



Letter to editor: confusions about the role of RNF149 in apoptosis and PI3K/AKT signaling

Xiaobin Guo¹ · Qian Yang¹ · Hongxin Yang¹

Received: 30 September 2023 / Accepted: 6 October 2023 / Published online: 20 October 2023
© The Author(s) 2023

Dear Editor,

We read with great interest the article of Zhu et al. [1] titled “RNF149 confers cisplatin resistance in esophageal squamous cell carcinoma via destabilization of PHLPP2 and activating PI3K/AKT signaling” in a recent issue of the journal. In this study, a lot of work has been done on the function and the mechanism of RNF149 in ESCC. However, we have some queries on the article.

Zhu et al. proposed RNF149 overexpression may contribute to apoptosis resistance role in ESCC via activating AKT signaling pathway. The results of Real-time PCR they demonstrated in Fig. 4D are confusing. It is well known that BIM is a pro-apoptotic member of the BCL-2 family, and BCL-2 is an anti-apoptotic member of the same family [2]. While in Zhu’s study, RNA expression levels of BIM and BCL-2 all increased in RNF149 overexpression ESCC cells, and all decreased in RNF149 downregulation cells. XIAP has the anti-apoptotic activity with negatively regulating the activation of caspase 3 [2]. But in Zhu’s study, XIAP decreased in RNF149 overexpression ESCC cells, and increased by downregulation of RNF149. Based on the conclusion of RNF149 producing apoptosis resistance, the results about RNA expression of BIM and XIAP are hard to understand. p27 and p21 are thought to suppress tumor growth and prevent cell cycle progression [3]. However, in Zhu’s study, RNA expression levels of p27 and p21 increased in RNF149 overexpression ESCC cells, and all decreased in RNF149 downregulation cells. The results do not support the conclusion “overexpression or inhibition of RNF149 confers CDDP resistance or sensitivity to ESCC”. In this part, the author proved the influence of RNF149 on expression of AKT downstream genes, but ignored relationship between these genes and apoptosis and cell cycle. This

results in confusions about the role of RNF149 in apoptosis and cell cycle and PI3K/AKT signaling.

Another query is, in Fig. 2B, stably expressed RNF149 and silencing RNF149 caused an increase or decrease in Eca109 cells respectively, while RNF149 protein expression level decreased or increased unexpectedly in RNF149 overexpression or downregulation Kyse510 cells. This may be an error.

Yours Sincerely,

Declarations

Conflict of interest the authors declare that they have no conflicts of interest to disclose.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

1. Zhu J, Tang J, Wu Y, Qiu X, Jin X, Zhang R. RNF149 confers cisplatin resistance in esophageal squamous cell carcinoma via destabilization of PHLPP2 and activating PI3K/AKT signaling. *Med Oncol*. 2023. <https://doi.org/10.1007/s12032-023-02137-z>.
2. Benedito A, Carneiro, Wafik S, El-Deiry. Targeting apoptosis in cancer therapy. *Nat Rev Clin Oncol*. 2020. <https://doi.org/10.1038/s41571-020-0341-y>.
3. Alberto Martín J, Odajima SL, Hunt P, Dubus S, Ortega M, Malumbres. Mariano Barbacid. Cdk2 is dispensable for cell cycle inhibition and tumor suppression mediated by p27(Kip1) and p21(Cip1). *Cancer Cell*. 2005. <https://doi.org/10.1016/j.ccr.2005.05.006>.

✉ Hongxin Yang
ny1882@163.com

¹ Department of pharmacy, Inner Mongolia Autonomous Region People’s Hospital, Hohhot, Inner Mongolia 010017, PR China

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.