

Toxicogenomic analysis of human intestinal epithelial FHs 74 Int cell responsiveness to sulfide

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Hydrogen sulfide (H₂S), a metabolic endproduct of sulfate-reducing bacteria in the large intestine, represents an environmental insult to the colonic epithelium linked with chronic disorders such as ulcerative colitis and colorectal cancer. We demonstrated previously that sulfide, at concentrations similar to those found in the human colon, induced genomic oxidative DNA damage in mammalian cells. The present study sought to define the early (30 min) and late (4 h) response of non-transformed intestinal epithelial cells (FHs 74 Int) to a genotoxic-but not cytotoxic-concentration of sulfide (500 μM Na₂S) using pathway specific quantitative RT-PCR arrays. Significant changes in gene expression were predominantly observed at 4 h, with the most notable being *PTGS2* (Cox-2; 7.9 fold upregulation), and *IL-1A* (interleukin 1 alpha; 5.2 fold downregulation). Functional pathway analysis indicated that sulfide modulates cell cycle progression and triggers both an inflammatory and DNA repair response. The analysis also highlights p53, p21, c-Fos, c-Jun, NFκ-B, and IL-8 as potential key molecules in normal cellular responses to sulfide. Overall, the present study identifies functional pathways by which sulfide may perturb cellular homeostasis and contribute to the onset of chronic intestinal disorders.