

Hydrogen sulfide induces direct radical associated DNA damage
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Hydrogen sulfide (H₂S) is produced by sulfate-reducing bacteria (SRB) in the large intestine and represents an environmental insult to the colonic epithelium. Clinical studies have linked the presence of either SRB or H₂S in the colon with chronic disorders such as ulcerative colitis and colorectal cancer, but underlying mechanisms remain undefined. We demonstrated previously that sulfide at concentrations similar to those found in the human colon generates genomic DNA damage in mammalian cells. The present study addressed the nature of the DNA damage by determining if sulfide is directly genotoxic or if genotoxicity requires cellular metabolism. We also asked if sulfide genotoxicity is mediated by free radicals and if DNA base pair oxidation was involved. Naked nuclei derived from CHO cells were damaged by very low sulfide concentrations (1 μM). This damage was effectively quenched by co-treatment with butylhydroxyanisole. Furthermore, sulfide treatment increased the number of oxidized bases recognized by Fpg (formamidopyrimidine [fapy]-DNA glycosylase). Together this work, confirms sulfide genotoxicity, and demonstrates that the toxicity is mediated by free radicals. These observations highlight the possible role of sulfide as an environmental insult that given a predisposing genetic background, may lead to genomic instability or the cumulative mutations characteristic of colorectal cancer.