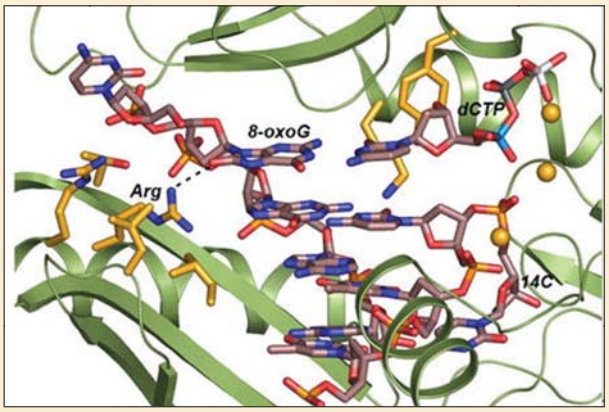
# biobits asbmb journal science

## Replicating Damaged DNA

DNA polymerases assist in DNA replication by catalyzing the polymerization of deoxyribonucleotides alongside a template DNA strand. Based on sequence homology, DNA polymerases can be subdivided into seven different families: A, B, C, D, X, Y, and RT. The Y family polymerases differ from others in that they are able to use damaged DNA as a template. For example, P2 DNA polymerase IV (Dpo4) can bypass 7,8-dihydro-8-oxodeoxyguanosine (8-oxoG), a major lesion arising from oxidative stress. In this JBC paper, the authors looked at the means by which Dpo4 is able to bypass this lesion with high fidelity, thus preventing mutation. Previous crystal structures had indicated that $Arg^{332}$ might play a role in stabilizing the 8-oxoG template base, allowing insertion of dCTP in the complementary strand. The results of the paper confirm that a bond between $Arg^{332}$ and 8-oxoG plays a role in determining the fidelity and efficiency of the Dpo4-catalyzed bypass.




**$Arg^{332}$ forms a bond with 8-oxoG during replication.**

**Hydrogen Bonding of 7,8-Dihydro-8-oxodeoxyguanosine with a Charged Residue in the Little Finger Domain Determines Miscoding Events in Sulfolobus solfataricus DNA Polymerase Dpo4**

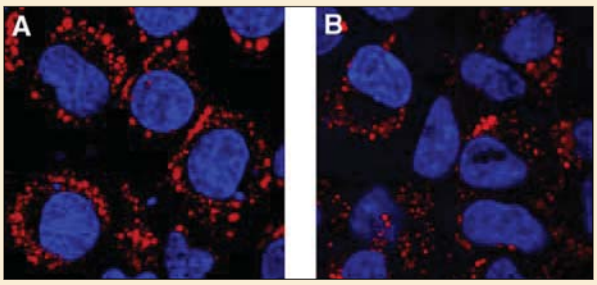
Robert L. Eoff, Adriana Irimia, Karen C. Angel, Martin Egli, and F. Peter Guengerich

*J. Biol. Chem.* 2007 **282**: 19831-19843

jbc

## The Side Effects of CETP Inhibition

Cholesteryl ester transfer protein (CETP) is a plasma protein that facilitates the transport of cholesteryl ester and triglyceride between lipoproteins. The protein picks up triglycerides from very low or low density lipoproteins (VLDL or LDL) and can exchange them for cholesteryl esters from high density lipoproteins (HDL) (and vice versa). Because HDL has a protective function in atherosclerosis and cardiovascular disease, the pharmacological inhibition of CETP has been investigated as a way to raise HDL levels. In this *JBC* paper, the authors use antisense CETP cDNA to suppress expression of the protein in adipocytes and document, for the first time, the importance of intracellular CETP in lipid transport and storage. They show that CETP deficiency affects the translocation of cholesteryl esters and triglycerides from the endoplasmic reticulum to their storage sites. With the extensive recent interest in raising HDL levels through CETP inhibition, the results of this study suggest that an increase in cellular cholesteryl ester storage may be one potential mechanism contributing to the adverse effects of CETP inhibitors such as Pfizer's torcetrapib.




**Triglyceride levels in CETP-deficient cells (B) are lower than in wild-type cells (A).**

**Possible Role for Intracellular Cholesteryl Ester Transfer Protein in Adipocyte Lipid Metabolism and Storage**

Lahoucine Izem and Richard E. Morton

*J. Biol. Chem.* 2007 **282**: 21856-21865

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