The regulating affects of receptor interacting protein 3 on retina ganglion cell-5 necroptosis following elevated hydrostatic pressure

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Necroptosis is an important neuronal death mode in retinal ischemia, but the mechanism still needs clarify. RIP3 is characterized as an N-terminal Serine/Threonine kinase, which participates in cell death signaling. Previous studies indicated RIP3 may participate in neuronal necroptosis, and the activation of caspase-8 could cleave RIP3 to inactive form. In the present study, we explored the effects of RIP3 in retinal necroptosis following elevated hydrostatic pressure (EHP) and discussed the possible role of caspase-8 on regulation of RIP3 activity. Necrosis levels detection were repeated with pretreatment of Nec-1 of 24 h to confirm the existence of necroptosis. The expression of RIP3, downstream molecules in the pathway of RIP3-induced necroptosis and necrosis levels of RGC-5 cells were detected by immunoblotting, immunofluorescence and flow cytometry at 6 h, 12 h or 24 h after EHP. Then, RNAi to rip3 was used for further confirming RIP3's effects on retinal necroptosis. Finally, caspase-8 inhibitor and activity peptide were applied to try to unveil the regulated mechanism of RIP3 activity. The results showed that, RIP3 expression was up-regulated and RIP3 enhance-labeled cells were coexisted with PI-positive cells after injury. PI-positive cells were reduced and ratios of necrosis were decreased after injury when treating with Nec-1 and rip3 RNAi. The ROS and PYGL levels in pathway of RIP3-induced necroptosis had been found to be decreased after rip3 knockdown. Caspase-8 inhibitor and activity peptide usage affected ratio of necrosis and levels of ROS or PYGL. Our results indicated RIP3 participated in RGC-5 necroptosis following EHP and caspase-8 may interference RIP3-induced necroptosis.

Biography
Lei Shang has completed his PhD from Central South University. He is the research worker of Hunan Cancer Hospital in the department of Translational Medicine Research, a premier Cancer Research Institute in Central South Region of China. He has published more than 10 papers in reputed journals.

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