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NCI'S INTERNATIONAL PROGRAM GROWING, WITH MORE AGREEMENTS, $8 MILLION IN CONTRACTS AND GRANTS

Since the inception of the National Cancer Program, NCI staff members have spent an increasing amount of time and energy (and more than $8.3 million in grants and contracts in fiscal 1975) on international activities. Formal bilateral agreements have been negotiated with the Soviet Union, Japan and Poland; collaborative research efforts with France have been expanded; NCI is talking with West Germany about developing cooperative programs; informal relations have been established with The Netherlands; and talks are in progress with Egypt.

"What are we getting from all this?" asked Lyndon Lee, member of the National Cancer Advisory Board. It was a question many have asked

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In Brief

SENATE SUBCOMMITTEE ADDS $100 MILLION FOR NCI OVER HOUSE BILL; NO FURTHER ACTION UNTIL SEPT.

SENATE HEW Appropriations Subcommittee added $100 million to the $703 million voted by the House for NCI for the 1976 fiscal year. With the $22 million which will be approved later for training, this would give NCI $825 million. The full Appropriations Committee did not act on the bill before Congress recessed to Sept. 3. If that figure holds up through committee and floor action, NCI probably would wind up with $775 million, half the difference between the House and Senate bills. That's close to the amount NCI has said it will need to maintain grant funding levels at approximately the same percentage it had in fiscal 1975. Some senators probably will try to add more for cancer to the bill when it reaches the floor in mid-September. . . . **MEANWHILE**, an organization called the National Cancer Petition has been formed to stir up support for increased cancer program funds. The organization is circulating a petition asking for annual spending by the federal government of $1.5 billion. Write to NCP, PO Box 85, Watertown, Mass. 02172, or phone 617-926-0815. The campaign was started by a Watertown man, Russell Arico, who has lost seven members of his immediate family to cancer. . . . **THE PAY** increase slipped through by Congress for its members and for federal executives will add from $1,500 to $2,500 to their salaries, frozen at $36,000 (for the executives —Congressmen and Senators get $42,500) since 1969. That will help somewhat, but it doesn't do anything about the jam at the top. Thousands of government employees, several levels removed from their supervisors, make as much as their bosses. At NCI, Director Frank Rauscher receives the same $36,000 pay as hundreds of his subordinates; in fact, no less than 165 get more than that, up to $47,500, by being MDs and members of the PHS commissioned corps. The cost-of-living increase, which will be from 5.5 to 8.5%, will be the same for everyone and the disparities will continue.

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ISRAEL TOP FOREIGN CONTRACTOR WITH 17; CANADA LEADS IN GRANTS WITH FIVE

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who feel there is a relative lack of sophistication in biomedical research in the USSR and elsewhere compared with that in the United States. Some have commented that NCI's work with the Russians "is our contribution to detente."

In fact, while NCI's contributions so far have outweighed that of foreign scientists in the collaborative efforts, it hasn't been entirely a one-way street.

"We've received a lot," NCAB Chairman Jonathan Rhoads answered Lee. "We've opened the channels. Foreigners have developed adriamycin and the Emi Scanner. The Institute in Melbourne has 56 people working on leukocytes and leukocyte precursors. There is some very good work going on in Stockholm, and we have hopes that one or two of the Russian drugs (obtained in the exchange agreement) will work out."

Gregory O'Conor, associate director for international activities, added that in lung cancer research, the agreement with the Japanese "appears very promising for what the U.S. will get out of it;" that through the use of seed money, projects of special interest to the U.S. are being developed in foreign countries; that he hopes to make better use of international organizations, especially the World Health Organization; that he hopes foreign scientists will soon be able to tap the International Cancer Research Data Bank through Cancerline; and that the comprehensive cancer centers will be playing a greater international role.

O'Conor pointed out that NCI has some joint protocols in progress in the United Kingdom and some British investigators are members of the cooperative clinical groups.

Considerable potential exists for collaborative research in Egypt, financed with counterpart funds, if the situation with Israel remains stable, O'Conor said. Counterpart funds are local currency obtained through U.S. foreign aid. Most counterpart funds have been used up by various U.S. agencies, including NCI, which had a big program in Israel financed in that manner through 1973. Counterpart funds are still paying for programs in India, Tunisia, Poland and Yugoslavia.

Israel leads all other foreign countries in the value of NCI contracts, with 17 contracts worth $1,653,000 in the 1975 fiscal year. Sweden was second with 12 worth $771,000, followed by Canada, 8, $496,000; Japan, 6, $401,000; Italy, 5, $380,000; Netherlands, 5, $372,000; Australia, 4, $367,000; UK, 7, $267,000; Uganda, 1, $252,000; France 3, $133,000; and other countries, 10, $458,000. International organizations have 13 contracts totaling $1,631,000.

Foreigners have 24 contracts in immunology, 14 in epidemiology, 7 in chemical carcinogenesis, 7 for the International Cancer Research Data Bank, 6 in virology, 6 in experimental therapeutics, 6 for clinical trials, 6 for special resources, 5 in molecular and cell biology, 2 in biochemistry, 2 in cytology, 1 to conduct meetings, 2 as liaison officers, and 2 for special projects.

Most foreign collaborative efforts are funded with contracts, although there is more than $1 million in grants awarded outside the U.S. Canada leads with 5, totaling $170,000, followed by Italy, 2, $151,000; Sweden, 2, $143,000; Belgium, 1, $132,000; Israel, 2, $118,000; France, 2, $70,000; UK, 3, $62,000; Australia, 2, $60,000; other countries, 6, $197,000; and UICC, 1, $35,000.

There are 10 grants in immunology, 3 in epidemiology, 3 for the cooperative groups, 3 in virology; 2 in experimental therapeutics, 2 in molecular biology, 1 in chemical carcinogenesis and 2 others.

Programs financed with counterpart funds in India include drug development, drug screening, chemotherapy, cancer registry, and treatment and control of oral cancer. Counterpart funds pay for epidemiology research in Poland, a breast cancer study in Tunisia, and experimental therapeutics in Yugoslavia.

O'Conor said, "The major problem we have with the USSR agreement is keeping it from growing to a disproportionate size in relation to our respective scientific needs." Program areas with the Russians include cancer chemotherapy, immunotherapy of human tumors, study of leukemia and tumor viruses in animals and man, mammalian somatic cell genetics related to neoplasia, epidemiology of cancer, and cancer control and cancer center organization.

With the Japanese, program areas are chemical carcinogenesis, cancer virology, cancer immunology, cancer therapy, analytical epidemiology, breast cancer, lung cancer, bladder cancer, high energy radiation therapy, cytology, and metastasis.

With Poland, program areas are cancer institute organization, epidemiology, and exchange of personnel and materials.

The International Agency for Research on Cancer (IARC) is working on seroepidemiology of Burkitt's lymphoma and nasopharyngeal carcinoma, epidemiology of esophageal cancer, evaluation of carcinogenic risk of chemicals to man, carcinogenicity testing, epidemiology clearing house, familiarity of breast cancer in Iceland, and meeting on cancer registries and occupational health.

The International Union Against Cancer (UICC) is working on a committee for international collaborative activities, epidemiology of Hodgkin's disease in Colombia, TNM staging classification, and synthesis of laboratory and clinical research on human tumors.

The World Health Organization is working on histological typing of tumors and international classification of oncological diseases.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg. NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CM-67037

Title: *Phase II and Phase III studies in patients with disseminated solid tumors*

Deadline: *Oct. 6, 1975*

NCI's Div. of Cancer Treatment will make available to interested contractors a request for proposal to conduct Phase II and Phase III studies in patients with the disseminated solid tumors such as large bowel cancer, bronchogenic carcinoma, breast carcinoma, pancreatic carcinoma, gastric carcinoma, prostatic carcinoma, bladder carcinoma, renal carcinoma, ovarian carcinoma, malignant melanoma, carcinoma of the cervix, endometrial carcinoma, head and neck carcinoma, soft tissue and bone sarcoma, or malignant lymphoma.

A minimum of 400 patients, representative of all or some tumor types previously defined, shall be required, with no less than 25 patients for any one tumor type. Protocols to be developed for these patients will include:

Phase II testing of new investigational drugs, Phase II testing of standard antitumor drugs not previously tested against the particular tumor type, and Phase II testing of new combination chemotherapy regimens as well as Phase III trials to determine the definitive activity of the above kinds of regimens.

Protocols will be developed by the investigators in concert with the project officer, and may also include combined modality approaches in which chemotherapy is combined with either surgery, radiotherapy, or immunotherapy.

Contract Specialist: Joseph Kerner
Cancer Treatment
301-427-7463

RFP NCI-CM-67048

Title: *The isolation of antineoplastic agents from marine and terrestrial invertebrates, vertebrates and insects*

Deadline: *Oct. 15, 1975*

The Drug Development Branch of NCI is seeking organizations having capabilities and facilities for the fractionation and isolation of antineoplastic agents from marine and terrestrial invertebrates, vertebrates and insects, and the determination of chemical structures of the antineoplastic agent from the above natural products.

The objectives of this project are to prepare by isolation enough of each compound to test for antitumor activity, to identify chemically, and to prove the structure if necessary and to prepare additional quantities, usually a few grams, of those compounds that require more biological testing to determine interest to NCI.

NCI will provide the marine and terrestrial materials and in vivo tumor bioassay. The contractor may or may not elect to use in-house in vitro bioassays.

The facility must have the capacity for storing, handling and grinding these natural products in amounts of 1-500 lbs. prior to extracting them, for performing all types of organic chemistry and for carrying out organic structure and identification work. A well instrumented analysis laboratory and an adequate library must be available.

The principal investigator must be trained in organic natural products chemistry preferably at the PhD level, from an accredited school, and must have extensive experience in isolating pure compounds from natural products and in organic chemical structure determination. It is anticipated that the total project will require a minimum of four technical man-years of effort per year.

Contract Specialist: S.R. Gane
Cancer Treatment
301-427-7463

RFP NCI-CB-63932-39

Title: *Radioimmunoassay of immunoglobulin molecules*

Deadline: *Sept. 30, 1975*

NCI is soliciting proposals from organizations having the capabilities to provide research support for the performance of double antibody radioimmunoassays for immunoglobulin molecules using procedures established intramurally at the NCI and using reagents provided by the intramural staff.

Offerors must have working experience in the procedures involved. Offerors must be located within one hour drive of NIH and will be required to pick up samples from the NIH twice a week.

Contracting Officer: Harold Simpson
Biology & Diagnosis
301-496-5565

VIRUS CANCER PROGRAM REPORT ON SCIENTIFIC ACTIVITIES CONTINUES

Portions of the report presented to the National Cancer Advisory Board on scientific activities of the Virus Cancer Program have appeared in previous issues of ***The Cancer Letter.*** That report continues here with a discussion of the relation of RNA viruses to human cancer, followed by a report on DNA viruses.

A discussion of possible treatment and control measures and other progress highlights will be published here in the next two weeks.

RNA Viruses: Relation to Human Cancer

The evidence that RNA viruses cause at least some animal cancers is very convincing. More species are continually being added to the list of those in which tumor-producing RNA viruses have been identified and there is good evidence that genetic material very closely related to RNA tumor viruses is present in all vertebrates. Since some of man's closest relatives have virus-produced cancers, there is every reason to believe that viruses cause cancer in man also.

The ease with which viruses can be isolated from a given species of animal varies markedly from species to species. The mouse releases viruses very readily: man has so far been one of the most difficult animals in which to find viruses. However, as new and more sophisticated procedures have come into use, previously unsuspected viruses have been uncovered.

Many of the known animal viruses grow well in human cells and can also transform them. When a virus is found growing in human tumor cells there is, therefore, always the problem of eliminating contamination by animal viruses. Since it is not possible to inject a virus into humans to test its oncogenic potential, other criteria have been developed for classifying viruses as human. There is, however, no clear-cut test for "humanness." Any human virus would be expected to be closely related to primate viruses and distantly related to other mammalian viruses in terms of nucleic acid homology and antigenic determinants. As we now know that the RNA viruses, including the proviruses in the cellular genome, can readily undergo genetic recombination with each other resulting in viruses that are of mixed origin, it is always necessary to test several properties of an unknown virus before classifying it. The question also presents itself: how much of a virus has to be human to call it human? Defective viruses are known, e.g., mammalian sarcoma viruses, which can only form complete viral particles with help from other viruses. The final particle of a defective virus can contain components belonging to its helper virus and could, therefore, give misleading results when tests for its origin are conducted. As more is known about the behavior of RNA tumor viruses the question of their natural host becomes more complicated. For example, RD-114, an endogenous cat virus, has nucleic acid sequences related to both cat and baboon DNA and p30 closely related to the p30 of an endogenous baboon virus but unrelated to p30 of other cat viruses. The curious properties of RD-114 can be explained if, millions of years ago, a primate virus infected an ancestral cat species from which the modern domestic cat evolved.

Evidence for human RNA tumor viruses. A variety of evidence has accumulated suggesting that human cells, like animal cells, contain RNA viral material and that this is involved in the initiation of malignant growth. The recent isolation of viruses from primates, man's closest phylogenetic relatives, argues strongly that man also harbors such viruses. As discussed above, DNA related to endogenous RNA tumor viruses has been shown to be present in normal human cells. Some investigators are also finding that normal cell membranes of several animals and of man contain substances that crossreact immunologically with a well-defined viral glycoprotein, gp69-71. The significance of the latter finding is not understood and confirmation of the validity of the results is needed before conclusions can be drawn.

In the normal human cell, the viral DNA sequences appear to be laregly repressed. If they have anything to do with cancer they should become activated when the cell undergoes transformation to the malignant state. The malignant cell should, therefore, contain appreciable amounts of typical products of RNA virus genes: RNA and protein molecules similar to those of the virus as well as the viral enzyme RDDP. Experiments to look for these components in human tumor cells have been done and positive results have been obtained in some cases. The best studied examples are human breast cancer and human acute myelogenous leukemia (AML).

Normal human milk and cells from malignant human breast tumors contain biochemically defined "particles" that contain 60-70S RNA and RDDP. In human milk a few particles that look like type B RNA viruses have also been seen under the electron microscope. The RDDP is like the viral enzyme in its substrate requirements and is unlike any normal cellular DNA polymerase. The RNA of the milk "particles" has sequence relationship to the RNA of breast cancer cells and the RNA found in breast cancer cells, in turn, has sequence homology to the RNA of MMTV and MP-MV. Benign breast tumor tissues do not have particles, RDDP or RNA homologous to MMTV or MP-MV. Recently it was reported that a human breast cancer cell line was able to produce viruses at a very low level. This has been difficult to reproduce as the conditions required for virus production are elusive.

The case for viral involvement in human AML appears even more convincing. "Particles:: containing 60-70S RNA and RDDP have been found in the leukemic cells of AML patients. The enzyme has been purified and studied extensively and found to be very similar immunologically to RDDP from two primate viruses–gibbon ape leukemia virus (GaLV) and woolly monkey virus (SSV). Hybridization studies showed that the RNA of the "particles" was closely related to the RNA of the same two primate viruses and more distantly to mouse leukemia virus RNA. As techniques became more refined it was possible to show that the human leukemia "particles" were more closely related to SSV than to GaLV or to any other virus tested, In all of the five cases tested, human AML cells have also been shown to contain p30 antigens specifically related to those of the SSV-GaLV group. The p30 proteins of this group of viruses cannot be distinguished immunologically.

Several cell lines developed from blood samples of one patient with AML have produced intact viral particles after prlonged growth in vitro. The particles are seen to bud from the cell membrane under the electron microscope. A factor from embryo cultures is required for the growth of these leukemic cells in vitro and the production of virus from them. The virus that is produced, like the "particles:: found in other AML patients, is very similar to SSV in its antigenic specificity and nucleic acid sequences, and is less closely related to GaLV. The relationship of the AML virus to woolly monkey virus is so close that the possibility of the two viruses being identifical cannot be completely ruled out. The woolly virus was obtained in California from a pet woolly monkey with fibrosarcoma and it is the only isolate obtained from this species of monkeys so far. It produces sarcomas and brain tumors in marmosets. In terms of the usual criteria of nucleic acid homology between virus and host DNA, the virus is not a bona fide woolly monkey virus, nor does it appear to belong to any other species tested. Even if the AML virus is identifical to the woolly monkey virus, the possibility that it has something to do with the human disease cannot be dismissed without further study.

DNA Viruses and Human Cancer

The last 10 years have seen the emergence of a large body of evidence linking the etiology of several human tumors to DNA viruses, especially those of the herpesvirus group. Prior to that time, the only evidence connecting herpesviruses to animal neoplasias was the finding of herpes-like particles in cells of the renal adenocarcinoma of the frog. The discovery of the Epstein-Barr virus (EBV) in cultured lymphoblastoid cells from patients with Burkitt's lymphoma in 1964 stimulated extensive studies to examine herpesviruses as possible etiologic agents of cancer in several animal species, including man. Herpesviruses recovered from wild cottontail rabbits, chickens, and higher primates are now known to be causally related to lymphoproliferative neoplasias in their respective hosts. These and other animal models have provided valuable experimental systems in which to study DNA virus-induced oncogenesis. At least two herpesviruses have been implicated as possible etiologic agents of certain types of human cancer—EBV with lymphoma and nasopharyngeal carcinoma, and herpes simplex type 2 virus with squamous cell carcinoma of the uterine cervix.

Two types of virus-cell interactions have been recognized following exposure of susceptible cells to members of the herpes group of viruses. Productive infection results in an inhibition of host cell DNA, RNA and protein synthesis, and a concomitant accumulation of virus-specific components. The net result of this interaction is the synthesis of infectious progeny virus and destruction of the host cells. Therefore, cell transformation and productive infection by herpesviruses would, of necessity, be mutally exclusive processes. In fact, oncogenic conversion by herpesviruses appears to result from a nonproductive (abortive) infection in which viral functions responsible for inhibition of host cell macromolecular synthesis are not expressed.

Stimulation of cellular DNA synthesis, acquisition of virus-induced antigens, incorporation of viral nucleic acids and transformation of normal cells into established cell lines have all been described in nonproductive infections. Activation of the synthesis of infectious virus by exposure to halogenated pyrimidines or irradiation is usually accompanied by cell death. In vivo, herpesviruses also establish covert latent infections in which infectious virions cannot be recovered except during periods of overt disease. Whether latent herpesvirus infections are the result of low level productive or nonproductive interactions remains undetermined. Although horizontal transmission represents the usual mode of spread of these viruses in vivo, vertical transmission of the genome in nonproductively infected cultured cells has been recorded.

Epstein-Barr Virus. Evidence has been steadily mounting for an etiologic role of EBV in Burkitt's lymphoma (BL) of African children and, to a lesser extent, in nasopharyngeal carcinoma (NPC). The association between EBV and Hodgkin's disease, chronic lymphocytic leukemia, and various non-malignant diseases has recently been questioned since some patients were found to have no antibodies to EBV and the elevated EBV titers observed in others may reflect the effects of these diseases on the immunological containment of a usually self-limited EBV infection. Finally, it has now been firmly established that EBV is the causative agent of the heterophile-positive, classical form of infectious mononucleosis (IM), a benign lymphoproliferative disease with predilection for adolescents and young adults.

The Epstein-Barr virus was discovered in the course of an intensive search for viruses associated with BL, a disease which is extremely rare outside of central Africa and parts of New Guinea. The climate-related geographical distribution of this highly endemic disease suggested that insects played some role in its dissemination. The involvement of an infectious agent was strongly supported by the time-space clustering and epidemic drift of the disease. However, the relatively restricted geographical incidence of BL compared to the ubiquitious nature of EBV strongly suggested the interaction of this virus with other cofactors or predisposing conditions to induce this malignancy. A similar pattern is suggested for NPC since this tumor occurs mainly in adults and at an increased frequency in Southern China and certain regions of Africa where primary EBV infection commonly occurs very early in life.

Seroepidemiologic surveys to study the relationship of EBV to BL and NPC became feasible with the

development of tests to detect antibodies to this virus in human sera. Patients were generally found to have elevated levels of antibodies to EB viral capsid antigens (VCA), cell membrane antigens (MA) and to the diffuse (D) or restricted (R) components of the EBV-induced early antigen (EA) complex. The spectra and titers of various EBV-related antibodies have been shown to be of diagnostic or prognostic value. For example, anti-EA activity is primarily directed against the D component in IM and Oriental NPC while antibodies to the R component prevail in BL and Caucasian NPC. Anti-VCA and EA titers are relatively low in the early stages of NPC and in long term survivors but increase gradually with progression of the disease. Similarly, an unfavorable prognosis for BL patients is indicated by a decline in anti-MA antibody production or an increase in anti-EA titer. Irradiation of BL and NPC in vivo has led to an increase of antibody titers against the EB virus-determined MA and VCA. Viral activation followed by antigen release or simple antigen release due to tumor disintegration may explain these effects.

The results of studies on BL and NPC tumor biopsies have been quite consistent. Virus particles, capsid and early antigens have been detected regularly in BL, but not NPC, tumors. Recently an EBV-determined nuclear antigen (EBNA) could be visualized by anticomplementary immunofluorescence in BL and NPC biopsies while an EBV-coded CF antigen, unrelated to VCA, MA or EA, has been measured in extracts prepared from BL tumors. The EBNA antigen shows a striking similarity with the T antigens in papova- or adenovirus-transformed cells. Multiple copies of EBV DNA have been demonstrated in virtually every BL and NPC biopsy and tumor cell line examined by molecular hybridization. Furthermore, recent experiments suggest the presence of EBV DNA in epithelial elements of nasopharyngeal carcinomas. This observation is especially important since only cells of the lymphoid series have been shown to undergo transformation by EBV in vitro.

Continuous lymphoblastoid cell lines have been established from BL or NPC biospies, from peripheral lymphocytes of IM patients, and from normal lymphoid cells exposed to EBV. In the latter case, transformation is prevented by prior exposure of the virus to neutralizing antibodies, to heat, or to ultrafiltration. Adult peripheral white cells may convert into these cell lines without the addition of extraneous virus, but the derived cells usually carry EBV. In contrast, cultures initiated from donors without EBV-directed antibodies or from cord blood or fetal organs fail to survive. The available data indicate that EBV is the sole or major determinant required for establishment of cell lines of lymphoid origin. Although the antigenic profile and virus productivity patterns vary among these cell lines, EBV-hemologous nucleic acid sequences are always detectable. Virus expression can be enhanced in some cases by arginine starvation, x-irradiation, or small doses of various synthetic matabolic inhibitors. Evidently the virus genome persists in these cells, is expressed in varying degrees, and, at least in vitro, is transmitted to progeny during cell division.

Recent efforts to demonstrate the oncogenic potential of EBV in vivo have met with notable success. Fatal tumors resembling reticulum cell sarcomas were observed in marmosets injected with IM-derived EBV which was propagated in simian cells. In addition, a fatal lymphoproliferative malignancy developed in an owl monkey following injection of cells from an EBV-producing culture of BL origin. If these results can be confirmed and shown to be related to the presence of EBV in the respective inocula, at least two animal models will become available to study the oncogenicity of EBV.

Although these observations strongly support an etiologic relation of EBV to African BL and to NPC, its role could be that of an accessory factor or passenger virus because high anti-EBV antibody titers are not always detected in BL patients and tumors of the Burkitt type do occur in temperate regions. In fact, a considerable proportion of European or American BL patients failed to show a seriological association with EBV. In addition, no EBV DNA has been found in has been found in American BL tissues even though this tumor is histopathologically similar to African BL. RNA sequences homologous to the genome of a murine leukemia virus have been identified in BL and NPC biopsies suggesting the possible interaction of a type C virus and a herpesvirus in the genesis of these diseases. In this regard, biopsies of two recent African BL patients failed to reveal EB viral DNA and EBNA, but another nuclear antigen was demonstrated in the tumor cells by the anti-complement immunofluorescence technique using sera from patients with acute myelogenous leukemia (AML).

The possibility that this leukemia-associated nuclear antigen (LANA) marks the presence of a human RNA tumor virus is supported by the recent isolation of a type C virus from the blood cells of a patient with AML. If we assume that infection by EBV primes the cell for neoplastic change, it is possible to conceive that one or more combinations of environmental and host factors could interact to promote oncogenesis. Thus, the association of EBV infection with more than one neoplastic disease becomes more plausible. Should this virus prove to be a necessary co-factor in the induction of disease, control of infection will be extremely important.

The Cancer Newsletter—*Editor* JERRY D. BOYD

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