

Accepted Manuscript

Tetrandrine inhibits deregulated cell cycle in pancreatic cancer cells: Differential regulation of p21^{Cip1/Waf1}, p27^{Kip1} and cyclin D1

Karnika Singh, Qin Dong, Prakash S. TimiriShanmugam, Sweaty Koul, Hari K. Koul



PII: S0304-3835(18)30245-3

DOI: [10.1016/j.canlet.2018.03.042](https://doi.org/10.1016/j.canlet.2018.03.042)

Reference: CAN 13832

To appear in: *Cancer Letters*

Received Date: 25 January 2018

Revised Date: 14 March 2018

Accepted Date: 26 March 2018

Please cite this article as: K. Singh, Q. Dong, P.S. TimiriShanmugam, S. Koul, H.K. Koul, Tetrandrine inhibits deregulated cell cycle in pancreatic cancer cells: Differential regulation of p21^{Cip1/Waf1}, p27^{Kip1} and cyclin D1, *Cancer Letters* (2018), doi: 10.1016/j.canlet.2018.03.042.

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

Current therapies in Pancreatic Cancer (PaCa) are ineffective due to deregulated cell cycle driven by landscape mutations. In this study, we show for the first time that tetrandrine (TET) inhibits proliferation of the PaCa cells and inhibits PaCa tumor growth. TET inhibits cell cycle transition at G1/S boundary. TET increased levels of p21^{Cip1/Waf1} and p27^{Kip1}, had no effect on the levels of CDK4/6 proteins and decreased the levels of cyclin D1 and pRb proteins. TET resulted in changes in mRNA levels of cyclin D1 and p21^{Cip1/Waf1} but had no effect on the mRNA of p27^{Kip1}. We show, for the first time in any system, that TET treatment downregulated Skp2, E3 ligase specific for degradation of p27^{Kip1} during the cell cycle. Taken together our results show, that TET indirectly impairs the activities of CDK4/6 to halt deregulated cell cycle and inhibit PaCa tumor growth. These results suggest that TET may serve, as a novel agent for treatment of PaCa, for which there is no effective cure to date.

Download English Version:

<https://daneshyari.com/en/article/8434483>

Download Persian Version:

<https://daneshyari.com/article/8434483>

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