagy-associated cell death using FACS and western blotting respectively. Together, these results suggest that IN00595 induces autophagy-dependent cell death via G9a dysfunction in PC3 cells. Therefore G9a inhibition can be an effective therapeutic strategy for cancer treatment.*

Keywords*: Posttranslational modifications, Methyltransferase, G9a, autophagy, cancer and genome organization.*

ISBN: 978-93-85822-60-5
Pages No. 72-72