Poster Abstracts

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OVEREXPRESSION OF TOLLIP PROVIDES A PROTECTIVE EFFECT ON PARAQUAT-INDUCED ACUTE LUNG INJURY

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Objectives: Toll-interacting protein (Tollip) is an important negative regulatory factor in TLRs/IL-1 R signal transduction pathway, which play an important role in the negative regulation of the inflammatory response. This study was designed to up-regulating Tollip expression by constructing gene recombinant adenoviral vector that carries Tollip gene of mice ,and to investigate the protective effect on paraquat-induced acute lung injury.

Methods: Forty-two SPF C57BL/6J mice, 8-12 weeks old, weighing 20 to 25 g, unlimited male and female, were randomly divided into seven groups(n=6 each): control group, PQ24h group,PQ72h group, PQ + Ad.V24h group, PQ + Ad.V72h group, PQ + Ad.mTollip24h group, PQ + Ad.mTollip72h group. 5×10^8PFU of Ad.mTollip (Ad.mTollip group) or Ad.V (Ad.V group) was injected intratracheally to establish mice Ad.mTollip infection model . Forty-eight hours after intratracheal administration of viruses, mice were injected intraperitoneally with 28 mg/kg PQ to establish acute lung injury model. The mice were sacrificed at 24 and 72 h after PQ challenge. Expression of Tollip in the lungs of mice was observed by using immunohistochemical staining, RT-PCR and Western blot; mice pulmonary histological changes were observed by HE staining and were scored by histopathologic grading; activity of myeloperoxidase was detected; NF-κB transcriptional activity in lungs was detected by EMSA; the level of IL-1β in serum and lung tissue homogenate was detected by ELISA.

Results: Through the immunohistochemistry, Real-time PCR and Western blot, we observed that expression of Tollip decreased and lower than the normal control group in PQ group and PQ+Ad.V group, but expression of Tollip was enhanced obviously ($P < 0.05$) in PQ+Ad.mTollip group compared with those in PQ group and PQ+Ad.V group; and after Ad.mTollip transfection, lung tissue injury in mice reduced, the activity of MPO and NF-κB decreased, the content of IL-1β in serum and lung tissue homogenate decreased in PQ+Ad.mTollip group compared with those in PQ group and PQ+Ad.V group.

Conclusion: Enhancement of Tollip expression in the lungs can reduce inflammation and pulmonary pathological damage in PQ-induced acute lung injury ,and provides a protective effect on PQ-induced ALI in mice.