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Union Internationale Contre le Cancer
International Union Against Cancer

INTERNATIONAL UNION AGAINST CANCER

The International Union Against Cancer is a non-governmental, voluntary organization devoted solely to promoting throughout the world the campaign against cancer in its research, therapeutic and preventive aspects. Over the years, the UICC has developed into a world-wide association with member-organizations in over 79 countries. It strives to achieve its aim by facilitating the exchange of information between national cancer organizations, holding international cancer congresses, conferences and symposia, standardizing nomenclatures and classifications, and by stimulating national efforts against cancer.

The UICC publishes the *International Journal of Cancer*, Monographs, Manuals, Technical Reports, and the *UICC Bulletin*. The International Union Against Cancer has received financial assistance for the publication of the *International Journal of Cancer* from the *U. S. National Institutes of Health*, the *Calouste Gulbenkian Foundation*, the *Swedish Cancer Society*, the *Canadian Cancer Society*, the *National Cancer Institute of Canada*, and the *Cancer Society of Finland*.

UNION INTERNATIONALE CONTRE LE CANCER

L'Union Internationale Contre le Cancer, au sein de laquelle sont groupées des sociétés membres de plus de 79 pays, est une organisation non gouvernementale sans but lucratif, qui se consacre exclusivement à encourager dans le monde entier la lutte contre le cancer: thérapeutique, prophylaxie et recherche. A cette fin, elle facilite les échanges d'informations entre sociétés nationales, organise des congrès, conférences et symposiums internationaux, unifie les nomenclatures et les classifications et stimule l'action menée contre le cancer sur le plan national.

L'UICC publie le *Journal International du Cancer*, des Monographies, Manuels, Rapports techniques, et le *Bulletin de l'UICC*. L'Union Internationale Contre le Cancer a reçu pour la publication du *Journal International du Cancer* l'aide financière des institutions suivantes: *the National Institutes of Health (USA)*, *Fondation Calouste Gulbenkian*, *the Swedish Cancer Society*, *Société Canadienne du Cancer*, *Institut National du Cancer du Canada*, et *the Cancer Society of Finland*.

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CHARACTERIZATION OF EBV-GENOME NEGATIVE "NULL" AND "T" CELL LINES DERIVED FROM CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND LEUKEMIC TRANSFORMED NON-HODGKIN LYMPHOMA

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Sixty-two explants from peripheral blood, bone marrow and cerebral fluid of children with acute lymphoblastic leukemia (ALL) and leukemic transformed non-Hodgkin lymphoma (NHL) were cultivated for at least 8 weeks. Although lymphatic cells persisted up to 16 weeks in tissue culture, no proliferation was observed in 54 cultures. From the remaining cultures, eight permanently growing cell lines were obtained. Five of these were EBNA (Epstein-Barr virus-specific nuclear antigen)-positive. Three, however, were EBNA-negative and lacked Epstein-Barr virus genomes. Two cell lines (KM-3 and SH-2) expressed neither B nor T cell characteristics. One line (JM) expressed T cell characteristics and complement receptors. The growing lymphatic cells represented leukemic cells, since the pattern of cytochemical staining and that of membrane receptors of lymphoblasts from the same donor prior to cultivation were identical. All leukemic cell lines were derived from patients in relapse. In contrast, no proliferation of leukemic cells occurred in explants from patients revealing the first manifestation of the disease. These results suggest enhanced growth potential of lymphoblasts resisting antileukemic therapy.

Acute lymphoblastic leukemia (ALL) contributes up to 35% of all childhood malignancies. Although the prognosis of ALL improved after introduction of more efficient radio- and chemotherapy (Pinkel *et al.*, 1972), about 50% of the patients relapsed within 5 years after first remission (Aur *et al.*, 1974). Similarly, a great number of children suffering from non-Hodgkin lymphoma (NHL) terminate in leukemic generalization. Therefore, early recognition of patients with high risk of relapse would be important for the prognosis and possibly also for an initial intensification of the therapy in this group. A considerable number of these patients express T cell surface markers (Borella *et al.*, 1973), although relapses occur in T-marker negative ALL as well. In the latter group different parameters (initial leukocyte count, age of the patient) may allow some prediction of prognosis. Nevertheless a better characterization of the lymphoblasts is urgently needed.

Leukemic cell lines represent an excellent tool in the search for tumor-specific characteristics. The almost unlimited quantity, the lack of contamination by normal leukocytes and their convenient availability are helpful in many experimental designs. As a prerequisite, however, the lack of Epstein-Barr virus (EBV) genomes and the identity of properties of cultured cells and primary tumor cells have to be ensured. Up to now these criteria have been fulfilled in only a few cell lines established from children with T-cell receptor-positive ALL or NHL (Foley *et al.*, 1965; Adams *et al.*, 1968; Minowada *et al.*, 1972, 1977). The permanent growth of T and B cell receptor-negative cells in childhood ALL has not been reported thus far. In this communication we describe the establishment of two leukemic "null" and of a T receptor-positive line.

MATERIAL AND METHODS

Origin and maintenance of the cell lines used as controls

The cell lines Raji (Pulvertaft, 1964), U-698 M (Nilsson and Sundström, 1974), Ramos (Klein *et al.*, 1975) and MOLT-4 (Minowada *et al.*, 1972) were kindly provided by Dr. H. zur Hausen, Erlangen. The cell cultures were incubated at 37° C and subcultivated once or twice weekly with medium RPMI 1640, supplemented with 10% inactivated fetal calf serum, 100 IU/ml penicillin and 100 μg/ml streptomycin.

Establishment of the cell lines

Blood and bone-marrow samples were centrifuged on a Ficoll-Hypaque gradient (Böyum, 1968) after 1:2 dilution in medium RPMI 1640, supplemented with fetal calf serum and antibiotics as described above. Ten samples derived from five patients were injected into Spongostan foam (Ferrosan, Malmö, Sweden) and layered on a grid of stainless steel according to the method of Nilsson (1971). The cultures were incubated at 37° C in a 5% CO_2 atmosphere and observed for at least 8 weeks. One-half to one-third of the medium was changed twice weekly.

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