



Interview of Professor Karl Salzwedel The Martin Delaney Collaboratory (MDC) program

Karl Salzwedel, PhD is Chief of the Pathogenesis and Basic Research Branch of the National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS) at the US National Institutes of Health (NIH) in Bethesda, Maryland. He has overseen the implementation of the Martin Delaney Collaboratories program at NIAID over the last four years and has spearheaded numerous funding initiatives focused on HIV cure research. Currently, he oversees a portfolio of approximately 325 grants and contracts totaling more than \$190 million per year in funding, including 20 Centers for AIDS Research (CFAR) and the NIH AIDS Reagent Program.

What was the genesis of the Martin Delaney Collaboratories?

In the summer of 2008, in conjunction with the International AIDS meeting in Mexico City, our Director at DAIDS, Carl Dieffenbach, together with Veronica Miller from the Forum for Collaborative HIV Research, organized a meeting of leading researchers to discuss the problem of HIV persistence and what would be needed to cure HIV infection. Afterwards, DAIDS initiated the lengthy process of developing an ambitious new program to accelerate HIV cure research. Attendees from the Mexico City meeting later penned a review in the March 6, 2009 issue of Science entitled "The Challenge of Finding a Cure for HIV Infection", highlighting the need for a partnership among government, academia, and industry in the form of an HIV latency "Collaboratory". That article was dedicated to the memory of prominent HIV activist, Martin Delaney, founder of Project Inform, who had recently died in January of 2009. Martin Delaney had long been an outspoken advocate for research focused on curing HIV infection. In June 2010, NIAID published a funding opportunity announcement (developed by my colleague Sandra Bridges) entitled "Martin Delaney Collaboratory: Towards an HIV-1 Cure". One year later, in July of 2011, the first three Collaboratory awards were announced.

What are the differences between the 3 Collaboratories, and what do they address?

One of the nice things about the three currently funded Martin Delaney Collaboratories is that they each have a different core research focus and, thus, complement one another quite nicely.

The Delaney Cell and Genome Engineering Initiative (defeatHIV), based out of the Fred Hutchinson Cancer Research Center in Seattle, WA is testing cell and gene therapy approaches to: 1) modify hematopoietic stem cells in a non-human primate bone marrow transplantation model so that the resulting immune cells become resistant to SHIV infection, and 2) target and inactivate integrated HIV provirus in latently infected cells. DefeatHIV is led by Keith Jerome and Hans-Peter Kiem in partnership with Sangamo Biosciences (Richmond, CA).

The Collaboratory of AIDS Researchers for Eradication (CARE), based out of the University of North Carolina in Chapel Hill, NC is focused on the mechanisms controlling HIV latency and is testing strategies to reverse latency using combinations of different agents to reactivate viral gene expression in latently infected cells. CARE is led by David Margolis in partnership with Merck Research Laboratories (West Point, PA).

The Delaney AIDS Research Enterprise (DARE), based out of UCSF in San Francisco, CA is focused on better characterizing the nature of the persistent HIV reservoir, particularly in lymphoid tissues, and is testing strategies to enhance the immune response to HIV to control viral rebound and reduce the size of the persistent reservoir. DARE is led by Steve Deeks, Mike McCune, and Rafick Sekaly in partnership with Merck Research Laboratories (West Point, PA).

How is the NIAID involved, and what is the budget dedicated to finding a cure compared to other priorities, like finding a HIV vaccine?

Unlike typical NIH research grants, the Martin Delaney Collaboratory program is a cooperative research agreement between NIH and the awardees. This means that the NIH Program Officials communicate regularly with the Collaboratory Principal Investigators, attend and facilitate Collaboratory meetings (including the biannual "Strategies for an HIV Cure" meeting held in the Washington, DC area), provide supplemental funding to selected projects, and mediate interactions with Scientific Advisory Panels and Community Advisory Boards (CABs).

The budget for HIV cure research at NIAID is still lower than that for HIV prevention and vaccines, which remains a top priority for the Institute. However, the proportion of funding dedicated to cure-related research has been steadily increasing every year. For the December, 2013 World AIDS Day, President Obama announced that an additional \$100 million in funding would be reallocated to HIV cure research over a period of 3 years. We are currently in the midst of that process, and some of those funds may contribute to the expansion of the Collaboratory program in 2016. On May 21, 2015, NIAID published the funding opportunity announcement for the next round of Collaboratory awards, entitled "Martin Delaney Collaboratories for HIV Cure Research". Applications are due by December 7, 2015. These will all be new awards, so we are hoping for a robust response from the research community. Depending on the quality of the applications as judged by peer review, we could potentially fund 3-5 Collaboratories for the next five years starting in July 2016.

What are the relationships between these research initiatives and the activists who usually claim that not enough is done?

When the Martin Delaney Collaboratory (MDC) program was first conceived, there was not a plan for community engagement, perhaps because of the nascent stage of cure research at the time – it seemed like it would be a long time before clinical trials would be initiated. However, shortly after the Collaboratory awards were made, my colleague Carla Pettinelli came to my office to share with me her historical perspective on the critical role that community activism had played in the development of antiretroviral therapies throughout the years of the epidemic. I thank her for opening my eyes to the need for CABs for each of the Collaboratories. We responded by providing supplemental funding to each of the Collaboratories to support individual CABs, as well as an overall MDC CAB made up of two representatives from each individual CAB.

In the next iteration of the program, my colleague Diane Lawrence and I have incorporated a community engagement plan as an integral part of the application. So, in a sense, we have effectively extended the Collaboratory model to include community as the fourth partner.