Schistosoma mansoni: Acetylation of SmHMGB1 and its role in inflammation

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The histone acetyltransferases CBP/p300 and PCAF/GCN5 are present in a multiprotein complex and function in concert with a variety of transcriptional factors. These coactivators act as acetyltransferases that acetylate histones and transcriptional factors. HMGB1 is a nonhistone DNA-binding protein that functions as a structural cofactor critical for proper transcriptional regulation in somatic cells. Despite its nuclear function, HMGB1 can also be passively or actively released to the extracellular medium signaling tissue damage or acting as a cytokine, respectively. The actively released protein plays an important role in the immune response activating macrophages, T and B cells, maturating dendritic cells, increasing vascular permeability and adhesion molecules expression. Two histone acetyltransferases from *Schistosoma mansoni* have been characterized: *Sm*CBP1/p300 and *Sm*GCN5. We showed that the HAT catalytic domain of both *Sm*CBP1 (HAT-*Sm*CBP1) and *Sm*GCN5 (HAT-*Sm*GCN5) were sufficient to acetylate *Sm*HMGB1 as well as the truncated proteins lacking its acidic tail and the B domain, only. To evaluate the role of acetylation in *Sm*HMGB1 cell trafficking, we transfected Hela cells with *Sm*HMGB1-GFP and a construct lacking the acid tail (*Sm*HMGB1?C). By fluorescence microscopy, we showed that *Sm*HMGB1 is natively present in the nucleus. However, in cells treated with sodium butyrate (a histone deacetylase inhibitor), SmHMGB1 were mainly found in the cytosol. *Sm*HMGB1?C was found in both, nucleus and cytosol in sodium butyrate-untreated cells. Alternatively, sodium butyrate-treated cells revealed that *Sm*HMGB1?C were found mainly in the cytosol. These findings suggest that acetylation of *Sm*HMGB1 participates in protein cell mobility and might play a role as a pro-inflammatory cytokine in schistosomiasis.

Key words: *Schistosoma mansoni;* HMGB1; Acetylation; Inflammation.