

Accepted Manuscript

miR-195 Potentiates the Efficacy of Microtubule-Targeting Agents in Non-Small Cell Lung Cancer

Xiaojie Yu, Yiqiang Zhang, Xiuye Ma, Alexander Pertsemliadis



PII: S0304-3835(18)30268-4

DOI: [10.1016/j.canlet.2018.04.007](https://doi.org/10.1016/j.canlet.2018.04.007)

Reference: CAN 13847

To appear in: *Cancer Letters*

Received Date: 12 January 2018

Revised Date: 30 March 2018

Accepted Date: 7 April 2018

Please cite this article as: X. Yu, Y. Zhang, X. Ma, A. Pertsemliadis, miR-195 Potentiates the Efficacy of Microtubule-Targeting Agents in Non-Small Cell Lung Cancer, *Cancer Letters* (2018), doi: 10.1016/j.canlet.2018.04.007.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

ABSTRACT

Microtubule-targeting agents (MTAs) are widely used for the treatment of non-small cell lung cancer (NSCLC). The response rate is only ~25%, mainly attributable to drug resistance. To identify determinants of resistance in NSCLC, we performed a high-throughput screen using a library of miRNA mimics. Here we report that miR-195 synergizes with MTAs to inhibit the growth of NSCLC cells *in vitro*, that increased expression of miR-195 sensitizes NSCLC cells to MTAs and that repression of miR-195 confers resistance to MTAs. We show that NSCLC tumors over-expressing miR-195 are more sensitive to MTA treatment and that induced expression of miR-195 in NSCLC tumors potentiates the anti-tumor effect of MTAs. Additionally, we demonstrate that miR-195 targets checkpoint kinase 1 (CHEK1) to regulate the response of NSCLC cells to MTAs, that over-expression of CHEK1 contributes to resistance to MTAs and that knock-down of CHEK1 synergizes with MTAs to repress cell growth. Our results highlight the importance of miR-195 in regulating the response of NSCLC cells to MTAs and underline the potential application of miR-195 as a biomarker for response to MTAs, and as a therapeutic adjuvant to MTA treatment.

Download English Version:

<https://daneshyari.com/en/article/8434373>

Download Persian Version:

<https://daneshyari.com/article/8434373>

[Daneshyari.com](https://daneshyari.com)