

Date Contract Initiated: March 1, 1971

BIONETICS RESEARCH LABS., INC. (NIH 69-2160)

Title: Support Services for SVCP

Contractor's Project Director: Dr. Robert Ting

Project Officers (NCI): Dr. George Todaro
Dr. Paul Levine
Dr. Robert Bassin

Objectives: To provide a laboratory that will collect, process and test cancer specimens from human and animal sources suspected of containing virus associated antigens.

Major Findings: EBV studies were carried out under the supervision of Dr. Paul Levine. One study initiated and completed during this year was a seroepidemiological study comparing EBV titers in American patients with Burkitt's lymphoma and age- and sex-matched patients with acute lymphocytic leukemia, African Burkitt lymphoma, and non-malignant diseases. The African Burkitt sera were significantly higher than the American Burkitt sera ($P < 0.005$). The role of EBV in human lymphoma was evaluated by immunological techniques detecting humoral and cellular immunity to the virus. The importance of careful clinical evaluation was emphasized by a study of twenty American patients with Burkitt's lymphoma and age and sex matched controls. Treatment and prognosis correlated with EBV titers in both lymphoma and leukemia patients, indicating that seroepidemiological studies which include single samples on a patient may be misleading. The studies clearly demonstrated that American patients with Burkitt's lymphoma, although their histopathology is indistinguishable from African patients, have different immune patterns to EBV.

Five individuals with low titers to EBV who were identified on an earlier study of Hodgkins disease were followed over a three year period. Half the patients developed high titers while the other half maintained low titers.

A study of leukemia in identical twins was initiated to determine whether an antigen could be detected in the cells of a leukemia twin which would not be identified in his normal HLA identical twin. Leukemia-associated antigens were detected in four of the seven families studied to date using the lymphocyte cytotoxicity test. In the animal system, this test is positive only when the lymphocytes are presensitized by an antigen, so that the reactivity of the family members against

the leukemic patient's cells but not against the normal twin's cells suggest that an environmental agent, perhaps a virus, is present.

Sera from 43/102 (42%) of breast cancer patients had antibodies to BeLev antigens. Sera from 29% of patient's with sarcomas had detectable antibodies, whereas, 13% of patients with benign breast diseases and 3.6% of normal blood bank donors reacted.

Significance to Biomedical Research and the Program of the Institute: Provides opportunity for systematic, large-scale effort to detect viruses or viral antigens in human or animal materials using tissue culture, immunological, biochemical and EM techniques. This is a major objective of the SVCP.

Proposed Course: Although this contract will continue to supply necessary supportive services to SVCP, the workscope has recently been divided into three major areas, each being co-directed by a senior investigator at Bionetics and an NCI project officer. Drs. Rein and Todaro will attempt to isolate, characterize, and purify the factor(s) in serum which overcome contract inhibition and regulate the growth of normal and transformed 3T3 cells in culture. Drs. Pienta and Bassin will attempt to rescue and isolate a viral genome in undifferentiated sarcomas from untreated patients by co-cultivation, hybridization, and other techniques. Drs. Levine and Ting will continue studies to detect tumor specific antigens in patients with leukemia, lymphoma and breast cancer. In the leukemia studies, special emphasis will be placed on testing patients who have an identical twin; in the lymphoma studies, the serums of patients in selected disease groups will be tested for antibodies to EBV.

Date Contract Initiated: June 27, 1969