

APRIL 2022



UNC CFAR NEWSLETTER

SPOTLIGHTING THE CFAR DEVELOPMENTAL AWARDEES

AWARENESS DAYS

May 18th, 2022

HIV Vaccine Awareness Day #HVAD

May 19th, 2022

National Asian and Pacific Islander HIV/AIDS Awareness Day #APIMay19

June 5th, 2022

HIV Long-Term Survivors Awareness Day #HLTSAD

June 27th, 2022

National HIV Testing Day #HIVTestingDay



CONFERENCES

14th Annual Social and Behavioral Science Research Network Meeting (SBSRN 2022)

May 26-27, 2022

In Person, Philadelphia, PA

Proclamation at the Intersections Faith Healing and HIV Conference

Sponsored by the Gilead COMPASS Faith Coordinating Center at Wake Forest School of Divinity

June 21-23, 2022

Register by June 1st, 2022

The 24th International AIDS Conference

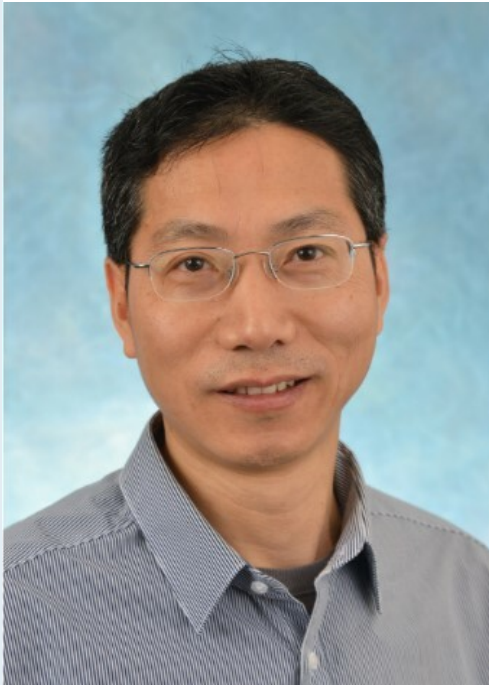
July 29-August 2, 2022

2022 National Ryan White Conference on HIV Care & Treatment

August 23-26, 2022

ERADICATION OF HIV BRAIN RESERVOIRS BY GENE EDITING

BY GUOCHUN JIANG PHD. UNC HIV CURE CENTER AND DEPARTMENT OF BIOCHEMISTRY AND BIOPHYSICS



Myeloid cells are the major reservoir for the persistent HIV-1 (HIV) infection in the central nervous system (CNS). The clearance of HIV reservoir in the myeloid cells, particularly the microglia (MG), is a critical step to achieve the cure of HIV in the CNS and to alleviate HIV-associated neurocognitive disorders (HAND). Efforts to target HIV reservoirs in the CNS continue to stymie HIV researchers. The current front-line strategy to attack HIV, “shock and kill,” raises safety concerns as the transient reactivation of latent HIV may lead to neurotoxicity in the brain. Gene editing to eradicate CNS HIV reservoirs is a promising approach, but it too brings several challenges. Suitable delivery systems being able to penetrate blood brain barrier (BBB) and target microglia without triggering undesirable neurotoxicity are not yet available, and the lack of physiologically relevant

model systems in which to test patient-derived microglia further compromise the development of strategies to eradicate HIV in the CNS. This CFAR microgrant-funded study aims to directly attack the latent HIV reservoirs in the brain microglia isolated from people living with HIV (PLWH) in the “Last Gift” cohort, altruistic, terminally ill individuals with HIV receiving antiretroviral therapy. This new tool may open a new avenue to eradicate HIV using physiologically relevant model system of human brain.

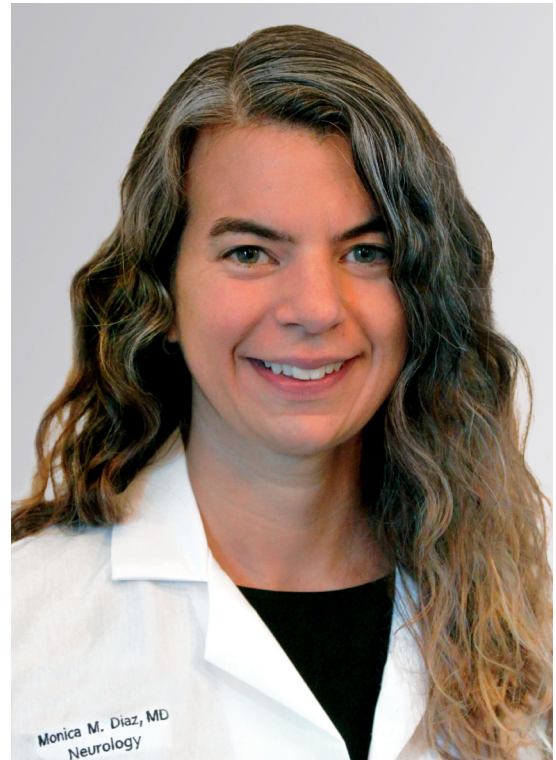
With the needed expertise, technical innovations, unique and novel platforms, we will develop and test a new gene editing system -- an AAV serotype being able to deliver microglia-specific promoter (Mp)-driven CRISPR/dCas (AAV-Mp-dCas) HIV editor -- that can specifically target microglia to disrupt HIV genome in the human brain. MG delivery of this new AAV-Mp-dCas gene editing system will be initially tested in vitro in the commercially available human primary MG and primary MG isolated from rhesus macaques, in comparison with human or monkey primary astrocytes. If successful, we will study its ability to eradicate HIV reservoirs in the MG derived from PLWH in the “Last Gift” cohort ex vivo. This study will address the critical knowledge and technology gaps in gene editing and targeted AAV delivery to microglia in the CNS HIV reservoirs, which is the first step to create an effective CRISPR/dCas tool for the eradication of HIV in the brain. For a long-term goal, we will develop a BBB-penetrating AAV packaged CRISPR/dCas HIV editor to disrupt HIV reservoirs in the brain in vivo.

PILOT STUDY FOR THE ASSESSMENT OF NEUROINFLAMMATION AND NEURODEGENERATION IN HIV-ASSOCIATED COGNITIVE IMPAIRMENT

BY MONICA DIAZ, M.D., M.S.

HIV is known to cause consequences to the brain, particularly difficulty with memory and activities of daily living which often requires a spinal tap (lumbar puncture). To understand the barriers of implementing lumbar punctures (LPs) for advancement of HIV neurology research, we propose to determine the knowledge and willingness of middle-aged and older people with HIV (PWH) attending the Infectious Disease clinics of UNC Health to undergo an LP for research purposes. Dr. Diaz proposes to enroll PWH who are 50 years of age or older with suppressed HIV virus in the blood. Participants will complete a short questionnaire assessing knowledge of LP procedures, and then watch a brief instructional video explaining the LP procedure that will be tailored to patients. The questionnaire will then be re-administered to the participant after watching the video.

We also propose to determine if there is a connection between inflammation and degeneration of nerve cells that may lead to cognitive impairment in PWH. In a sub-group of 40 randomly selected participants who completed the questionnaire above, we will determine if they may have signs of cognitive impairment (memory problems) by administering neuropsychological testing and completing an LP performed by Dr. Diaz. All spinal fluid and blood samples will be sent to the UNC CFAR core laboratory for analysis. We will then determine if neurofilament light (NFL) protein, a neurodegeneration sign or marker, is elevated in those who are detected as having cognitive impairment on neuropsychological testing compared with cognitively healthy PWH. These NFL levels will be compared with other markers of inflammation in the spinal fluid and blood. This study will help determine whether there may be a connection between degeneration of neurons (nerve cells) and inflammation present in the central nervous system of PWH.



GENOMICS OF GENITAL ULCER DISEASE OF UNKNOWN ETIOLOGY AMONG PERSONS WITH HIV OR AT HIGH RISK FOR HIV-INFECTION IN

**BY SARAH E. RUTSTEIN,
MD, PHD**



Genital ulcer diseases (GUDs) continue to cause substantial morbidity and mortality worldwide, and are regarded as a common presentation of sexually transmitted infections (STIs). In particular, epidemiological and biological data have shown that GUD increases HIV transmission and acquisition. GUD are also more

common among people living with HIV infection. Despite the global impact of GUD, and the disproportionate burden of disease among persons with HIV, our understanding of the etiology and epidemiology of GUD is outdated and incomplete.

In the best-case scenario, using both molecular and serologic diagnostics for GUD, one-third of patients never have an infectious etiology identified. Alternative approaches are needed to identify potential pathogens and explore non-infectious causes. Genomic techniques can help our understanding of these unidentified cases by identifying potential infectious etiologies missed by traditional diagnostic techniques, informing diagnostic tool development and improving treatment strategies and outcomes.

In this study, we are enrolling persons infected with HIV or at high risk of HIV acquisition who present to a public STI clinic in Lilongwe Malawi with evidence of GUD on examination. We will use serology, targeted real-time polymerase chain reaction (PCR), and genomic sequencing from ulcer swabs to identify bacterial, viral and fungal etiologies of GUD. Patients will be followed for two weeks after receipt of standard GUD treatment to assess treatment response and ulcer resolution.

TELLURIDE AIDS BENEFIT

**BY JOEY HARPER—STUDENT RESEARCH ASSISTANT, UNC CFAR
SOCIAL AND BEHAVIORAL SCIENCE RESEARCH**

The Telluride AIDS Benefit gathers people from across the globe to raise money and awareness for the ongoing AIDS and HIV epidemic. I have been involved in the organization since my first exposure during an AIDS Education day in Middle School and used my involvement as a peer mentor and advocate for key populations in Southwest Colorado as an introduction to research in the field during my time at the University of North Carolina at Chapel Hill. I recently traveled to Colorado to volunteer in TAB's 28th year of the benefit, which raised over \$300,000 to support education, awareness, and access to medication in beneficiaries across Colorado and Sub-Saharan Africa.



In 1994, the entire Telluride community surrounded Presley to show support in his battle against his disease and mounting medical bills. Three years later, Robert Presley died from complications relating to the disease, but the organization lives on to support individuals across rural Colorado and sub-Saharan Africa alike. In the growing list of beneficiaries, TAB honors Presley's indomitable spirit and love for exuberant fashion through an Annual Gala Fashion Show. Companies from across the country donate clothing, local artists create elaborate "wearable art pieces", and the community comes together to recognize the ongoing challenges faced by HIV/AIDS in both Colorado and beyond.

While at UNC, I have worked as a Research Assistant at CFAR in the Social and Behavioral Core and recently completed a Thesis on structural barriers influencing adherence in perinatally infected HIV positive infants in Southern Africa. I honor the Telluride AIDS Benefit, and the animated energy and palpable passion of the long-time locals involved as being the inspiration for my research interests and involvement throughout college, and now post-grad. Please check out the website if interested in further information!

<https://www.tellurideaidsbenefit.org>

Another piece I wrote during my internship at (RED) this summer:<https://www.red.org/reditorial/telluride-aids-benefit>

