Md Zahid Akhter et al., Transcriptomics, 2:2
http://dx.doi.org/10.4172/2329-8936.S1.003

OMICS International
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International Conference on
Transcriptomics

July 27-29, 2015 Orlando, USA

Selective inhibition of HMGA1 by triplex forming oligonucleotides induce apoptosis in human cervical cancer

Md Zahid Akhter and Moganty R Rajeswari
All India Institute of Medical Sciences, India

High mobility group protein A1 (HMGA1) is a non-histone chromosomal protein also known as 'architectural' transcription factor that facilitates the assembly of 'enhanceosome'. Expression of HMGA1 is elevated in a number of human malignancies, however, is practically absent in healthy adults. In the present study, we made an attempt to inhibit hmga1 expression in cancer by using anti-gene strategy. Two triplex forming oligonucleotides (TFOs), TFO-1 and TFO-2 were chosen to target the promoter region of HMGA1 at positions, -284 to -304 and -2800 to -2826 respectively. Stability of DNA triplexes were characterized using UV-Vis spectroscopy, Circular Dichroic spectroscopy, Isothermal titration and Differential scanning calorimetry and was confirmed by gel retardation assay using -32P [ATP]. Expression analysis of HMGA1 was evaluated in HeLa cells using MTT assay, Flow cytometry, Western blot and RT-PCR. Results reveal a higher binding affinity of TFO-1 to HMGA1 as compared to that of TFO-2 which correlates well with the greater efficacy of TFO-1, both in terms of HMGA1 expression and apoptosis. Further, the combination treatment of TFO-1 and adriamycin illustrates an additive effect on HMGA1 expression. Present results indicate that TFO-mediated inhibition of HMGA1 expression is a promising strategy for the development of novel anticancer therapeutics.

Biography

Md Zahid Akhter has completed his PhD from Department of Biochemistry, All India Institute of Medical Sciences, New Delhi, India in 2014. He is pursuing Post-doctoral studies in Center for Molecular Medicine, National Institute of Immunology, New Delhi, India.

zahidaasim@gmail.com

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