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HU plays a key role in nucleoid organization and compaction in the radiation-resistant bacterium Deinococcus radiodurans

A major player in bacterial nucleoid organization is the histone-like HU protein. In the radiation resistant bacterium, *Deinococcus radiodurans*, HU is an essential protein that largely coats the genomic DNA and plays a central role in regulating the remarkable plasticity and high level of compaction of this bacterium's nucleoid. Using conventional and super-resolution microscopy approaches, we have indeed revealed that its nucleoid is highly compact at all times, but also surprisingly dynamic, adopting distinct configurations as it progresses through its cell cycle [1]. Furthermore, we recently observed that a major remodeling of the nucleoid induced by exposure to intense UV-C light was accompanied by marked changes in HU mobility, underlining the critical role played by HU-DNA interactions in structuring the nucleoid [2]. Using a combination of biochemistry, structural biology and molecular dynamics simulations, we are now investigating HU's mode of DNA binding at the molecular level. For this purpose, we have assembled HU onto supercoiled plasmid DNA and examined the HU-DNA assemblies by cryo-electron microscopy (cryo-EM). Particularly stunning spiral-like assemblies were observed repeatedly at a defined HU:DNA ratio. Image analysis reveals at least two distinct DNA binding modes: one in which HU binds loosely to the DNA duplex and another in which HU tightly bends the dsDNA. Mutational studies are now underway to determine whether the unusual lysine-rich N-terminal tail of *D. radiodurans* HU may be responsible for one of these two binding modes.

[1] Floc'h et. al., Nat Comm., 2019. 10.1038/s41467-019-11725-5
[2] Vauclare et. Al., NAR, 2014. 10.1093/nar/gkae379

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