## COMPARISN OF SENSITIVITY OF BONE MARROW CELLS AND MYELOID LEUKAEMIA CELLS TO ULTRAVIOLET IRRADIATION

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Our previous results have shown that bone marrow cells are very sensitive to UV-irradiation. UV-doses as small as 5 $J/m^2$ abolished stem cell division, and cells transplanted in syngeneic or allogeneic lethally X-irradiated recipients produced small numbers of colonies, and the recipients died. Myeloid leukaemia cells were exposed to UV-doses of 5, 20, 80, 160, 320, 640 and 1,280 $J/m^2$, and transplanted into RF mice. All mice died with typical symptoms of leukaemia and in the usual time period. If Uv-irradiated leukaemia cells were transplanted into lethally X-irradiated mice, all mice died earlier than irradiated mice without UV-treated cells, but splenomegaly was not observed. Higher doses of UV irradiation were also examined, such as 2,000, 4,000, 8,000, 16,000, 32,000 and 64,000 $J/m^2$. Recipients of UV-irradiated leukaemia cells died with leukaemia, but 5 or 10 days later than the recipients of leukaemia cells not irradiated with UV. If the recipients were X-irradiated and transplanted with leukaemia cells irradiated with these high doses of UV, mice died significantly earlier than the control, only irradiated mice, but splenomegaly was not observed. However, if X-irradiated mice were injected with syngeneic bone marrow along with UV-irradiated leukaemia cells, they survived several days longer than mice irradiated only, and all mice developed splenomegaly. The results suggest that myeloid leukaemia cells are resistant to UV-irradiation, or that UV-irradiation results in reactivation of an oncogenic virus.

## EPITHELIAL CELL PROLIFERATION OF COLORECTAL MUCOSA IN NORMAL SUBJECTS AND IN PATIENTS WITH POLYPS OR CANCER OF THE LARGE BOWEL

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In normal individuals the cytoproliferative activity of colorectal mucosa is limited to the lower portions of the crypts and almost absent in the surface. It has been suggested that in some groups of subjects at increased risk for colorectal cancer, the prolifrative zone is expanded to the whole length of the gland. Using an autoradiographic approach we evaluated: (1) the proliferative activity of different large bowel segments in normal controls; (2) the pattern of cell proliferation in patients with polyps or cancer of the large bowel. For the purpose of investigation intestinal crypts were divided in 5 equal compartments from the base (compartment 1) to the surfce (compartment 5). The labelling Index for the crypt compartment (L.I.-C.C.: ratio of labelled - i.e. proliferating - cells to total cells in each compartment) was similar in the various large bowel tracts. L.I.-C.C. was significantly ($P<0.001$) higher in polyps and in cancer patients than in controls. In conclusion, rectal samples are probably representative of the kinetic activity of the entire large bowel. In polyp or cancer patients an upwards expansion of the proliferative zone has been observed; this was more evident in compartment 5, which has a high discriminatory power between subjects with or without intestinal neoplasms.

## FREQUENCY OF COLORECTAL CANCER AMONG FIRST-DEGREE RELATIVES OF PATIENTS WITH CANCER OR POLYPS OF THE LARGE BOWEL

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The recent institution of a Colorectal Tumour Registry in our Health Care District gave us the opportunity to test if the frequency of cancer (particularly of the intestine) is higher in first-degree relatives of patients with large bowel malignancies than in the general population. For all the registered patients a careful clinical history was taken and the genealogic tree was traced. Each patient was matched to a control of the same age and sex. During 1984-85 a total of 271 cases of cancer and 301 of polyps were registered; there were 4156 first degree relatives in the diseased group and 4224 in the control group. Among the relatives of cancer patients we found 118 cases of colorectal cancer as compared to 28 in controls (Relative Risk, RR, 4.5; $P<0.001$). The same trend was seen both in parents and, more markedly, in siblings (RR 2.5 and 9.0 respectively). A similar excess of colorectal cancer was observed in relatives of patients with polyps, whereas no difference was seen in the frequency of other tumours. In conclusion, we observed a fourfold increse of colorectal cancer in

close relatives of patients with large bowel malignancies. This excess of cases suggests that genetic factors may be involved in about 20% of the registered colonic tumours.

## ARA-C INDUCED DIFFERENTIATION OF A NEW HUMAN NEUROBLASTOMA CELL LINE (GI-ME-N)

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Cytosine-arabinoside (ARA-C) effects on a new human neuroblastoma (NB) cell line (GI-ME-N) recently established in our laboratory, have been extensively tested. Low doses of ARA-C allowing 100% cell viability induce morphological differentiation and growth inhibition; differentiated cells appear larger and flattened with elongated dendritic processes; such cells appeared within 48 hrs after a dose of ARA-C as low as 0.1 µg/ml. The new morphological aspect reached the maximum expression after 5 days of culture being independent of the addition of fresh drug to the culture. A decrease in [3]H-thymidine incorporation was also observed within 48 hr, the cell growth being completely inhibited by the 5th day. Membrane immunofluorescence with specific monoclonal antibodies showed several dramatic changes in NB-specific antigen expression after 4 days of treatment with ARA-C. Concurrent studies including transmission electron microscopy, appearance of 68, 120 and 200 kD, neurofilaments and catecholamines determination will contribute to further definition of this system. Our data suggest that low ARA-C doses promotes in vitro differentiation of human NB cells resulting in an interesting alteration of the malignant phenotype.

## SYNGENEIC TUMOUR INHIBITION AFTER TRANSFER OF IN VITRO INDUCED SPECIFIC T CELLS AND IN VIVO LAK CELLS

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Inhibition of polyoma growth after transplantation in CBA mice was achieved in 70% of animals treated with IL-2 and T cells induced in culture. transferred cells derived from donors with DTH to TAA and were stimulated with TAA. Soluble TAA with both specificities (polyoma and H-2K) have affinity to cell receptors. Antitumour effects and DTH in recipients are dependent on the period of time of the culture of T cells and dosage of IL-2.

## PRESENCE OF A BREAST CARCINOMA ANTIGEN IN BODY FLUIDS

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The anti-breast carcinoma monoclonal antibody, NCRC-11 defines complex, high molecular weight glycoprotein antigens associated with secretory glandular epithelia, as well as with most epithelial malignancies. These components have been identified in, and purified from, normal body fluids including urine and skim milk. Analysis of these materials from normal fluids or tumours by sodium dodecyl sulphate polyacrylamide gel electrophoresis and immunoblotting with the NCRC-11 antibody revealed that the major antibody binding species were present as a single band or doublet of low electrophoretic mobilities.

Since it was shown that NCRC-11 antigens were released from tissues in a soluble form, the possibility that these antigens, when secreted from a developing tumour into the circulation, might represent a diagnostic marker for breast cancer was evaluated. For this purpose, the NCRC-11 antibody was employed in a solid phase 'sandwich' radioimmunoassay, whereby antigen in the serum of cancer patients was captured by adsorbed NCRC-11 antibody, and the antigen was then detected by the subsequent binding of radiolabelled NCRC-11 tracer antibody. The findings obtained indicated that NCRC-11 antigens were elevated in the serum of advanced breast cancer patients in comparison to healthy control females. Thus, access to the circulation was available to NCRC-11 antigens released from the tumour but not to equivalent products released from normal epithelia.

## COMPARISON OF GEOCHEMICAL AND CANCER INCIDENCE DATA IN FINLAND

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As a joint effort of the Finnish Cancer Registry and the Geochemistry Department of the Geological Survey of Finland a research project has been started in which the role of elements in the soil will be studied as risk or protective factors in different cancers. Soil samples were collected from