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Photo-induced self-repair of CPD lesion in T=TAG DNA sequence

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Abstract:

Photochemistry[1] of nucleobases has a long history and is widely studied in the context of damage and photostability of DNA. DNA bases absorb in solar radiation in the UV range, leading to several photophyisical and photochemical processes resulting in formation of mutagenic and carcinogenic photoproducts like cyclo butane pyrimidine dimer (CPD) and 6-4 photolesion. Nature has developed several self-defence mechanisms against photo damage. Some sophisticated enzymes, such as photolyase[2], developed by nature during chemical evolution, are very selective for a particular repair and operate via electron transfer mechanisms. An oligonucleotide sequence (T=TAG) having inherent capability to repair lesions was first reported by Bucher et al[3]. The authors proposed a sequence specific sequential electron transfer mediated repair mechanism which was recently theoretically supported by Szabla et al[4]. However, the details of the mechanisms are yet to be elucidated and the sequence specificity has yet to be rationalized. By using a judicious combination of linear-response and real-time time-dependent density functional theory (TDDFT) methodology we present a detailed description of the mechanism including the states involved at the various stages, factors influencing the rates of forward and backward electron transfer as well as the driving force of the CPD repair. Our results indicate that in addition to sequence dependence of the repair the mechanism might depend on the conformations adopted by the oligonucleotide as has been previously suggested.

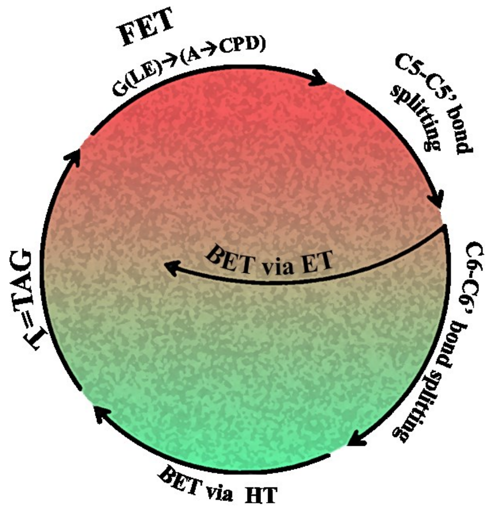

Figure: Schematic diagram of complete photocycle of CPD repair in T=TAG DNA sequence

References: **(1)** Crespo-hernndez, C. E. et al. *Chem. Rev.* **2004**, *104* (4), 1977–2020 **(2)** Liu, Z.et al. *Proc. Natl. Acad. Sci.* **2011**, *108* (36), 14831–1483 **(3)** Bucher, D. B. et al *J. Am. Chem.Soc.* **2016**, *138* (1), 186–19 **(4)** Szabla, R. et al. *Chem. Sci.* **2018**, *9* (12), 3131–3140