

## Identification of a Possible Human Population Hyper-Susceptible to Formaldehyde

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### ABSTRACT

Formaldehyde is a highly reactive outdoor and indoor environmental pollutant found in automobile emissions, tobacco smoke, building materials, adhesives, and many other sources. Recently, formaldehyde has been reevaluated as a known environmental human carcinogen due to a positive association between the extent of exposure to workers and their death from nasopharyngeal cancer. Formaldehyde has been determined to cause DNA damage by forming covalent crosslinks between the DNA and proteins. This damage then putatively leads to the transformation of the cell into a cancer cell.

Every cell in our body will endure a myriad of DNA damaging events every day. To combat this damage, cells have evolved several DNA repair mechanisms. Each of these mechanisms makes use of a number of different enzymes (proteins) to catalyze the reactions necessary to complete the repair. Although genetically normal individuals appear to successfully deal with DNA-protein crosslinks, not much is known about how they are repaired. In an attempt to determine which of the repair mechanisms is used by the cell, we made use of a series of cell lines - each cell line being mutated so that it is made deficient in one of the repair enzymes. Each of the repair mechanisms was represented in this work. We found that cells that are deficient in the repair mechanism called homologous recombination are particularly hypersensitive to (easily killed by) formaldehyde. Of particular interest is the hypersensitivity of cells mutated in the genes named BRCA1, BRCA2 and FANCD2. The BRCA genes get their name from BRCAst CAncer and each has been found to be mutated in certain people with the inherited form of the disease and individuals with these mutations are more likely to develop the disease during their lifetimes. FANCD2 is named for the disease known as Fanconi's Anemia and is one of the genes that may be mutated, leading to this deficiency. Fanconi's Anemia is characterized by developmental abnormalities, susceptibility to certain cancers and bone marrow failure. All three gene products are required for homologous recombination DNA repair and a defect in any of the three may cause deficiency in this repair mechanism.

Our data suggests that homologous recombination is the primary mechanism for the repair of DNA-protein crosslinks. Just as important is the discovery that individuals deficient in BRCA1/2 or FANCD2 may be hyper-susceptible to mutations caused by formaldehyde. With this in mind, those who are responsible for the regulation of this chemical may want to reconsider acceptable environmental levels to better protect the more sensitive among us.

### Are FEMA trailers 'toxic tin cans'?

