MS6-P3 X–ray Crystallographic Analysis of the Chromatosome

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The packaging of eukaryotic DNA into chromatin consists of the nucleosome as the basic repeating unit. The nucleosome has a core region, comprised of ~146 base pairs of DNA wrapped around a protein octamer of core histones, in addition to a variable length of linker DNA. The linker DNA connecting adjacent nucleosome core regions is on average ~50 base pairs in length in higher eukaryotes and can be occupied by a linker histone. By modulating chromatin structure, dynamics and recognition by other nuclear factors, the core and linker histones regulate genomic function. The first atomic model of the nucleosome core (particle) was published in 1997 [1], paving the way for the structural solution of a great variety of nucleosome core constructs composed of variant/modified histones and different DNA sequences [2,3]. This has consequently revolutionized our understanding of nucleosome activity, and yet 19 years later we are still lacking an atomic level understanding of how linker histones interact with nucleosomes.

In mammals, there are 11 linker histone variants, which can display cell type and cellular status dependent expression, site-specific localization in the nucleus as well as specific interactions with different nuclear factors to foster gene-specific regulation. In addition, the linker histones can undergo an enormity of post-translational modifications that further expand the regulatory landscape. Nonetheless, the general function of the linker histones is largely that of compacting nucleosomes into condensed chromatin states, which are generally repressive to gene expression. An atomic model of the chromatosome, the minimal assembly of a nucleosome with a linker histone, could significantly advance our understanding of chromatin function, and we present here the first X-ray crystal structure of a chromatosome [4].

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MS6-P4 Unique base pairing interactions at the third position of codon-anticodon helix

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Post-transcriptional modifications at the wobble position of tRNAs play a substantial role in deciphering the degenerate genetic code on the ribosome. The number and variety of modifications suggest different mechanisms of action during mRNA decoding of which only a few were described so far. Uridine at the wobble positions of various tRNAs is almost always modified in bacteria and eukaryotes[1]. In many cases tRNAs with the modified uridines read two codons ending with purines A or G and in some rare cases modifications help to recognize all four nucleotides A, G, C and U at the third codon position[2]. Previously it was shown that preferential form of the third wobble pair with a fully modified uridine approached a standard Watson-Crick-like geometry if this uridine was paired with guanosine[3,4]. Here we describe a new type of a base pair at the third wobble position of a codon-anticodon duplex in the 70S ribosome decoding center. Our structures demonstrate that the reversed "wobble" pair mnm^5s^2U34•G(+6) adopts its own geometry, different from the standard G34•U(+6) pair[5] at the third codon-anticodon position. We show that mnm^5s^2U forms an unusual pair with guanosine at the wobble position that expands general knowledge on the degeneracy of the genetic code and specifies a powerful role of tRNA modifications in translation.

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