Experimental Model for Induction of Lymph Node Metastases with a Human Heterotransplanted Melanoma in Rat

In previous papers POPP et al. reported a new rat tumour IOB hR 18 derived from a human melanocarcinoma transplanted in WAG rats by intra-embryonic route[1-3]. Tumoural outgrowth became evident in suckling rats. Isologous transplantations were performed in embryos, new-born and adult animals, as well as in adult Wistar rats and were always followed by tumoural take. At present the tumour has a history of 25 generations, being maintained in Wistar rats by s.c. challenge every 3 weeks.

The tumour does not metastasize; it grows within a capsule and may sometimes reach the size of the host, killing it in about 30 days.

Microscopic examination showed an abundantly pigmented melanocarcinoma. After several rat passages, the aspect became that of a massive anaplasic carcinoma, the cells being arranged in rows or in close, well vascularized clones.

Studying the development of intratestis inoculated tumours[4-10], we were able to set up an experimental model of abdominal lymph node metastases of IOB hR 18 tumour.

Material and methods. Sixty adult Wistar-London rats from the Oncological Institute closed colony were used.

A tumoural fragment of about 1 g was minced and then ground in saline. After 5 min sedimentation, 0.2–0.3 ml of the supernatant were picked in a syringe with a No. 16 needle and injected into each testicle.

Results. The intratesticle grafts of IOB hR 18 tumour resulted in 100% takes, while the percentage of abdominal lymph node metastases was of the order of 90%. The bilaterally inoculated animals developed metastases in 15–20 days. The size of metastatic tumours reached that of a dry nut, while the para-aortic and para-renal lymph node metastases ranged between that of a pea and that of a nut. 25% of the inoculated animals developed a tumour cell rich ascites of 0.5–10 ml. The metastases achieved by the above procedure are very similar to the lymph node metastases developing in human melanoma and carcinoma.

This experimental model of intratesticular tumours inoculation is of practical importance because of its neatness and its homogenous and constant results, which permit investigations of free neoplastic cells (malignant monerocytoma[11]) and, in the experimental study, of the pathogeny and therapy of tumoural metastasis.

Résumé. Le travail décrit une technique expérimentale qui permet d'obtenir de grosses métastases ganglionnaires chez le rat après inoculation intratesticulaire de la tumeur IOB hR 18. Ce modèle expérimental peut être utilisé dans diverses études concernant la pathogénie et la thérapie des métastases.

A. RIVENZON, V. COMISEL and I. POPP

Oncological Institute, Bucharest 62 (Rumania), 8 July 1968.

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Binding of 1-3,4-Dihydroxyphenylalanine and Dopamine in Cytoplasmic Granules of Paneth Cells

Several tissues have the ability to take up and bind catecholamines (CA) but it is now generally accepted that this binding occurs predominantly in the adrenergic nerve system. The mammalian intestinum contains 5-hydroxytryptamine (5-HT) storing enterochromaffin cells[1] and in rodents there are also 5-HT-containing mast cells[2]. Certain cells in the glandular part of the rat stomach are capable of storing monoamines in vivo[3] and some human intestinal epithelial-like cells store 1-3,4-dihydroxyphenylalanine (D) in vitro[4]. The intestinal epithelium and the intestinal glandular cells normally contain neither CA nor 5-HT in chemically or histochemically demonstrable amounts. In the present study the binding of i.v. administered D and dopamine (DA) was studied in the duodenum of the mouse with special reference to cytoplasmic particles of Paneth cells.

150 mice, 20–25 g, were studied. The animals received no food for 24 h before experiments. D and DA (15–150 mg/kg) were injected slowly into the tail vein of mice and the animals were killed 10 and 30 min, 1, 2.5, 4 and 8 h later by decapitation. The freeze-drying procedure followed the principles given by ERÄNKÖ[5]. Duodenal pieces, 5 mm in length, including the entire transverse section of an opened intestinal wall, were frozen in isopentane precooled in liquid nitrogen and dried in vacuo at $-40\,^{\circ}C$ for 2 days. Specimens were warmed up to room temperature in vacuo for 5 h and after treatment in formaldehyde vapour derived from paraformaldehyde for 1 h at 80 °C. 5-μ sections were cut and the paraffin wax was removed by xylene before fluorescence microscopy. Histochemically monoamine oxidase (MAO) activity was demonstrated by the method of GLENNER et al.[6]. In inhibition experiments of MAO mice were pre-treated with a 500-mg/kg dosis of Niamid® 4 h before amine administration.

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