HU proteins are the most abundant DNA-binding proteins in prokaryotic organisms, playing an essential role in processes of DNA replication, repair, and recombination\(^1\). In bacteria, where only HU proteins serve the function of nucleoid-associated proteins, genetic deletion of this protein was shown to be lethal\(^2\).

These small (about 90 amino acids per monomer) basic dimeric proteins are annotated in majority of bacteria genomes. The three-dimensional structures of a number of HU proteins as well as their mutants and complexes with DNA were solved. All HU protein dimers form compact bodies, including several intertwined α-helices, two three-stranded β-sheets, and two disordered arms, which are flexible in the absence of DNA. Due to the existence of HU homologs possessing moderate or high thermal stability, the small size of the protein molecules, and the similarity of three-dimensional structures, HU proteins may serve as a convenient model for investigating the structural basis of thermal stability.

Recently, we established the three-dimensional structure of the histone-like HU protein from the mycoplasma Spiroplasma melliferum KC3 (HUSpm) at 1.4 Å resolution and evaluated thermal stability of the protein by differential scanning calorimetry (DSC)\(^3\). According to DSC data, HUSpm has a high thermal denaturation temperature comparable with those of HU proteins from thermophilic bacteria. Like other members of the HU protein family, HUSpm is a stable dimer containing a central hydrophobic core stabilized by hydrogen bonds. Detailed analysis revealed that the spatial structure of the HUSpm dimer is similar to that of its bacterial homologs but distinguished by higher strength of hydrophobic interactions in the dimer interface. Additionally, no salt bridges are present at the HUSpm dimer interface, while larger number of hydrogen bonds is formed. In order to find the structural basis of HUSpm thermal stability, we identified amino acid residues potentially responsible for this feature and proved their importance for protein thermal stability by site-directed mutagenesis and subsequent DSC analysis.

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3. Boyko K. et al (2016), Scientific Reports, 6, 36366; doi: 10.1038/srep36366