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78

High mobility group protein 1: A collaborator in nucleosome dynamics and estrogen-responsive gene expression

William M Scovell

Abstract

High mobility group protein 1 (HMGB1) is a multifunctional protein that interacts with DNA and chromatin to influence the regulation of transcription, DNA replication and repair and recombination. We show that HMGB1 alters the structure and stability of the canonical nucleosome (N) in a nonenzymatic, ATP-independent manner. As a result, the canonical nucleosome is converted to two stable, physically distinct nucleosome conformers. Although estrogen receptor (ER) does not bind to its consensus estrogen response element within a nucleosome, HMGB1 restructures the nucleosome to facilitate strong ER binding. The isolated HMGB1-restructured nucleosomes (N' and N'') remain stable and exhibit a number of characteristics that are distinctly different from the canonical nucleosome. These findings complement previous studies that showed (i) HMGB1 stimulates *in vivo* transcriptional activation at estrogen response elements and (ii) knock down of HMGB1 expression by siRNA precipitously reduced transcriptional activation. The findings indicate that a major facet of the mechanism of HMGB1 action involves a restructuring of aspects of the nucleosome that appear to relax structural constraints within the nucleosome. The findings are extended to reveal the differences

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