ELECTRON TUNNELING PATHWAY AND ROLE OF ADENINE IN REPAIR OF DAMAGED DNA BY PHOTOLYASE

ZHEYUN LIU, CHUANG TAN, XUNMIN GUO, YA-TING KAO, JIANG LI, LIJUAN WANG, and DONG-PING ZHONG, *Department of Physics, Chemistry, and Biochemistry, The Ohio State University, Columbus, OH 43210.*.

Through electron tunneling, photolyase, a photoenzyme, restores damaged DNA into normal bases.[a b] Here, we report our systematic characterization and analyses of three electron transfer processes in thymine dimer restoration by following the entire dynamical evolution during enzymatic repair with femtosecond resolution. We observed the complete dynamics of the reactants, all intermediates and final products, and determined their reaction time scales. Using (deoxy)uracil and thymine as dimer substrates, we unambiguously determined the electron tunneling pathways for the forward electron transfer to initiate repairing and for the final electron return to restore the active cofactor and complete the repair photocycle. Significantly, we found that the adenine moiety of the unusual bent cofactor is essential to mediating all electron transfer dynamics through a super-exchange mechanism, leading to a delicate balance of time scales. The active-site structural integrity, unique electron tunneling pathways and the critical role of adenine assure these elementary dynamics in synergy in this complex photorepair machinery to achieve the maximum repair efficiency close to unity.

[a] Z. Liu, C. Tan, X. Guo, Y.-T. Kao, J. Li, L. Wang, A. Sancar, and D. Zhong, *Proc. Natl. Acad. Sci. USA* **108**, 14831 (2011)
[b] J. Li, Z. Liu, C. Tan, X. Guo, L. Wang, A. Sancar, and D. Zhong, *Nature* **466**, 887 (2010)