

Center for AIDS Research
 Albert Einstein College of
 Medicine
 1300 Morris Park Avenue
 Belfer Bldg. Room 605A
 Bronx, NY 10461
 Tel: 718-430-2740
 Fax: 718-430-2374

Harris Goldstein, M.D.
 Director

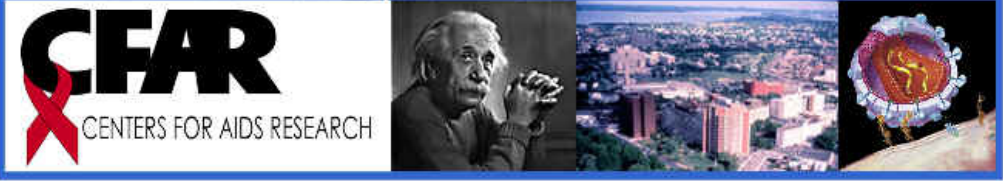
William Jacobs, Ph.D.
 Associate Director

Ms. Georgia Veroutis
 Administrator

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Albert Einstein College of Medicine OF YESHIVA UNIVERSITY



Einstein/MMC CFAR Newsletter

VOLUME 1, ISSUE 1

JULY 2004

Message From The Director: Harris Goldstein, M.D.

It has been a little over a year since the Einstein/MMC CFAR grant was funded by the NIH. The Einstein/Montefiore CFAR is designed to provide an infrastructure to promote the HIV-related research effort of investigators at Einstein and Montefiore. The specific goals of the CFAR are: 1) To provide scientific leadership and an institutional infrastructure to foster collaborative and translational research among basic scientists and clinical investigators; 2) To establish and maintain core facilities that provide CFAR investigators with ready access to user-friendly, efficient and affordable laboratory, biostatistical and clinical services. These Cores are centralized facilities operated by experienced personnel that perform specialized assays, services and techniques for basic and clinical researchers, obviating the time-consuming need for investigators to establish and validate these technical procedures and services in their own labs. These cores also serve as a centralized source that provide CFAR investigators with ready access to HIV-1 clinical isolates, vectors, patient samples and unique reagents;

3) To provide intellectual and financial support for HIV-related research, identify and investigate emerging research opportunities, mentor and support junior investigators and recruit investigators not currently involved in HIV-related research; 4) To disseminate information about HIV-1 transmission, prevention and therapeutic interventions to the medical community and the general population.

During the past year, the four basic science cores, Flow Cytometry, Virology, Animal Biohazard and Immunology/Pathology were set up in dedicated space provided by the school while the Clinical Investigation Core was set up at MMC. The Developmental Core funded two pilot projects, one by Dr. Ekaterina Dadachova examining the utility of antibodies linked to radionucleotides for targeting and eliminating HIV-1-infected cells and another pilot project by Dr. Aharon Freedman to study the use of monoclonal antibodies for the treatment of MTb infection. The Einstein/MMC CFAR organized a very successful CFAR AIDS Club seminar series occurring every

other week consisting of a 30 minute presentation by a CFAR investigator predominantly involved in basic research and a 30 minute presentation by a CFAR investigator predominantly involved in clinical research. This approach provided a forum that presented material of immediate interest to both basic and clinical researchers. It was an extremely successful seminar series that was usually attended by over 40 investigators and has been extremely effective in stimulating collaborations and interactions. In addition, this seminar series is accredited for CME activity. During the past year, the Einstein/CFAR has hosted and co-hosted seminars from a wide range of outstanding AIDS investigators. Further progress and details about the CFAR Cores are detailed in the newsletter. The success of our CFAR is dependent upon participation by our faculty investigators. I welcome any suggestions and ideas of how the CFAR can help expand AIDS-related research efforts at Einstein and at Montefiore. We look forward to your participation.

Welcome To The Einstein/CFAR Web Site

To provide a centralized source of information about Einstein/MMC AIDS investigators, CFAR Core services, CFAR seminars and activities and AIDS research, we have developed and published the Einstein/CFAR web site at www.aecom.yu.edu/home/CFAR. The Cores are divided into Basic Science Cores – Animal/Biohazard, Flow Cytometry, Immunology/Pathology and Virology and a Clinical Core-the Clinical Investigation Core. Each Core has a separate page that details the services offered by the Core and contact information for the Core personnel.

The web site also has a central-

ized listing of Einstein/CFAR Investigators broadly designated by area of interest- Virology, Developmental Therapeutics, Epidemiology and Opportunistic Infections. Each Investigator's name either links to the web page hosted by the SGGs or to a unique web page that provides a portal for students/fellows interested in doing research access to information about active research projects being pursued by faculty members.

The site also lists the complete schedule of the CFAR AIDS Club and of CFAR-hosted seminars. Links are provided to the web pages of two Einstein NIH-funded training pro-

grams directed by Dr. Prasad, (NIH AIDS Training Program For Pre- and Post-doctoral Fellows and the AIDS International Training and Research Program), to the other NIH-funded CFARs and to useful research sites including the NIH AIDS reagent program, various HIV molecular and sequence databases, HIV clinical trials and vaccine overviews, and general research links.

The Einstein/CFAR website is a resource for Einstein and MMC AIDS investigators and please feel free to forward any new information, corrections or comments to the CFAR administrator Ms. Georgia Veroutis.

Upcoming Einstein/MMC CFAR Retreat



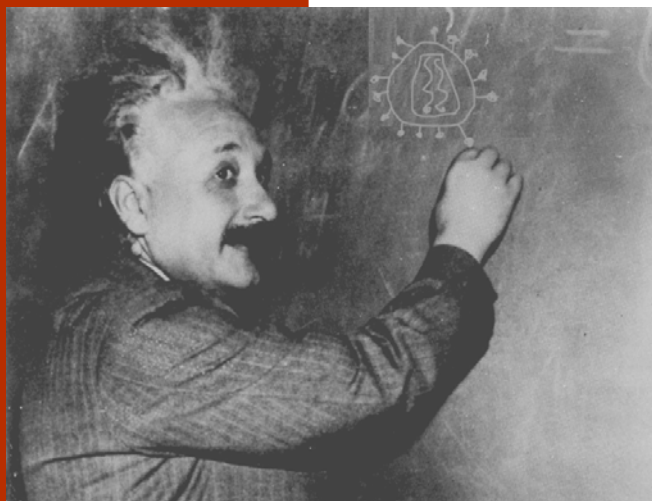
Wave Hill— site of the upcoming CFAR Retreat October 12, 2004

Our first Einstein/MMC CFAR Retreat has been scheduled for October 12, 2004 at Wave Hill in Riverdale. **Please reserve this date in your calendars!** Drs. Steve Porcelli and Barry Zingman are coordinating the planning of the program. To educate CFAR members about Core Capabilities, Core Directors will present a summary of their core capabilities, discuss

new services offered and provide CFAR members with the opportunity to suggest new services to develop. In addition, CFAR pilot grant awardees will present a short progress report about their projects. The retreat will also include breakout sessions of small groups consisting of a mixture of basic and clinical researchers to stimulate interaction and the development of

new collaborations. The groups would be given a chance to develop a collaborative research project and then all group leaders would report their proposals to the entire retreat. This approach should encourage interaction and facilitate the development of new research approaches. Further details will be disseminated as they become available.

Plans For The CFAR AIDS Club In The Coming Year



One of the major goals of the CFAR AIDS Club is to stimulate interactions among AIDS investigators at Einstein and Montefiore. To this end, in the past year we scheduled two 30 minute presentations at each CFAR AIDS Club ses-

sion, one from a basic scientist and one from a clinician. These sessions were successful in generating new collaborations and interactions among Einstein and MMC researchers. Nevertheless, we feel that there is room to increase the capacity of this forum to stimulate interaction. To accomplish this, we have modified the format of the CFAR AIDS Club to include a moderator for each session. Members of the Executive Committee will serve as moderators whose goal will be to actively suggest possible areas of collaboration based on the presentations at the CFAR AIDS Club. In addition, every third meeting will take place at MMC to facilitate attendance by MMC-based investigators.

The CFAR AIDS Club in the coming year will also provide a forum to educate AIDS investigators about the services provided by the CFAR Core facilities. The Directors of the Flow Cytometry, Virology, Immunology/Pathology, Animal Biohazard and Clinical Investigation Cores will present an overview of the services provided by their cores and examples of research projects facilitated by access to Core facilities and/or services. These will be 30 minute presentations interspersed among the CFAR AIDS Club research presentations by investigators. **We look forward to your attendance and participation in these meetings for which CME credit is available.**

Expansion Of CFAR Research Seminars

During the past year the Einstein/MMC CFAR has hosted seminars from a group of outstanding investigators. These included **Dr. Anthony Fauci** (Director, NIAID, NIH), four CFAR Directors, Drs. **Eric Hunter**, (UAB) **Mario Stevenson** (U. Mass), **Bruce Walker** (Harvard) and **Richard D'Aquila** (Vanderbilt), leading TB investigators, Drs. **Carl Nathan** (Chairman of Microbiology at Weil Medical College), **Joel Ernst** (Director of Infectious Diseases, NYU), **John Moore** (Professor of M&I, Weil Medical College of Cornell University), and leading virologists, Drs. **John Coffin** (Chief, HIV DRR Host Virus Interaction Branch, NCI, NIH) and **Roger**

Pomerantz (Director of Infectious Diseases and the Center for Human Virology, Jefferson Medical College). These seminars were embedded in extant Departmental seminar slots and were co-sponsored by the Einstein/MMC CFAR with various Einstein Departments. We plan to continue this approach and will be happy to co-sponsor speakers presenting AIDS-related seminars at Einstein and MMC. For the coming year, we have decided to expand the seminar series in a way designed to stimulate interaction between the speaker and CFAR members and to address a request from clinical investigators who expressed their difficulty in attending noon seminars

at Einstein. Therefore we will initiate a monthly afternoon CFAR seminar series hosting presentations by prominent AIDS researchers that will be scheduled for 4:00 p.m. The seminar will be followed by a reception where refreshments will be served to provide an opportunity for CFAR members to meet and talk to the speakers.

The Albert Einstein College of Medicine and Montefiore Medical Center are proud to inaugurate the Einstein/MMC Center for AIDS Research

Welcome
Dominick P. Purpura, M.D.
 The Honorable and Stanley H. Katz Dean

Introductory Remarks
Harris Goldstein, M.D.
 Director, Einstein/MMC Center for AIDS Research
 Professor and Vice Chairman, Department of Pediatrics
 Professor, Department of Microbiology & Immunology

Keynote Address
Anthony S. Fauci, M.D.
 Director
 National Institute of Allergy and Infectious Diseases
 at the National Institutes of Health

**Monday, November 17, 2003
 4:00 - 5:00 P.M.
 Robbins Auditorium**

Everyone Invited. Reception to follow.

CFAR
 CENTER FOR AIDS RESEARCH

Einstein/MMC CFAR Cores Increase Services

In response to requests by Einstein/MMC CFAR investigators, several Cores have expanded the services that they offer.

Further progress and de-

tails for each of the CFAR Cores are elaborated below in the newsletter. The success of our CFAR is dependent upon participation by our faculty investigators. We welcome

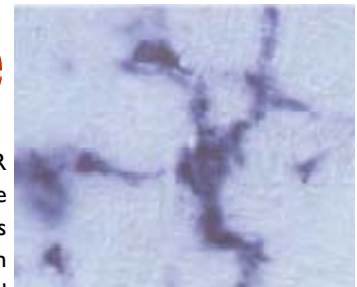
any suggestions and ideas of how the CFAR can help expand AIDS-related research efforts at Einstein and at Montefiore.

CFAR Immunology and Pathology Core

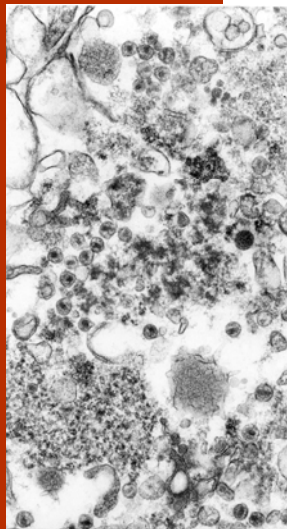
The Immunology and Pathology Core directed by Drs. Joan Berman (berman@aecom.yu.edu) and Sunhee Lee (slee@aecom.yu.edu) expanded the services available to include preparation of the vibratome sections of tissues. In conjunction with cryostat and paraffin-embedded sections, vibratome sections maximize the antigen

preservation as well as preservation of the superb morphologies of tissues and cells. Because of the thickness (30-40 microns) of the sections, they offer additional details and higher sensitivities for antigen detection. A new vibratome is located in the P3 Immunology and Pathology Core facility exclusively for processing infected

tissues for the CFAR members. The vibratome joins the Cryostat that is available for cutting frozen sections from infected tissues. Consultation from the Core Directors is available to help investigators determine the suitability of these methods for individual projects.



CFAR Virology Core



Electron micrograph of HIV-1 produced in the Virology Core

The Virology Core directed by Drs. Harris Goldstein (hgoldste@aecom.yu.edu) and Tanya Dragic (tdragic@aecom.yu.edu) has expanded its services by obtaining the technology to measure plasma viral HIV loads using branched chain technology. In addition, this technology can be modified for the measurement of plasma levels of hepatitis C. This system is FDA approved and can be used for clinical and research studies in patients. We are currently using this system for an NIH-funded study for which Julia Arnsten is

the PI. In addition, for measurement of research samples at a much lower cost, the Core has developed the capacity for real-time PCR measurement of HIV viral loads at sensitivities down to 100 copies. The Core can also provide support to investigators requiring measurement of other mRNA including cytokine and chemokine levels using real-time PCR techniques and using Affymetrix microarray analysis for determining differential gene expression. For a clinical study being developed by Barry Zingman, the Core is developing the capacity to

measure TREC in T cells to quantify thymic output in patients. The Virology Core also offers HIV pseudotypes for single cycle entry assays using a variety of envelopes from X4, R5 and R5X4 isolates, as well as envelopes of VSV, SFV and MLV. Retroviral vectors, including SIN vectors, expressing different reporter genes are available. Furthermore, The Virology Core offers cell lines expressing different combinations of CD4 and CCR5 or CXCR4 coreceptors for use in entry assays, as well as coreceptor-expressing cell lines for gp120 binding assays.

“The facility has also recently acquired a new FACSCalibur flow cytometer.”

CFAR Flow Cytometry Core

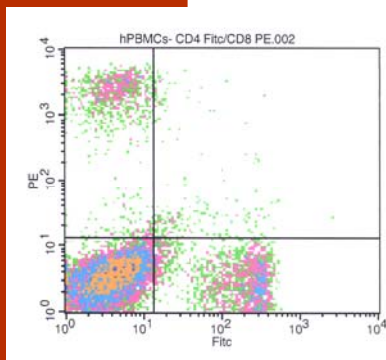
The CFAR Flow Cytometry Core directed by Dr. Steven Porcelli (porcelli@aecom.yu.edu) now has been expanded to include two functioning analytical flow cytometers for phenotypic studies of blood samples or cell suspensions.

The FAC-Scan flow cytometer can be used for up to three color fluorescence analysis,

and has had recent software upgrades that include MultiSET for obtaining absolute values of CD4 and CD8 T cells from freshly obtained whole blood samples. This instrument is relatively easy to use, and CFAR investigators are encouraged to have members of their laboratory groups sign up for training by the facility's resident technician (Ms. Isa Arias). The facility has also recently acquired a new FACSCalibur flow cytometer. This is a dual laser instrument with four color analysis capability. This instrument also has

limited sorting capability, and is useful for purifying relatively small numbers (e.g., several hundred thousand or less) of cells based on surface staining with antibodies to specific markers. The facility has initiated a pilot study for Dr. Kathy Anastos to study the correlation between CD28 expression on CD4+ and CD8+ T cells and clinical outcomes in women receiving HAART. An NIH funded study led by Dr. Julia Arnsten that is soon to be initiated will also use the core for measurement of CD4 and CD8 T cell levels.

Two-color analysis of monocytes done in the Flow Cytometry Core



CFAR Animal Biohazard Core

The Animal Biohazard Core directed by Dr. John Chan (jchan@aecom.yu.edu) provides a facility and support staff permitting researchers to perform studies requiring the use of mice infected with HIV, MTb and other AIDS associated pathogens. In addition,

it can also provide investigators with **SCID mice** and other immunodeficient mice as well as mice carrying gene deletions targeting specific cells populations and immune modulators. The facility has added a second bubble for gnotobiotic breeding of these colonies.



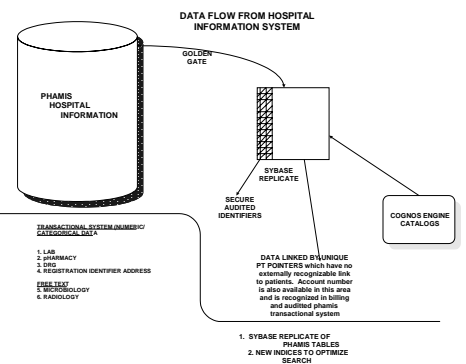
CFAR Clinical Investigation Core

The Clinical Investigation Core directed by Dr. Robert Klein (rklein@montefiore.org) continues to offer CFAR investigators extensive services in assisting with study design, data management, statistical analysis, and identification of and access to thousands of well-defined human subjects with or at risk for HIV infection and/or to their specimens. The technician who now is available to provide access to and extraction of data from medical center databases has completed extensive training and is prepared to process approved requests that could include exploration and linking of various clinical databases.

For example, all HIV-1 viral loads, CD4+ lymphocyte counts, demographic information, and any other clinically obtained laboratory values or pathological results from all patients with isolation of *M. tuberculosis*, *Cryptococcus*, or any other specific microorganism from any clinical specimen could be obtained for all patients seen at any of our medical center facilities.

Dr. Julia Arnsten, Coordinator of the Division of Substance Abuse component of the Clinical Investigation Core, has recently been named the Head of the Division of General Internal Medicine in the

Department of Medicine. She is planning on hiring in the near future several new junior faculty members with clinical and epidemiological research interest in HIV and substance abuse related research. These investigators are expected to be users of Clinical Investigation Core resources and additional potential clinical collaborators for basic investigators.



CFAR Developmental Core

The Developmental Core directed by Dr. Vinyaka Prasad (prasad@aecom.yu.edu) continues the mission of the core to provide support for junior investigators and collaborative and translational HIV/AIDS research at Einstein. An RFA was put out earlier this year to support three projects for up to \$35,000 each. There was an enthusiastic response to this RFA and we received seven excellent applications. The applications were re-

viewed by both internal and external reviewers and the Developmental Core Review Committee and three applications covering diverse investigational topics were funded. Dr. Joshua Nosanchuk (Department of Medicine, Infectious Diseases) will examine voriconazole therapy for *Cryptococcosis* and *Histoplasmosis*, Dr. Mark Einstein (Assistant Professor, Department of Obstetrics & Gynecology and Women's Health, Gynecological Oncology) will inves-

tigate immunotherapeutic approaches for the management of HPV-induced cervical neoplasia in HIV-infected women and Dr. Laura Santambrogio (Assistant Professor, Department of Pathology) will determine the role of exosomes in HIV release from multivesicular bodies in CNS microglial cells.

Investigators who were unsuccessful or who did not submit an application, please look forward to our next RFA in the fall.