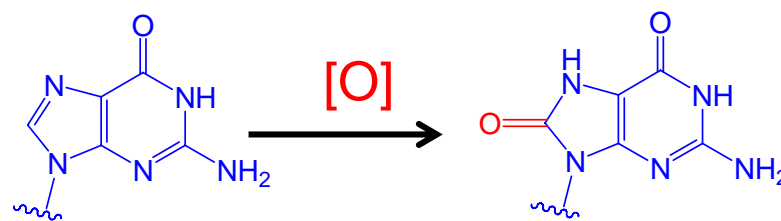


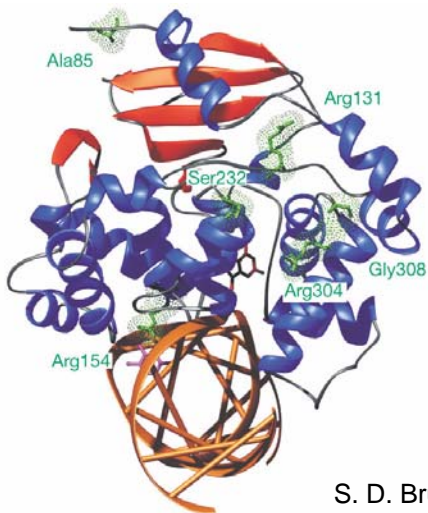
# Characterization of Variants of Human 8-oxoguanine DNA Glycosylase 1 (hOGG1) Identified in Cancer Patients

## Professor Karl Haushalter, Harvey Mudd College, CHE-0353662 Research Experience for Undergraduates

Everyday our DNA is relentlessly attacked by reactive oxygen species (ROS). ROS oxidize exposed guanine residues to form the mutagenic lesion 8-oxoguanine. Our cells remove this damaged base using human 8-oxoguanine glycosylase 1 (hOGG1). Different polymorphisms of hOGG1 have been found in cancer patients and cancer cell lines. No direct correlation between having a polymorphism of hOGG1 and having an increased risk of carcinogenesis has been determined at the present time, but not much research has been done characterizing these variants either.



The 8-oxoguanine lesion forms from oxidation of a guanine base in DNA



**Undergraduate student Katie Mouzakis (HMC)** characterized the Ser326Cys, Arg154His, Ala85Ser, Ser232Thr, and Arg46Gln hOGG1 variants using wildtype hOGG1 as a benchmark. The ultimate goal of this project is to compare the DNA repair activity, thermostability, and binding affinity of each of the different variants with that of wildtype hOGG1. She has conducted research to show that the Arg46Gln, Ser326Cys and Ser232Thr hOGG1 variants are thermolabile, while the Ala85Ser and Arg154His hOGG1 variants and wildtype hOGG1 are not thermolabile. She has also begun kinetic studies determining the rates that the DNA repair enzymes can excise an 8-oxoguanine base using DNA substrates that are radiolabeled or fluorescently labeled.

S. D. Bruner, D. P. G. Norman, G. L. Verdine, "Structural basis for recognition and repair of the endogenous mutagen 8-oxoguanine in DNA," *Nature*, **403**, 859-866 (2000)