TRANSPLANTATION OF HAMSTER LUNG LESIONS INDUCED BY $^{239}PuO_2$ OR BENZ(a)PYRENE

Investigators:
K. E. McDonald and C. L. Sanders

None (0%) of 1000 recipients of lung lesions from $^{239}PuO_2$-exposed hamsters that were transplanted into other hamsters' cheek pouches, developed tumors, whereas 90% of transplants from benz(a)pyrene-induced lung lesions were malignant.

The incidence of lung tumors in Syrian Golden hamsters given intratracheal ^{210}Po has been reported as high as 75%, while the lung tumor incidence observed in hamsters following inhalation of comparable doses of $^{238}PuO_2$ or $^{239}PuO_2$ was <5%. One criterion of malignant transformation is transplantability. The purpose of this investigation was to determine whether lesions induced by inhaled $^{239}PuO_2$ in the hamster lung are truly malignant or merely metaplastic.

One hundred young, female, Syrian Golden hamsters were exposed, nose-only, to an aerosol of $^{239}PuO_2$; initial alveolar depositions ranged from 12 nCi to 150 nCi ^{239}Pu. At monthly or bimonthly intervals, starting at 5 mo after inhalation of $^{239}PuO_2$, groups of 10 hamsters were killed. The most severe (from gross appearance) lung lesions were removed, bisected and one portion was transplanted into the cheek pouch of an unexposed recipient hamster. The other portion was embedded in paraffin for histopathological examination (Annual Report, 1978). A control group of 10 hamsters was given serial intratracheal instillations of benz(a)pyrene (BaP) + Fe_2O_3. Grossly obvious BaP-induced lung tumors were transplanted into the cheek pouches of unexposed hamsters. Lung lesions were tested and examined up to 13 mo following initial exposure. The degree of epithelialization and adenomatosis was determined for the original sample transplanted and for the tissue removed after 3 wk growth within the cheek pouch.

A total of 1000 recipient transplants from 100 donor hamsters following exposure to $^{239}PuO_2$, and 10 recipient transplants from two lung-tumor-bearing hamsters following BaP instillation, were histopathologically evaluated. The most severe lesions in but focal regions of adenomatosis; some of these lesions exhibited epithelialization following transplantation (Figures 17 and 18). BaP-induced lung tumors were of the squamous-cell type, and grew up to 1-2 cm in diameter within the recipient transplants. Histologically, transplanted BaP-induced tumors were similar to those seen in donor lungs (Figures 19 and 20).

The degree of epithelialization and adenomatosis was greatest in BaP + Fe_2O_3 hamster lungs, followed by Fe_2O_3 alone, then by $^{239}PuO_2$; few such lesions were seen in control hamsters (Table 15). None (0%) of the 1000 transplants from 100 donor hamsters exposed to $^{239}PuO_2$ developed malignant transformations; all of these transplants exhibited some degree of necrosis, calcification and replacement of epithelial tissue with connective tissue at 3 wk. In contrast, 9 of 10 (90%) BaP tumor transplants developed large tumor growths in hamster cheek pouches. None of the Fe_2O_3 or unexposed control lung transplants developed malignant transformations.

An earlier study with inhaled PuO_2 failed to demonstrate the induction of primary lung tumors in more than a few hamsters. However, there was a dose-dependent increase in adenomatosis which might represent a premalignant condition. However, our transplant studies have failed to demonstrate any malignant potential for these lesions. We therefore conclude that, based on the criteria of histopathology and transplantability, inhaled plutonium dioxide induces few primary lung tumors in the hamster at any radiation dose. The hamster is therefore a poor animal model for the study of pulmonary carcinogenesis following inhalation of alpha-emitting radionuclides.

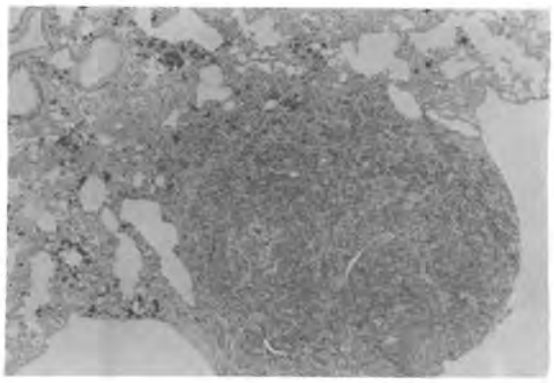

FIGURE 17. Lung Tumor Extending into Pleural Cavity Following Intratracheal Instillation of Benzo (a) pyrene + Fe_2O_3. 40X

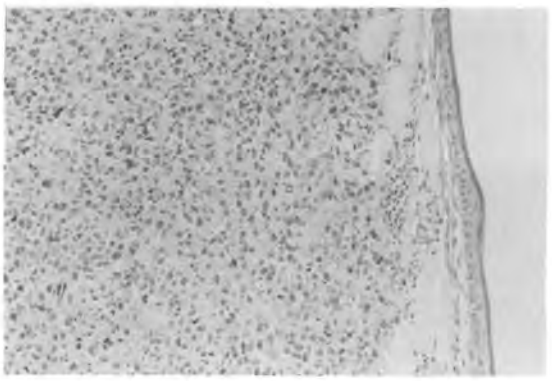

FIGURE 18. Transplanted Lung Tumor (from Figure 17) in Hamster Cheek Pouch. Tumor was about 1 cm in diameter at 3 wk after transplantation. 160X

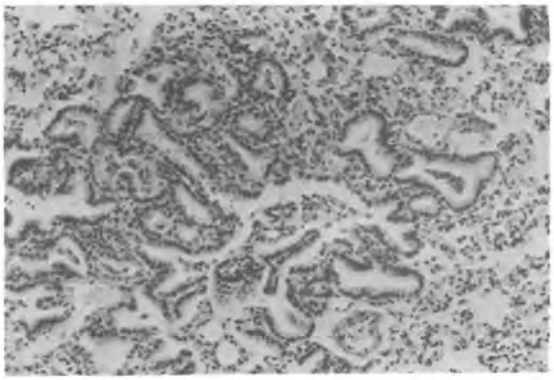

FIGURE 19. Hamster Lung Exposed to $^{239}PuO_2$ Showing Bronchiolization and Adenomatous Metaplasia. 160X

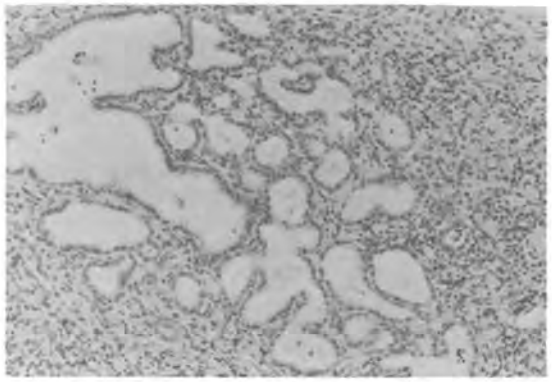

FIGURE 20. Transplant from Hamster Lung Exposed to $^{239}PuO_2$ Showing Bronchiolization at 3 wk after Transplantation. This is an example of the most pronounced epithelial proliferation seen in any transplant lung tissues from $^{239}PuO_2$-exposed hamsters. 160X

TABLE 15. Degree of Adenomatosis in Donor Lungs and Epithelialization in Hamster Lung Transplants (at 3 wk After Transplantation)

	Mean[(a)] ± SD, Epithelial Proliferation	
Treatment	Donor Lung (N)	Transplant Lung (N)
Unexposed Controls	0.72 ± 0.31 (10)	0.71 ± 0.30 (100)
$^{239}PuO_2$	1.26 ± 0.38 (100)	0.81 ± 0.30 (1000)

(a) Grading system:
1 - very slight
2 - slight
3 - moderate
4 - marked
5 - extreme