Abstract Type : Poster exhibition
Abstract Submission No.: A-0719
Abstract Topic : Basic Research

Therapeutic effect of Navitoclax through suppression of senescence and fibrosis in diabetic nephropathy model

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Objectives : Diabetic nephropathy (DN), a major complication of diabetes, is recognized as the leading cause of chronic kidney disease. DN induces senescence and epithelial-mesenchymal transition (EMT) in renal tubular epithelial cells, leading to morphological changes such as renal fibrosis. To improve diabetic nephropathy, it is necessary to verify whether anti-senescence therapeutic strategies can effectively attenuate renal injury caused by senescence and EMT. Therefore, we aim to investigate the anti-senescence effects and attenuation of EMT induced by Navitoclax in a streptozotocin (STZ)-induced DN mouse model.
Methods : To establish animal models of DN, C57BL/6 mice were injected with STZ (50 mg/kg) for 5 consecutive days. One week after the final injection, the mice were orally administered Navitoclax (50 mg/kg) for 20 weeks. Tissue sections were blocked and incubation with the following primary antibodies: p53, p21, α-SMA. After incubation, the sections were treated with fluorescent-labeled secondary antibodies and mounted with DAPI for imaging. Proteins were loaded onto SDS-PAGE gels for electrophoresis, followed by immunoblot analysis.
Results : The results showed a reduction in the expression of α-SMA and p53 following Navitoclax treatment. In the DN group, the expression of E-cadherin was reduced; however, Navitoclax treatment increased E-cadherin. Additionally, Navitoclax treatment resulted in decreased p21 expression and increased TUNEL expression. The expression levels of p53, p21, and Bcl-2 were elevated in the DN groups, but they were significantly reduced after Navitoclax treatment.
Conclusions : Navitoclax effectively attenuated EMT in the STZ-induced diabetic nephropathy model through its anti-senescence effects.