

CFAR CONNECTIONS

A Newsletter of the UAB CFAR

World Renowned AIDS Activist Mary Fisher Visits the UAB CFAR and Speaks in Birmingham



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Mary Fisher – an author, artist and speaker who travels the world advocating for those who share her HIV-positive status -- visited the UAB CFAR administrative offices and the UAB 1917 Clinic on February 20, 2008. Mary was in town to give a speech at the Birmingham Rotary Club, and to visit colleagues and friends at the CFAR and her UAB-based philanthropy, the Mary Fisher Clinical AIDS Research and Education (CARE) Fund.

Introduced to the Rotarians by CFAR Director Dr. Michael Saag, MD, Mary noted that she had known him so long, as her cousin and physician, that “when I come to Birmingham, I think of it as coming home.” In a speech several said left them humbled and inspired, Mary challenged listeners to find some way to “make a difference” in the HIV/AIDS pandemic – in Alabama, in Africa, or wherever they could.

When Mary Fisher addressed the Republican National Convention in August 1992, she spoke of the AIDS virus that she contracted in marriage and that she believed would soon leave her two young sons orphans. In a speech that moved many in the audience to tears, she noted that the AIDS virus “does not care whether you are Democrat or Republican.

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Insights, updates and news for HIV/AIDS research and clinical investigators



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It does not ask whether you are Black or White, male or female, gay or straight, young or old ... HIV asks only one thing of those it attacks: Are you human?" Thanks to life-prolonging drugs, that speech was merely the opening act on Mary's career of advocacy.

Traveling around the world, she has devoted her life to raising awareness of those most at risk of AIDS and the death it brings – the poor and oppressed and, especially, women and girls. In May 2006, the United Nations recognized her decade-and-a-half of worldwide advocacy by appointing her an ambassador of its Joint Programme on HIV/AIDS (UNAIDS). Mary's words, photographs and art have filled five books. Mary's art is exhibited and collected around the world, and several of her sculptures are in the permanent collection at the UNAIDS headquarters in Geneva, Switzerland.

Mary founded the CARE Fund, based at UAB, to support long-term research for the care of people living with HIV, especially women, in both the United States and Africa. She travels frequently to Zambia, where she works with the UAB-backed Centre for Infectious Disease Research in Zambia (CIDRZ). As part of her commitment to enable HIV-affected women in Africa to support themselves and their families, Mary taught women in Rwanda and Zambia to hand-bead bracelets brought to the U.S. market by Fair Winds Trading, Inc., through partnerships with *O, The Oprah Magazine*, and Macy's.com. She continues to personally train HIV-positive women in Lusaka support groups to make bracelets, then sells them on her Web site (www.maryfisher.com) to provide income for the women.



Message from the Director Dr. Michael Saag

As the adage goes, "the only thing constant is change." And the UAB CFAR has gone through some significant changes over the past several months! Often times, change represents loss and is associated with grief. We certainly grieve the loss of Mike Bertram, Jeannette Lee, Michael Kilby, and Craig Wilson as leaders within our Center. Mike Bertram has moved to the UAB Comprehensive Cancer Center where he is now the Administrative Director there and doing a fine job. Jeannette is moving to the University of Arkansas where her husband is the new Chair of Radiology and she will be joining their Biostats group. Michael Kilby is going to the Medical University of South Carolina where he will be Division Director of ID. And Craig Wilson has become the new Director of the UAB Sparkman Center and has given up his leadership role as Director of the International Core. We wish all of these CFAR leaders well in their new roles and are grateful to them for years of remarkably productive service and dedication.

Change also represents opportunities ... and the CFAR has embraced these unexpected changes with identification of new leadership in 2008. Dr. Donna Porter is our new Administrative Director, Dr. Paul Goepfert is the new leader of our Clinical Core, Dr. Jeff Stringer has taken over the International Core, Drs. David Allison and Gary Cutter are assuming the leadership of the Biostatistics Core, and Dr. Casey Morrow is taking over the reins of the Developmental Core. These new leaders are highlighted throughout this newsletter. Dr. Morrow and Dr. George Shaw have been appointed to serve as new members of the CFAR Executive Committee and Dr. Olaf Kutsch is joining Allan Zajac as the Co-Director of the Flow Cytometry Core. All of these leaders are committed to making the UAB CFAR the best it has ever been. A key focus of all of the leaders is to improve the functionality and the communications of the Center for its members. In this way, we are looking forward to a productive year with our new "Connections" newsletter and our new-and-improved website, www.uabcfar.org!

Here's to a great year!



Donna C. Porter, PhD has recently joined the CFAR as the new Administrative Director. Dr. Mike Bertram, the former Administrative Director, left the position to join the UAB Comprehensive Cancer Center in a similar capacity. Dr. Porter is a UAB alumna with a BS in Biology (1987) and a PhD in Molecular Biology (1994). Dr. Porter did her thesis work in virology with Dr. Casey Morrow, (Dept of Cell Biology). After she graduated, Dr. Porter, Dr. Morrow, and another graduate student from the same lab, Dr. David Ansardi, developed and characterized a technology based on poliovirus (a picornavirus) for therapeutic gene expression. The results of the work was so promising, they sought legal rights and monies to seed a startup biotech company in 1998. The company setting allowed for pharmaceutical development of the technology on a commercial scale for patients with neurological diseases and disorders, such as brain tumors. Dr. Porter and Dr. Ansardi left their academic positions, as a Research Assistant Professors in Microbiology at UAB, to work for the company full-time.

As often happens with companies developing pharmaceutical products that take many years for FDA approval, the company wasn't able to sustain itself financially and was closed by 2005. The experience stirred her entrepreneurial spirit so, instead of returning the university, she took a few years off to help her husband, an attorney, follow a dream to open his own business in downtown Birmingham.

Last fall, Dr. Porter was ready to leave the family business and pursue her own interests again just

Dr. Donna C. Porter joins the UAB CFAR as the new Administrative Director

as the UAB CFAR had an opening for Administrative Director. Dr. Porter is happy to come back to UAB. She has followed the work of the UAB CFAR since 1997, when her first research funding as a postdoctoral fellow was a CFAR developmental award for pilot studies in AIDS vaccine vector research.

Events of Note

THE CFAR EXTERNAL ADVISORS MEET IN BIRMINGHAM

THE CFAR External Advisory Committee met in Birmingham on February 23, 2008.

The purpose of the meeting was to conduct annual strategic planning for the center.

The members of the committee are:

Dr. Paul Volberding UCSF,

Dr. King Holmes, UW,

Dr. Kathleen Sikkema Duke Univ.,

Dr. Robert Siliciano, Johns Hopkins Univ.,

Dr. Jerry Zack, UCLA.

Dr. Eric Hunter, Emory Univ.

2007-2008 Developmental Grant Program Awardees



Terje Dokland, Ph.D., Associate Professor of Microbiology. Development of a broadly effective vaccine against HIV has been very difficult due to the high variability of the envelope (Env) proteins (gp41 and gp120) and the ways the virus evades the immune system. One promising strategy for vaccine development is the use of virus-like particles (VLPs) that display HIV immunogens on their surface. Chimeric envelope proteins that include transmembrane and cytoplasmic domain sequences from other viral envelope proteins are incorporated into VLPs at higher levels than native Env proteins and elicit higher levels of neutralizing antibodies. We will use cryo-electron microscopy (EM) in combination with tomographic reconstruction methods to study the structures of such chimeric VLPs. This will allow us to begin to understand the structural determinants for envelope protein incorporation and immunogenicity in HIV virions and VLPs which will be important in the continued development of VLP- based vaccines

Mirjam-Collete Kempf, Ph.D., MPH, Research Assistant Professor of Epidemiology. Although antiretroviral therapy (ART) has had a tremendous impact on the decrease in perinatal HIV transmission, few studies have

examined ART adherence among HIV-infected pregnant women, particularly during postpartum care. While a decrease in ART adherence after delivery of a child has been suggested in the literature, barriers to postpartum ART adherence have not been evaluated yet. Since ART adherence among HIV+ mothers is critical to the survival of mother and infant, it is important to understand the HIV treatment experience of mothers in the postpartum period. The aim of this study is to evaluate contextual factors contributing to postpartum ART non-adherence in HIV+ women who have given birth to a child within the last 5 years while seeking care in Birmingham or Montgomery, AL.



Michael Niederweis, Ph.D., Associate Professor of Microbiology.

Mycobacterium tuberculosis (*Mtb*) has infected about two billion people and causes the death of about two million people every year. Unfortunately, HIV infection drastically reduces the number of CD4 T-cells which are of vital importance for the control of infection with *Mtb*. Tuberculosis (TB) is the most

common co-infection in HIV-positive individuals. Control of these diseases now demands increased investment and new research efforts. TB caused by MDR strains of *Mtb* increases treatment time and costs dramatically. We have identified the first such Outer Membrane (OM) channel of *Mtb*. OM channels have served as targets of drug development efforts due to their crucial role in drug efflux systems. This is likely to play an important role for multidrug resistance of *Mtb* and for understanding solute transport across the OM, which will make it an attractive drug target.

Jacqueline Parker, Ph.D., Associate Professor of Pediatrics-Infectious Disease. The desperate need for an effective AIDS vaccine has emerged as a public health objective of the highest priority in the global community.



These studies will test the hypothesis that HIV-1 Gag-specific immune responses elicited by vaccination with a replication-competent, neuroattenuated Herpes Simplex Virus (HSV) that expresses HIV-1 Gag can be augmented by co-immunization with cytokine-expressing HSV vectors. Studies are outlined that will determine the effect of pre-existing immunity to HSV on the host immune responses elicited. Vectors targeting the gut mucosa as the site of primary immunization will also be explored during these studies.



Sadeep Shrestha, Ph.D., Assistant Professor of Epidemiology.

Immunological and clinical outcomes in the natural history of HIV infection and progression to AIDS can vary considerably both at individual and population levels, suggesting a role of host genetics. Several gene polymorphisms have been shown to influence the immunopathogenesis of HIV/AIDS: however the influences are inconsistent and may be population-specific. Strong evidence suggests that the risk of developing AIDS is influenced by IL10 promoter polymorphisms in European Americans, but not in other ethnic groups. The immunoregulatory involvement of IL10, a pleiotropic cytokine with both pro- and anti-inflammatory immune activities, in several pathogenic infections could have led to selective adaptation and genomic evolution of the gene and its related family in certain populations. This study proposes to examine genetic variants in IL10 and related gene families among African Americans within the REACH cohort, to elucidate the heterogeneous influence in HIV disease outcomes.

Changes for CFAR Core Leadership

Casey D. Morrow, PhD, Professor of Cell Biology and Microbiology will serve as the new Director of the **CFAR Developmental Core**. His laboratory has studied HIV replication for more than 15 years and has over 100 publications. Dr. Morrow has served on many NIH study sections and is currently a holder of a Merit award. Dr. Morrow is the PI of the Basic Mechanisms in AIDS Pathogenesis (BMAP) training grant, supporting pre and post-doctoral fellows in HIV research for over 15 years. Dr. Morrow is well-suited to lead the Developmental Core which provides oversight for the application and selections for the CFAR Developmental Grant Awards program. Twenty-two graduate students have received their PhDs from Dr. Morrow's laboratory and he has mentored 5 post-doctoral fellows during his career.



David Allison, PhD, Professor of Biostatistics will serve as the new Co-Director of the **Biostatistics Core**. Dr. Allison currently serves as Head of the Section on Statistical Genetics, and Director of the NIH-funded Clinical Nutrition Research Center. He has authored over 300 scientific publications and edited five books. He has won several awards, including NSF's 2006 Presidential Award for Excellence in Science, Mathematics, and Engineering Mentoring (PAESMEM). Dr. Allison's current research interests include statistical genetics, clinical nutrition research, genomics, obesity and longevity. Co-Director for the Core, **Gary Cutter, PhD** also brings extensive knowledge and experience in conducting clinical trials and statistical and research methodologies to the Core. Dr. Cutter is Professor of Biostatistics and Head of the Section on Research Methods and Clinical Trials at the UAB SOPH Department of Biostatistics. He has directed numerous Statistics and Data Management Centers for national research collaborations. He has a strong interest in the design, measurement and interpretation of clinical trials, epidemiological studies and evaluation research. He has served the NIH on advisory panels, study sections as a chartered member and ad hoc reviewer; and on a variety of Data and Safety Monitoring Committees. He is an advisor for numerous pharmaceutical companies on design and conduct of Clinical



Trials and serves on their Data and Safety Monitoring Committees.



Jeffrey Stringer, MD, will serve as the new Core Director for the **International Core**. Dr. Stringer is a Professor of Obstetrics & Gynecology at UAB. Based full-time in Zambia since 2001, Dr. Stringer is an internationally recognized expert in clinical and operations research in the prevention of mother-to-child HIV transmission (PMTCT) and HIV treatment. With his many partners and collaborators he has developed one of the largest HIV prevention and treatment programs in the world. Dr. Stringer serves as Director of the Centre for Infectious Disease Research in Zambia (CIDRZ), a nonprofit clinical, research and training center run by UAB faculty in conjunction with the Zambian government. With funding from the President's Emergency Plan for AIDS Relief (PEPFAR), the U.S. Centers for Disease Control and Prevention (CDC), and the Elizabeth Glaser Pediatric AIDS Foundation, CIDRZ has enrolled tens of thousands of patients in long-term HIV care. It supports treatment at 50 clinics in 22 Zambian districts. **Benjamin Chi, MD** who is in residence at CIDRZ, will also participate in the leadership of Core.

Paul Goepfert, MD was recently named Director of the **Clinical Core**, replacing Dr. Michael Kilby who is leaving UAB for another position. To the leadership of the



Core, Dr. Goepfert brings his expertise as an established investigator focusing on translational research. He joined the UAB faculty in the Division of Infectious Diseases in 1997 and has subsequently published extensively in the field of HIV immunopathogenesis and vaccines. He currently serves as the Director of the Alabama Vaccine Research Clinic whose main objective is to perform clinical testing of preventative vaccines. He also maintains a laboratory performing translational research on HIV vaccines and immunology. Because his translational research is completely dependent on clinical samples, he has gained tremendous experience obtaining and maintaining clinical samples for scientific research. Dr. Goepfert will maintain the quality and availability of clinical samples for both UAB HIV investigators and those outside of our institution. Core leadership will also include co-investigators **Michael Mugavero, MD** and **Laura Bachmann, MD**.

Introducing New CFAR Members

Randy Cron, MD, PhD
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Dr. Cron earned a PhD in immunology from the University of Chicago and an MD degree from the University of California at Los Angeles. He completed a pediatric internship and residency at Lucile Packard Children's Hospital at Stanford University Hospital, California, and a pediatric rheumatology fellowship at Children's Hospital and Medical Center, University of Washington, Seattle. He was a Howard Hughes Medical Institute postdoctoral fellow at Stanford University Medical Center. He comes to UAB from the University of Pennsylvania School of Medicine, where he was assistant professor of pediatrics.

The Cron lab is interested in unraveling the role of host CD4 T cell transcription factors usurped by HIV-1 to drive its own LTR transcription. Specifically, we study NFAT and NFkB factors which are critical to HIV-1 transcription in primary peripheral blood CD4 T cells.

We have also identified a c-maf transcription factor binding site located just upstream of the dual NFkB/NFAT proximal LTR binding sites. We are studying the interaction of c-maf with specific NFAT and NFkB members in providing a transcriptional advantage to HIV-1 in IL-4 producing CD4 T cells, which uniquely possess c-maf. This work looks to explain the increased replication of HIV-1 noted in IL-4 producing Th2 and Th0 T cell subsets.

Chad Steele, PhD
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Dr. Steele is a native of Louisiana and received a BS in Chemistry from Northeast Louisiana University followed by a MS and PhD in Microbiology/Immunology from Louisiana State University Health Sciences Center – New Orleans. Dr. Steele spent the last 4 years as an Assistant Professor in the Department of Pediatrics at the University of Pittsburgh.

Dr. Steele's research includes a long-standing interest in lung host defense against the HIV-associated opportunistic fungal pathogen *Pneumocystis carinii*. A large portion of his research centers on characterizing innate immune responses to *P. carinii*.

Current projects include examining host defense against *P. carinii* in mice deficient in the beta-glucan receptor Dectin-1, determining the effects of cigarette smoke on innate host defense against *P. carinii*, determining mechanism(s) of innate immune regulation by Src-family tyrosine kinases and Tyro 3-family tyrosine kinases and determining the role of MCP-1 and IL-6 in innate defense against *P. carinii*. He has also initiated studies to define the Th1/Th2 axis in CD4 T cell-mediated host defense against *P. carinii*.

Additional studies also include examining the transcription factors Stat4 and Stat6 in CD4 T cell responses to *P. carinii* and determining the role of the transcription factor T-bet in CD4 T cell-mediated defense against *P. carinii*. Future studies will investigate the role of Stat4 and T-bet in CD4 T cell-dependent pulmonary inflammation in a Scid reconstitution model as well as the role of Stat4 and T-bet in anti-*P. carinii* antibody responses.