Celastrol induces apoptosis-mediated cell death in multi-drug resistance human nasopharyngeal cancer cells

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Introduction

Nasopharyngeal carcinoma (NPC) belongs to squamous cell carcinoma that occurs in the epithelial lining of the nasopharynx. Because of the anatomical position close to the cervical lymph node, some patients have a distant metastasis at the time of diagnosis that leads to treatment failure. Although early stages have a high curability and excellent prognosis, advanced NPC urgently requires new drugs developed to reinforce the effectiveness of therapy without noticeable side effects.

Aim

Celastrol, a chemical compound isolated from the root extracts of Tripterygium wilfordii (Thunder god vine) and Celastrus regelii, has been reported to possess anticancer potential. The aim of the present study was to determine the anticancer activity of celastrol and further elucidate the underlying molecular mechanisms.

Materials & Methods

MTT assay

Flow cytometer

Western blot

Results & Discussion

In this study, we first demonstrated that celastrol potently suppressed cell viability in NPC cell lines. Treatment of cells with celastrol induced G2/M arrest and apoptosis (A-D). Further studies showed that celastrol increased the expression of cleaved caspase-3, -8, -9 and subsequently activated apoptosis. Moreover, we found that celastrol-induced activation of Bax, Bim and t-Bid involved in the apoptosis. The expression of anti-apoptotic proteins Bcl-2 was significantly reduced, but expression of Bcl-XL was no significantly change after treatment of celastrol. Celastrol treatment also increased the expression of Fas, DcR2, DR5, RIP and TRADD (E).

Conclusion

The cytotoxic effect of celastrol on MDR-NPC cells is mainly due to apoptosis, mediated by Fas-Fas ligand and mitochondrial pathway. These results suggested that celastrol could be a potential anticancer agent for NPC.

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