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The effect of SIRT3 on CsA induced renal cell apoptosis

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Objectives : Cyclosporine A (CsA), a calcineurin inhibitor, is widely used for organ transplantation and to treat autoimmune diseases. However, long-term therapeutic use of CsA results in chronic nephrotoxicity, which may be related to renal cell apoptosis, but the apoptotic mechanism is still not clear. SIRT3, a mitochondrial deacetylase, protects the mitochondria from oxidative stress by enhancing mitochondrial homeostasis.

Methods : We designed an in vitro study using MDCK cells to describe the effect of SIRT3 on renal cell apoptosis by CsA. For detecting cyclosporine toxicity, MDCK cells were treated with 20 mM CsA, and we observed increased caspase-3 levels in CsA-treated cells.

Results : CsA-treated cells were then transfected with SIRT3, and decreased MDA levels were detected, indicating significant improvement in cell viability. Western blot analysis revealed that the expression of cytochrome C, bax, cleaved-caspase-3 was decreased in cells transfected with SIRT3 than in control cells. Moreover, we measured decreased annexin-V levels by confocal microscopy in cells transfected with SIRT3

Conclusions : In conclusion, the results obtained in this study indicate that SIRT3 may influence the apoptotic mechanism of cyclosporine-induced nephrotoxicity. Further studies need to be conducted to evaluate the in vivo protective effects of SIRT3 on cyclosporine-induced renal cell apoptosis.

Keywords : Cyclosporine A, calcineurin inhibitor, SIRT3, apoptosis