BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

**NAME:** Kashuba, Angela

**eRA COMMONS USER NAME (credential, e.g., agency login):** ANGELA_KASHUBA

**POSITION TITLE:** John A. and Deborah S. McNeill Jr Distinguished Professor and Chair

**EDUCATION/TRAINING** *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>Completion Date MM/YYYY</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Toronto, Toronto, Ontario</td>
<td>BS</td>
<td>05/1990</td>
<td>Pharmacy</td>
</tr>
<tr>
<td>SUNY Buffalo, Amherst, NY</td>
<td>PHMD</td>
<td>05/1995</td>
<td>Clinical Pharmacy</td>
</tr>
<tr>
<td>Women's College Hospital, Toronto, Ontario</td>
<td>Resident</td>
<td>06/1991</td>
<td>Hospital Pharmacy Residency</td>
</tr>
<tr>
<td>Bassett Research Center, Cooperstown, NY</td>
<td>Postdoctoral Fellow</td>
<td>06/1997</td>
<td>Clinical Pharmacology</td>
</tr>
</tbody>
</table>

**A. Personal Statement**

The CFAR Clinical Pharmacology and Analytical Chemistry (CPAC) Core assists and supports our domestic and international investigators with all aspects of preclinical and clinical pharmacology research. I have over 20 years of experience working in antiretroviral preclinical and clinical pharmacology (in both healthy volunteers and patient populations), and have published over 200 peer reviewed manuscripts. I have been Director of the Clinical Pharmacology and Analytical Chemistry Core for the UNC CFAR for over 15 years. In my laboratory, all analytical methods are validated according to FDA criteria, and we are CLIA (#34D1022136) and CAP (LAP#7521077;AU-ID#1589458) accredited. I have amassed a team and set of tools that are uniquely suited to supporting HIV investigators in all aspects of clinical pharmacology research, including providing novel bioanalytical methods. As a result of my experience, I am aware of the importance of communication, collaboration, constructing realistic research plans, timelines, and budgets that apply to the current application, and will ensure that this Core performs successfully and provides added value to researchers.

**B. Positions and Honors**

**Positions and Employment**

- **2004 - 2009** Director, Clinical Pharmacology and Analytical Chemistry Core, UNC Center for AIDS Research, University of North Carolina at Chapel Hill (UNC-CH), Chapel Hill, NC
- **2011 - 2015** Vice Chair for Research and Graduate Education, Division of Pharmacotherapy and Experimental Therapeutics, Eshelman School of Pharmacy, UNC-CH, Chapel Hill, NC
- **2011 -** Professor of Pharmacy, with Tenure, Eshelman School of Pharmacy, UNC-CH, Chapel Hill, NC
- **2011 -** Co-Director, Clinical Pharmacology Fellowship Program (T32 NIGMS and NICHD), UNC-CH and Duke University, Chapel Hill, NC
C. Contribution to Science

1. DRUG EXPOSURE IN PUTATIVE VIRAL RESERVOIRS. I have developed an approach to measuring drug exposure in secondary body compartments, including the male and female genital tracts, and the gastrointestinal tracts, considered putative reservoirs for HIV replication. These data have allowed optimal selection of antiretrovirals for clinical study in HPTN052 and have provided an explanation for why certain PrEP studies in women (FemPrEP, VOICE) failed.


2. ASSESSMENT OF DRUG DISTRIBUTION FOR HIV PREVENTION STRATEGIES. In studies of HIV eradication strategies, we have characterized the pharmacokinetics of antiretrovirals and other small molecules in animals and clinical studies.


3. NOVEL BIOANALYTICAL APPROACHES. My laboratory specializes in bioanalytical assay development in difficult biological matrices. We have developed high-level multiplex methods to measure up to 17 antiretrovirals in a single sample, and developed methods to measure intracellular ARV exposure in red cells - a powerful adherence tool obtained from a normally-discarded portion of a blood sample. Recently, we have developed a novel small molecule imaging technique to visualize drug distribution in putative viral reservoirs. This technology will allow us to evaluate pharmacokinetics and pharmacodynamics in unperturbed tissue.


4. EX-VIVO METHODS FOR PK-PD ANALYSIS. We have been evaluating approaches to understand drug distribution in tissues and pharmacokinetic-pharmacodynamic relationships that inform drug dosing in clinical studies. Recently, we developed tissue models to capture clinically relevant data.


Complete list of published work in NCBI Collections:

D. Research Support
Ongoing Research Support
5 P30-AI050410-19 08/01/11 – 07/31/21
NIAID (PI: Ronald Swanstrom); Role: Core Director

UNC Center for AIDS Research Core E: Clinical Pharmacology/Analytical Chemistry
The Clinical Pharmacology/Analytical Chemistry Core of the UNC CFAR is designed to provide a centralized facility to advise, support and perform pharmacological and analytical studies of AIDS related clinical and basic science research projects. Projects range from in-vitro correlations of drug disposition, drug interactions and drug toxicity to clinical pharmacokinetic-dynamic evaluations of interactions, efficacy, toxicity and the development of drug resistance.

5 U01 AI103390-05 01/10/13-12/31/18
NIH (PI: Adimora); Role: Investigator

University of North Carolina Women's Interagency HIV Study (UNC WIHS)
The Women's Interagency HIV Study (WIHS) is a longitudinal, observational cohort study of women infected with and at risk for HIV infection in the United States. The purpose of WIHS is to understand the current epidemiology of HIV infection, disease progression, treatment use and outcomes, and related co-morbidities among U.S. women with HIV.

5 R01AI111891-02 3/15/2014-2/28/2019
NIH/NIAID (PI: Kashuba)
Multi-Species Mechanisms of Drug Bio-distribution in HIV Tissue Reservoirs
This project aims to identify what species differences and pharmacologic barriers exist in extracellular and intracellular antiretroviral biodistribution and efficacy in eliminating active HIV reservoirs.

1UL1TR002489-01  03/01/2018- 02/28/2023
NIH (PI: Buse); Role: Mentor
North Carolina Translational & Clinical Sciences Institute (NC TraCS)
This grant provides 5 years of support for UNC’s CTSA award, the NC Translational and Clinical Sciences (TraCS) Institute. Dr. Kashuba serves within the Education Program of the NC TraCS Institute and mentors KL2 Scholars.

2K12HD001441-17  9/30/2015 – 7/31/2020
NIH (PI: Boggess); Role: Co-PD
UNC Building Interdisciplinary Research Careers in Women’s Health (K12)
Dr. Kashuba will serve as Associate Research Director and Resource Laboratory Network Director for this K12 project.

Novel Mass Spectrometry Imaging Methods to Quantify Antiretroviral Adherence
It is important to identify if someone is taking a medication regularly and as prescribed to optimize their health and wellbeing. Sometimes, patients have trouble remembering if and when they miss doses; other times, even though patients are taking their medication, it is not getting into the body in the right amount. Quickly monitoring medications in 5-10 hair strands using our novel imaging technology called IR-MALDESI will allow patients and their doctors to see how much medication they are exposed to over 1 or more months, and help identify challenges to taking medication in both research and clinical settings. This proposal will optimize and explore the acceptability and feasibility of using IR-MALDESI for monitoring medications in hair.

Collaboratory of AIDS Researchers for Eradication (CARE)
Including scientists from leading universities and Merck Research Laboratories, Qura Therapeutics, and Macrogenics, the Collaboratory of AIDS Researchers for Eradication (CARE) will seek to eradicate HIV infection by developing and testing therapies that will permanently destroy the viral reservoir.

Long term persistence of HIV in the liver and the clinical impact on HIV-HBV co-infection
One of the main challenges in the management of HIV is that it has long lived forms that persist in the face of antiviral therapy. Several studies suggest that the liver may be a reservoir of HIV even on long term ART. To determine whether HIV persistence in the liver on ART is a consequence of sub therapeutic levels of ARV in liver, as previously described for lymphoid tissue and rectal tissue, we propose to measure ARV levels in human liver, plasma and PBMC samples both pre and following at least 2 years ART by both LC-MS/MS and IR-MALDESI IMS methods.