Induction of DNA Double–Strand Breaks by Asbestos, Silica and Titanium Dioxide: Do They Provide an Early Predictive Marker of Carcinogenic Potential?.

V. Vallyathan, Ph.D.[1], Z. Msiska, Ph.D.[1], M. Pacurari, Ph.D.[1] and V. Castranova, Ph.D.[1]. Email: vav1@cdc.gov

[1]NIOSH, Morgantown, WV; [2]NIOSH, Morgantown, WV; [3]NIOSH, Morgantown, WV and [4]NIOSH, Morgantown, WV.

Rationale: Induction of DNA double strand breaks (DSBs) is a very rapid response to DNA damage that occurs in cells subjected to many types of toxic insults, such as radiation, exposure to toxic substances and other stresses. The inability to repair these breaks can lead to tumorigenesis.
Methods: One of the earliest responses to DNA DSBs is the phosphorylation of a histone, H2AX, at serine 139, yielding a focal product (γ–H2AX) that can be detected by a fluorescent antibody. In this study we compared the induction of DSBs in normal lung cells (SAE) and cancer cells (A549) after exposure to crocidolite asbestos (a known carcinogen), silica (a suspected carcinogen), or titanium dioxide (an inert particle) recently alleged to be carcinogenic in animals.
Results: The results indicate that asbestos induced greater DNA DSBs than silica and TiO_2 regardless of cell type. DNA DSBs due to asbestos were higher in normal cells than in the cancer cells. In contrast, silica and TiO_2 induced higher DNA DSBs in cancer cells than in normal cells. The production of reactive oxygen species (ROS) was also found to be highest in cells exposed to asbestos followed in potency by silica and TiO_2. The generation of ROS was higher in normal cells than in cancer cells. Apoptosis, as measured by caspase 3/7 activity, was highest in asbestos–exposed cells followed in potency by TiO_2 and silica. Cell viability assays indicate that asbestos caused the greatest cytotoxicity in both cell types.
Conclusions: The results of this study indicate that asbestos has a greater carcinogenic potential than silica and TiO_2 to exhibit by its ability to produce sustained genomic instability.

This abstract is funded by: NIOSH and US Army Medical Research.