

HU multimerization shift controls nucleoid compaction

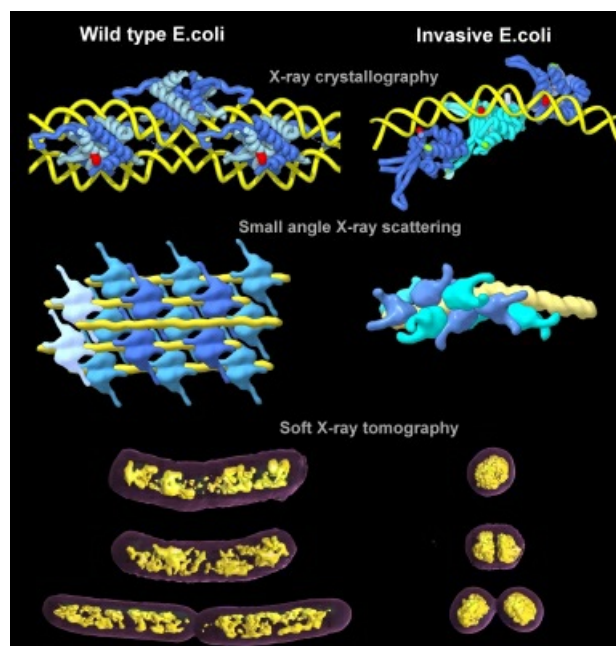
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Molecular mechanisms controlling functional bacterial chromosome (nucleoid) compaction and organization are surprisingly enigmatic, but depend partly upon conserved, histone-like proteins HU α and HU β and their interactions that span the nano and meso scales from protein-DNA complexes to the bacterial chromosome and nucleoid structure. Here, we determined crystal structures of these chromosome-associated proteins in complex with native duplex DNA. Distinct DNA-binding modes of HU α - and HU β elucidate fundamental features of bacterial chromosome packing regulating gene transcription. By combining crystal structures with solution X-ray scattering results, we determined architectures of HU-DNA nucleoproteins in solution under near physiological conditions. These macromolecular conformations and interactions result in contraction at the cellular level based upon *in vivo* imaging of native unlabeled nucleoid by soft X-ray tomography upon HU β and ectopic HU α 38 expression. Structural characterization of charge-altered HU α - DNA complex reveals an HU molecular switch suitable to condense nucleoid and reprogram noninvasive *Escherichia coli* into an invasive form. Collective findings suggest that shifts between networking, cooperative and non-cooperative DNA-dependent HU multimerization control DNA compaction and supercoiling independently of cellular topoisomerase activity. By integrating X-ray crystal structures, X-ray scattering, mutational tests, and X-ray imaging that span from protein-DNA complexes to the bacterial chromosome and nucleoid structure, we show that defined dynamic HU interaction networks can promote nucleoid reorganization and transcriptional regulation as efficient general microbial mechanisms to help synchronize genetic responses to cell cycle, changing environments, and pathogenesis.

Hammel, M., D. Amlanjyoti, F. E. Reyes, J. H. Chen, R. Parpana, H. Y. Tang, C. A. Larabell, J. A. Tainer and S. Adhya (2016). *Sci Adv* 2(7): e1600650.



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