Ability of HMGB1 protein to bind to intrinsically bent and non-bent DNA sites in the AMPD2 gene amplicon


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ABSTRACT. HMGB-like proteins are architectural chromatin factors, and their function is heavily dependent on their ability to interact with DNA (especially non-canonical DNA structures). HMGB1 is involved in many DNA processes, and dysregulation of HMGB protein expression has profound effects on cellular transcription, resulting in severe developmental defects as well as cancer. During DNA replication, elements that form the origin are still not well defined in metazoans. Sites with A (adenine) or T (thymine) repeats cause intrinsic curvatures in the DNA and are described to be involved in the replication machinery by providing binding sites to replication proteins. As a result, the DNA molecule shows intrinsically bent DNA sites, caused by periodic repeats of 2 or more As/Ts (dA/dT) as well as intrinsically non-bent DNA sites (INBDs), due to a succession of curvatures that cancel each other. In the present study, we mapped 11 INBDs present in the AMPD2 gene that are related to each replication origin (oriGNAI3, oriC, oriB, and oriA). Following characterization of
INBDSs, we tested the ability of HMGB1 to bind to the bent (\(b_1\), \(b_2\), \(b_4a\), \(b_4b\), \(b_5\), \(b_6\), \(b_7\), and \(b_8\)) and non-bent DNA fragments (\(nb_7\), \(nb_{11}\), \(nb_1\), \(nb_2\), \(nb_4\), and \(nb_5\)) via electrophoretic mobility shift assays. All fragments showed efficient binding to HMGB1. However, the non-bent DNA fragments \(nb_2\), \(nb_4\), and \(nb_5\) showed slightly reduced binding efficiency.

**Key words:** HMGB1; Intrinsically bent DNA; AMPD2 amplicon; Intrinsically non-bent DNA; DNA replication