S1d1-3

Control of Regioselectivity of Heme Oyxgenase by Reconstruction of Hydrogen-Bonding Interactions between Substrate and Enzyme

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Regioselective reactions catalyzed by enzymes are very important biologically and chemically. Therefore, molecular mechanisms of regioselective reactions have been studied for various enzymes with various spectroscopic methods. We have studied the molecular mechanism of heme oxygenase (HO), which catalyzes regioselective degradation of heme (iron protoporphyrinIX) to α-biliverdin, CO, and free iron ion. We have found two essential amino acid residues, Asp-140 and Arg-183 in rat-HO, for the α-regioselective heme degradation. We showed that the Asp-140 and Arg-183 residues control oxygen activation process and the substate (heme) binding process via hydrogen-bonding interactions, respectively. With combination of the Asp-140 and Arg-183 residues, the α-meso position of the heme is placed at the nearest position from the activated oxygen species, resulting in the α-regioselective reaction. This mechanism let us imagine that we can switch the regioselectivity of HO if we can control an orientation of the heme in HO so that the other meso position is placed at the nearest position from the activated oxygen species. To realize this idea, on the basis of the crystal structure of the wild type HO, we designed a mutant, in which the other meso position is placed at the nearest position from the activated oxygen species. In this presentation, we will show our strategy for controlling the orientation of the heme and regioselectivities of the mutants prepared according to the strategy.

S1d1-4

Investigation of DNA damage induced by heavy ions

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The double strand breaks (DSBs) of DNA are considered to be the most important initial damage of all biological effects induced by radiation. Heavy ions with high LET can deposit more energy in medium and have complex track structure. It is especially necessary to investigate the DNA damage induced by heavy ion. Using ^{7}Li of 19MeV (LET=120keV/μm, in aqueous solution) and ^{12}C of 84MeV (LET=240keV/μm) generated by HI-13 tandem accelerator of China Institute of Atomic Energy (CIAE), three conditions of pUC19 plasmid DNA samples including aquiform, dry and adding free radical scavenger (mannitol) with various concentrations are irradiated at different doses from 10 to 1000Gy in atmosphere environment. After irradiating, these DNA samples are analyzed with atomic force microscopy (AFM) and the gel electrophoresis. The changes of three forms of DNA, supercoiled (intact DNA), open circular (OC,DNA with SSB) and linear form (L,DNA with DSB), as the dose are observed. The distribution function of DNA fragment length is gained by the AFM direct observation of the DNA fragments. In order to evaluate the relative biological effectiveness (RBE) of DNA damage induced by heavy ions, pUC19 plasmid DNA is irradiated also by γ rays. Thus the dose and LET dependence on the DSBs induced and protection function of the free radical scavenger are obtained. The direct and indirect interactions of heavy ion with different DNA samples are estimate. Using the random breakage model the length distribution of short DNA fragments induced by ^{7}Li ions is analyzed.

S1d1-5

Water and Weak Interactions

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From the dynamical analysis of a motor protein (kinesin) we found that motor protein could change the amplitude of the intramolecular interaction in a large range corresponding to different water populations around. We make a simple calculation for the electrostatic interaction energy between two charged residues at two different hydration states to give a quantitative description about how large the change of the energy could be. At the back door of the catalytic site of kinesin there is a 'latch' formed by a pair of oppositely charged residues, R216 and E253. During a period of catalysis the distance between the two residues changes from 0.4nm to 0.9nm, which correspond to the close and open states of the back door respectively. To calculate the electrostatic energy we must determine what dielectric constants could be used for the two cases. For bulk water the dielectric constant is 80. However, for the water forming the hydration shell, which is about 0.4 nm thick, the dielectric constant is 5. With these values we calculated the electrostatic energy for the close state as 70 kJ/mol and that for the open state as 2 kJ/mol. These two values are of reasonable orders since the former is large enough for closing the back door against thermal disturbs and the latter is of the same order as that of the thermal motion energy. This result shows that different water populations may result in large change for weak interactions and protein could make use of this special function of water to implement important conformational changes.

S1d1-6

A Statistical Model on the Protein-Water Network due to Hydrogen Bonds

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Based on a statistical theory proposed on a single component hydrogen bonding(HB) system, we consider the relevant properties of the network of protein and water molecules due to hydrogen bonds. For the protein-water systems, we point out that, which can undergo a sol-gel phase transition process with the corresponding critical condition and the scaling laws are obtained. In detail, we derive the equilibrium free energy and the cluster size distribution of the protein-water system. In addition, by means of an invariant property of the size distribution, we found the sol-gel transition is a kind of geometrical phase transition. Furthermore, some statistical parameters that are closely related to elastic properties of the protein-water network are carried out, which include the number of the effective cross-linkages, the numbers of elastic active chains and dangling chains as well as the mers of them. Final, a numerical calculation on these parameters is presented for a modeled system.