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Interaction of Histone H1 with Chromatin-associated Protein HMGB1 Studied by Microscale Thermophoresis

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Abstract : HMGB1 is an architectural protein in chromatin, acting also as a signaling molecule outside the cell. Recent reports from several laboratories provided evidence that a number of both the intracellular and extracellular functions of HMGB1 may depend on redox-sensitive cysteine residues of the protein. MALDI-TOF analysis revealed that mild oxidization of HMGB1 resulted in a conformational change of the protein due to formation of an intramolecular disulphide bond by opposing Cys23 and Cys45 residues. We have demonstrated that redox state of HMGB1 could significantly modulate the ability of the protein to bind and bend DNA. We have also shown that reduced HMGB1 could easily displace histone H1 from DNA, while oxidized HMGB1 had limited capacity for H1 displacement. Using microscale thermophoresis (MST) we have further studied mechanism of HMGB1 interaction with histone H1 in free solution or when histone H1 was bound to DNA. Our MST analysis indicated that reduced HMGB1 exhibited in free solution > 1000 higher affinity of for H1 (KD ~ 4.5 nM) than oxidized HMGB1 (KD <10 □M). Finally, we present a novel mechanism for the HMGB1-mediated modulation of histone H1 binding to DNA.

Keywords : HMGB1, histone H1, redox state, interaction, cross-linking, DNA bending, DNA end-joining, microscale thermophoresis
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