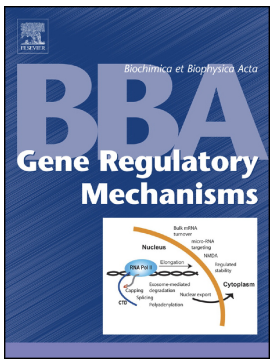

HMGB1-mediated DNA bending: Distinct roles in increasing p53 binding to DNA and the transactivation of p53-responsive gene promoters

Michal Štros, Martin Kučírek, Soodabeh Abbasi Sani, Eva Polanská

PII: S1874-9399(17)30396-6
DOI: https://doi.org/10.1016/j.bbagrm.2018.02.002
Reference: BBAGRM 1229

To appear in:

Received date: 13 November 2017
Revised date: 2 February 2018
Accepted date: 2 February 2018

Please cite this article as: Michal Štros, Martin Kučírek, Soodabeh Abbasi Sani, Eva Polanská , HMGB1-mediated DNA bending: Distinct roles in increasing p53 binding to DNA and the transactivation of p53-responsive gene promoters. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Bbagrm(2017), https://doi.org/10.1016/j.bbagrm.2018.02.002

HMGB1-mediated DNA bending: distinct roles in increasing p53 binding to DNA and the transactivation of p53-responsive gene promoters

Michal Štros*, Martin Kučírek, Soodabeh Abbasi Sani, and Eva Polanská

Laboratory of Analysis of Chromosomal Proteins, Institute of Biophysics of the Czech Academy of Sciences, Brno, Czech Republic

Abbreviations: HMG, high mobility group; WT, wild-type; oxiHMGB1, oxidized HMGB1; HMGB1ΔC, HMGB1 lacking the acidic C-terminal tail; EMSA, electrophoresis mobility shift assay.

Keywords: HMGB; p53; DNA bending; DNA-protein interaction; promoter transactivation.

Corresponding author:

* Tel. +420 517 183 or + 420 777 159 816 (mobile).

E-mail address: stros@ibp.cz

A B S T R A C T

HMGB1 is a chromatin-associated protein that has been implicated in many important biological processes such as transcription, recombination, DNA repair, and genome stability. These functions include the enhancement of binding of a number of transcription factors, including the tumor suppressor protein p53, to their specific DNA-binding sites. HMGB1 is composed of two highly conserved HMG boxes, linked to an intrinsically disordered acidic C-terminal tail. Previous reports have suggested that the ability of HMGB1 to bend DNA may explain the *in vitro* HMGB1-mediated increase in sequence-specific DNA binding by p53. The aim of this study was to reinvestigate the importance of HMGB1-induced DNA bending in relationship to the ability of the protein to promote the specific binding of p53 to short DNA duplexes *in vitro*, and to transactivate two major p53-regulated human genes: *Mdm2* and *p21/WAF1*. Using a number of HMGB1 mutants, we report that the HMGB1-mediated increase in sequence-specific p53 binding to DNA duplexes *in vitro* depends very little on HMGB1-mediated DNA bending. The presence of the acidic C-terminal tail of HMGB1 and/or the oxidation of the protein can reduce the HMGB1-mediated p53 binding. Interestingly, the induction of transactivation of p53-responsive gene promoters by HMGB1 requires both the ability of the protein to bend DNA and the acidic C-terminal tail, and is *promoter*-specific. We propose that the efficient transactivation of p53-responsive gene promoters by HMGB1 depends on complex events, rather than solely on the promotion of p53 binding to its DNA cognate sites.