bonds but AT base pair formed incomplete hydrogen bonds under the mechanical force. Trajectories tended to escape the energetic mountain and took heterogeneous pathways on rugged energy landscape. Entropy maps showed that the entropy was negatively correlated with the number of hydrogen bonds, whereas the total energy was not correlated. This result might indicate that the DNA structure is entropically stabilized by hydrogen bonds.

1C1324 Flexural rigidity of dsDNA measured by winding single molecule on a nanometer size bearing

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The mechanical properties of DNA are classically described by worm-like chain (WLC) model which uses a single parameter; the persistence length, to characterize the filament's resistance to bending by thermal energy. However, the property of locally bent DNA by relatively higher force than thermal force was not clear yet. Recent studies by AFM and cyclization of DNA showed sharply bent DNA is more flexible than predicted from WLC model; however, it was hard to control the bending force and the shape of DNA filaments. Thus, we developed a single-molecule method to directly apply force and control the radius of curvature of single dsDNA by winding on a nanometer size bearing (*i.e.* F_1 -ATPase); thereby measure the flexural rigidity of DNA. In our system, the stator $\alpha_3\beta_3$ ring of the rotary motor protein F_1 -ATPase was fixed on the glass surface, and a magnetic bead was attached to the rotor γ subunit. One end of DNA was also connected to the rotor γ , and wound by the rotary magnetic tweezers. Another end of DNA was attached to a polystyrene bead which was controlled by the optical trap, thus we can measure both the tension and the change in the tether length of winded DNA. From the analysis of rotation numbers and the change of tether length, we can determine the radius of winded DNA. As a result, the radius of winded DNA decreased from 9.5 to 4.5 nm when the tension increased from 1.8 to 6 pN. In this force range, our preliminary results were well fitted with WLC model, which gave a value of persistence length of ~60 nm.

1C1336 ゲノムクロマチンの凝縮が生み出す新たな放射線耐性

P38 Chromatin compaction protects genome DNA from radiation damage

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The human body is made up of 60 trillion cells, each of which has 2 m of long genome DNA. Recently, we proposed that irregularly folded nucleosome fibers, in which DNA is wrapped around core histones, form compact chromatin domains in the nuclei. What is the advantage of this kind of chromatin domain? Here we report that the chromatin compaction protects genome DNA from radiation damage. To test the chromatin compaction effect on DNA damage protection, condensed and decondensed chromatins were manipulated on glass surfaces and exposed to X-ray (gamma-ray). DNA double strand breaks (DSBs) were quantitatively detected by using TUNEL (Terminal deoxynucleotidyl transferase dUTP nick end labeling) assay. Surprisingly, frequency of X-ray-induced DSBs in the fully decondensed chromatin was 16-fold higher than that in the condensed chromatin, indicating that chromatin compaction itself has a prominent radiation-damage protection effect. Our finding demonstrate another meaning of the genome DNA compaction, regarding a novel DNA damage protection mechanism, which could be beneficial for all living organisms in the long run.

1C1348 長いDNAはどのようにして染色体の中に折り畳まれているのか？

How is a long strand of genomic DNA organized into a chromosome?

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How a long strand of genomic DNA is compacted into a mitotic chromosome remains one of the most basic questions in biology. To explain the mitotic chromosome structure, one of the classical models holds that 11-nm nucleosome fibers are compacted into 30-nm chromatin fibers, which are folded progressively into larger fibers (100, 200-250 and 500 nm) to form the final mitotic chromosomes. However, when we observed frozen hydrated human mitotic cells using cryo-electron microscopy, which enable direct high-resolution imaging of the cell structures in a close-to-native state, we did not

find any higher-order structures, or even 30-nm chromatin fibers, but just a uniform disordered texture (Eltsov et al., *Proc. Natl. Acad. Sci. USA*, 2008; Maeshima et al., *Current Opinion in Cell Biology*, 2010). To further investigate the mitotic chromosome structure, we performed small angle x-ray scattering or SAXS, which can detect regular internal structures in non-crystalline materials in solution. Purified human mitotic chromosomes were exposed to the synchrotron radiation beam at SPring-8 in Japan. Again, the results were striking: we detected no structural feature larger than 11 nm even on a chromosome-diameter-scale. Our finding provides a nucleosome irregular folding model, which promises more dynamic and more flexible genome organization than allowed by static regular structures (Maeshima et al., *Cold Spring Harbor Symposia on Quantitative Biology*, 2011).

1C1412 Local conformational changes of proteins in DNA interfaces

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DNA-protein interaction plays a key role in many cellular functions such as transcription, replication, recombination and DNA packaging. Understanding the mechanisms by which the protein recognizes DNA is one of the main topics in biology. With increased amount of crystal structures, conformational changes of proteins in DNA interfaces are suggested to be one of important factors in DNA recognition. To better understand a role of the flexibility of proteins in DNA recognition, quantitative analyses of local conformational changes in DNA interfaces of proteins are required.

In order to analyze such conformational changes in DNA interfaces, we extracted crystal structures of DNA-unbound and DNA-bound states from PDB. The backbone structures were described by 7 letters that were pre-defined according to conformations of consecutive overlapping fragments of 4-residues. Using the letter codes, any conformational change from DNA-unbound state to DNA-bound state was described as one of 49 patterns of changes. We statistically analyzed the frequency of these conformational changes in DNA interfaces and protein surfaces. As a result, we found 7 structural changes preferred in DNA interfaces compared with that of protein interfaces.

1C1424 Hsp90のN末端ドメインとリガンド分子の分子動力学シミュレーション

Molecular dynamics simulations of the N-terminal domain of Hsp90 with ligand molecules

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Heat Shock Protein 90 (Hsp90) is an ATPase-coupled molecular chaperone. Molecular chaperones are proteins which help client proteins fold. These proteins work to keep the client proteins folded and active in living cells. Heat shock proteins are molecular chaperones and have important functions to help client proteins fold and prevent them from the dangerous aggregation of immature proteins. Hsp90 is a specialized chaperone that has a more specific function in contrast to other Hsp molecules. Binding with ATP and hydrolysis of ATP to ADP are required for the normal function of Hsp90. The ATPase-coupled conformational rearrangement from the open to the closed state of Hsp90 dimer occurs. In addition, Hsp90 is an interesting target for the therapy of virus infectious disease and cancer. For example, it is involved in the replication of influenza virus. Blocking the binding of ATP to Hsp90 causes the inhibition of ATPase activity. Then, the replication of viruses is inhibited. The formation of Hsp90-nucleotide complex is important for its function. The purpose of our study is to investigate the molecular mechanisms of the formation of Hsp90-nucleotide complex. We performed the all-atom model molecular dynamics simulations of the N-terminal ATP-binding domain (NTD) of Hsp90 with nucleotides to elucidate the molecular mechanism of the formation of Hsp90-nucleotide complex. We will discuss the conformational differences between the NTD with nucleotides.

1C1436 粗視化モデルによる複数のヌクレオソームのシミュレーション

Coarse-grained simulations of multi-nucleosome systems

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In eukaryotic cell, the genome is packaged into chromatin assisted by histone proteins. The basic unit of chromatin is nucleosome, in which DNA duplex is wrapped around histone core proteins, H2A H2B, H3, and H4, and strings of