

Director's Overview

**Year 1
July 1, 2005 – June 30, 2006**

Kent J. Weinhold, Ph.D.

Introduction

The Duke University Center for AIDS Research (CFAR) is completing its initial year of NIH funding that began on July 1, 2005. Duke previously enjoyed over a decade of CFAR support ending in June of 2001, during which time NIH-sponsored AIDS-related research at Duke grew substantially and flourished in a broad variety of clinical and basic research areas. Unfortunately, the nearly four-year hiatus in CFAR support saw much of the established infrastructure as well as the synergy among intramural investigators undergo significant deterioration. Thus, a major goal in this first year of the new CFAR funding is to prioritize and re-establish those critical elements that have served the Duke AIDS-related research community so well in the past. With this in mind, it is important to emphasize that significant changes in both the direction of AIDS research and the needs of the Duke AIDS research community have taken place over the past 4 years such that this newly established CFAR and its overall direction will be substantially different from its predecessor that ended in 2001.

The new Duke CFAR will take full advantage of the translational aspects of many of the ongoing intramural AIDS-related research efforts. To this end, I have chosen John A. Bartlett as my Co-Director. John is a well-recognized clinical researcher whose many talents provide the necessary balance and clinical perspective to complement my background in basic research. A primary area of emphasis for the new CFAR, and one that was largely non-existent within the prior CFAR, is Global Health. International HIV-1 research collaborations in Tanzania and South Africa will undergo significant expansion over the next 5 years with active CFAR support. The University and the Medical Center will join in these efforts as they complete plans to establish a Global Health Institute at Duke that will address the many different challenges that impact on health care around the world. Another area that has undergone significant expansion in the past 9 months is HIV vaccine research. Within weeks of the beginning of CFAR funding, Bart Haynes received an NIH award establishing the Center for HIV/AIDS Immunology (CHAVI) at Duke under his direction. This 7-year award establishes a multi-institutional, virtual vaccine institute consortium focused on greatly accelerated, in-depth studies to identify the correlates of immune protection against HIV infection and develop an efficacious preventive vaccine based on those findings. Although there has been an undercurrent of HIV vaccine research at Duke since 1986, CHAVI represents a highly significant expansion of these efforts and the single largest NIH award within the Duke CFAR portfolio. In addition to the other scientific areas that constitute the CFAR Research Programs, a comprehensive program in Training and Mentoring, established by John Hamilton to insure the continued development of young clinical and basic scientists dedicated to all aspects of AIDS-related research, stands as a focal point within the overall goals of the new CFAR.

Ongoing Activities and New Developments

In the course of composing the CFAR application, I became aware of a large number of new AIDS-related investigators who arrived at Duke during the 4-year hiatus in CFAR funding, and who were largely unknown to the intramural AIDS research community. As a means of introducing the new CFAR to Duke investigators while at the same time re-discovering the scope of AIDS research on campus, the first official CFAR activity was to convene a CFAR Fall Scientific Retreat on September 13 that was open to all investigators involved in

any aspect of basic or clinical AIDS research at Duke. We had 40 presenters and over 110 attendees of this one-day meeting. The feedback from the retreat was largely very positive and a number of active intramural collaborations were begun as a result of the meeting. The attendees generally felt that a yearly retreat of this kind would definitely serve a heretofore-unmet need of the AIDS research community at Duke. Therefore, a CFAR Fall Scientific Retreat will become an annual event. Further details on the retreat can be found under the report from the Administrative Core. In addition to the Fall Scientific Retreat, a monthly CFAR Seminar Series as well as a series of informal CFAR Chalk Talks were both initiated. The seminar series, in particular, has been highly successful and well attended (see Administrative Core report). CFAR has also been active in sponsoring AIDS-related lectures and symposia on campus, including the Matthews Lecture, the Global Health Speakers Series, and the recent Global Health Symposium. All of these efforts have added greatly to the overall visibility of the CFAR within Duke. The CFAR International Program, led by John Bartlett, has created a multiple mechanisms to expand opportunities for CFAR investigators to participate in international HIV/AIDS research. This program also supports conferences and workshops to develop research infrastructure and promote research exchange. Details of these activities can be found in the report from the Clinical Core.

Perhaps one of the more challenging aspects of the first year of the Duke CFAR has been the organization and implementation of the various Core activities. Each Core presented its own unique challenges, nearly all of which were met in a timely manner. Of necessity, the Administrative Core was both the first Core to become functional and, by far, the most active of the Cores. The Development Core, led by John Hamilton, became operational soon thereafter, and was able to provide first year funding to several investigators through the internally peer-reviewed small and innovative grants program. The three CFAR service Cores (Flow Cytometry, Molecular Virology, and Biostatistics/Computational Biology) began meeting the technical needs of intramural investigators by the early Fall of 2005. Efforts to establish each of these as Shared Resources within Duke were greatly confounded by the complicated structural and regulatory oversight requirements of the institution. Lastly, the Clinical Core was active in Year 1 in meeting the needs of CFAR investigators domestically as well as in facilitating technology transfer to the international site in Moshe, Tanzania.

As highlighted above, the most significant change that has occurred at Duke since the inception of the new CFAR is the CHAVI award with Bart Haynes as its Principal Investigator and Director. The intramural aspects of this multi-institutional scientific consortium represent the largest single component within CFAR, and involve no fewer than 25 Duke CFAR members are directly involved with CHAVI. Among the other institutions participating in CHAVI are Harvard University, the University of Alabama at Birmingham, and the University of North Carolina, all of which are currently active CFAR sites. Thus, the Duke-based CHAVI will serve as a direct conduit for inter-CFAR collaborative activities at a number of different levels. Organizationally, CHAVI resides within the Human Vaccine Institute, a portion of which (ie. the AIDS-related activities) resides within the Duke CFAR.

Of particular note, this initial year of CFAR support has greatly facilitated the interactions between AIDS investigators at Duke and UNC, and thus between the two CFARs. David Margolis from UNC was the January speaker in the Duke CFAR Seminar Series, while Michael Cohen and Ron Swanstrom are key participants in CHAVI. An additional link between the Duke and UNC CFARs was established during Year 1 through the Duke CFAR Flow Cytometry Core. The BD LSRII analyzer and BD FACSAria cell sorter in the Duke Core are the only BSL-3 instruments available at the two institutions capable of multiparameter flow analysis/sorting (up to 19 parameters) of HIV-1 infected specimens. Following informal discussions with Ron Swanstrom (UNC CFAR Director) and John Schmitz (Director of the UNC CFAR Immunology Core), the Duke CFAR Flow Cytometry Core has made their services available to UNC CFAR investigators. As a result, David Margolis and his group have begun using our FACSAria to perform live cell sorting of HIV-1 infected patient PBMC in their efforts to study the latent viral reservoir. All indications are that this will be a continuing

activity over the next years. At least one additional group from UNC has also used our BSL-3 cell sorting facility.

As detailed in the report from the Flow Cytometry Core, the current FACSria cell sorter is on loan to the CFAR from Dr. Haynes, who will re-locate the instrument in early 2007 when construction of the Regional Biocontainment Laboratory (RBL) is completed. Once in the RBL, use of this cell sorter will be exclusively dedicated to research in emerging infections and biodefense. To replace the sorter, I have submitted a Shared Instrumentation Grant application for funds to purchase a new FACSria with an optical platform that will match that of the existing LSRII in the Flow Core. The School of Medicine has committed an additional \$50,000 to purchase a Baker Bioprotect containment hood to house the new instrument. If the application is funded, the purchase of this instrument will coincide with the re-location of the existing sorter. If unsuccessful, I will seek additional institutional support to lease an instrument with an option for future purchase.

During its initial year, the Duke CFAR has been very active in the area of Community Outreach. A partial listing of those activities is presented below.

- Duke AIDS Research and Treatment (DART) Center Community Advisory Board (CAB) is the forum through which CFAR receives feedback from the community on all activities. CAB members learn about CFAR clinical research activities, provide input on planned research activities, and serve as a liaison to potential research subjects. CFAR is a co-sponsor of their quarterly meetings, and the CFAR Outreach Coordinator Patricia Bartlett provides assistance and support. Co-Director John Bartlett attends all meetings.
- The Annual Holiday Party serves as a unique opportunity for patients and their families to enjoy community support and celebrate with the holiday spirit. The Annual Holiday Party is planned and overseen by the CFAR Outreach Coordinator, with the support of the CAB. Last year's event was attended by 500 persons. CFAR Co-Director Bartlett gives an annual report on research progress during the party, and community members interact extensively with CFAR members during the evening.
- The Annual Community Treatment Update takes place in March after the Conference on Retroviruses and Opportunistic Infections (CROI), and is co-sponsored by the Duke CFAR. The Duke CFAR Outreach Coordinator organizes the meeting, and Duke CFAR Co-Director Bartlett and UNC CFAR Co-Director Joseph Eron discuss relevant findings from CROI with the community. Last year approximately 200 persons attended.
- The Beyond the Forum Treatment Update occurs annually in August and reviews either the World AIDS Conference or the IAS Conference on HIV Pathogenesis and Treatment. It is organized by the CFAR Outreach Coordinator and the CAB. This Update focuses on a more sophisticated discussion of research results with a prolonged question and answer period. CFAR Co-Director Bartlett is one of the speakers participating in this event, and the event is co-sponsored by CFAR.
- Patricia Bartlett is the Adult ACTU and CFAR Outreach Coordinator, and she is the principal liaison with numerous community groups. Mrs. Bartlett coordinates all DART CAB meetings and assists with their activities, (please see the activities listed above). She serves currently as Chair of the Project Straighttalk Community Advisory Board, a Member of the Partnership for a Healthy Durham, and a Board Member at the international CAB site hosted by the non-governmental organization KIWAKKUKI.

- Julia Giner, a study coordinator in the Duke University Adult Infectious Diseases Clinic, serves as a Member of the El Centro Board. El Centro serves the health care needs of the Latino community in Durham, and she advocates for HIV prevention, care and research in her position as a Board Member. She is also assisting with the development of research capacity at the Kilimanjaro Christian Medical Centre in Moshi, Tanzania, and is a Board member for KIWAKKUKI.
- Peer Effectiveness Training (PETS) is a 3 phase educational program directed at persons living with HIV infection. PETS teaches on diverse topics including basic clinical principles of HIV infection, self advocacy in health care, adherence, safer sex precautions, substance abuse diagnosis and treatment, and recognition of emotional distress within oneself and the available resources for treatment. It has trained over 400 persons, representing mainly African Americans and Latinos living with HIV infection. CFAR Co-Director Bartlett has served as the Principal Investigator for this project.
- Resistance Against Pressure (RAP) is a primary prevention project directed to African American youth. It provides education regarding the ABC's of prevention in culturally appropriate settings, especially churches, and beauty and barbershops. CFAR Co-Director Bartlett serves as the Principal Investigator for this project.
- Partners in Caring (PIC) is an outreach project for persons living with HIV infection through the Pastoral Services Department at Duke University Medical Center. Partners in Caring has overseen the PETS and RAP projects, and has critical links to the faith-based community throughout North Carolina. CFAR Co-Director Bartlett and Outreach Coordinator Bartlett are important liaisons with PIC.
- The Northern Outreach Clinic (NOC) is located at Maria Parham Medical Center in Henderson, North Carolina, an area with relatively high HIV incidence and a medically underserved, largely African American and Latino population. Through Duke University, the NOC receives Ryan White Title II and III funding for care delivery. CFAR Co-Director Bartlett is Principal Investigator for the Ryan White Title II and III Awards.
- The Southern Regional Area Health Education Clinic (SRAHEC) is located in Fayetteville, North Carolina, and serves an underserved area with relatively high HIV incidence. The SRAHEC HIV/AIDS Program is staffed by infectious diseases physicians from Duke. CFAR Co-Director Bartlett was the founder of this program, although other faculty members now provide staffing including CFAR Developmental Core Director Hamilton.
- The Early Intervention Clinic, located at the Durham County Public Health Department, receives Ryan White Title III funding through its parent organization, the Lincoln Community Health Center. CFAR Co-Director Bartlett, CFAR Developmental Core Director Hamilton, and CFAR Member Hicks have intermittently provided care and back-up support for this clinic. Dr. Bartlett still provides back-up supervision for the 2 nurse practitioners who staff the Early Intervention Clinic, and many clinical research subjects are referred from here to Duke.
- CFAR Clinical Research Director and Clinical Core Co-Director Coleen Cunningham serves as a Member of the AIDS Care Unit Advisory Council for the State of North Carolina. Mr. Scott Pollard, a social worker on the Duke University Adult Infectious Diseases Clinic staff, also serves as a Member of this Council.

Principal Investigator/Program Director (Last, First, Middle): Weinhold, Kent J.

- Mary Washington, a peer counselor within the Duke University Adult Infectious Diseases Clinic, Co-Chairs North Carolina AIDS Action Network. She provides a critical liaison between the Duke University CFAR and community needs.
- Within the Duke University Adult Infectious Diseases Clinic, a Men's Support Group is coordinated by Gordon Lipscomb MSW.
- The KCMC/KIWAKKUKI Community Advisory Board provides guidance to Duke University CFAR international efforts. The Duke CFAR is represented by 2 members on the Board, Ms. Bartlett and Ms. Griner, and by Drs. John Crump and John Bartlett, who regularly attend meetings.

Finally, the Duke CFAR has also been instrumental in facilitating the recruitment of underrepresented minority physicians and researchers. Below is a listing of the successful recruiting activities during Year 1.

- Ope Johnson recruited as a Minority Health Research Fellow
- Dr. Habib Ramadhani attended Department of Medicine Course on Clinical Research techniques and now serves as ISAAC Study Coordinator
- Dr. Humphrey Shao named as THIRST Study Coordinator, Co-Director of ISAAC Mycology and Mycobacteriology Programs
- Drs. Habib Ramadhani and Humphrey Shao named as candidates for Master's in Health Sciences, Clinical Research Training Program
- Dr. Florida Muro recruited as LPV/RTV Study Coordinator
- Dr. Olola Oneko attended Department of Medicine Course on Clinical Research techniques, and now serves as the KCMC Site Investigator for ACTG 5207
- Drs. Seif Shelalaghe and Venance Maro attended Department of Medicine Course on Clinical Research Techniques. Dr. Maro is Co-Director of the ISAAC Malaria Program

Major Research Results and Scientific Accomplishments

During the first 9 months of funding for this new CFAR, the most notable research results and scientific accomplishments are not so much in the form of CFAR-supported publications, but in the implementation of the critical components of the Duke CFAR, especially through the activation of the Scientific Cores. For the very first time, Duke and the surrounding Research Triangle area have access to a BSL-3 cell sorting facility where cells from samples containing infectious HIV-1 (or other pathogens) can be safely isolated in a viable state. Even in its earliest days of existence, this facility provides an essential service to Bryan Cullen in his isolation of lentiviral vector-transduced cell populations as well as to David Margolis in his high throughput isolation of purified cell subpopulations from HIV-1 patients that comprise the latent viral reservoir. The new technologic leap that now permits us to analyze up to 20 different parameters of a cell population simultaneously is likewise a major scientific accomplishment that places a significantly improved analytic tool in the hands of CFAR investigators. The state-of-the-art services offered through the Molecular Virology Core were not previously available to the community of Duke AIDS investigators and will, most certainly facilitate both basic and

clinical studies in the future. The formation of a Biostatistics and Computational Biology Core where none previously was available to Duke AIDS researchers represents a significant value added aspect of the new CFAR. Lastly, the tremendous growth of the international program within the Clinical Core will serve to further align the CFAR mission with that of the University and the Medical Center in their formation of a Duke Global Health Institute.

Since most of the Cores have been activated for less than 7 months, the CFAR supported studies that will produce the significant scientific publications are presently ongoing. It is anticipated that such publications should begin to appear throughout Year 2 and continue to increase with each year of CFAR support.

Future Plans

Aside from the re-establishment of the Duke CFAR, the single most important scientific event that will have the greatest overall effect on AIDS research at Duke in the future is the recent CHAVI award to Bart Haynes, the Director of the Duke Human Vaccine Institute. Most certainly, nearly all components of the Duke CFAR will be affected by this enormous scientific undertaking. The challenge to the Duke CFAR is to meet the upcoming infrastructure and support demands of the planned CHAVI investigations, while still serving the research needs of Duke AIDS-related investigators who are not a part of CHAVI. This may translate into expansion of several Core services and will, most certainly, require more extensive strategic planning.

Recruitment remains a high priority for the Duke CFAR, but one that was confounded in Year 1 by the efforts of the University and Medical Center to establish the Duke Global Health Institute (DGHI) and identify a Director. Once a Director of DGHI is named, the recruitment priorities within CFAR will be re-evaluated by the CFAR Executive Committee.

Efforts will be made over the next year to significantly increase the participation of both our international collaborators as well as our trainees in the different activities of the CFAR. This may include a special scientific forum for these groups, perhaps as part of this year's Fall Scientific Retreat. We will also re-evaluate the current structure of the Chalk Talks and develop strategies for increased participation. Lastly, there are at least two potential antiretroviral compounds that could move from pre-clinical to clinical testing in Year 2. CFAR resources will be committed to facilitate these important translational activities.

Director's Overview

Year 2

July 1, 2006 – June 30, 2007

Kent J. Weinhold, Ph.D.

Introduction

During its second year of existence, the Duke Center for AIDS Research (CFAR) continued to expand many of the initiatives begun in Year 1 and began a number of new activities designed to better meet the needs of the Duke HIV/AIDS research community. Membership in the Duke CFAR has continued to grow as our efforts to identify and engage new investigators have become more effective. The arrival of several key investigators on campus (see below) has further bolstered global health efforts on campus and has greatly strengthened our HIV/AIDS research efforts in the areas of social and behavioral sciences. The site visit of the Duke CFAR by the NIH on June 27, 2006 was particularly important in guiding our Year 2 activities, as the advice from the site visit team was instrumental in our alteration of a number of activities, such as expansion of our Small Grants Awards Program and establishment of Shared Resources for Core operations. With flat NIH budgets and paylines of 14% or less, there is tremendous concern that funding difficulties will represent a significant disincentive for young investigators to pursue a career in research. Since these scientists represent the next generation of HIV/AIDS investigators, it is imperative that the Duke CFAR discover new ways to support and encourage young scientists. This will remain one of the primary missions within the Duke CFAR. Overall, the most significant accomplishment of the past year has been the establishment of CFAR's highly successful working relationships with CHAVI, the Global Health Institute, the AIDS Clinical Trials Unit and AITRP. Each of these is active within CFAR and CFAR has established itself as the central hub of HIV/AIDS research activities at Duke.

Ongoing Activities and New Developments

On November 1st of last year, Dr. Michael Merson arrived on campus to begin serving as the Director of the new Duke AIDS Global Health Institute. During his recruitment as well as the time immediately preceding his arrival, I had the opportunity to meet with him on several occasions to discuss the overall organization of the Duke CFAR in order to identify different ways in which the CFAR and DGHI could interact. Dr. Merson brings to Duke a broad-based experience and distinguished career in Global Health. He served as Director of the World Health Organization's Global Program on AIDS and, most recently, was Director of Yale's Center for Interdisciplinary Research on AIDS (CIRA), funded through NIMH. Although not previously associated with a CFAR, Dr. Merson has very rapidly become familiar with the NIH CFAR Program by serving as Chairman of the committee conducting the most recent NIH review of new and competitive renewal CFAR proposals. Because of the overall importance of global health to the CFAR mission and to maximize CFAR-DGHI interactions, Dr. Merson is now a member of the Duke CFAR Executive Committee.

Although many of the basic research areas that comprise the Scientific Programs of the Duke CFAR are highly developed, having matured over the course of many years of productive investigations, one important area of research that is still in its infancy within the Medical Center is the social and behavioral science aspects of HIV/AIDS research. The arrival of Dr. Kathleen Sikkema at Duke last November signaled an important new initiative in this area. Dr. Sikkema, now a Professor in the Duke School of Nursing, became an active participant in the Duke CFAR, even prior to her arrival. In September she served as a judge for the poster session at the CFAR Fall Retreat where she also gave a brief talk on a number of her ongoing projects. That same month she attended a CFAR Behavioral Sciences meeting in Philadelphia, representing both the Yale CIRA and the Duke CFAR. Following many discussions with Dr. Sikkema and other CFAR investigators, we felt that there was a specific need for a Social and Behavioral Sciences Core within the Duke CFAR. This plan was presented to and approved by the CFAR Executive Committee. Dr. Sikkema has generously agreed to

take on the task of directing this new Core beginning July 1, 2007. The complete proposal can be found in the Appendix to Core A.

During the past year research activities within the Center for HIV/AIDS Vaccine Immunology (CHAVI) at Duke have intensified as new discovery protocols are enrolled and the complex immunologic and virologic analyses have begun in earnest. A number of the CFAR Cores, particularly the Flow, Molecular Virology, and Clinical Cores, have played an important role in getting these important comprehensive studies underway. As many of the CHAVI assays are subject to stringent quality control/quality assurance measures, (much like those already established for the HVTN studies performed at Duke), Dr. Marcella Sarzotti-Kelsoe has organized the QA/QC efforts for HVTN, CHAVI and the Gates initiatives into one centralized program termed the CFAR-GAP (CFAR-GCLP-compliant Assay Program). Plans are in progress to make CFAR-GAP materials such as SOPs and forms available through the CFAR website. Because of the increasing focus on GCLP-compliance, especially for assays performed in association with clinical protocols, the Duke CFAR has added a new Scientific Program, the Quality Assurance Program, to its organizational structure. This Program will be co-Directed by Dr. Sarzotti-Kelsoe and Thomas Denny, and will serve the interests of Duke HIV/AIDS investigators engaged in activities requiring QA/QC oversight and/or consultation.

The CFAR Seminar series, the Matthews Lecture, and the monthly Chalk Talks have all continued to grow in popularity, as evidenced by increased attendance. Seminar speakers have included Drs. Rafi Ahmed, James Hoxie, and David Bangsberg. The monthly Chalk Talk series has enjoyed much success in a number of areas. As word has spread about these after-hours informal discussions, more people from different disciplines have begun participating. We have also enlisted discussion leaders from industry (Dr. Celia LaBranche, GSK) and the UNC CFAR (Dr. Miriam Braunstein). For the next year, we are contemplating opening up the Chalk Talks to members of the UNC CFAR. If we proceed with these plans, we will need to locate another venue, since we are presently at capacity in our current location.

The Fall Retreat was, once again, our most successful venture of the year. Participation increased significantly over the previous year and a number of new scientists were in attendance. For the first time we included a poster session focused on work from trainees and junior faculty, and the top four posters were selected for oral presentation. Gift certificates to the Medical Center Bookstore, were awarded as prizes to the oral presenters and the top poster non-presenter. Support for this retreat (i.e. breakfast, lunch, refreshments, presenter prizes, etc.) came from the School of Medicine. The Retreat also featured keynote speeches by Drs. Michael Merson, Kathy Sikkema, and Michael Greenberg, with a luncheon address by Mr. Benjamin Mkapa, the former President of the Republic of Tanzania.

Following the advice of the NIH Site Visit Team and with approval from the CFAR Executive Committee, the Development Core committed more resources to funding Small Grants and Pilot Projects during Year 2. We originally committed \$100,000 to the Small Grant award program, enough to fund 4 projects. Following the NIH site visit in June, it was decided to commit an additional \$100,000, taken from the pool of recruiting monies, to fund new projects. Thus for Year 2 a total of 6 Small Grant Awards (\$25K each) and 1 Pilot Project Award (\$50K) were awarded, bringing the total projects funded in the first two years to eleven.

We have begun to see productivity among the recipients of the Small Grant Awards. Dr. Floyd Wormley, an award recipient in Year 1, successfully competed for his first R01 award from the NIH, using data derived from his CFAR grant as the basis for his R01 application. In addition seven publications have resulted directly from the CFAR funded projects, with several others in the process of submission or peer-review. As we continue to expand this mechanism of support in upcoming years, we are hopeful that such support will serve as an important incentive to this generation of young scientists to remain dedicated to HIV/AIDS research.

A number of recruitment initiatives were begun in Year 2. Under the leadership of its Chair, Dr. Thomas Petes, the Department of Molecular Genetics and Microbiology (MGM) began recruitment for two junior faculty positions in the Fall of 2006. Several members of the Duke CFAR participated in all aspects of the interview and selection process. From a field of impressive applicants, offer letters were sent to two highly qualified young scientists (Drs. Sara Sawyer and Marco Vignuzzi), both of whom have a background and continued

interest in AIDS-related research. The credentials for these individuals were presented to the CFAR Executive Committee who decided to commit \$100,000 of CFAR funds and \$100,000 in matching funds from the School of Medicine to the recruitment of these exemplary young scientists. The distribution of these funds between the individual recruitment packages was left to the discretion of Dr. Petes. Offer letters have been sent to both individuals and we are awaiting their respective decisions. Successful recruitment of either of these scientists would represent a solid investment in the future of HIV/AIDS research at Duke. We are, of course, hopeful that both candidates will accept their offers.

In addition to the two basic science recruits mentioned above, the Duke CFAR in conjunction with the Duke Global Health Institute is attempting to recruit Dr. David Bangsberg, a well-recognized AIDS clinical investigator who has also established a site in southwestern Uganda dedicated to the care and treatment of HIV-infected patients. In March the Duke CFAR hosted Dr. Bangsberg as a Visiting Professor and sponsored his 2-day visit to campus that culminated in his CFAR Seminar entitled 'International Perspectives on Adherence and Resistance to HIV Antiretroviral Therapy'. The Department of Medicine, the Global Health Institute, and the CFAR are all currently engaged in assembling a recruitment package for Dr. Bangsberg that will hopefully be ready by July 1. The successful recruitment of Dr. Bangsberg would represent a significant addition to both the Division of Infectious Diseases in the Department of Medicine and the Global Health Institute at Duke.

Activities within the CFAR Flow Cytometry Core have increased significantly during Year 2. In addition to serving the needs of HIV/AIDS investigators on campus, Core C has also been engaged in furthering research collaborations with industry as well as with members of the UNC CFAR. Retrospective studies of clinical samples generated from trials of the antiretroviral drug Enfuvirtide have become the focus of ongoing collaborative efforts with both Roche and Trimeris, focusing on polychromatic flow cytometric technologies developed within the CFAR Flow Cytometry Core. The BSL3 sorting facility continues to serve as a valuable resource to both Duke and UNC CFAR investigators. In particular, the laboratory of Dr. David Margolis at UNC has come to depend on the facility as he continues in his characterization of the latent viral reservoir. Interactions between the Duke and UNC CFARs also extend to pilot studies of the novel humanized mouse model developed by Lishan Su and colleagues at UNC. These very early experiments aimed at examining HIV-specific cellular immune reactivity in Rag2- γ C double knockout mice reconstituted with human CD34+ hematopoietic stem cells and infected with HIV-1 will continue into Year 3 of the CFAR. The CFAR Flow Core has also been instrumental in generating pilot data for CHAVI studies of apoptosis during very early HIV-1 infection. These efforts have been focused on the physical and phenotypic characterization of potentially immunosuppressive microparticles produced during the apoptotic process.

The CFAR Molecular Virology Core has continued to facilitate new collaborations within the CFAR community. In addition to the extensive sequencing activities of Dr. Gao, the viral infectivity services of Dr. Tomaras' laboratory has performed analyses for Duke investigators in departments not traditionally associated with HIV/AIDS research efforts, including Dr. Shaw in the Department of Chemistry and Dr. Haystead in the Department of Pharmacology. The RNA interference technology offered by Dr. Cullen's laboratory has likewise spanned several different departments and multiple disciplines.

The Biostatistics and Computational Biology Core has been quite active in Year 2 on a number of different fronts. In particular, Dr. Kepler and his colleagues have been actively involved in the experimental design, data analysis, and/or document preparation for 5 NIH grant applications from CFAR investigators. The team has additionally played a key role in performing data analysis, manuscript preparation, and abstract submission in support of an additional four ongoing NIH grants.

Of the many ongoing activities within the CFAR Clinical Core, the one that has perhaps had the greatest impact on the domestic research efforts at Duke is the hiring of Kareema Whitfield in September as the dedicated CFAR Coordinator who is available to assist CFAR investigators with IRB submissions, maintenance of regulatory documents, and recruitment of subjects into studies in support of CFAR initiatives. Her efforts have been instrumental in supporting the establishment of a Duke long-term non-progressor (LTNP) cohort for Duke investigators. She has also provided demographic information and assisted with consenting patients

enrolled into a number of different studies. She fills an extremely critical need among CFAR investigators in her role as liaison between the clinics and the basic researchers within the Duke CFAR. Her duties also involve activities at the Moshi site for which she maintains and updates critical documents in support of the KCMC database protocol.

The Duke CFAR has been proactive in soliciting and supporting greater involvement by under represented minorities. The following are examples of these efforts that took place during Year 2 of CFAR funding:

Kareema Whitfield (see above) is the Clinical Core Coordinator and African American. She completed an undergraduate degree in social work, and prior to her current position, worked as a research assistant and adherence counselor at Duke. In her current position she initiates formal and informal interactions between the Clinical Core and other Core members to facilitate and develop collaborative projects, provides training and regulatory support to other staff members and helps with recruitment for HIV-related clinical trials in both the Adult and Pediatric HIV Clinics.

Opemipo Johnson is an African American Medical Student at Duke who has worked with the CFAR both prior to enrolling in Medical School and now, as she completes her first year. She was initially a research assistant in the Division of Pediatric Infectious Disease during which time she applied for and received NIH funding and training as an under represented minority. While in that program, she worked closely with the CFAR Clinical Core in Moshi, Tanzania, assisting with a variety of on-going research projects and completing her own research project and to evaluate lymphocyte count and other low-cost markers as predictors of low CD4 count in HIV-infected children. Her work resulted in a first author presentation at the World AIDS Conference in Toronto and a manuscript currently under review.

Gayani Tillekeratne is an American but from Sri Lanka. She is currently a 4th year medical student at Duke University Medical School but completed her 3rd year of medical school training in Moshi Tanzania under the mentorship of 2 CFAR investigators (Drs. Cunningham and Crump). She helped with a variety of ongoing projects but played a major role in a home- based care study that resulted in a first author presentation at the World AIDS meeting in Toronto and a retrospective study to identify predictors of disease progression in HIV-infected children who initially present with mild disease (Stage 1 and 2). Manuscripts are under review for both projects.

Blandina Mmbaga is African and is in her final year of Pediatric Residency training at KCMC in Moshi, Tanzania. She previously worked indirectly with the Clinical Core, but in the past year has pursued concentrated research training in collaboration with the Duke CFAR in order to prepare herself for a faculty position in 2007 at Tumani. There she will conduct HIV related research in collaboration with Duke Investigators. The CFAR directly and indirectly contributed to her research training as she completed a 6-week research methods course at Duke. Due to her training, experience, and collaboration with Duke investigators, she was elected to be a member of the DAIDS-funded IMPAACT Network. She will clearly be a future leader in Pediatric HIV research on the African continent.

Thumbi Ngund'u is African, originally from Kenya but now running a successful immunology research laboratory in Durban, South Africa. Dr. Ngund'u visited Duke in 2007 as a guest of CHAVI, but during that time he was able to interact with Dr. John Bartlett (CFAR Clinical Core Director) to collaborate on Dr. Ngund'u's research capsule submission for IMPAACT and discuss potential future collaborations.

Drs. **Humphrey Shao** and **Habib Ramadhani** from KCMC are enrolled in the Master's in Clinical Research Program at Duke.

Cathrine Hoyo is a new Duke CFAR investigator. She is a molecular epidemiologist from Zimbabwe who is an Assistant Professor in Community and Family Medicine, and the recipient of a Small Grant Award from CFAR.

Many of the Community Outreach activities highlighted in the Year 1 Progress report are continuing. These activities include,

- Duke AIDS Research and Treatment (DART) Center Community Advisory Board (CAB) is the forum through which CFAR receives feedback from the community on all activities. CAB members learn about CFAR clinical research activities, provide input on planned research activities, and serve as a liaison to potential research subjects. CFAR is a co-sponsor of their quarterly meetings, and the CFAR Outreach Coordinator Patricia Bartlett provides assistance and support. Co-Director John Bartlett attends all meetings.
- The Annual Holiday Party serves as a unique opportunity for patients and their families to enjoy community support and celebrate with the holiday spirit. The Annual Holiday Party is planned and overseen by the CFAR Outreach Coordinator, with the support of the CAB. Last year's event was attended by 500 persons. CFAR Co-Director Bartlett gives an annual report on research progress during the party, and community members interact extensively with CFAR members during the evening.
- Patricia Bartlett is the Adult ACTU and CFAR Outreach Coordinator, and she is the principal liaison with numerous community groups. Mrs. Bartlett coordinates all DART CAB meetings and assists with their activities, (please see the activities listed above). She serves currently as Chair of the Project Straighttalk Community Advisory Board, a Member of the Partnership for a Healthy Durham, and a Board Member at the international CAB site hosted by the non-governmental organization KIWAKKUKI.
- Julia Giner, a study coordinator in the Duke University Adult Infectious Diseases Clinic, serves as a Member of the El Centro Board. El Centro serves the health care needs of the Latino community in Durham, and she advocates for HIV prevention, care and research in her position as a Board Member. She is also assisting with the development of research capacity at the Kilimanjaro Christian Medical Centre in Moshi, Tanzania, and is a Board member for KIWAKKUKI.
- The Southern Regional Area Health Education Clinic (SRAHEC) is located in Fayetteville, North Carolina, and serves an underserved area with relatively high HIV incidence. The SRAHEC HIV/AIDS Program is staffed by infectious diseases physicians from Duke. CFAR Co-Director Bartlett was the founder of this program, although other faculty members now provide staffing including CFAR Developmental Core Director Hamilton.
- CFAR Clinical Research Director and Clinical Core Co-Director Coleen Cunningham serves as a Member of the AIDS Care Unit Advisory Council for the State of North Carolina. Mr. Scott Pollard, a social worker on the Duke University Adult Infectious Diseases Clinic staff, also serves as a Member of this Council.
- Mary Washington, a peer counselor within the Duke University Adult Infectious Diseases Clinic, Co-Chairs North Carolina AIDS Action Network. She provides a critical liaison between the Duke University CFAR and community needs.

In addition, a few new efforts were initiated.

- Dr. Nathan Thielman spoke at this year's Adult Infectious Disease Holiday Party for patients and staff.
- Drs. Kathy Sikkema and David Wohl spoke at the Community Treatment Update.
- Dr. Merson participated in a press conference for a new statewide campaign, 'Get Real. Get Tested', sponsored by the North Carolina Department of Health and Human Services. The platform is to encourage North Carolinians to become educated about and get tested for HIV and AIDS. Lastly,
- Julia Giner and Patricia Bartlett have spent much of the past year in Tanzania working with KIWAKKUKI

Principal Investigator/Program Director (Last, First, Middle): Weinhold, Kent J.

(Kilimanjaro Women's Group Against AIDS). They have been helping to organize the Center and hire and train counselors to work with the local community. www.kiwakkuki.org.

The Strategic Planning process within the Duke CFAR has driven many of the initiatives highlighted in this overview section. Among the highlights of the Year 2 Strategic Planning efforts that were vetted through the CFAR Executive Committee were: 1) formation of the new Social and Behavioral Sciences Core to be directed by Dr. Sikkema, 2) commitment of recruiting funds in support of the recruitment of two outstanding HIV/AIDS basic researchers, 3) plans to commit funds to the recruitment of Dr. Bangsberg, 3) formation of a new CFAR QA Program headed by Marcella Sarzotti-Kelsoe and Tom Denny, 4) continuation of the highly successful CFAR Fall Retreat, and 5) finalization of the External Advisory Board meeting on June 29th. The new CFAR Core was funded for one year from funds in the CFAR unobligated balance. It is anticipated that this Core will become self-sufficient after this initial year of funding through the charge back mechanism established specifically for the Duke CFAR following last year's NIH site visit. We also anticipate that other service Cores (e.g. Flow Cytometry and Molecular Virology) will generate sufficient revenues through charge backs such that each may require a lesser investment of CFAR funds. If this expectation is borne out, the CFAR funds will be used to either create additional Cores or to bolster existing ones. One plan under consideration by the Executive Committee, should Core funds be freed up, is to take the international efforts out of the Clinical Core and form a new International Core. Another idea under consideration is to expand the Flow Core into an Immunology Core and include immunologic testing services beyond flow cytometry. Also, these monies could be re-invested into expansion of the Small Grant Award program. Any such changes will be in response to specific needs within the Duke HIV/AIDS research community and will be properly vetted through the CFAR Executive Committee.

Finally, we include in this overview section a composite Table of all Duke CFAR members, their type of participation, and their Core usage. As we've noted in the beginning of this section, the membership of the Duke CFAR has grown significantly and now stands at 140 active members. Several of our new members were identified either through Dr. Merson's contacts at DGHl or through the new NIH spreadsheet of 'Allowable' funded HIV/AIDS research at Duke. We will continue in our efforts to reach out to additional investigators, including those who may not be directly involved in HIV/AIDS research, but may have an interest in collaborating with one or more CFAR investigators. We also want to continue to be proactive in encouraging young investigators, including undergraduates, graduate students, medical students, medical residents, and post-doctoral trainees to actively participate in CFAR-sponsored events. Support and scientific interaction with these young investigators in training will be essential to the continuation of high-quality investigations in the future.

Director's Overview

Year 3

July 1, 2007 – June 30, 2008

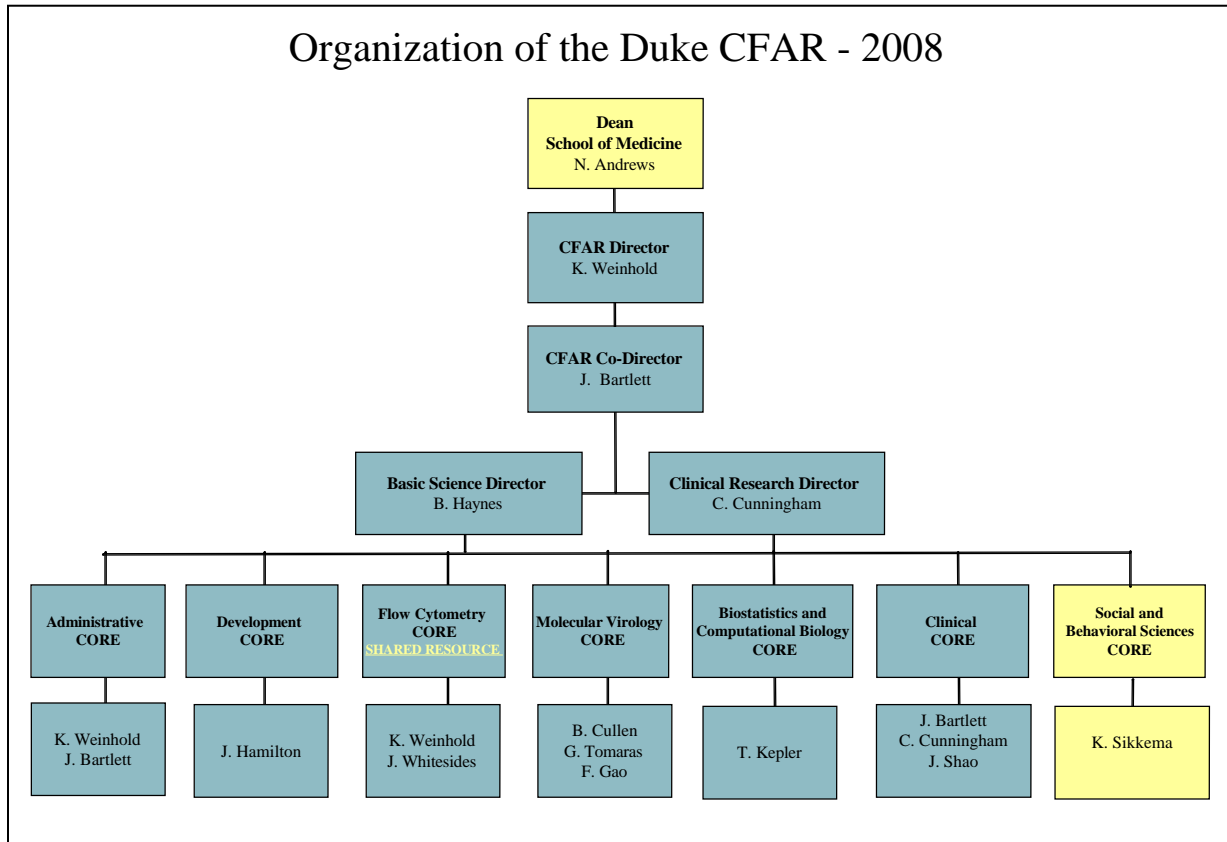
Kent J. Weinhold, Ph.D.

Introduction

During its third year of existence, the Duke Center for AIDS Research (CFAR) continued in its efforts to better serve and support the expanding interests of the Duke HIV/AIDS Research community. The CFAR experienced growth, reaching a membership of 173 investigators, many being brought in from the Social Science and Global Health research arenas. Perhaps the most significant event during Year 3 was the thorough and insightful review of the CFAR by our External Advisory Committee (EAC). The largely positive report generated by the EAC was instrumental in assisting the CFAR in securing an additional level of Institution Support through the School of Medicine (SOM) and its new Dean, Dr. Nancy Andrews. A continuing high priority of the Duke CFAR is the support and mentoring of young investigators who will represent the next generation of HIV/AIDS researchers. The Annual CFAR Fall Scientific Retreat as well as the CFAR Small Grants and Special Projects Initiative represent two of the major means of encouraging and supporting bright, young scientists within the community of Duke HIV/AIDS researchers. The overall Strategic Planning process by the CFAR Executive Committee (EC) matured greatly during the past year as CFAR faculty development support played an important role in bringing a young basic scientist (Dr. Micah Luftig) to Duke, and the CFAR EC has pledged additional faculty developmental support for four new, young faculty candidates engaged in HIV/AIDS research who are presently considering offers from various Departments and Institutes at Duke.

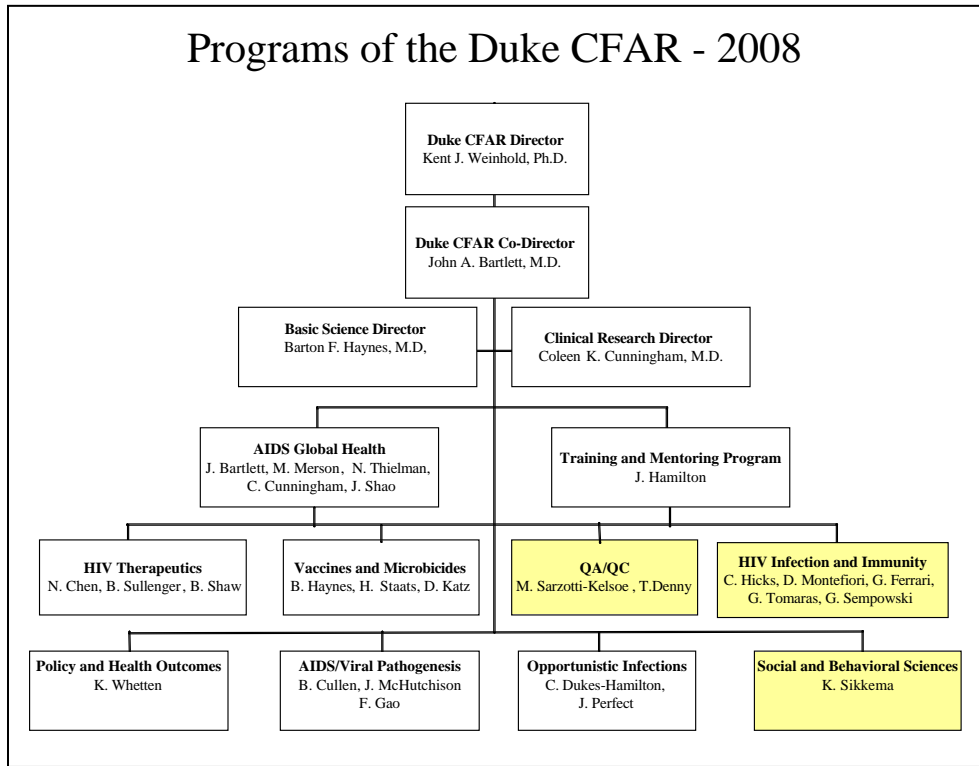
Ongoing Activities and New Developments

A number of organizational changes have taken place in the Medical Center and the Duke CFAR during Year 3 as a result of changes in the leadership of the School of Medicine as well as the formation of a new Core and the change in status of an existing CFAR Core. As mentioned above, the Duke School of Medicine has a new Dean, Dr. Nancy Andrews, who replaced R. Sanders Williams as Dean on October 1, 2007. As CFAR Director, I have had the opportunity to meet with Dean Andrews as well as her Executive Vice Dean for Administration, Mr. Scott Gibson. As detailed in the report from the Administrative Core, these meetings specifically addressed the Institutional Support concerns raised by the EAC report, and resulted in an increased SOM commitment to the Duke CFAR in the form of \$300,000 in matching funds for Years 3-5 in support of new faculty development and the Small Grants Program. The new Dean is committed to continued SOM support for the CFAR and has encouraged us to meet with her at any time to discuss any changes needs of the Center. Overall, we are greatly encouraged by the desire of the Dean to play an ongoing role in the further evolution of the Duke CFAR. On July 1, 2007, Dr. Kathy Sikkema became Director of the new Social and Behavioral Sciences Core (Core G) of the Duke CFAR. Funding for this Core became possible as we transitioned another Core, the Flow Cytometry Core (Core C), into a new Shared Resource. This permitted us to withdraw the initial CFAR investment from Core C and to re-invest those funds into the support of new Core G. This change was in keeping with the directive in the CFAR RFA to eventually have service Cores transition into Shared Resources as a means of beginning new Core initiatives. These changes (highlighted in yellow) are reflected in the CFAR 2008 Organizational Chart depicted below.



During the past year, we have also re-evaluated and re-structured our CFAR Programs in order to maximize collaborative interactions among the CFAR membership. To this end, we have combined the 'Acute Infection', 'Dendritic Cells and Germinal Centers' and 'Humoral and Cellular Immunity' Programs into a single new Program named 'HIV Infection and Immunity'. We also now include the new QA/QC Program run by Marcella Sarzotti-Kelsoe and Tom Denny, as well as the new Social and Behavioral Sciences Program under the direction of Kathy Sikkema. These changes are highlighted in yellow in the figure entitled 'Programs of the Duke CFAR – 2008' on the next page of this report.

The Duke CFAR continues to play a critical leadership role on campus. As evidence of this, the SOM recently sanctioned search committees for two separate faculty recruitments that could have a great positive impact on the future character of the Duke CFAR. The first committee, chaired by Bart Haynes, is charged with recruiting a new Infectious Disease Division Chief within the Department of Medicine to replace John Hamilton who is stepping down to focus his attention on largely administrative matters, including his continued CFAR participation as Director of the Developmental Core. Although it is unclear at this very early stage whether the next ID Chief will come from the HIV field or will have expertise in some other area associated with emerging infections, the CFAR Director and several CFAR members were selected to serve on this important committee. The second search committee, chaired by the CFAR Director, has a membership comprised exclusively of CFAR members and is charged with the recruitment with a mid-career scientist who would join in the HIV/AIDS research endeavors at Duke, taking on a significant leadership role such that the he or she would eventually lead the next generation of Duke scientists when Drs. Haynes and Weinhold complete their respective careers at Duke. In addition to the two SOM-sanctioned search committees, the alliance between the CFAR and the Duke Global Health Institute has been significantly strengthened in Year 3 by the appointment of the CFAR Co-Director (John Bartlett) as Associate Director of Research at the DGHI.



The CFAR Seminar Series, the Chalk Talks, and the Matthews Lecture all grew with respect to individual attendance. The number of CFAR Seminars decreased somewhat over the previous year, as repeated requests to the membership failed to produce additional suggested speakers. To remedy this as we move forward, we will form a CFAR Events Committee responsible for scheduling intra- and extramural seminar speakers and chalk talk discussants. Oversight of this committee will be accomplished through the Administrative Core. The after hours Chalk Talks have grown in popularity, especially with the graduate students, post-docs and young faculty members. One particular Chalk Talk held in January and addressing the topic of the failed STEP vaccine trial, attracted nearly 70 CFAR members representing basic and clinical investigators as well as community representatives. The Matthews Lecture (co-sponsored by the CFAR) featured Dr. Dennis Burton speaking on 'HIV Vaccine Design and the Neutralizing Antibody Problem' and enjoyed significant growth in attendance in its third year. CFAR also co-sponsored the sixth annual 'Mini-Symposium on Pathogenic Human Viruses' that featured Drs. Gabuzda and Stevenson speaking on AIDS-related topics.

By far our most successful venture as a Center during Year 3 was our CFAR Fall Scientific Retreat. This is the single-most important event that brings the largest segment of the overall Duke CFAR membership together in a scientifically rigorous forum. This year, attendance topped out at 143 participants, not counting speakers. We altered the format somewhat over that used for the previous year in order to encourage greater participation by the trainees and junior faculty. A total of 23 scientific abstracts were received and the top four were selected for oral presentation, while the remaining 19 were presented as posters. All of the oral presenters as well as the top poster presenter were awarded gift cards to the Medical Center Bookstore. To reflect the changing face of the Duke CFAR, both poster and keynote presentations by social and behavioral scientists were included among the scientific areas covered. At the Retreat, we also introduced a new CFAR initiative that we have termed the 'New Grant Pre-Submission/Post-Review Service' that is intended to provide advice from senior Duke investigators to any CFAR members submitting or re-submitting NIH grant

applications. The details of how this service will operate are highlighted in a flyer that is posted on the CFAR website and included in the materials at the end of this section. Although we received very strong support to initiate this process, no CFAR investigators have, to date, elected to avail themselves of these services. We plan to continue to highlight this initiative to CFAR members via e-mail communications, the website, and the new CFAR Newsletter in hopes that word of its value will spread throughout the Center once the first few investigators utilize this new support mechanism. All of the financial support for the Retreat comes from the SOM as part of their ongoing Institutional Support of the CFAR. A more detailed accounting of the Retreat Program can be found in the material included at the end of this report from the Administrative Core.

As we did in Year 2, we have continued to commit \$200,000 from the Developmental Core in support of the Small Grants and Special Projects Program. This has allowed us to expand our specific offerings to 3 separate submission deadlines throughout the year. A total of 15 applications were received during Year 3, and 9 were judged as meritorious and worthy of support. Productivity among the Small Grant recipients during Year 3 included an R21 award (Huang), an R01 award (Kondo), several peer-reviewed publications (Crump, Huang, Katz, and Kondo), and presentations at National and International Conferences.

During its series of meetings throughout Year 3, the CFAR Executive Committee (EC) further refined its Strategic Planning process and focused its attention on the emerging opportunity to support the faculty development packages of 4 possible new faculty recruits who are all conducting HIV-related research. If successful, these recruitments being conducted by several Departments and Institutes would add greatly to the scientific persona of the Duke CFAR, especially in the areas of social/behavioral science and global health. Since all four of the recruits are women, they would also contribute to greater gender balance among Duke CFAR investigators. A description of each of these pending young faculty recruits can be found as part of the report from the Developmental Core.

We were successful in our efforts to support the development package for a basic science recruit, Dr. Micah Luftig, now an Assistant Professor in the Department of Molecular Genetics and Microbiology. Even though his official start date in the department wasn't until October 1, 2007, Micah enthusiastically participated in the CFAR Fall Scientific Retreat on September 13th as an oral presenter, a poster presenter (two different AIDS-related projects), and a reviewer. As a new faculty member, he is being mentored by Dr. Bryan Cullen, and through their scientific interactions they jointly submitted a proposal in response to the CFAR-Comprehensive Cancer Center Collaboration RFA. The CFAR leadership looks forward to involving Micah in many different CFAR activities, including an invitation to have him join the new CFAR Events Committee (see above) responsible for identifying and scheduling Seminar speakers and Chalk Talk discussants.

The high level of research activity seen in the Flow Cytometry Core last year has continued throughout Year 3 of CFAR funding. The most significant administrative and/or organizational event that took place with respect to Core C was the change in its status to a recognized Shared Resource in the Medical Center. This became official on January 1, 2008 and it backed by support through the Department of Surgery, the 'home' Department of the Duke CFAR. The CFAR Flow Core continues to interact with many different investigative groups within the CFAR. The Core and its staff serve as a valuable resource to Duke investigators interested in developing polychromatic flow cytometry panels for a variety of different applications. The BSL3 sorting facility and its continuing support of the ongoing studies of Dr. David Margolis remains a formidable conduit for inter-CFAR interactions between the Duke and UNC CFARs. Of particular note are two manuscripts, co-authored by Ms. Janet Ottinger (Core Manager), that have recently been published in Cytometry and have great relevance to the evolving polychromatic flow technologies available within the Core. Also of note are the interactions between the Flow Core and Dr. Cliburn Chan in the Biostatistics and Computational Biology Core in which Dr. Chan is developing a means for management of the large data files generated in conjunction with the polychromatic assay panels.

The Molecular Virology Core (Core D) continues to serve the needs of multiple Duke CFAR investigators. The extensive sequencing efforts of Dr. Gao's laboratory supported 11 different research projects during Year 3. Additionally, the HIV infectivity portion of the Core established several new collaborative interactions, resulting in both grant submissions and publications. Finally, the RNAi technology available through the Core

saw increased usage throughout Year 3, supporting at least 7 different research projects and resulting directly in two publications in high profile journals.

In addition to becoming part of a nationwide group of CFAR statisticians and meeting with CFAR biostatisticians from eleven different universities during the 2007 Joint Statistical Meeting, the Biostatistics and Computational Biology Core (Core E) supported the work of 6 different projects throughout Year 3. Assistance was provided by Dr. Kepler and his group in the areas of both study design as well as data analysis. Several of these efforts resulted in presentations at international meetings and one of the projects was nested within an R01 submission.

The CFAR Clinical Core (Core F) accomplished a great deal during Year 3. In addition to increased Core usage, a number of new investigators have been recruited from Duke and KCMC to participate in HIV-related clinical investigations. The Core has been very active within the CFAR, participating extensively in the Fall Scientific Retreat and the Chalk Talk series, as well as seminars within the DGHI. Three new Core personnel were hired during the past year to further assist with specimen acquisition and regulatory affairs. This Core remains the principal point of contact with the community, including the pediatric and adult CABs.

The new Social and Behavioral Sciences (SBS) Core (Core G) has made tremendous progress during its first 9 months of existence. In addition to their active involvement in increasing both the scope and visibility of socio-behavioral research at Duke, it is of particular note that their efforts thus far have supported the submissions of 5 NIH/HHS research proposals, a developmental grant, and the funding of 3 additional awards. Six SBS faculty have also been added to the CFAR membership roles. At least 6 different research projects have benefited directly from Core G services. We are delighted with the very rapid establishment of this Core and its effective outreach to the Duke HIV/AIDS research community.

The continuing development of international collaborations is an explicit priority of the Duke University CFAR, principally focused on the Kilimanjaro HIV/AIDS Program in Moshi, Tanzania. The specific mechanisms used by the CFAR to stimulate international collaborations include;

- a) **Support for CFAR members who live overseas** and catalyze the development of new research projects, as well as advise on the practical aspects of project implementation (Bartlett and Crump);
- b) **Visits by CFAR members** to the Kilimanjaro Christian Medical Centre (KCMC) to develop and implement new projects (Cunningham, Thielman, Ferrari, Hoyo, John and Carol Hamilton, Whetten);
- c) **CFAR-sponsored fora** for investigators to exchange ideas regarding international research (CFAR Research Retreat, Seminars, Chalk Talks);
- d) **Mentorship for young and new investigators** from Duke and KCMC by CFAR members (Bartlett, Ferrari, Thielman, Cunningham, John and Carol Hamilton, Hoyo, Whetten, Sikkema, Gao);
- e) **Support for the KCMC Research Ethics Committee Secretariat** to enable her to conduct their activities according to the standards of the Office of Human Research Protections (OHRP).

Within each mechanism, CFAR members have provided communication assistance, study design input, data analysis, suggestions for new assays, educational materials, and research supplies that have contributed to new projects. The success of these CFAR-supported mechanisms is demonstrated by the expanding number of new and young investigators (please see the mentoring examples listed below), the diversification of the portfolio of research activities (please note the addition of studies on cervical cancer and HPV-related squamous cell carcinoma of the conjunctivae), and the development of multidisciplinary research teams (Operational Research proposal to the Elizabeth Glaser Pediatric AIDS Foundation [EGPAF] involving investigators from Departments of Obstetrics and Gynecology, Pediatrics and Medicine). By stimulating discussions on research results and potential opportunities, providing support to CFAR members, coordinating research collaborations, mentoring new and young investigators, and offering assistance with protocol development and regulatory communications, the Duke University CFAR has provided critical assistance to expanding international activities. Examples of specific activities by CFAR members that have added value include the following;

- a) Mentorship of new and young investigators (Dr. Habib Ramadhani mentored by John Hamilton, Bartlett, Crump and Thielman as he completed a Masters' degree at Duke in the Clinical Research Training Program [CRTP]; Dr. Humphrey Shao mentored by John Hamilton, Bartlett, Crump and Thielman as he also completed the CRTP; Dr. Bernard Njau mentored by Sikkema, Thielman and Whetten and will be coming to Duke for 6 months training in the CFAR Behavioral and Social Sciences Core; Moses Sichangi mentored by Ferrari and assisting with assay development at KCMC, resulting in research presentations in South Africa and Switzerland, and will be coming to Duke as a PhD candidate; Drs. Joseph Obure and Pendo Mlay mentored by Hoyo at Duke for training in cervical cancer research; Dr. Elizabeth Reddy mentored by Cunningham, Crump, Thielman, Carol Hamilton and Bartlett as she implements a project supported by a CFAR Small Grant Award).
- b) New supplements to the AIDS International Training Research Program (AITRP) on cervical cancer and human papilloma virus-associated squamous cell carcinoma of the conjunctivae that were developed with the assistance and leadership of CFAR members Bartlett and John Hamilton.
- c) Operational Research proposal to EGPAF to coordinate family planning and prevention of mother to child transmission at KCMC developed by CFAR member Bartlett.

The Duke University CFAR continues to participate in efforts to enhance the recruitment of underrepresented populations within the community of CFAR investigators. These efforts include the following activities;

- a) **CFAR investigator Haynes is serving as the faculty advisor to the Duke University Chapter of the Student National Medical Association.** In this role, he is encouraging African American students to consider careers in HIV/AIDS-related investigation.
- b) **Numerous CFAR investigators are serving as mentors for Tanzanian research trainees.**
- c) **With every CFAR-supported faculty recruitment, strong emphasis is placed on the identification and consideration of candidates from historically underrepresented populations.**

Outreach to local communities in Durham and Moshi continues through the following mechanisms;

- a) **Community Advisory Boards (CAB)** for the Clinical Research Sites at Duke (IMPAACT and ACTG) and KCMC (combined ACTG and IMPAACT). CFAR supports these activities through the regular participation of CFAR investigators, by providing specific investigator expertise when requested by the CAB membership, by inviting CAB members to comment on proposals in development, and by inviting CAB members to CFAR-sponsored activities.
- b) **Involvement of the community in specific CFAR-sponsored activities.** For example, during a CFAR Chalk Talk on failure of the Merck vaccine trial, the Vice Chair of the Duke ACTG CAB (Mr. Royce Hardin) participated as a panel member, representing both the CAB and persons living with HIV infection.
- c) **Participation in community-sponsored events** such as the Annual Community Treatment Update in Durham, the El Centro Health Fair for the Latino community in Durham, World AIDS Day celebrations in Durham and Moshi, and the KIWAKKUKI Annual General Meeting in Moshi. In each of these events, CFAR investigators provide education and materials regarding HIV infection and the role of research in generating new knowledge. These educational efforts encourage routine HIV testing, the rapid referral of infected persons into care, the treatment of co-morbidities such as mental illness and substance abuse, and the acceptance of HIV-infected persons within the community.
- d) **Participation in the Vanderbilt CFAR meeting on HIV and the African American Spiritual Community.** The Duke CFAR was represented by Dr. Cameron Wolfe in this important meeting, and he will present his experiences in a future CFAR Chalk Talk.

Finally, we include in this overview section both the NIH Spreadsheet of Funded HIV/AIDS Research at Duke as well as a composite Table of all Duke CFAR members, their type of participation, and their Core usage. As we've noted in the beginning of this section, the membership of the Duke CFAR has grown significantly and now stands at 173 active members. Several of our new members were identified through the new NIH spreadsheet of funded HIV/AIDS research at Duke. All of these investigators have accepted our written invitations to become members of the Duke CFAR and have indicated their potential use of CFAR

Cores and anticipated participation in CFAR activities throughout the upcoming year. We will continue in our efforts to reach out to additional investigators, including those who may not be directly involved in HIV/AIDS research, but may have an interest in collaborating with one or more CFAR investigators. We also want to continue to be proactive in encouraging young investigators, including undergraduates, graduate students, medical students, medical residents, and post-doctoral trainees to actively participate in CFAR-sponsored events. Support and scientific interaction with these young investigators in training will be essential to the continuation of high-quality investigations in the future. Although these pre-doctoral students don't qualify for full membership in the Duke CFAR (restricted to post-graduate scientists receiving or eligible to receive NIH funding) and are, therefore, not included in our accounting to the NIH of CFAR members, they do represent a vital part of the lifeblood that drives the Duke CFAR through their active participation in the Annual CFAR Fall Scientific Retreat as well as the CFAR Seminar and Chalk Talk series. In order to give these highly valuable CFAR colleagues a greater sense of belonging to the larger community of Duke HIV/AIDS investigators, we will now offer them the status of Associate Members. They will still not be tallied in our accounting of Full Members for NIH reporting, but this new membership designation will become a highly recognized prestigious activity listed in their developing resumes and *Curriculum Vitae*, while also recognizing their highly valuable contributions to the Duke CFAR.

Director's Overview

Year 4

July 1, 2008 – June 30, 2009

Kent J. Weinhold, Ph.D.

Introduction

The fourth year of the Duke CFAR saw continued growth and expansion in the infrastructure support of intramural HIV/AIDS clinical and basic research activities. Likewise, the overall Strategic Planning process that has served as the lifeblood of the Duke CFAR was greatly intensified during Year 4, in preparation for submission of our competitive renewal application due at the NIH by June 15, 2009. We have made important and exciting substantive changes to the overall organization of the Biostatistics and Computational Core (Core E) that should greatly facilitate increased utilization of these valuable support services. We have also changed the manner in which we support the Flow Cytometry Core (Core C), moving from a 100% Shared Resource Facility that was falling short of meeting its goal of total self-sufficiency in overall support to a 'mixed' model of support that is based on a partial funding through the Duke CFAR and re-investment of revenues generated through the Core's fee-for-service activities. In January, we had our second bi-annual meeting with the CFAR External Advisory Committee (EAC) during which we received a thorough review of our ongoing activities, many based on recommendations from the initial EAC meeting, and many important suggestions on how the Duke CFAR might submit the strongest possible competitive renewal application for funding the further growth of CFAR Programs over the next 5 years. A final copy of the EAC report is included in the Appendix to the Administrative Core report.

Lastly, the Duke CFAR continues to benefit greatly from the partnership that has been established with the Division of AIDS (DAIDS) and the 8 co-funding/participating NIH Institutes and Centers (ICs). From the viewpoint of the Duke CFAR, the joint meeting at the NIH on January 30th provided several critically important elements. First, the recognition and approval by our NIH partners of the many accomplishments that drove the evolution of our Center over the 40 months of its existence provided significant reinforcement of our extensive, broad-based efforts thus far. Perhaps even more importantly, the NIH team provided valuable guidance and insights into the critical elements that we need to consider as we articulate the overall organization and vision of the Duke CFAR in the context of the competitive renewal application. As an example of how greatly we value the guidance of our NIH partners, we are submitting this Annual Progress Report one month early so that we can possibly receive a critical review of our Year 4 accomplishments as well as the identification of any perceived weaknesses that we might correct prior to the submission of the CFAR renewal application. Although we are quite naturally disappointed that, according to the new Program Announcement and the new manner in which our Funded Research Base (FRB) is calculated, the Duke CFAR will fall short of the criteria needed to move up to the Tier II level of funding, we remain confident that the Duke CFAR can continue to experience significant future growth over the next 5 years in providing critical infrastructure support to the intramural community of basic and clinical HIV/AIDS research investigators.

Ongoing Activities and New Developments

Events of the past year have signaled a period of significant change within the Medical Center – especially with respect to leadership in both the Clinical and Basic Science Departments. Formal searches are presently underway for a total of 8 Departmental Chair positions. Although there are undoubtedly a multitude of reasons for this level of turnover in leadership, a likely contributor is the reduced level of NIH funding over the past 5 years and the accompanying pressures these shortfalls place on departmental leaders who are charged with finding additional sources of support for young faculty members in an atmosphere of continuing economic recession. Throughout this period of change, the CFAR membership has continued to play a vital leadership role within the Medical Center. One or more members of the Duke CFAR populate all 8 of the ongoing

Departmental Chair Search Committees. Additionally, CFAR members have played an important role in participating in the search for several key Division Chief positions – most notably the search for a new Chief of the Division of Infectious Diseases within the Department of Medicine. This search committee was chaired by Bart Haynes and had no fewer than 6 CFAR investigators as members, including the CFAR Director. Following a comprehensive national search, the committee developed a ‘short list’ of 6 highly qualified candidates who visited Duke, met with intramural investigators and administrators, and presented overviews of their ongoing research portfolios. Although the initial charge to the committee by the Dean of the School of Medicine (SOM) was to identify the most highly qualified scientific leader in the broad arena of Infectious Diseases and Microbial Pathogenesis, the top two candidates unanimously ranked by the entire committee both have made significant contributions to the field of HIV/AIDS research. Negotiations between the SOM and the top candidate are nearing completion, and we are hopeful that the new ID Chief will be named within the next two months. If one of the two highly accomplished HIV/AIDS investigators is named Division Chief, the Duke CFAR plans to immediately engage the new Chief by naming them Co-Director of the CFAR Developmental Core. Either of these two candidates will bring significant scientific leadership and mentoring skills to this position. John Hamilton, who stepped down as ID Chief, will remain as Director of the CFAR Developmental Core and will work with the new Chief in formulating future support and mentoring initiatives by the Core. We are very excited by this new opportunity to add to the already highly developed support endeavors of Core B. The search committee (mentioned in the Year 3 Progress Report) chaired by the CFAR Director and charged with identifying an accomplished mid-career HIV/AIDS investigator to join the ongoing research efforts at Duke and eventually occupy a leadership position in the CFAR has been placed on hold until the new ID Chief is named and the co-investigators are identified who might join the Chief at Duke. We anticipate renewing these search efforts by September of this year.

As it has been since its inception during the initial year of support, the Fall Scientific Retreat remains the most significant CFAR event of the funding year. It is estimated that over 150 Duke investigators, graduate students, postdoctoral fellows, and staff were in attendance at this year’s Retreat. The program (see Administrative Core Appendix for agenda) was largely built around brief scientific presentations from past and present recipients of CFAR Small Grant support, and these were divided into a morning and an afternoon session. As part of the talks, awardees were asked to include a final slide that listed any CFAR support-related publications and grants, as well as anticipated manuscripts and grant submissions. This information was used by the Developmental Core for the current Progress Report, and will be used in constructing our competitive renewal application. Interspersed between the 2 scientific overview sessions was a series of presentations by 3 of the 4 most recent recruits – namely Drs. Blankenship, McKellar, and Merli. This session was aimed at introducing the new recruits and their respective research portfolios to the Duke CFAR membership. The fourth recruit, Dr. Christina Meade, began her new Duke faculty duties on December 1st, and was not available to participate in this year’s Retreat. Following the ‘New Recruit’ session, Drs. Merson and Haynes gave highly insightful overview presentations on “Future Perspectives in Global Health” and “Future Perspectives in Human Vaccine Research and Development”, respectively. The Retreat also included a poster session as well as presentations by 4 pre-selected abstract submitters. Prizes were awarded for the best oral and poster presentations. The theme for this year’s upcoming Fall Scientific Retreat will be ‘Interactions’ and will focus on the collaborations and partnerships that CFAR members have with other Centers and Institutes at Duke.

As mentioned in the introductory section of this Director’s Overview, the second biannual meeting of our External Advisory Committee (EAC) was held on January 13, 2009, with 5 of the 6 members in attendance. Dr. Koup was the only absentee, due to a late-emerging scheduling conflict involving a trip to China on behalf of the VRC. As with the initial EAC meeting near the end of Year 2, the daylong session of review and discussion resulted in a number of highly valuable recommendations to the CFAR leadership in several key areas. In particular, the committee made very strong suggestions on enhancing administrative staff support as well as further ways to increase overall Institutional Support as we construct our competitive renewal application. The EAC also made substantive recommendations regarding streamlining of the Small Grant application review process as well as increasing the amount of individual awards and issuing targeted RFAs as a means of filling in specific programmatic gaps that become evident. The committee also supported the re-organization efforts of the Biostatistics and Computational Biology Core as well as the re-structuring of CFAR support for the Flow Cytometry Core into a more realistic ‘mixed’ CFAR-Shared Resource type of model. The

CFAR leadership greatly appreciated the very strong positive comments regarding the accomplishments of the past 3 years, including the very high praise for the formation and very early successes of the new Social and Behavioral Sciences Core directed by Dr. Sikkema.

The CFAR Seminar Series, Chalk Talks, and the Matthews Lecture were all active throughout Year 4, although the numbers of CFAR Seminars and Chalk Talks dropped off somewhat due to only sporadic responses to our continued requests to CFAR members for suggested speakers and topics. To address this shortfall, a CFAR Events Planning Committee has been formed to more proactively develop regular seminar and chalk talk schedules. The new committee is chaired by Dr. Georgia Tomaras, and includes Drs. Guido Ferrari, Charles Hicks, and Melissa Watt as members. Additional members will be added in the next few months. The Committee has already scheduled Drs. Mauro Schechter and Mario Roederer for CFAR Seminar presentations for the end of CFAR Year 4. A schedule for regular monthly Chalk Talks is currently being developed, and the expanded committee will also take over the role of planning for the Fall Retreat – a task that has previously fallen to the CFAR Director. Dr. Max Cooper, this year's Matthews Lecturer, presented to the largest audience in the 4-year history of this prestigious series. Dr. Robert Gallo has already agreed to give the next Matthews Lecture scheduled in November 2009. The Duke CFAR also co-sponsored a number of lectures and related events during Year 4. These are all presented under the Administrative Core.

The four new recruits highlighted in last year's report are now all firmly in place at Duke and in various stages of integration within the CFAR. A critical recruit for the Moshi international site remains as a high priority, as defined by the CFAR EC. We are hopeful to secure this key individual by September of this year. The CFAR Small Grants and Special Projects Program funded a total of 12 proposals thus far during year 4 and, at the suggestion of the EAC, we are about to release an additional Year 4 RFA that targets 3 specific HIV/AIDS-related research areas – namely, 1) Bioinformatics, 2) HIV/HCV Co-Infection, and 3) Novel HIV Therapeutics. We have increased the amounts for these awards from the standard \$25,000 to a new cap of \$40,000 per award.

NIH Programs and Areas of Interest to the Co-Funding and Participating Institutes and Centers (ICs)

The Duke CFAR Funded Research Base (FRB) for FY 2008 reflects a heavy concentration of effort on NIAID sponsored research programs, accounting for \$31,470,777 of the \$34,827,620 (90.3%) of total allowable costs. The largest portion of NIAID-related funding is represented by the Center for HIV/AIDS Vaccine Immunology (CHAVI) U19 award with Dr. Bart Haynes as its Principal Investigator. The remaining portfolio includes the broad programmatic areas of vaccine development, novel therapeutics development, therapeutic trials, and opportunistic pathogens. The NCI sponsored projects address various aspects of cancer therapies and immunotherapies. NIMH sponsored research by Duke CFAR investigators support outcomes measures/coping programs domestically and internationally. Dr. Whetten's program on HIV/AIDS and Orphan Care represents the only current NICHD sponsored HIV/AIDS research at Duke. HIV-associated drug abuse as well as the development of novel HIV/AIDS therapeutic agents comprise the NIDA portfolio within the Duke CFAR. Each of these funded HIV/AIDS studies is supported by one or more CFAR Service Cores. Presently, there are no Duke CFAR HIV/AIDS-related research projects supported by either NCCAM or NHLBI, but a number of NHLBI and NCCAM sponsored non-HIV/AIDS studies are supported by several of the CFAR Service Cores – most notably the Flow Cytometry, Biostatistics and Computational Biology, and SBS Cores.

Major Research Results and Scientific Accomplishments

Members of the Duke CFAR published a number of important findings over the past year. Among them are significant new insights in the following areas – namely, 1) HIV/AIDS pathogenesis, 2) broadly reactive anti-HIV antibody reactivities, and 3) bioinformatics and statistical modeling for analysis of polychromatic flow cytometry data. The paper by Gasper-Smith *et al* (J. Virol. 82:7700-7710, 2008) highlighted for the first time the very early apoptotic events of the acute infection period that lead to the production of plasma microparticles during peak HIV viremia, thus representing one of the earliest events leading to the cascade of profound early immunologic compromise and loss of virologic control. These observations suggest that the 'window of

opportunity' for intervention prior to irreversible immunologic damage is far narrower than originally believed, and thus limit the possible countermeasures that might impact on this process. A central question to overall vaccine design is why broadly reactive HIV neutralizing antibody reactivities are so rare in HIV infected patients and non-existent in response to candidate vaccines evaluated clinically to date. The manuscript by Shen and colleagues currently in press in *J. Virol.* documents for the first time anti-gp41 antibodies in an HIV infected patient that mediates broad viral neutralizing activity and fine specificity for the so-called 2F5 epitope. These findings as well as follow-up studies based on these results could have a profound impact on the design of future HIV vaccine immunogens. Two significant publications resulted in part from collaborations between the Flow Cytometry and the Biostatistics and Computational Biology Cores (Chan *et al*, *Cytometry A* 73A:693-701, 2008 and Frelenger *et al*, *Source Code for Biology and Medicine* 3:10, 2008). While the polychromatic flow cytometry platforms developed, standardized, and implemented within the CFAR Flow Cytometry Core represent extremely powerful tools for both basic and clinical HIV/AIDS investigators, the broad application of these technologies is severely hampered by the existing analytic software available for data analyses of these extraordinarily large data sets. Cliburn Chan in the Biostatistics and Computational Biology Core has developed a Bayesian-based analytic software that can rapidly (*i.e.* overnight) analyze with high precision data sets that ordinarily took weeks to analyze. The overall significance of these new analytic tools is not trivial and will greatly facilitate further application of polychromatic flow cytometry platforms in a broader arena of scientific investigations.

Scientific Programs

The Scientific Programs comprising the Duke CFAR remain unchanged during Year 4, having been consolidated during Year 3 to facilitate potential synergy within and among specific programmatic areas. The Duke CFAR does not provide funding support for the Programs. As we approach the CFAR competitive renewal, we will identify opportunities to further consolidate the overall programmatic structure of the Duke CFAR. We will also begin to invite non-HIV/AIDS investigators at Duke to become members of specific Programs in order to attract accomplished scientists from outside the field to begin closer interactions (and hopefully productive collaborations) with Duke CFAR members.

Future Plans

In each of the sections above, I have attempted to project future plans for specific CFAR areas. Obviously, the overall vision for the Duke CFAR over the next 5 years will constitute a highly important component of our competitive renewal application. We have accomplished much during this initial 4 years of CFAR support, but we anticipate developing a highly vigorous agenda in the future that will further broaden the scope of support for Duke HIV/AIDS investigators and, in turn, increasing their high level of productivity and significant contributions to the field. We look forward to continuing our partnership with the NIH in these future efforts.