17.

A HIGH-CAPACITY SEMI-MICRO METHOD FOR THE ASSAY OF TUMOR CELL PENETRATION. K. Tullberg, R. Obrist, J.P. Obrecht, M.M. Burger*.Div. of Oncology, Dept.of Internal Medicine of the University and Dept. of Biochemistry, Biocenter of the University*, CH-4031 Basel, Switzerland.

It was demonstrated that penetration of B16 melanoma cells through 3um membrane-filters involves parameters contributing to metastasis (Tullberg and Burger, Invasion and Metastasis 5:1, 1985). It is unknown whether this also holds true for various human tumors. Current work to investigate this prompted the present methodological improvement, feasible for large-scale, semi-micro and semi-automatic tests. The new method uses a 80x25 mm nuclepore membrane, which rests on a 2 mm stainless steel plate and is covered by a silicon rubber gasket and a 5 mm steel plate, all with 10 holes of 8 mm Ø. Gasket and 5 mm plate are both fitted and secured over screws protruding from the lower plate. The assembly fits in a 10 cm culture dish. Filters are sterilized separately in 70% ethanol and not autoclaved, which avoids wrinkles due to heat deformation. The new device differentiates with similar sensitivity between low and high metastatic B16 lines as did the previous method (old assay: 102±8 vs. 538±37 cells; new assay: 86±11 vs. 534±25 cells). Four improvements are featured: 1. Ten measurements are obtained in a single assay. 2. Different cells can be tested in the same dish, minimizing inter-dish differences. 3. A total count of the penetrating cells is possible, due to the smaller surface. 4. Strictly planar filters make automatic cell counts by image analysis possible. Supported by the Roche-Foundation.

18.

RELEASE OF PROTEINASES BY CULTURES OF HUMAN CELL LINES DERIVED FROM SQUAMOUS CARCINOMAS OF THE TONGUE AND LARYNX. A. Baici, Department of Rheumatology, University Hospital, CH-8091 Zürich, Switzerland.

Squamous carcinomas of the head and neck are invasive tumors characterized frequently by destruction of contiguous cartilage and bone (a relatively uncommon mode of spread in solid tumors at other sites), diffuse infiltration of local soft tissues, invasion of lymphatics and blood vessels and metastasis to regional lymph nodes. Seven human cell lines derived from squamous carcinomas of the tongue and larynx were examined for their ability to produce and secrete proteinases. All cell lines were able to release cysteine proteinase and plasminogen activator-like activities. All lines differed from each other in the amount of enzymes secreted, in the kinetics of the secretion, in the quality of the enzymes produced and in the intracellular pools of these activities. The considerable and consistent differences between the abilities of the tumor cell lines to secrete relevant proteolytic activities may possibly be related to the capacity of the cells to invade and destroy soft tissue and bone. For instance, the line HN-4 showed the highest potential to secrete both cysteine proteinase and plasminogen activator. This correlates well with other independent data showing that this line manifests the highest in vitro bone resorbing activity and fibrinolytic potential among the tumor cells considered.

19.

INVASION OF THE CHICK CHORIOALLANTOIC MEMBRANE (CAM) BY HEp-3, A HUMAN TUMOR CELL LINE. J.E. Testa, J.-F. Cajot and B. Sordat, Swiss Institute for Experimental Cancer Research, CH-1066 Epalinges, and the Division of Hematology, CHUV, CH-1010 Lausanne, Switzerland.

The invasive behavior of a number of human and murine tumor cell lines on the chick chorioallantoic membrane (CAM) was examined by light and electron microscopy. Most of the lines tested were unable to form tumors when cell suspensions were placed on the CAM surface. Of the tumorigenic cells, HEp-3, a human epidermoid carcinoma cell line (established from a CAM tumor), regularly formed large, rapidly growing tumors and was the only line capable of crossing the chorionic epithelium. These cells could also invade the mesodermal vasculature of the CAM and infiltrate the chick lung, liver and, in particular, the kidney. Within the embryonic organs HEp-3 formed diffuse, loosly associated cellular patches rather than well defined metastatic foci. HEp-3 is hypertetraploid and produces large quantities of human urokinase-like plasminogen activator.

Three HEp-3 sublines have been established *in vitro* : 1) HEp-3/SC 2 established from a subcutaneous (s.c.) nude mouse tumor; 2) HEp-3/SC2-LM from a lung metastasis in a nude mouse; and 3) HEp-3/KSC 1 from an infiltrated embryonic chick kidney implanted s.c. in a nude mouse. The invasive behavior of these sublines on the CAM has been examined. The karyotypes, plasminogen activator activities and 2-dimensional gel electrophoresis protein maps of the sublines and the parental HEp-3 line have also been compared.

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20.

EXPERIMENTAL REPRESSION OF METASTASIS BY A SECOND IMPLANT OF THE SAME TUMOR. R. Keller. Immunobiology Research Group, Institute of Immunology and Virology, University of Zurich, Schönleinstr. 22, CH-8032 Zurich, Switzerland.

In a rat fibrosarcoma model (D-12), the incidence of spontaneous macroscopic metastases, located predominantly in regional lymph nodes, is low; it is however markedly increased after surgical removal of the primary tumor inoculum. The present study shows that the rapid outgrowth of macroscopic metastases occurring after surgical resection of the primary tumor implant is effectively repressed by a second implant of live D-12 cells into a remote site. Contrariwise, implantation of heavily irradiated D-12 cells or the prolonged delivery of D-12 ascites fluid had no repressive effect on metastatic tumor growth. This is further evidence for a basic role of tumor/tumor interrelations in determining the final outcome of the interaction of tumor and host.