Accepted Manuscript

Dacomitinib antagonizes multidrug resistance (MDR) in cancer cells by inhibiting the efflux activity of ABCB1 and ABCG2 transporters

Ying-Fang Fan, Wei Zhang, Leli Zeng, Zi-Ning Lei, Chao-Yun Cai, Pranav Gupta, Dong-Hua Yang, Qingbin Cui, Zuo-Dong Qin, Zhe-Sheng Chen, Louis D. Trombetta

PII: S0304-3835(18)30043-0

DOI: 10.1016/j.canlet.2018.01.021

Reference: CAN 13689

To appear in: *Cancer Letters*

Received Date: 15 November 2017

Revised Date: 30 December 2017

Accepted Date: 8 January 2018

Please cite this article as: Y.-F. Fan, W. Zhang, L. Zeng, Z.-N. Lei, C.-Y. Cai, P. Gupta, D.-H. Yang, Q. Cui, Z.-D. Qin, Z.-S. Chen, L.D. Trombetta, Dacomitinib antagonizes multidrug resistance (MDR) in cancer cells by inhibiting the efflux activity of ABCB1 and ABCG2 transporters, *Cancer Letters* (2018), doi: 10.1016/j.canlet.2018.01.021.

Dacomitinib antagonizes multidrug resistance (MDR) in cancer cells by inhibiting the efflux activity of ABCB1 and ABCG2 transporters

Ying-Fang Fan[a,b,1], Wei Zhang[b,c,1], Leli Zeng[b,d], Zi-Ning Lei[b], Chao-Yun Cai[b], Pranav Gupta[b], Dong-Hua Yang[b], Qingbin Cui[b,e], Zuo-Dong Qin[f], Zhe-Sheng Chen[b,*], Louis D. Trombetta[b,*]

[a.] *Department of Hepatobiliary Surgery, Zhujiang Hospital, Southern Medical University, Guangzhou 510282, China*

[b.] *Department of Pharmaceutical Sciences, College of Pharmacy and Health Sciences, St. John's University, Queens, NY 11439, USA*

[c.] *Institute of Plastic Surgery, Weifang Medical University, Weifang, Shandong 261041, China*

[d.] *MOE Key Laboratory of Bioinorganic and Synthetic Chemistry, School of Chemistry, Sun Yat-Sen University, 510275, P. R. China*

[e.] *School of Public Health, Guangzhou Medical University, Guangzhou, Guangdong, 511436, China*

[f.] *College of Chemical and Biological Engineering, Hunan University of Science and Engineering, Yongzhou, Hunan, 425199, China*

Corresponding author. Department of Pharmaceutical Sciences, College of Pharmacy and Health Sciences, St. John's University, Queens, New York, NY 11439, USA. Fax: +1 718 990 1877.

Corresponding author. Department of Pharmaceutical Sciences, College of Pharmacy and Health Sciences, St. John's University, Queens, New York, NY 11439, USA. Fax: +1 718 990 1877.

E-mail addresses: chenz@stjohns.edu(Z.S. Chen.), trombetl@stjohns.edu(L.D. Trombetta).

[1] The first two authors contribute equally to this work.

Abbreviations: MDR, multidrug resistance; ABC, ATP-binding cassette; EGFR, epidermal growth factor receptor; TK, tyrosine kinase; TKI, tyrosine kinase inhibitor

Abstract

The development of multidrug resistance (MDR) to chemotherapy remains a major challenge in the treatment of cancer. Numerous mechanisms have been recognized that cause MDR, but one of the most important mechanisms is overexpression of adenosine triphosphate (ATP)-binding cassette (ABC) transporters, through which the efflux of various anticancer drugs against their concentration gradients is powered by ATP. In recent years, small molecular tyrosine kinase inhibitors (TKIs) have been developed for treatment in various human cancers overexpressing epidermal growth factor receptor (EGFR). At the same time, some TKIs have been shown to be capable of inhibiting ABC transporter-mediated MDR. Dacomitinib