

Identification and specificity of action

The about 1300 publications dealing with cell therapy comprise experimental and clinical papers, which are specified hereafter under relevant points of view:

Experimental data:

1. Physiological (biological) experimental studies –
2. Research of morphological elements –
3. Immunological studies.

1. Physiological (biological) experimental studies

Attention is drawn to the following, highly specified in part, experimental studies:

- a) Biostatistical and methodical data (KMENT) –
- b) Activity studies on rats by means of lyophilised organic preparations (KMENT, 1956) –
- c) Tests on the activity of guinea-pig thyroid glands using radio-isotopes (J 131) after treatment with siccacell preparations (KMENT, 1958) –
- d) Objective demonstration of revitalisation by cell injections in animals (KMENT, 1960) –
- e) The substantiation of the revitalising effect on animals after cell injections (KMENT, 1963, 1967) –
- f) Quantitative electron-microscopic studies on cardiac mitochondria of rats after cell injections from placenta or testicular tissues (KMENT, 1966) –
- g) Studies on the revitalising effect of myocardial cells, myocardial nuclei and myocardial mitochondria in rats (KMENT, 1974) –
- h) The dispersion of tritiated cardiac,

liver and renal cells in old rats (KMENT, LEIBETSEDER and STEININGER, 1972) –

- i) The analysis of the spontaneous activity of old and revitalised rats by means of electronic registration (KMENT and HOFHECKER, 1972) –
- k) Trace elements in heart, liver and brain of rats in various ages and after revitalisation by cell injections (KMENT, HOFHECKER and NIEDERMÜLLER, 1973) –
- l) Studies on the effect of revitalisation upon the absorption, dispersion and excretion of penicillin V in rats (KMENT and NIEDERMÜLLER, 1973) –
- m) Article on the method of registering cinematographically the activity of rats as part of the research into revitalisation (JELENIK, 1971) –
- n) The effect of organic extracts and sera on the metabolism of organic cultures (WRBA, 1961–1962) –
- o) Experimental gerontological studies on the revitalization (KMENT, 1977).

These extensive experimental studies on the revitalizing effect, which are so far unique in gerontology, have demonstrated from various angles the possibility of influencing functionally aging tissues and organs. As in addition to the untreated controls, cellular suspensions (lyophilisates) of various organs were used, these results give also a relative explanation of the specificity of the effect.

2. Research of morphological elements

The following papers dealing with experiments on morphological elements relate to morphological effects of cell implantations:

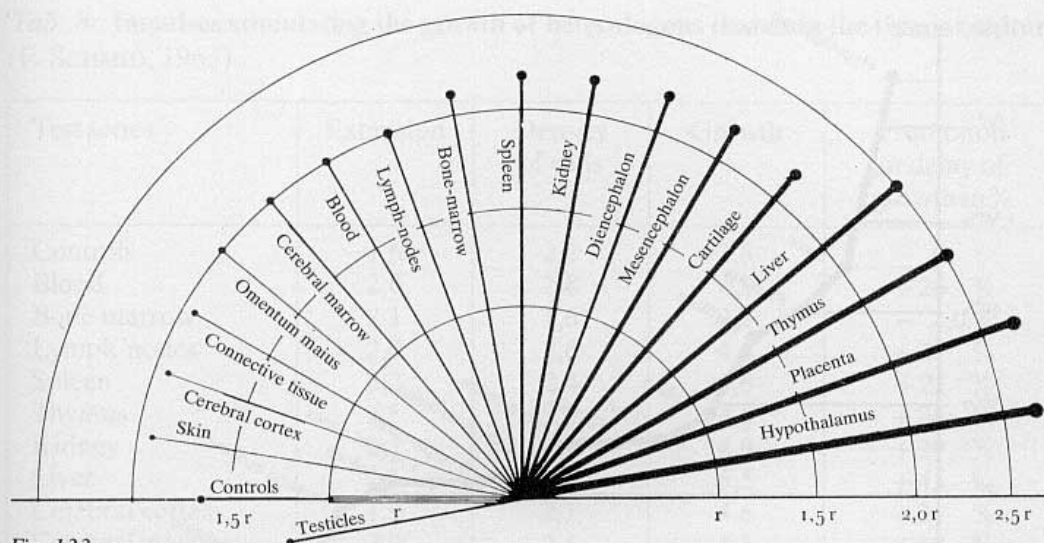


Fig. 133:

Extension of the zones of emigration in bone-marrow of rats on addition of fetal, heterological, lyophilized tissues as against the controls.

- a) Growth impulses and prolongation of life of cell cultures (CARELL; LETTRÉ, 1954; SCHMID F., 1962, 1963, 1967; v. LANGENDORFF, 1974) (fig. 129–132, 133, 134) –
- b) Increase of growth in corresponding organs (ANDRES, 1953, 1955, 1963); fig. 135 –
- c) Morphological studies on the substantiation of a different effect of extracts of lymphatic organs (GOSLAR, 1959, 1969) –
- d) Induction of the organic growth by implantation of homologous tissues (NEUMANN, 1957, 1958, 1959, 1963, 1967) –
- e) Influence of tissue injections on experimental hepatic lesions (NEUMANN, 1963, 1967) –
- f) The organo-specific effect of implanted rabbit endometria on the uterus of castrated rabbits (BERNHARD and KRAMPITZ, 1958, 1959, 1960, 1963, 1967) –
- g) Influence of placenta cells on the angiopathies of experimental angiosclerosis (DORNBUSCH, KLEINSORGE, 1956, 1963, 1967; WIETEK and TAUPITZ, 1957) –
- h) Growing processes in mice treated with fresh cells (DITTMAR, 1956, 1963) –
- i) Influences on leukaemia in animals (SCHMID F., 1963, 1967); fig. 289–294 –
- k) The effect of cell injections on tumours in rats (HOEPKE, 1955, 1963, 1967) –
- l) The effect of mast-cell substances on the growth of tumours (LANDSBERGER, 1963, 1967) –
- m) Light- and electron-microscopic studies on cell therapy; studies on mitochondria (LANDSBERGER, 1974) –
- n) Gerontological tests on mitochondria in the liver of rats (ADAMIKE, 1963; BURGER, 1965) –
- o) Quantitative electron-microscopic studies on liver mitochondria of rats after injections of placental and testicular tissues (HARTMANN, 1964; LECHNER, 1965) –
- p) Histological cross-sections of guinea-pig organs after injections of lyophilized placental cells (KLUDAS, 1954) –

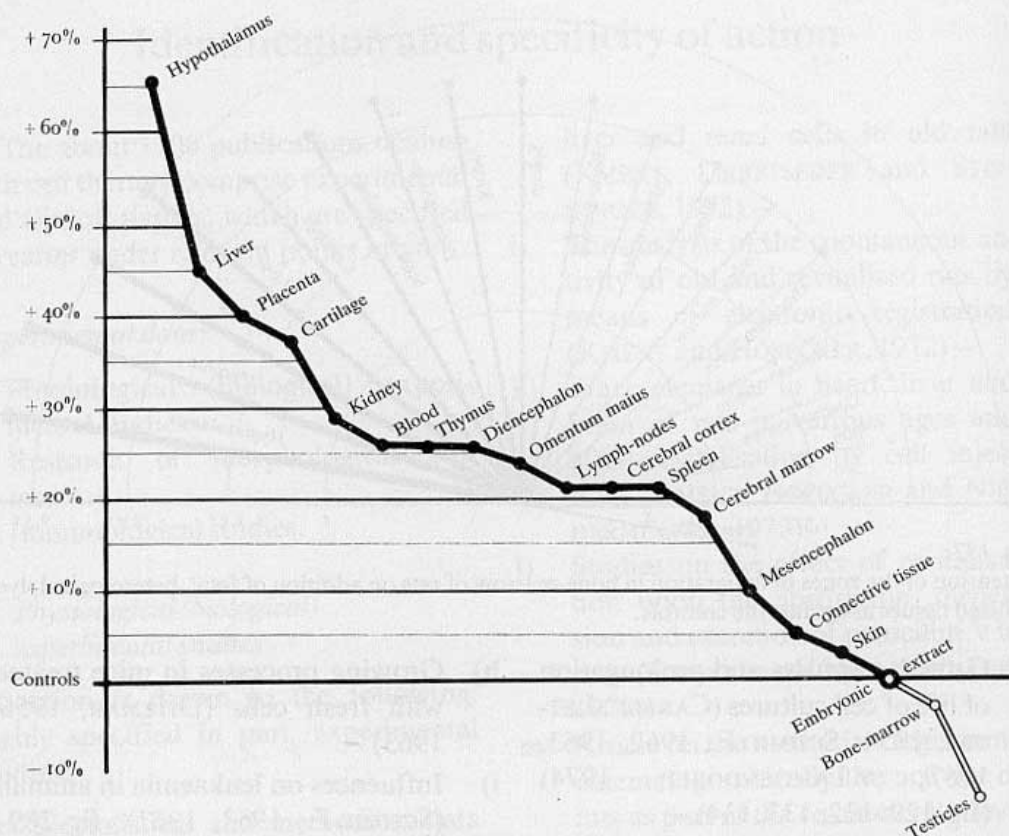


Fig. 134:
Growth indices from density and extension of the zones of emigration in explants of rat bone-marrow on addition of various heterologous tissue as against the controls.

- q) Studies on the vaginal epithelium of mice under lyophilised organic material (KMENT, 1958) –
- r) Data and tests on animals respecting the therapeutic applicability of isolated mitochondria (LAUDAHN, 1956).
- s) The effect of Fetal Mesenchymal Cells on a Hodgkins-like Lymphoma culture (LANGENDORFF, W. v., 1978)
- t) The effect of Fetal Mesenchymal Cells on the Morphology, Growth Characteristics and Function of an Experimental Wilm's Tumor culture (LANGENDORFF, W. v., 1979)

3. Immunological studies

Immunological viewpoints have been playing an increasingly important part

during the last years, more so because cell therapy is concerned with the transplantation of heterogeneous tissue. The following experimental studies are worth mentioning:

- a) The immunological reactions coming into question for cell therapy (H. SCHMIDT, 1963) –
- b) Special immuno-biological problems of the implantation of heterologous tissue (J. STEIN, 1963); this paper mentions also the immunologically interpreted complications known by that time –
- c) The immunological mechanism of the cell (F. SCHMID, 1963) –
- d) The dependence of the immunoreactions on the amount of blood in the implant (A. VALLS CONFORTO, 1963) –

Tab. 8: Impulses stimulating the growth of heterologous tissues in the tissular culture
(F. SCHMID, 1963)

Test series	Extension	Density of cells	Growth	Promotion or delay of growth in %
Controls	1,6	2,2	3,8	0
Blood	2,0	2,8	4,8	+ 26 %
Bone-marrow	2,1	1,6	3,7	- 2,0 %
Lymph-nodes	2,0	2,6	4,6	+ 21 %
Spleen	2,2	2,4	4,6	+ 21 %
Thymus	2,5	2,3	4,8	+ 26 %
Kidney	2,2	2,7	4,9	+ 29 %
Liver	2,5	3,0	5,5	+ 45 %
Cerebral cortex	1,9	2,7	4,6	+ 21 %
Cerebral marrow	2,0	2,5	4,5	+ 18 %
Diencephalon	2,2	2,6	4,8	+ 26 %
Hypothalamus	2,7	3,6	6,3	+ 66 %
Mesencephalon	2,2	2,0	4,2	+ 10 %
Skin	1,9	2,0	3,9	+ 2,6 %
Testicles	1,2	2,0	3,2	- 13 %
Placenta	2,7	2,6	5,3	+ 40 %
Omentum maius	2,0	2,7	4,7	+ 24 %
Connective tissue	1,9	2,1	4,0	+ 5,3 %
Cartilage	2,2	3,0	5,2	+ 37 %

- e) The formation of antibodies after cell injections (KANZOW and KINDLER, 1958) –
- f) Change of the heterohemagglutination titre after injections of lyophilized organic cells (MÖSE, WENNIG and STEIN, 1957, 1958) –
- g) Oncofetal antigens (RENNER, 1973, 1974) –
- h) Immunological effect of fetal cells (RENNER, 1977) –
- i) Interferon (EMÖDI, 1977) –
- k) Methods of immunological identification (SEELIG, 1977) –
- l) Clinical aspects of a tumour-immunising therapy with lyophilized fetal cells (RENNER, 1979)
- m) Terapia celular con Resistocell e inmunidad en oncología (FUENTE-PERUCHO, de la, A. et al., 1979).
- n) Immunobiological synopsis (SCHMID, F., 1980).
- o) Regeneration, Immunstimulation und Interferon-Induktion (LANDSBERGER, A; 1980)
- p) Immunstimulation und Interferon-Induktion in der Tumorthherapie (HAGER, D., 1981)
- q) Interferon-Induktion durch xenogenes Gewebe (Resistocell) (WACKER, A., 1982)
- r) Immunmodulation and Restoration with Resistocell (GIANOLI, A. C. a. PEREZ-CUADRADO, S., 1982)

A detailed representation of immunological questions will be given hereafter.

Fig. 133–135, legends and Tab. 8 comprise experimental examples of impulses stimulating the growth of heterologous tissues and the specific effect.

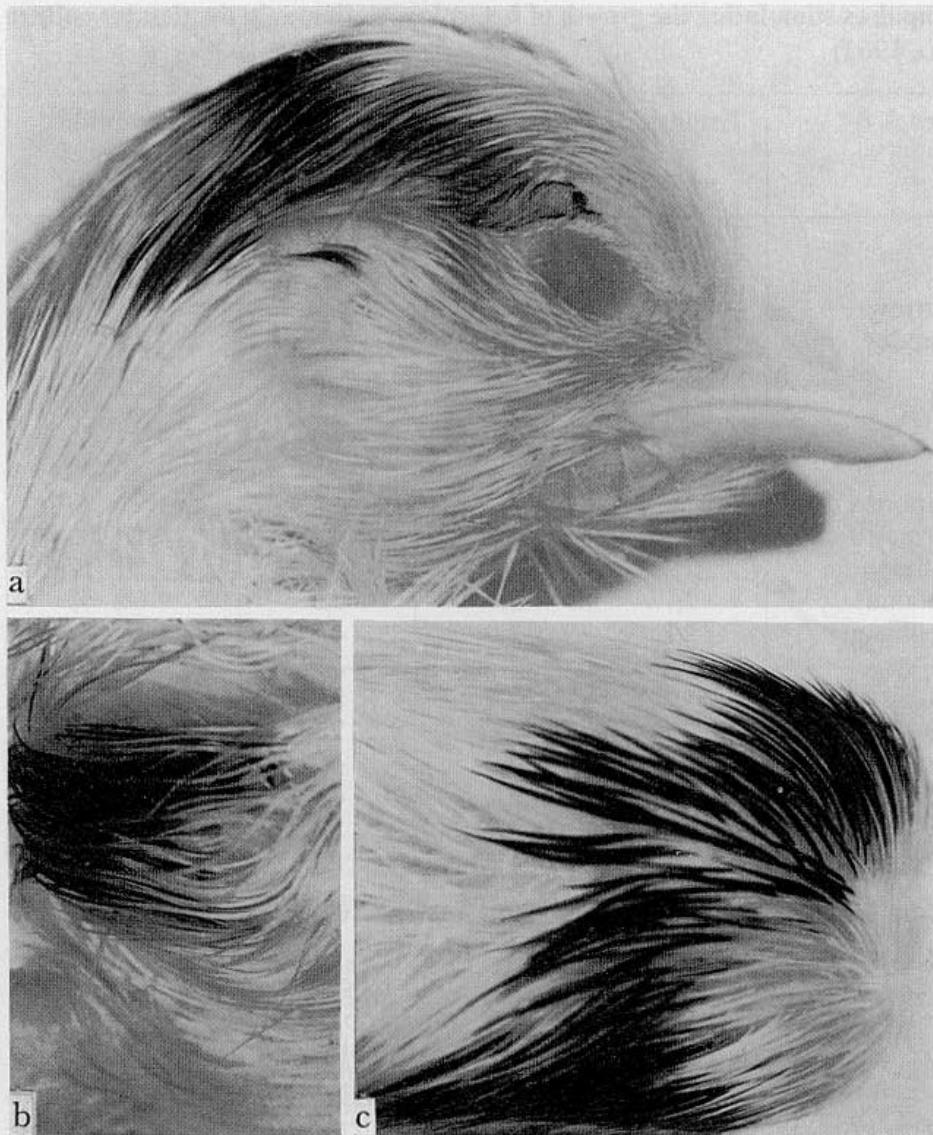


Fig. 135 (a-c):

Inoculated cell material is utilised in the areas of the body where it structurally belongs.

Intravenous injection of melanoblasts of a 2 days old donor (Barred Plymouth Rock and Brown Leghorn) into a 3 days old white Leghorn embryo shows an extensive deposition of pigment in the white hens. (From WEISS and ANDRES, 1952, from SCHMID and STEIN: Cell Research and Cell Therapy, Ott Publishers Thoune, Switzerland 1967).