fraction and DSB-repair efficiency are dramatically decreased by chrysotile asbestos in the DNA DSB repair deficient cells as compared with wild-type cells (Okayasu et al. 1999). A very early step in the response of mammalian cells to DNA DSBs is the phosphorylation of histone H2AX at serine 139 at the sites of DNA damage (Lowndes and Toh 2005). Using γ-H2AX as a biomarker for DNA DSBs, our data showed that the accumulation of γ-H2AX was greatly increased by chrysotile treatment in MEF cells, which was inhibited by concurrent treatment with catalase. These findings provided strong corroborating evidence of the DNA damaging effects of chrysotiles through the oxyradical pathway.

Chromosomal rearrangements have been closely associated with the progression and maintenance of cancer (Radford 2004). One of the major difficulties in detecting *in vivo* somatic mutations in chromosomal DNA is the lack of systems capable of identifying and isolating mutated genes with high efficiency. Spi^- selection based on deletions extending into or through both the *redBA* and *gam* genes is an efficient mutation assay system for detecting small to kilobase-sized deletions in different cells, organs, and tissues (Nohmi and Masumura 2004). Although during packaging, the individual genes and vectors are segregated from each other and assayed for mutation independently, the target genes in the *gpt* delta system are present in multiple copies in tandem arrays and amount to a potential target of approximately 3.8 Mb. In reality megabase deletions cannot be distinguished from kilobase deletions because of the size limitation of lambda phage to be packaged. Thus, it is likely that the deletions that are induced by asbestos fibers in the present study may include intergenic deletions whose sizes are > 10 kb. As gene mutation, mitotic recombination, chromosome loss, and interstitial deletion largely contribute to the development of malignancy, the establishment of the *gpt* delta transgenic mouse mutation model may provide novel, mechanistic information on asbestos-induced genotoxicity in the future.

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