interaction that involved the TCR and MHC class II. Indeed, polarization of the TCR was seen within 15 min of cocultivation of Jurkat T cells with superantigen staphylococcal enterotoxin E (SEE)-prepulsed Raji B cells. In the same experimental conditions, within 15 min, the $p12^{I}$ protein expressed in Jurkat T cells coactivated with SEE-prepulsed Raji B cells, polarized together with CD3e to the IS. IS enriched for $p12^{I}$ was also observed at 30 min from cocultivation. As expected, IS formation was not observed in the absence of SEE.

HTLV-1-Encoded $p30^{II}$ is a Post-Transcriptional Negative Regulator of Viral Replication

The stoichiometry and the catalytic activity of Tax, the viral transactivator, determine T cell progression through the G1 phase of the cell cycle (reviewed in X). The Rex protein promotes viral production by regulating the transport of genomic and envelope viral mRNAs to the cytoplasm and influences the expression of other cellular genes (reviewed in X). Because Tax is highly immunogenic, it was hypothesized that HTLV-1 in addition to interfering with CTL recognition through $p12^{I}$ may have evolved a dedicated genetic function to reduce the expression of viral proteins (including Tax) and become transiently dormant. This would help the virus-infected cells evade host immune surveillance, a strategy commonly used by DNA viruses. To this end, the effect on viral replication of the HTLV-1 $p30^{II}$ protein, encoded by the doubly spliced mRNA from ORF II, was investigated. $p30^{II}$ was chosen because the nuclear and nucleolar localization of this protein suggested that it might have regulatory function(s). We demonstrated indeed that HTLV-1 has evolved a genetic function to restrict its own expression by a novel post-transcriptional mechanism. The HTLV-1-encoded $p30^{II}$ is a nuclear-resident protein that binds to and retains in the nucleus the doubly spliced mRNA encoding the Tax and Rex proteins. Because Tax and Rex are positive regulators of viral gene expression, their inhibition by $p30^{II}$ reduces virion production, and this is true also in human T cell lines HUT102, C91PL, and MT2 chronically infected with HTLV-1. In a collaborative study with P.L. Green and M.D. Lairmore, we also showed that the HTLV-1 $p30^{II}$ represses by a post-transcriptional mechanism HTLV-2 expression and that HTLV-2 also encodes a protein ($p28^{II}$) able to suppress both HTLV-2 and HTLV-1 replication.

The HTLV-1 $p30^{II}$ has a negative effect on viral replication. Therefore, it could be thought of as a "latency protein." Mechanistic studies on $p30^{II}$ function and regulation and whether inhibition of $p30^{II}$ function may reveal hidden infected cells to host immune surveillance are subjects that need further investigation. Our demonstration that $p30^{II}$ binds to the splice junction for the Tax/Rex mRNA and not to the $p21^{Rex}$ RNA demonstrates specificity. However, the precise nature of this interaction has not been unveiled.

National Cancer Institute Initiatives for International and AIDS-Related Cancer Research

Jodi B. Black

The global burden of cancer is large and projected to grow larger. Each year there are approximately 10 million new cancer cases and more than 6 million deaths worldwide. In many developed countries, including the United States, cancer accounts for more than 20% of all deaths. Although all-site cancer rates are generally lower in less developed countries, these regions are projected to incur the most rapid increase in cancer rates over the next few decades. Cancer in developing countries is expected to represent 70% of the global cancer burden by 2030. Developing countries also bear the majority of the global burden of HIV infections and associated co-morbid conditions including cancer. Thus, the National Cancer Institute (NCI) supports cancer and AIDS related malignancy research outside the United States by highly qualified foreign nationals. In addition, the NCI supports collaborative research involving US and foreign investigators and the training of US scientists abroad and foreign scientists in the US.

The Office of International Affairs (OIA) of the NCI coordinates the Institute's worldwide activities in a number of arenas, including: 1) liaison with foreign and international agencies; 2) coordination of cancer research activities under agreements between the US and other countries; 3) planning and implementation of international scientist exchange programs; 4) sponsorship of international workshops; and 5) dissemination of cancer information. A major objective of the OIA of the NCI is enhancing capacity for cancer research in countries around the world especially in developing/emerging nations because discoveries anywhere can help people everywhere.

The OIA also coordinates the AIDS oncology activities of the NCI. This article outlines resources available from the NCI to enhance international collaborations and to stimulate research and increase our knowledge of cancer pathogenesis, treatment and control with emphasis on resource poor areas and cancer in the context of HIV infection.

OIA sponsors two international scientist exchange programs for applicants with at least three years postdoctoral cancer research experience. The Oncology Research Faculty Development Program prepares participants for careers as independent investigators and for leadership positions in cancer research. The Short Term Scientist Exchange Program promotes collaborative research between established U.S. and foreign scientists from developing countries by supporting, in part, exchange visits of cancer researchers to foreign laboratories (1 week to 6 months). To learn more about these programs visit the website at http://cancer.gov/oia.

The NCI also developed the Summer Curriculum in Cancer Prevention Fellowship Program which offers courses open to foreign trainees. The Principles and Practice of Cancer Prevention and Control course is a 4 week session that provides a broad overview of available resources, scientific data, and quantitative and qualitative methods. This is followed by the 1 week Molecular Prevention Course which provides background in molecular biology and genetics of cancer. Over 200 scientists from 48 countries have participated in this program. Additional information about course registration is available at http://cancer.gov/prevention/pob.

Epidemiology Research

The Viral Epidemiology Branch, located at the NCI, conducts multidisciplinary studies of carefully selected domestic and foreign populations, with the goal of clarifying the relationship of infectious agents, especially viruses, to human cancer and other conditions. To learn more about ongoing research activities of this branch please visit http://www.dceg.cancer.gov/viral.html.

The Multi-center AIDS Cohort Study (MACS) <http://statepi.jhsph.edu/macs/macs.html> and the Women=s Interagency HIV Study (WIHS), https://statepiaps.jhsph.edu/wihs/ are joint ventures with the National Institute of Allergy and Infectious Diseases (NIAID). The MACS began in 1984 and is an ongoing, multi-center perspective study of the natural and treated histories of HIV infection in homosexual and bisexual men. The WIHS is a multi-center study established in 1993 designed to carry out comprehensive investigations of the impact of HIV infection in women and to monitor changes in the natural history of HIV and associated conditions occurring as a result of treatment advances and longer survival. Both of these groups have malignancy working groups.

Clinical Research

The AIDS Malignancy Consortium (AMC) is a multicenter clinical trials network, developed in 1995, that identifies hypothesis driven therapeutic approaches to treat cancer in AIDS patients and conducts multicenter phase I, II and III clinical trials and laboratory correlative studies. Their interests include both the AIDS defining malignancies, Kaposi's sarcoma, lymphoma, and anogenital lesions and cancers, as well as non-AIDS defining cancers now evident in HIV-positive population as their lifespan is extended by highly active anti-retroviral therapy (HAART). Additional information about the AMC can be obtained at http://www.amc.uab.edu

The HIV and AIDS Malignancy Branch which is part of the NCI, conducts laboratory and clinical research in AIDS, AIDS-related malignancies, and viral-induced tumors. The principal aims of this translational research program are to develop novel therapies for these diseases based on an understanding of their pathogenesis. To learn more about the NCI investigators and specific research interests please visit http://ccr.cancer.gov/labs/lab.asp?labid=63

Resources and Infrastructure

The AIDS and Cancer Specimen Resource (ACSR) is the nation's leading multisite resource for tissues, fluids, and clinical data collected from HIV-positive patients with cancer. The ACSR was established in 1994 to identify and to improve access to well-characterized tissues, fluids, and associated demographic and clinical data collected from HIV-positive patients and HIV-negative controls. The ACSR contains over 100,000 specimens collected from cohort studies, clinical trials, and other research sources (including international research). Information on available specimen types and how to obtain them is available at http://acsb.ucsf.edu.

The AIDS Oncology Resources Handbook http://ctep.cancer.gov/forms/aidsoncohndbk.pdf is a comprehensive listing of the clinical and laboratory resources that receive NCI funding. The handbook contains a brief synopsis of all the research studies and recent accomplishments. It also provides a personnel contact information list and describes the NCI AIDS budget and the percentage of spending on grants, contracts, and the intramural program. The Centers for AIDS Research <http://www.niaid.nih.gov/research/cfar/> is an infrastructure program that provides administrative and shared research support to synergistically enhance and coordinate AIDS research projects at 20 academic institutions across the US. The CFAR has accomplished this through core facilities that provide expertise, resources and services not otherwise readily obtained through more traditional funding mechanisms.

International Training and Capacity Building

The NCI partners with the Fogarty International Center in the AIDS international research and training program http://www.fic.nih.gov/programs/aitrp/aitrp.html and the International Clinical Operational and Health Services Research Training Award for AIDS and TB.

http://www.fic.nih.gov/programs/ICOHRTA-AIDS-TB/ICOHRTA-AIDS-TB.html. Both of these programs build basic science and clinical science research capacity in resource poor areas with significant HIV/AIDS prevalence.

The NCI has sponsored The International Conference on Malignancies in AIDS and Other Immunodeficiencies http://www.nci.nih.gov/oia since 1997 to foster scientific exchange and international collaboration. The conference is designed to be a forum for the presentation of basic, epidemiologic, and clinical aspects of research on malignancies in HIV infected and other immunosuppressed individuals with an emphasis on viral oncology relevant to AIDS malignancies.

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