World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:10, No:09, 2016

Oncogenic Role of MicroRNA-346 in Human Non-Small Cell Lung Cancer by Regulation of XPC/ERK/Snail/E-Cadherin Pathway

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Abstract : Determinants of growth and metastasis in cancer remain of great interest to define. MicroRNAs (miRNAs) have frequently emerged as tumor metastatic regulator by acting on multiple signaling pathways. Here, we report the definition of miR-346 as an oncogenic microRNA that facilitates non-small cell lung cancer (NSCLC) cell growth and metastasis. XPC, an important DNA damage recognition factor in nucleotide excision repair was defined as a target for down-regulation by miR-346, functioning through direct interaction with the 3'-UTR of XPC mRNA. Blocking miR-346 by an antagomiR was sufficient to inhibit NSCLC cell growth and metastasis, an effect that could be phenol-copied by RNAi-mediated silencing of XPC. In vivo studies established that miR-346 overexpression was sufficient to promote tumor growth by A549 cells in xenografts mice, relative to control cells. Overall, our results defined miR-346 as an oncogenic miRNA in NSCLC, the levels of which contributed to tumor growth and invasive aggressiveness.

Keywords : microRNA-346, miR-346, XPC, non-small cell lung cancer, oncogenesis
Conference Title : ICCDD 2016 : International Conference on Cancer Drug Designing
Conference Location : Tokyo, Japan
Conference Dates : September 05-06, 2016