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Resveratrol repressed viability of U251 cells by miR-21 inhibiting of NF-κB pathway

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Abstract Resveratrol (RSV), a polyphenol, is known to play an important role in inhibiting proliferation and inducing apoptosis of glioma cells. The aim of this study was to explore the mechanism of RSV on U251 cells apoptosis. RSV showed a dose-dependent decrease in U251 cell viability. It could reduce IκB phosphorylation, nuclear P65 protein levels and NF-κB transcriptional activity, which suggested that signaling pathway are involved in RSV-induced apoptosis. In addition, RSV could inhibit miR-21 expression and down-regulation of miR-21 expression could suppress NF-κB activity. Interestingly, over-expression of miR-21 can reverse the effect of RSV on NF-κB activity and apoptosis in U251 cells. These results suggest that RSV can effectively induce apoptosis of U251 cells and modulation of miR-21 possibly contributes to this antitumor action.

Keywords Glioma · Resveratrol · miR-21 · NF-κB · Apoptosis

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Introduction

Glioblastoma (GBM), one of the most malignant brain tumors, is almost always fatal in adults [1]. The conventional strategies for the treatment include surgical resection, radiotherapy, and chemotherapy. For these treatments, the rate of cure and side effects are still unsatisfactory, and the median survival time of patients is no more than 1 year from diagnosis [2]. Therefore, it is urgent to clarify the key mechanism of the apoptosis in glioma cells as well as establishment of the appropriate blocking channels as the proper way to achieve a radical cure for GBM.

Resveratrol (*trans*-3,40,5-trihydroxystilbene, RSV) is an edible polyphenolic phytoalexin present in grapes, peanuts, red wine, and a variety of food sources and can resist numerous age-associated diseases, including cardiovascular disease, Alzheimer, and cancer [3–5]. It has been reported that RSV plays an important role in inhibiting proliferation and inducing apoptosis of glioma cells [6, 7].

MicroRNAs (miRNAs) are a new class of endogenous, non-coding RNAs involved in post-transcriptional gene regulation by binding to a target site in the 3′-UTR of target mRNAs [8]. Recent evidence has revealed that miRNAs may function as regulatory molecules and act as tumor suppressors or oncogenes [9]. One of these microRNAs, miR-21, is overexpressed in GBM cell lines and human GBM tumor tissues, and exerts anti-apoptotic effects by inhibiting expression of LRRFIP1, whose product is an inhibitor of NF-κB signaling [10, 11]. When the expression of miR-21 was down-regulated in human glioma cells, it was showed to reduce cell proliferation both in vitro and in vivo [12].

The transcription factor NF-κB is activated in carcinogenesis, including GBM and NF-κB, may be an important pharmacological target for this disease [13]. Activation of