Table II. Content of intercellular dermal components in 6-day cultured skin explants supplemented whith CS or E nutritional medium

	CS	E
NANA	0.019[a]	0.015
Uronic acids	0.021	0.025
Hexosamines	0.033	0.015
NANA/Ur ac	0.90	0.60
NANA/Hexos	0.54	0.62
Ur ac/Hexos	0.63	1.04

[a] mg/mg of proteins; each walue is the mean of 2 independent experiments each in duplicate.

and a minor amount of uronic acids is present in CS cultured explants in comparison with E cultured ones (Table II). Assuming the amount of sialic acid as an index of GP content, of uronic acids of GAG, and the amount of hexosamines as an index of both GP and GAG content, we can deduce that in CS explant GP accumulate to a greater extent than GAG. A similar situation has been previously demonstrated in vivo[4]. The concentration ratio HA/CSA in vivo (6-day 1; 10-day 1.52; 14-day 1.62) confirms the prevalent accumulation of HA.

Our results clearly demonstrate a correlation both in vivo and in vitro between the histochemical and biochemical features of dermal skin and the onset of epidermal differentiation and the dependence in vitro of mesenchyme modification on environmental factor(s) present in the chicken serum. They therefore support the suggested mechanism that environmental factor(s) can activate mesenchymal cells to produce substance(s) able to act specifically upon epidermal differentiation[5].

Riassunto. È stata evidenziata una correlazione fra caratteristiche istochimiche e composizione biochimica del mesenchima e l'instaurarsi del differenziamento dell'epitelio nella cute di pollo sia in vitro, in espianti prelevati al 6° giorno di incubazione e mantenuti in terreno nutritizio contente siero, che in vivo.

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Interrelationship Between Mean Arterial Blood Pressure, Blood Flow, and Vascular Resistance in Solid Tumor Tissue of DS-Carcinosarcoma

Capillary morphometrics and blood flow measurements in implantation tumors of DS-carcinosarcoma in rat kidneys show the following results: With increasing tumor wet weight, the volume of the vascular space decreases exponentially, the reduction of the vascular bed being especially distinct during the first period of the tumor growth[1]. During tumor growth in the kidney, there results an exponential enlargement of the mean intercapillary distances about the factor 2.5–3.0, as well as a lengthening and an increase in diameter of the capillaries. The rarefaction of the terminal vascular bed with increasing tumor weight or age is attended by an exponential decrease of the total tumor blood flow, the regional microcirculation of the outer areas of the tumor showing higher blood flow values than the inner parts[2]. The present investigation attempts to analyze the interrelationship between mean arterial blood pressure, tumor blood flow, and vascular resistance in tumor tissue of DS-carcinosarcoma under standardized in vivo conditions during different stages of growth.

Materials and methods. Ascites cells of DS-carcinosarcoma are implanted into rat kidneys where they are maintained 'tissue-isolated'[3,4]. After an average of 7–12 days, the infiltrating and destructively growing tumor cells completely replace the kidney tissue, and the tumor mass is connected to the host by only a single artery and vein. Total tumor blood flow (TBF) is determined by cannulating the tumor vein by means of a burette, using a roller pump and a constant pressure buffering chamber. The operative procedure, the blood flow determination and monitoring of the mean arterial blood pressure (MABP) are described elsewhere[5].

To study the influence of the mean arterial blood pressure on total tumor blood flow under in vivo conditions, blood flow measurements in 10 animals (anesthetized with pentobarbitone sodium, 25–30 mg/kg i.p.) are performed using a bubble flow meter. Multiple measurements of the bubble passage in the burette are made not only when blood pressure values spontaneously occur in the thoracic aorta but also after changing the perfusion pressure. After decreasing the mean arterial blood pressure by controlled bleeding, or after increasing it by blood transfusion from other tumor bearing animals, we always wait for steady state conditions before blood flow is measured at a new pressure level.

Results. Under steady state conditions the dependence of tumor blood flow on mean arterial blood pressure is examined at normal respiratory gas parameters in the arterial blood. As can be seen from the representative

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experiments in Figures 1 and 2 (upper parts), the blood flow through tumors with different weight or age shows linear dependence on the mean arterial blood pressure within the range of 40 to 135 mm Hg. According to the tumor weight, the blood flow values of both the tumors differ at the same mean arterial blood pressure. Autoregulation of blood flow, as is typical of the host organ, can no longer be observed.

The ratio of perfusion pressure to tumor blood flow indicates the vascular resistance of the tumors. With increasing mean arterial blood pressure, vascular resistance decreases from 160 to 141 PRU[6] for the light tumor (Figure 1, lower part) and from 574 to 219 PRU for the older, heavier one (Figure 2, lower part). Correspondingly, the tumor blood flow increases with rising perfusion pressure, the vascular resistance decreasing at the same time.

Discussion. The blood flow values of DS-carcinosarcoma in rat kidneys correspond with other data that were obtained not only in several 'tissue-isolated' implantation tumors but also in tumors growing spontaneously[7–13]. Compared to parenchymatous organs, the behaviour of the vascular system during tumor growth can explain the low tumor blood flow and its dependence on the weight. The tumor mainly holds the large vessels of the host organ only. In case of progressive growth of the tumor cells, especially in quickly growing tumors, vascularization can no longer keep up with the rapid proliferation of the cells. In consequence of their expansive growth, the tumor cells widen the existing capillary network, in the sense of a general vascular reduction, to such an extent that the tumor blood flow, related to the weight, must decrease to the same degree. Moreover, this increasing rarefaction of the tumor vessels during growth is proved by the increase of vascular resistance from 145.5 to 234.5 PRU (MABP = 100 mm Hg) at an increase in weight from 2.5 to 8.2 g. A comparison with the vascular resistances of important rat organs calculated from already known blood flow data at corresponding mean arterial blood pressures (liver[14]: 8.2 PRU, kidneys[15]: 11.7 PRU, brain[16]: 51.8 PRU, and heart[17]: 52.6 PRU) illustrates the influence of the general reduction of the vascular space and rarefaction of the terminal vascular bed on hemodynamics and on the tissue perfusion rate of solid tumors.

Zusammenfassung. In vivo-Untersuchungen der Tumordurchblutung an Implantationstumoren eines DS-Carcinosarkoms in der Rattenniere zeigen eine deutliche

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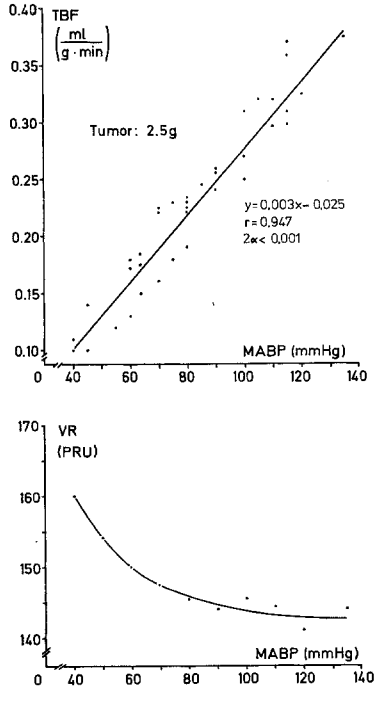

Fig. 1. Effect of mean arterial blood pressure (MABP) on blood flow (TBF) through a young tumor of 2.5 g (upper part). Dependence of vascular resistance (VR) in tumor tissue of DS- carcinosarcoma on mean arterial blood pressure (MABP) in the thoracic aorta (lower part).

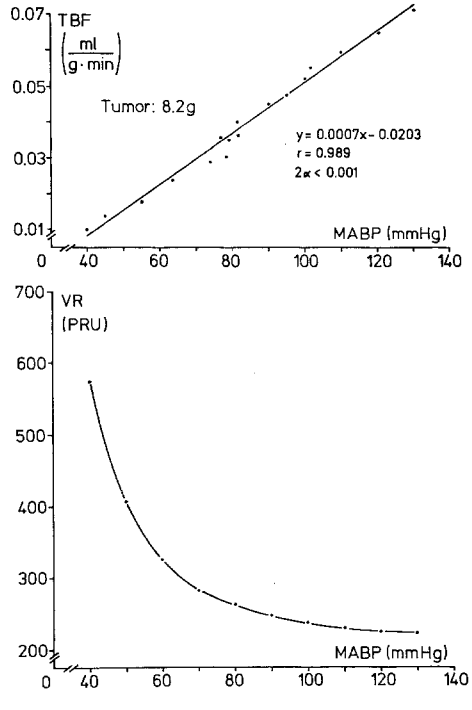

Fig. 2. Effect of mean arterial blood pressure (MABP) on blood flow (TBF) through an old tumor of 8.2 g (upper part). Dependence of vascular resistance (VR) in this tumor on mean arterial blood pressure (MABP).

Abhängigkeit der Durchblutungsgrösse vom Tumorgewicht. Bei Variation des arteriellen Mitteldrucks zwischen 40 und 135 mm Hg steigt die Durchblutung der einzelnen Tumoren linear mit zunehmendem Perfusionsdruck an. Eine zunehmende Rarefizierung der terminalen Strombahn mit ansteigendem Tumorgewicht wird belegt durch eine starke Zunahme des Strömungswiderstandes, der schon bei sehr jungen Tumoren wesentlich höhere Werte als bei verschiedenen Organen aufweist.

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A Study of the Primordial Germ Cells During their Migratory Phase in Steel Mutant Mice

The primordial germ cells (PGCs) of the mouse embryo can first be identified in the caudal end of the primitive streak, allantoic bud and yolk sac splanchnopleure around day 8 of gestation[1–5]. When first detected, the PGCs number about 100. On day 9 they reach the hind gut splanchnopleure and number about 500. On day 10 they reach the dorsal mesentery, mesenteric root and coelomic angles and number about 1,000. By day 11 the gonadal ridges are heavily populated with about 2,000 germ cells[2–5]. The migratory phase of germ cell development appears to end during day 12 at which time they number about 5,000[2]. The germ cells are known to divide along the migration path before infiltrating the gonadal ridges[5].

Mice carrying 2 mutant genes at the Steel (*S1*) locus are sterile, anemic and lack hair pigment[6]. The sterility, which is due to the absence of germ cells in the mature gonad[7,8], may be due to a failure in the proliferative and/or migratory capacity of the PGCs[9].

The present work is a study of mutant Steel mice and their normal littermates to further elucidate the process of primordial germ cell development.

WC/Re – *S1*/+ females and C57BL/6J – *S1*^{d}/+ males were mated overnight. The presence of a vaginal plug at 08.00 h indicated day 0 of gestation. Pregnant females were killed by cervical dislocation exactly 9, 10 and 11 days later (08.00 h). The embryos and surrounding membranes from two 9 day litters, and 4 each of 10 and 11 day litters, were fixed in 95% ethanol, embedded in paraplast (M.P. 50–52 °C) and sectioned at 10 µm.

PGCs are recognized cytologically from their high content of alkaline phosphatase[3]. Sections were stained for this enzyme in Fast Red TR salt coupled to α-Napthyl

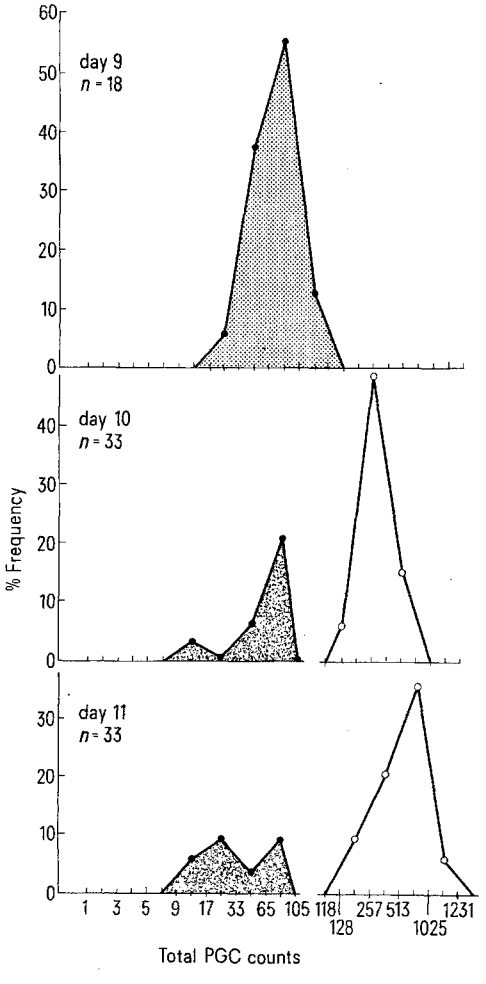

Fig. 1. The percent frequency of total PGC counts arranged on a logarithmic scale, showing a bimodal distribution of PGCs on days 10 and 11.

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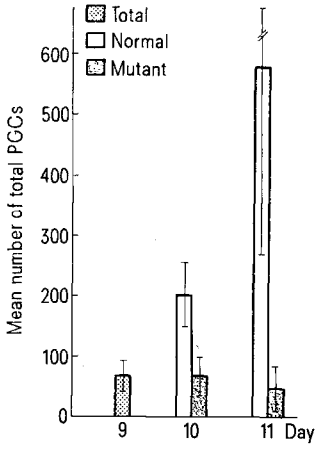

Fig. 2. An increase in the number of normal germ cells is seen on day 10 and 11 whereas the mutant PGCs remain about the same.