DNA Damage and its Enzymatic Repair : Path toward a Preservation of Genetic Information Molecular Dynamics Simulation

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■ 概要

□ ionizing radiation and oxidative products of cell metabolism damage DNA and cause mutations and chromosomal aberrations in cells and organisms;

□ recognition of damage is first step of repair during which repair enzyme recognizes lesion and forms stabile DNA-enzyme complex;

□ presented work shows results of molecular dynamics simulation of two DNA lesions (8-oxoguanine (8-oxoG) and apurinic/apyrimidinic (AP) site), either as single or multiple lesion, and their recognition by repair enzyme;

■ アルゴリズム

□ AMBER 7, molecular dynamics (MD) code;

□ all atoms simulation;

□ GAUSSIAN 03, *ab initio* calculations;

□ F-BMVS – FUJITSU Bio-Molecular Visualization Software;

□ Hi-PATS – HITACHI Parallel Application Tracking and Steering (visualization software)

■ 計算規模

□ simulated system size - several 100,000 atoms;

□ real biological simulated time - several nanoseconds;

DNA+hOGG1 (complex)   STEP=500ps
8-oxoG   arginine, lysine
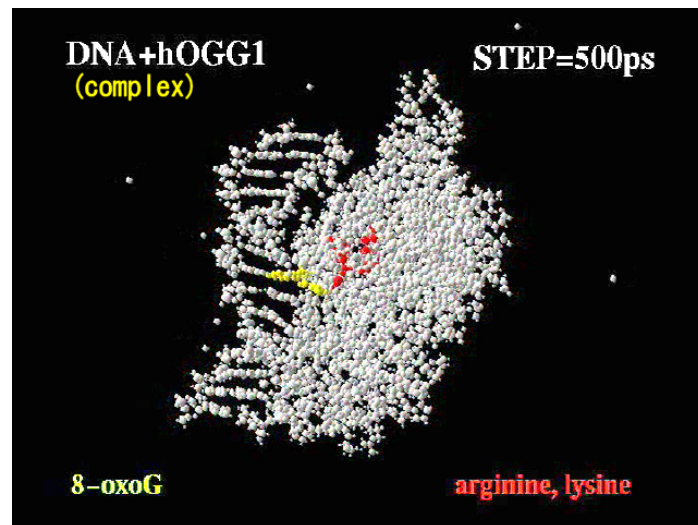
■ どんなことが期待されるか？

□ to identify significant structural and energetical changes that may facilitate the onset of entire repair process;

□ to describe molecular changes in their dynamical scale that are undergoing prior and upon recognition of lesion;

□ to determine the role of electrostatic interaction between DNA damage and active site of enzyme in recognition;

□ theoretically propose and describe the most probable enzymatic repair pathway;