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Clonochis sinensis lysophospholipase A upregulates IL-25 expression in macrophages as a potential pathway to liver fibrosis

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Statement of the Problem: Liver fibrosis is an excessive wound-healing reaction requiring the participation of inflammatory cells and hepatic stellate cells (HSCs). The pathogenesis of liver fibrosis caused by viruses and alcohol has well been elaborated, but the molecular mechanisms of *Clonorchis sinensis*-induced liver fibrosis are poorly understood. Lysophospholipase A (LysoPLA) which is characterized as deacylating lysophospholipids plays a critical role in virulence and pathogenesis of parasites and fungi; however, the roles of *C. sinensis* lysophospholipase A (CsLysoPLA) in *C. sinensis* induced liver fibrosis remain unknown.

Methodology & Theoretical Orientation: Mouse macrophage cell line (RAW264.7) was cultured and treated with CsLysoPLA. IL-25 and signaling pathway were detected by quantitative real-time PCR, Western blotting or immunofluorescent staining. Human hepatic stellate cell line (LX-2) was cultured and exposed to IL-25. The activation markers of LX-2 cells were examined with quantitative real-time PCR, Western blotting and immunofluorescent staining. The migration was analyzed by Transwell plate.

Findings: We show that treatment of RAW264.7 cells with CsLysoPLA significantly induced IL-25 expression. The elevation of PKA, B-Raf, and ERK1/2 mRNA levels and phosphorylations of B-Raf and ERK1/2 were detected in CsLysoPLA-stimulated RAW264.7 cells. Whereas, PKA inhibitor H-89 weakened the phosphorylations of B-Raf and ERK1/2 and AKT activator SC79 attenuated the phosphorylation of ERK1/2 in RAW264.7 cells. Both H-89 and SC79 could inhibit IL-25 up-regulation induced by CsLysoPLA. In addition, stimulation of LX-2 cells with IL-25 up-regulated the expression of mesenchymal cell markers including α-smooth muscle actin (α-SMA) and collagen type I (Collagen-I) and promoted migration of the cells.

Conclusion & Significance: Our results propose that CsLysoPLA activates HSC by up-regulation of IL-25 in macrophage through PKA-dependent B-Raf/ERK1/2 pathway and plays a potential promotion role in hepatic fibrosis during the *C. sinensis* infection.

Biography

Yan Huang is currently working in the Department of Parasitology, Zhongshan School of Medicine, Sun Yat-sen University, Guangzhou, China. She has her expertise in genome, functional genomics of *Clonorchis sinensis* (Chinese liver fluke) and pathogenesis of food-borne parasitic diseases.

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