The structural reminiscence of nucleosome architecture throughout the course of eukaryotic evolution suggests its pre-eukaryotic origin. This fact is further supported by the prevalence of primitive archaebacterial histones with conserved histone fold domains. Herein, the crystal structure of Methanothermus fervidus histone B/DNA (HmfB/DNA) complex has been presented. The structure represents one of the archaebacterial histone-DNA complexes. The high degree of structural resemblance of HmfB/DNA complex with eukaryotic nucleosomes may further be envisaged to trace the evolutionary origin of nucleosome.

Figure | Structural comparison of archaebacterial chromatin and nucleosome. A. Helical array of (HmfB)6/DNA complex. B. Crystal structure of archaebacterial nucleosome, consisting of three HmfB homodimers bound to 90bp DNA. C. Crystal structure of nucleosome, consisting two H2A/H2B heterodimers and two H3/H4 heterodimers bound to 147bp DNA.
Compaction of genetic material inside the cellular dimension is a universal problem faced by each living organism. Eukaryotes solved this problem by packing their enormous amount of genomic materials into multiple highly condensed nucleoprotein complexes, the chromosomes. Four small structurally related histone heterodimers (two copies of H2A/H2B and H3/H4) wrap ~147 base pairs (bp) of DNA in a tight nucleoprotein complex to form Nucleosome, the basic repeating unit of eukaryotic chromosome (Luger et al., Nature 389, 251, 1997). Packaging of eukaryotic genome in the nucleosomal context exerts highest level of DNA compaction but imparts a great challenge to access the genomic information by other key cellular pathways ranging from cell division to DNA repair (Ordu et al., Biophys. Rev. 8, 33, 2016). The presence of the core histone variants (Koyama et al., J. Biochem 163, 85, 2018) and post translational modification (PTM) of histone tails (Mersfelder et al., Nucleic Acids Res. 34, 2653, 2006) plays pivotal role in the eviction of nucleosomes on the wake of DNA transaction machineries. Mechanistic details of the emergence of histone variants and the PTMs of histone tails through the course of evolution of genomic complexity is being sought to understand their role in eukaryotic genome compaction and the regulation of gene expression. Intriguingly, the nucleosome structure and the structure of its core histone components remained the same (RMSD <2Å) throughout the course of eukaryotic evolution which may indicate their origin predates the origin of the first eukaryote. In addition, the discovery of smaller histone analogues in primitive archaebacterial organisms further supports the hypothesis, making archaebacterial histones ideal candidates to study the evolution of modern nucleosome.

In this context, we solved the crystal structure of archaebacterial histone (HmfB)/DNA complex (PDB ID, 5T5K) (Fig1) and uncover the role of this complex in archaebacterial gene expression in vivo (Mattiroli et al., Science 357, 609, 2017). HmfB is one of the histones other than HmfA from the hyperthermophilic archaeon Methanothermus fervidus. The HmfB/DNA complex is strikingly similar with eukaryotic nucleosome (RMSD ~ 2Å) with principal DNA binding amino acid residues and their mode of interaction with the DNA molecule are well conserved between these two structures (Fig1B and Fig. 1C). The structural reminiscence of histone-DNA interaction clearly indicates that the nucleosome structure as the fundamental genome compaction principle is not a eukaryotic innovation; rather it has been well preserved in primitive archaebacterial organisms. However, unlike stringent heterodimeric eukaryotic core histones, HmfB is a single tailless histone which in the crystal structure forms homo-hexamer to bind 90 bp DNA in nucleosome like fashion. Moreover, unlike nucleosome which packs the DNA like discrete ‘beads on a string’ like pattern, HmfB hexamers form a left-handed helical ramp onto which DNA wraps in a left-handed superhelix (Fig1A). The importance of this superhelical structure was further established by disrupting the superhelix through the introduction of structurally non-compatible amino acids at the interface of the superhelical layers without hampering the basic HmfB/DNA interactions. Mutant archaebacterial cells harboring the superhelix disrupting amino acid substitutions show significant alteration in gene expression patterns compared to the wild type, indicating the importance of the HmfB/DNA superhelix in archaebacterial gene expression (Mattiroli et al., Science 357, 609, 2017).

Interestingly, some species of archaebacterial have 1-6 copies of histone analogues, some which heterodimerizes to bind DNA and contain the histone tails just like eukaryotic counterparts (Nishida et al., Jl. Gen. Appl. Microbiol. 63, 28, 2017). Structure based functional characterization of these archaebacterial histone variants holds immense scope to divulge evolution pathway of the DNA compaction module which is now thought to commence with single tailless-histone containing archaebacterial chromatin [(HmfB)6/DNA] to multiple tailed-histone containing modern nucleosome.