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The How and Why of Asbestos Carcinogenesis

Tom K. Hei, Ph.D.

Center for Radiological Research, College of Physicians and Surgeons
Department of Environmental Health Sciences, Mailman School of Public Health
Columbia University

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10 - 11:30 am
Chamblee 106 Rooms 1A/1B

Asbestos is an important environmental hazard in the U.S. and remains the primary occupational concern in many developing countries. Although asbestos is carcinogenic to humans, the underlying mechanisms of fiber carcinogenesis are not known. Studies using mammalian cell models have suggested that fiber dimensions, surface properties, physical durability, and cell and tissue responses are important criteria for the carcinogenicity of the fibers. Studies using oncogenic transformation as an endpoint have shown that asbestos fibers can induce malignantly transformed foci in certain rodent cells and that oxygen radicals are important in the toxicity, oncogenic transforming and mutagenic effects of asbestos fibers. The mutagenic effects of asbestos in mammalian cells have been demonstrated using several model systems that can detect large multilocus deletions. There is evidence that extranuclear targets play an essential role in the initiation of oxidative damages that mediate fiber mutagenesis. Downregulation of BigH3 protein, a secreted protein induced by transforming growth factor-Beta has been found to be causally linked to the tumorigenic phenotype in asbestos treated human bronchial epithelial cells. These findings provide a direct link between chromosomal abnormalities that have frequently been demonstrated in fiber exposed human and rodent cell lines and carcinogenicity in vivo. Although the United States E.P.A. has limited the industrial use of asbestos since the mid-1970's, the recent contamination incidence in Libby, Montana highlights the need for a better understanding of the mechanism of fiber carcinogenesis, which is essential for the developments of better interventional and preventive measures.