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Commentary: Lico A causes ER stress and apoptosis via up-regulating miR-144-3p in human lung cancer cell line H292

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ABSTRACT

Natural compound licochalcone A (lico A), a main constituent of flavonoids, has been proved to induce ER stress and apoptosis in cancer cells. However, the underlying anti-tumor mechanism of lico A remains to be clarified in detail. A recently-published report from the journal Frontiers in Pharmacology evaluated the miRNA-based mechanism for lico A on its anti-cancer effect. They found that lico A significantly promoted the tumor-suppressor miR-144-3p expression, so as to up-regulate ER stress-response protein CHOP (CCAAT/-enhancer-binding protein homologous protein) by down-regulating nuclear factor E2-related factor 2 (Nrf2), finally inducing apoptotic cell death in lung cancer. Their findings pave the path toward a more understanding of miRNA-based drugs for cancer treatment in the future.

A commentary on Lico A causes ER stress and apoptosis via up-regulating miR-144-3p in human lung cancer cell line H292. by Chen G, Ma Y, Jiang Z, Feng Y, Han Y, Tang Y, Zhang J, Ni H, Li X and Li N (2018). Front. Pharmacol. 9:837. doi: 10.3389/fphar.2018.00837.

MicroRNAs (miRNAs) are evolutionarily conserved small non-coding RNAs, playing key roles in many cellular processes, such as development and stress response. Additionally, numerous studies have been collectively showing that miRNAs form central nodal points in cancer development [1]. MiRNAs-based anti-cancer therapeutics is being evaluated, either alone or in combination with current strategies, to improve the curative effect and prognosis in diverse types of malignancies [2]. Recent studies demonstrated that several natural product-

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derived compounds exhibit the promising anti-cancer biological activity through targeting miRNAs and influencing their down-stream signaling pathways [3]. However, more studies towards the miRNA-based mechanism for natural agents are object of intense investigation.

In a recent report, Chen et al. evaluate the detailed functions of miR-144-3p on the anti-cancer effect of lico A, a main constituent of natural flavonoids [4]. By means of a lung cancer-associated miRNAs screen in H292 cells, they found that lico A could significantly promote the expression of tumor-suppressor miR-144-3p, so as to up-regulate CHOP expression, an ER stress-response protein, finally inducing apoptotic cell death. Co-transfection experiments indicated that lico A potentially enhances pre-miR-144 dicing, thus increasing the mature miR-144-3p level. Subsequently, genetic and pharmacological inhibition of miR-144-3p severely interfere the growth inhibitory of cancer cells caused by lico A. Further biochemical tests showed that lico A could impair the expression of nuclear factor E2-related factor 2 (Nrf2), a validated target of miR-144-3p, and its down-stream several signal molecule.

Given higher doses of the drugs can increase response to therapy [5], the authors next evaluate the dose-dependent inhibitory effects of lico A in H292 cells. The mean applied doses of lico A in the high-dose (HD) and low-dose (LD) groups were 40 μM vs. 10 μM, respectively. Comparison of the HD- and LD-groups reveals a greater potential anti-proliferation effect after treatment with HD-lico A. However, HD-lico A could not induced obvious apoptosis as LD-lico A did in H292 cell lines. The reason for this discrepancy might be unclear, but some data suggested that it might be because that pro-apoptosis function mediated by CHOP is well inhibited by HD-lico A. To test such hypothesis, the authors performed a docking analysis and found that HD-lico A could be well docked into the basic region leucinzipper (BRLZ) domain of CHOP protein, consequently prevent its down-stream apoptotic factors from being activated.

To summarize, these data reported by Chen G et al. pave the path toward a more understanding of the roles of miRNAs on the anti-cancer drug lico A. Though further studies are required to establish their specific functions in the clinical setting, new miRNA-based drugs would represent a prospective therapeutic strategy for cancer treatment in the future.

Author contributions

ZJX designed the work. YLY wrote the manuscript. ZCG and ZJX revised the manuscript. All authors reviewed and approved the final version of the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bj.2018.11.002.

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