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Tumor induction in Swiss mice by filtrable agent and Salmonella typhimurium.

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Abstract

Combined inoculation of a cell-free extract of leukotic tissue of D103 mice and Salmonella typhimurium into adult Swiss mice induced leukosis and solid tumors. The induced solid tumors were histologically multifarious, and were transplantable in Swiss mice, but not in other strains of mice.

KEYWORDS: tumor, cell-free extract, salmonella

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—— BRIEF NOTE ——

TUMOR INDUCTION IN SWISS MICE BY FILTRABLE AGENT AND *SALMONELLA TYPHIMURIUM*

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Abstract. Combined inoculation of a cell-free extract of leukotic tissue of D103 mice and *Salmonella typhimurium* into adult Swiss mice induced leukosis and solid tumors. The induced solid tumors were histologically multifarious, and were transplantable in Swiss mice, but not in other strains of mice.

Key words: tumor, cell-free extract, Salmonella

We have reported the development of murine leukosis following ingestion of human cancers (1–4). The synergetic action of a filtrable agent and *Salmonella typhimurium* appeared to be necessary for the development of this leukosis (5). In the present study, combined inoculation of a cell-free extract of D103 leukotic tissue and *Salmonella typhimurium* into Swiss mice induced leukosis and solid tumors. These results are reported in this paper.

A 20% homogenate of the spleen and liver of leukotic D103 mice was prepared in cold physiological saline solution and passed through a millipore filter (HAWP) to produce a cell- and bacteria-free extract. *Salmonella typhimurium* isolated from the spleen and liver of leukotic D103 mice was suspended in physiological saline solution to a concentration of about 14×10^5 bacilli/ml. The cell-free extract and the bacterial suspension were inoculated intraperitoneally into 3- or 4-month-old Swiss mice at a dose of 0.3–0.5 and 0.01–0.03 ml respectively.

As shown in Table 1, neither 15 Swiss mice inoculated solely with the cell-free extract nor 10 inoculated solely with *Salmonella typhimurium* developed any recognizable disease. However, of 51 Swiss mice inoculated simultaneously with both cell-free extract and *Salmonella typhimurium*, 19(37%) developed leukosis in 4–15 (average 7) days, and 6 (12%) developed intraperitoneal solid tumors in 72–374 (average 143) days.

The leukosis developing in Swiss mice was macroscopically and microscopically similar to the murine leukosis we reported previously (1–3). The solid

tumors appeared to be developing on the peritoneum (Fig. 1) without any recognizable distant metastases, and were transplantable into Swiss mice, but not other strains of mice. The histology of the tumors was multifarious: fibroblas-

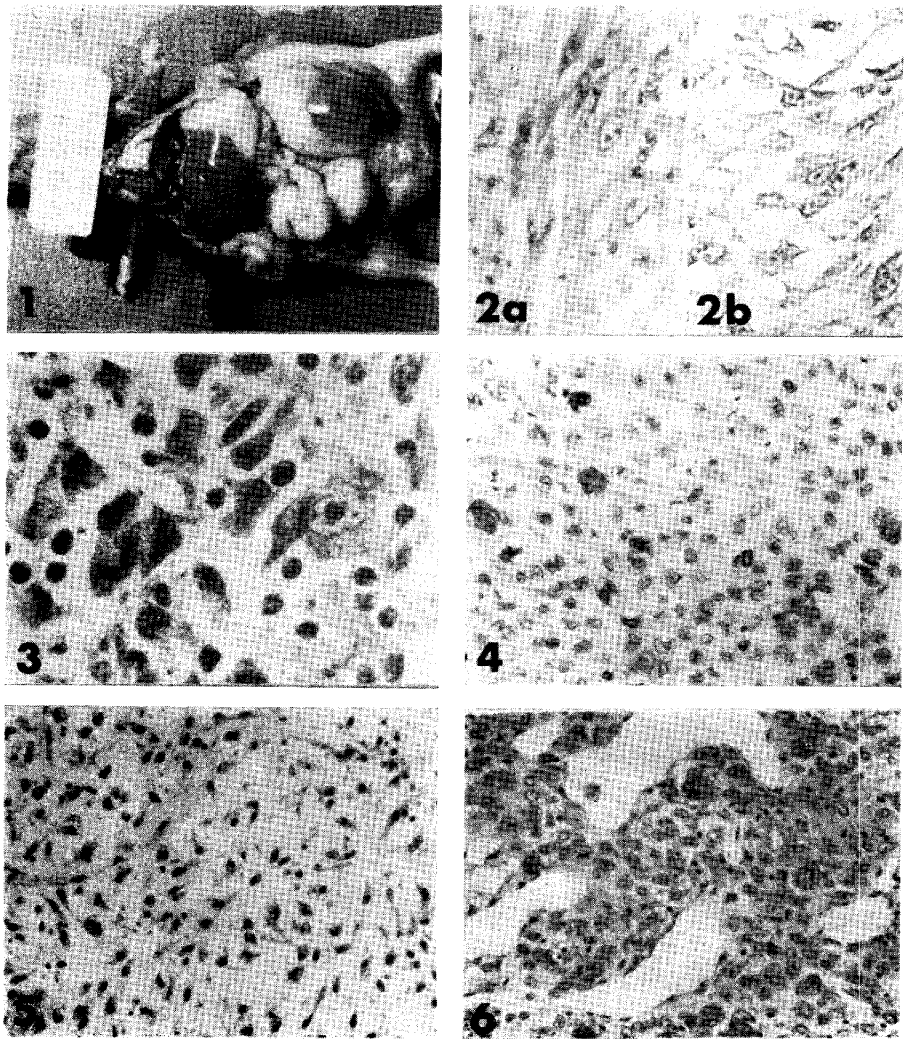

Fig. 1. Intraperitoneal tumors developing in a Swiss mouse 72 days after combined inoculation of cell-free extract and *Salmonella typhimurium*.

Fig. 2. Large mesenchymal cells constituting the main parts of tumors. (a) Fibroblastic cells. (b) Fibroreticular cells. Hematoxylin-Eosin (HE) stain. ×200.

Fig. 3. A part resembling pleomorphic cell sarcoma. HE stain. ×100.

Fig. 4. A part resembling chondrosarcoma. HE stain. ×200.

Fig. 5. A part resembling myxoma. HE stain. ×200.

Fig. 6. A part resembling hemangiopericytoma. HE stain. ×200.

TABLE 1. TUMOR INDUCTION IN SWISS MICE BY COMBINED INOCULATION OF CELL-FREE TISSUE EXTRACT AND *Salmonella typhimurium*

Materials inoculated	No. of inoculated	Tumor		Days from inoculation to death or sacrifice from tumors (average)
		Tumor type	No. of developing tumors (%)	
Cell-free extract[a]	15	Leukosis	0	
		Solid tumors	0	
Salmonella typhimurium[b]	10	Leukosis	0	
		Solid tumors	0	
Cell-free extract + Salmonella typhimurium	51	Leukosis	19 (37)	4- 15 (7)
		Solid tumors	6 (12)	72-374 (143)

a Cell-free extract of the liver and the spleen of leukotic D103 mice.

b *Salmonella typhimurium* isolated from the liver and the spleen of leukotic D103 mice.

tic or fibroreticular sarcoma partly intermingled with areas resembling hemangioendo/pericytoma, chondroma, myxoma and pleomorphic cell sarcoma (Figs. 2-6).

Summary. Our previous studies have suggested that the synergetic action of a filtrable agent and *Salmonella typhimurium* might be necessary for the development of leukosis in D103 (5). In the present study, the combined inoculation of leukotic tissue extract and *Salmonella typhimurium* induced both leukosis and solid tumors in Swiss mice. Thus it again appears that bacterial infection might stimulate the induction of neoplasms. Salmonella possesses facultative intracellular parasitic properties, and these might be responsible for its enhancing the induction of neoplasms by our filtrable agent, although the mechanism is not clear at present.

Harvey has reported the development of solid tumors in mice inoculated with murine leukemia virus (6).

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