Role of Phosphorylation of *Schistosoma mansoni* HMGB1 Protein

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The High Mobility Group B family (HMGB1, 2 e 3) represents a class of evolutionarily highly conserved and abundant chromosomal proteins in eukaryotes. In vertebrates, HMGBs are characterized by non-sequence-specific binding to DNA through one or two domains termed HMG boxes. HMGBs act by bending the DNA and disrupting the structure of chromatin. HMGBs are involved in DNA transcription, replication, recombination and repair. Besides its nuclear role, HMGB1 can also be secreted by certain cells, and plays important roles in inflammation and tumor metastasis. Our group has recently cloned and characterized the *Schistosoma mansoni* HMGB1 (*Sm*HMGB1). *Sm*HMGB1 recognizes and binds preferentially to supercoiled DNA and is also able to bend short double stranded DNA fragments. Vertebrate HMGB proteins have been reported to be posttranslationally modified by phosphorylation, acetylation, methylation and ADP-ribosylation. Data suggest that these modifications might be involved in cellular trafficking. *In silico* analysis of *Sm*HMGB1 phosphorylation revealed putative sites for casein kinase 2 (CK2). Indeed, we demonstrated that *Sm*HMGB1 is an *in vitro* substrate for CK2 at serine residues 172 and 174. Furthermore, we determined that phosphorylation had no effect in the ability of *Sm*HMGB1 to promote DNA supercoiling or bending. Total extract of *S. mansoni* was able to phosphorylate *Sm*HMGB1 and this modification was blocked by specific CK2 inhibitors. This data suggest that endogenous schistosome CK2 plays a significant role in *Sm*HMGB1 phosphorylation. Phosphorylation of *Sm*HMGB1 seems to be also involved in cellular trafficking, as shown by GFP transfections. Our results suggest that CK2 phosphorylation might be responsible for the shuttle of SmHMGB1from the nucleus to the cytosol.

Keywords: *Sm*HMGB1, CK2, phosphorylation