THE COUNCIL FOR TOBACCO RESEARCH – U.S.A., INC.

September 23, 1981

HK01360096

PUBLICATION BY GRANTEE (1943)

The following paper has been published with acknowledgment of support by The Council for Tobacco Research - U.S.A., Inc.

DNA REPLICATION AND UNSCHEDULED DNA SYNTHESIS IN LUNGS OF MICE EXPOSED TO CIGARETTE SMOKE

A murine model system was used here to study the effects of chronic cigarette smoke exposure on enzymatic activities in lung tissue associated with DNA replication and DNA repair. For this work, mice were chronically exposed to measured amounts of machine-generated whole Kentucky reference 2A1 cigarette smoke. DNA replication and unscheduled DNA synthesis (UDS) were measured in lung tissue in vitro using a short-term organ culture method. Within one week of beginning smoke exposure, DNA replicative activity, as indicated by incorporation of ^{3}H-thymidine into total lung DNA, was increased more than two-fold over sham-exposed controls and remained elevated as long as smoke exposure was continued. Treatment of lung tissues in vitro with either the lung carcinogen 4-nitroquinoline-1-oxide or methylmethane sulfonate stimulated UDS, presumably as the result of DNA repair activity. Until the 10th to 12th week of smoke exposure, at which time the accumulated deposition of total particulate material in the lung was approximately 40 mg, the level of UDS stimulated by the alkylating chemicals declined to approximately 50% of that seen in lung tissue from sham-exposed control mice. If the mice were removed from smoke exposure, DNA replicative activity returned to normal levels within one week, but the UDS response to DNA damage remained depressed up to five months after ending smoke exposure. The results presented here show that both transient and apparently permanent changes are produced in mouse lung as the result of chronic exposure to cigarette smoke.

Rasmussen, R. E. (973) et al.

Cancer Research 41(7):2583-3588, 1981.

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