Synopsis of Original Research Paper

Cellular repair mechanisms of oxidative DNA damage induced by UVA

Hiroshi Ide

Graduate School of Science, Hiroshima University

Solar ultraviolet radiation with wavelength between 320-400 nm (UVA) passes through stratospheric ozone without absorption and reaches the earth's surface. When exposed to UVA, reactive oxygen species (ROS) generated by endogenous photosensitizers cause damage to DNA, mostly oxidative base lesions, in living organisms. In this study, the damage specificity has been elucidated of two base excision repair enzymes [endonuclease III homolog 1 (NTH1) and 8-oxoguanine glycosylase 1 (OGG1)] that are potentially involved in removal of UVA-induced oxidative DNA lesions. Duplex oligonucleotide substrates containing unique lesions were incubated with the enzymes and products were analyzed by denaturing polyacrylamide gel electrophoresis. Pyrimidine lesions such as urea, thymine glycol, 5,6-dihydrothymine, and 5-hydroxyuracil were efficient substrates for NTH1, and purine lesions such as 7,8-dihydro-8-oxoguanine and formamidopyrimidine were also good substrates for OGG1. Interestingly, further analysis of the damage specificity revealed that NTH1 recognized formamidopyrimidine, a purine lesion, and OGG1 recognized the pyrimidine lesions except thymine glycol but in a paired base-dependent manner. These results suggest that NTH1 and OGG1 may be able to act as a mutual backup enzyme, albeit not perfectly, in cells. The repair activity for 5-formyluracil, a major UVA-induced oxidative lesions, was also investigated using mouse tissues. Incubation with the crude cell extracts from several tissues including brain, heart, lung, thymus, and liver all resulted in incision of a substrate at the 5-formyluracil site, demonstrating the presence of repair activity for this lesion. Several lines of evidence suggested that the observed activity for 5-formyluracil resided on a novel enzyme that had not been identified before.