

Accepted Manuscript

New Compound ChIA-F Induces Autophagy-dependent Anti-cancer Effect *via* Upregulating Sestrin-2 in Human Bladder Cancer

Xiaohui Hua, Jiheng Xu, Xu Deng, Jiawei Xu, Jingxia Li, David Q. Zhu, Junlan Zhu, Honglei Jin, Zhongxian Tian, Haishan Huang, Qin-shi Zhao, Chuanshu Huang



PII: S0304-3835(18)30525-1

DOI: [10.1016/j.canlet.2018.08.013](https://doi.org/10.1016/j.canlet.2018.08.013)

Reference: CAN 14027

To appear in: *Cancer Letters*

Received Date: 1 May 2018

Revised Date: 16 July 2018

Accepted Date: 9 August 2018

Please cite this article as: X. Hua, J. Xu, X. Deng, J. Xu, J. Li, D.Q. Zhu, J. Zhu, H. Jin, Z. Tian, H. Huang, Q.-s. Zhao, C. Huang, New Compound ChIA-F Induces Autophagy-dependent Anti-cancer Effect *via* Upregulating Sestrin-2 in Human Bladder Cancer, *Cancer Letters* (2018), doi: 10.1016/j.canlet.2018.08.013.

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

ChlA-F is a novel conformation-derivative of Cheliensisin A, styryl-lactone isolates that show potent anti-tumor potential *in vivo* and *in vitro*. However, the anti-cancer activity and its potential mechanisms underlying ChlA-F action have never been explored. In the present study, we evaluated the potency of ChlA-F on autophagy-mediated anchorage-independent growth inhibition in human high-grade invasive bladder cancer (BC) cells. We found that ChlA-F treatment significantly inhibited anchorage-independent growth of human BC cells by inducing autophagy in a Sestrin-2 (SESN2)-dependent fashion. Our results revealed that ChlA-F treatment specifically induced SESN2 expression via increasing its transcription and mRNA stability. On one hand, ChlA-F treatment markedly attenuated Dicer protein abundance, in turn abolishing miR-27a maturation and further relieving miR-27a binding directly to SESN2 mRNA 3'UTR, thereby promoting SESN2 mRNA stabilization. On the other hand, ChlA-F treatment promoted Sp1 abundance and consequently mediated SESN2 transcription. These results demonstrate that its activation of the autophagic pathway through specifically promoting SESN2 expression mediates the anti-cancer effect of ChlA-F, which offers insights into the novel anti-cancer effect of ChlA-F on BC, as well as providing therapeutic alternatives against human BC.

Download English Version:

<https://daneshyari.com/en/article/8943848>

Download Persian Version:

<https://daneshyari.com/article/8943848>

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