Resveratrol Stimulates the Release of Tumor Necrosis Factor-α, Interleukin-6 and Interleukin-10 By Activated Hepatic Stellate Cells

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Introduction: Hepatic stellate cells (HSC) play an important role in chronic liver injuries. Once activated, HSC greatly contribute to liver fibrosis development. Interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) participate on HSC activation. Oppositely, interleukin-10 (IL-10) has an anti-fibrogenic activity, inducing activated HSC to apoptosis. HSC not only respond to these cytokines but also secrete them, revealing a tightly regulated interaction. Our previous results showed the cytotoxic effects of resveratrol (RSV), a phytoalexin found in red fruits skins, in GRX cells, an activated HSC model. This situation could contribute to liver fibrosis resolution. **Objectives:** In this study, we sought to investigate/explore the RSV effects towards liver fibrosis resolution through the point of view of HSC autocrine signaling. We evaluated the RSV effects (0.1 to 50 µM) in GRX ability on releasing TNF-α, IL-6 and IL-10 in the culture media. We also measured the protein expression of two fibrogenic markers: Colagen-I and α–actin. **Material and Methods:** The GRX cells were treated with 0.1, 1, 10, 50 µM of RSV for 24 or 120 hours. The TNF-α, IL-6 and IL-10 was determined with respective Kit ELISA. The media of last day of culture was used for analysis. Immunocytochemistry for Colagen-I and α-actin protein was performed and image immunofluorescence was quantified using ImageJ.**Results and Discussion**: Our results showed that while resveratrol induced a reduction of IL-6 concentration, the TNF-α and IL-10 concentrations were increased in culture media of GRX cells treated for 24 and 120 hours. Also, RSV induced an increase in protein expression for Colagen-I and α–actin. **Conclusion:** These results reveal a new explanation in the anti-inflammatory effects of resveratrol in HSC and its possible role in autocrine signaling that would contribute to fibrogenic regulation.

Keywords: Hepatic stellate cells, Interleukin-6, interleukin-10, Liver fibrogenesis Resveratrol, tumor necrosis factor-α

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