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Shimkin M B & Stoner G D. Lung tumors in mice: application to carcinogenesis bioassay. *Advan. Cancer Res.* 21:1-58, 1975.
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This review article summarizes the information available in 1975 on the biology of mouse lung tumors and their use in the detection of environmental chemical carcinogens. It has served as a reference base for numerous subsequent investigations of mouse lung tumorigenesis, ranging from studies on the genetic basis of lung tumor susceptibility in mice to carcinogenesis bioassays of environmental chemicals. [The *SCI*® indicates that this paper has been cited in over 200 publications.]

Mouse Lung Tumorigenesis— A Tribute To Michael Shimkin

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I joined Michael B. Shimkin as a postdoctoral fellow at the University of California, San Diego, in 1970. Mike developed a quantitative lung tumor bioassay in strain A mice for the detection of environmental chemical carcinogens in the 1940s, and he was interested in using the assay to determine structural/functional activity relationships of environmental chemicals. He was intrigued by the fact that only minor differences in chemical structure could have a profound effect on carcinogenic activity. For example, he showed that ethyl carbamate is a potent carcinogen in the lung tumor bioassay whereas methyl carbamate is inactive. The observed differences in lung tumor susceptibility among the various inbred strains of mice were also of great interest, and Mike thought that genetic and biochemical studies to unravel the bases for these differences could be of importance in understanding cancer. Finally, as a pragmatist, Mike liked the fact that the lung tumor bioassay is a rapid, quantitative, and cost-effective method for detecting the carcinogenic potential of environmental chemicals and wanted to see its use for this purpose expanded. Therefore, he suggested that we write a review article to summarize the current state of knowledge of mouse lung tumorigenesis in 1975. It was his desire (and mine) that the article stimulate other researchers with different expertise to become involved in studies of mouse lung tumorigenesis.

Mike was very prolific. After spending a few weeks (off and on) in the library compiling reference data on index cards, he wrote most of the chapter in three days. His first draft was essentially a final draft. Needless to say, my smaller portion of the chapter took somewhat longer to write.

The objectives of the review article have been largely fulfilled. Since 1975 there have been numerous investigations of mouse lung tumorigenesis encompassing a variety of fields.[1-3] Morphological studies suggest that mouse lung tumors are derived both from alveolar type II cells and bronchiolar Clara cells, as opposed to type II cells only (as indicated in our chapter). However, this remains a matter of controversy. Immunologic, morphometric, and genetic studies have shown that susceptibility to chemically induced lung tumors among inbred mouse strains is related to the immune system, basal proliferation rates of alveolar type II cells, and the expression of at least three *Pas* (pulmonary adenoma susceptibility) genes. Activation of the K_1-*ras* proto-oncogene has been observed in both spontaneous and chemically induced lung tumors in mice, and the activating mutations in this gene are unique for each class of carcinogen. Inbred strains with high lung tumor susceptibility have a different allelic form of the K_1- *ras* gene than do those with low lung tumor susceptibility. Finally, since 1975, the lung tumor bioassay has identified a few additional carcinogens in our environment; however, it has proved to be relatively insensitive to certain classes of chemicals that are active in long-term carcinogenesis bioassays.

Michael Shimkin died in January 1989.[4] Among his numerous interests and accomplishments in cancer research and education, none was any more important to him than his work on chemically induced mouse lung tumors. In this regard it is only fitting that a symposium entitled "Mouse Lung Tumorigenesis" is being held in his honor at the National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, this week (March 27-28, 1990).

1. **Stoner G D & Shimkin M B.** Strain A mouse lung tumor bioassay. *J. Amer. Coll. Toxicol.* 1:145-9, 1982. (Cited 35 times.)
2. **You M, Candrian U, Maronpot R R, Stoner G D & Anderson M W.** Activation of the K_1-*ras* protooncogene in spontaneously occurring and chemically-induced lung tumors of the strain A mouse. *Proc. Nat. Acad. Sci. USA* 86:3070-4, 1989.
3. **Malkinson A M.** The genetic basis of susceptibility to lung tumors in mice. *Toxicology* 54:241-71, 1989.
4. **Weinhouse S.** Michael B. Shimkin, 1913-1989. *Cancer Res.* 49:3143, 1989.

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