HMGB1 is as a Key Player in the Pathogenesis of Schistosomiasis Liver Fibrosis

Vicentino, A.R.R.[1], Carneiro, V.C.[1], Santos da Silva, D.A.R[2], Guilherme, R.F[3], Benjamim, C.F.[3], Pyrrho, A.S.[4], Estanislau, J.A.S.G.[5], Pereira, T.A.[6], Lambertucci, J.R.[6], de Oliveira, R.C.[7], Fantappié, M.R.[1*]

[1]Instituto de Bioquímica Médica Leopoldo de Meis, [2]Instituto de Biofísica Carlos Chagas Filho, [3]Departamento de Farmacologia Básica e Clínica, [4]Faculdade de Farmácia, Departamento de Higiene Social e Análise Clínica, Universidade Federal do Rio de Janeiro, Brasil. [5]Instituto de Ciências Biológicas, Departamento de Morfologia, [6]Faculdade de Medicina, Universidade Federal de Minas Gerais, Brasil. [7]Centro de Pesquisas Renné Rachou, Fundação Oswaldo Cruz, Minas Gerais, Brasil.

INTRODUCTION. Schistosomiasis is a chronic hepatic disease caused by *Schistosoma mansoni*. The disease remains a major and neglected health problem in many tropical areas. The adult worms lay hundreds of eggs every day, which causes an intense inflammatory response and subsequent fibrosis that is usually associated with the mortality in schistosomiasis. The inflammatory mediators produced during schistosomiasis activate the Hepatic Stellate Cells (HSC), which play an important role during liver fibrosis. The High-mobility group box 1 (HMGB1) protein was originally identified as a DNA-binding protein that functions as a transcription regulator in somatic cells. Importantly, HMGB1 can be actively secreted into the extracellular milieu acting as multifunctional cytokine that contributes to mediate inflammatory processes, including liver fibrosis. The inhibition of HMGB1 could offer an alternative strategy to the treatment of schistosomiasis. **OBJECTIVE.** Evaluate the role of HMGB1 in the liver fibrosis during schistosomiasis. **METHODS.** Immunohistochemistry, ELISA, Western Blot, Survival Curve. **RESULTS AND DISCUSSION.** We showed for the first time that HMGB1 is increased in the sera of mice and humans infected with schistosomiasis. The inhibition of HMGB1 by the anti-inflammatory drug DIC (4,5 dihydroisoxazole) decreased the levels of HMGB1 in the sera of the infected mice, as well as the inflammatory responses against the eggs deposited in the liver. The pro-fibrotic parameters such as the α-SMA deposition and IL-13 production were also decreased in mice treated with DIC. Most importantly, the HMGB1 inhibition resulted in the survival of schistosome infected mice. **CONCLUSION.** HMGB1 is released from hepatocytes and seems to act as an important mediator of liver fibrosis. HMGB1 could, therefore, be rationalize as a promising therapeutic strategy to treat schistosomiasis.

Key words: schistosomiasis, liver fibrosis and HMGB1.
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