Free Radic Biol Med. 2013 Oct;63:401-9. doi: 10.1016/j.freeradbiomed.2013.05.031. Epub 2013 May 28.

Genotype-phenotype analysis of S326C OGG1 polymorphism: a risk factor for oxidative pathologies.

Simonelli V[1], Camerini S, Mazzei F, Van Loon B, Allione A, D'Errico M, Barone F, Minoprio A, Ricceri F, Guarrera S, Russo A, Dalhus B, Crescenzi M, Hübscher U, Bjørås M, Matullo G, Dogliotti E.

Author information

1 Department of Environment and Primary Prevention, Istituto Superiore di Sanità, 00161 Rome, Italy.

Abstract

8-Oxoguanine DNA glycosylase (OGG) activity was measured by an in vitro assay in lymphocytes of healthy volunteers genotyped for various OGG1 polymorphisms. Only homozygous carriers of the polymorphic C326 allele showed a significantly lower OGG activity compared to the homozygous S326 genotype. The purified S326C OGG1 showed a decreased ability to complete the repair synthesis step in a base excision repair reaction reconstituted in vitro. The propensity of this variant to dimerize as well as its catalytic impairment were shown to be enhanced under oxidizing conditions. Mass spectrometry revealed that the extra cysteine of the variant protein is involved in disulfide bonds compatible with significant conformational changes and/or dimerization. We propose that the S326C OGG1 catalytic impairment and its susceptibility to dimerization and disulfide bond formation in an oxidizing environment all concur to decrease repair capacity. Consequently, the C326 homozygous carriers may be at increased risk of oxidative pathologies.

KEYWORDS: DNA repair; Disulfide bond profile; Free radicals; Genotype–phenotype analysis; Single-nucleotide polymorphisms

PMID: 23726996 DOI: 10.1016/j.freeradbiomed.2013.05.031