BIOGRAPHICAL SKETCH

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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.)*

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

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 - 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

2011 -	Co-Director, Preclinical and Clinical Pharmacology Core, Martin Delaney Collaboratory to Eradicate HIV-1 Infection (CARE; U19 NIAID), UNC-CH, Chapel Hill, NC
2012 -	Adjunct Professor, Infectious Diseases, Department of Medicine, School of Medicine, UNC- CH, Chapel Hill, NC
2013 -	John A. and Deborah S. McNeill Jr Distinguished Professor, UNC Eshelman School of Pharmacy, UNC-CH, Chapel Hill, NC
2015 -	Chair, Division of Pharmacotherapy and Experimental Therapeutics, UNC Eshelman School of Pharmacy, UNC-CH, Chapel Hill, NC

Other Experience and Professional Memberships

1999 - 2006	Pharmacology Committee Member, Vice-Chair, Pharmacology Lab Director, AACTG
2000 -	Member, Organizing Committee, International Workshop on HIV In Women
2001 -	Diplomat, American Board of Clinical Pharmacology
2004 -	Member, Plan for HIV-Related Research on Women and Girls, NIH/OAR Planning Committee 2006 - Member, Organizing Committee, International Workshop on Clinical Pharmacology of HIV Therapy
2008 - 2010	Member, Publications Committee, American Society for Clinical Pharmacology and Therapeutics
2010 - 2014	Member, ADDT Study Section, NIH/NIAID
2011 -	Chair, Clinical Pharmacology Best Practices Working Group, NIH/DAIDS
2013 -	Invited Member, Advisory Committee on Research on Women's Health, NIH Office of Research on Women's Health

Honors

2007	Pam Herriott Award for Outstanding Service, UNC Department of Infectious Diseases
2009	Leon I Goldberg Young Investigator Award, American Society for Clinical Pharmacology and Therapeutics
2013	Academic Leadership Fellow, UNC Chapel Hill Institute for the Arts and Humanities

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.

   a. Patterson KB, Prince HA, Kraft E, Jenkins AJ, Shaheen NJ, Rooney JF, Cohen MS, Kashuba AD. Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. Sci Transl Med. 2011 Dec 7;3(112):112re4. PubMed Central PMCID: PMC3483088.
   b. Kashuba AD, Patterson KB, Dumond JB, Cohen MS. Pre-exposure prophylaxis for HIV prevention: how to predict success. Lancet. 2012 Jun 30;379(9835):2409-11. PubMed Central PMCID: PMC3652584.
   c. Corneli AL, Deese J, Wang M, Taylor D, Ahmed K, Agot K, Lombaard J, Manongi R, Kapiga S, Kashuba A, Van Damme L. FEM-PrEP: adherence patterns and factors associated with adherence to a daily oral study product for pre-exposure prophylaxis. J Acquir Immune Defic Syndr. 2014 Jul 1;66(3):324-31. PubMed Central PMCID: PMC4059551.

d. Rahangdale L, De Paris K, Kashuba AD, Nelson JA, Cottrell M, Sykes C, Emerson C, Young SL, Stevens T, Patterson KB, Cohen MS. Immunologic, virologic, and pharmacologic characterization of the female upper genital tract in HIV-infected women. J Acquir Immune Defic Syndr. 2015 Apr 1;68(4):420-4. PubMed Central PMCID: PMC4334681.

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.

a. Archin NM, Liberty AL, Kashuba AD, Choudhary SK, Kuruc JD, Crooks AM, Parker DC, Anderson EM, Kearney MF, Strain MC, Richman DD, Hudgens MG, Bosch RJ, Coffin JM, Eron JJ, Hazuda DJ, Margolis DM. Administration of vorinostat disrupts HIV-1 latency in patients on antiretroviral therapy. Nature. 2012 Jul 25;487(7408):482-5. PubMed Central PMCID: PMC3704185.
b. Spina CA, Anderson J, Archin NM, Bosque A, Chan J, Famiglietti M, Greene WC, Kashuba A, Lewin SR, Margolis DM, Mau M, Ruelas D, Saleh S, Shirakawa K, Siliciano RF, Singhania A, Soto PC, Terry VH, Verdin E, Woelk C, Wooden S, Xing S, Planelles V. An in-depth comparison of latent HIV-1 reactivation in multiple cell model systems and resting CD4+ T cells from aviremic patients. PLoS Pathog. 2013;9(12):e1003834. PubMed Central PMCID: PMC3873446.
c. Denton PW, Long JM, Wietgrefe SW, Sykes C, Spagnuolo RA, Snyder OD, Perkey K, Archin NM, Choudhary SK, Yang K, Hudgens MG, Pastan I, Haase AT, Kashuba AD, Berger EA, Margolis DM, Garcia JV. Targeted cytotoxic therapy kills persisting HIV infected cells during ART. PLoS Pathog. 2014 Jan;10(1):e1003872. PubMed Central PMCID: PMC3887103.
d. Archin NM, Bateson R, Tripathy MK, Crooks AM, Yang KH, Dahl NP, Kearney MF, Anderson EM, Coffin JM, Strain MC, Richman DD, Robertson KR, Kashuba AD, Bosch RJ, Hazuda DJ, Kuruc JD, Eron JJ, Margolis DM. HIV-1 expression within resting CD4+ T cells after multiple doses of vorinostat. J Infect Dis. 2014 Sep 1;210(5):728-35. PubMed Central PMCID: PMC4148603.

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.

a. Jung BH, Rezk NL, Bridges AS, Corbett AH, Kashuba AD. Simultaneous determination of 17 antiretroviral drugs in human plasma for quantitative analysis with liquid chromatography-tandem mass spectrometry. Biomed Chromatogr. 2007 Oct;21(10):1095-104. PubMed PMID: 17582235.
b. Adams JL, Sykes C, Menezes P, Prince HM, Patterson KB, Fransen K, Crucitti T, De Baetselier I, Van Damme L, Kashuba AD. Tenofovir diphosphate and emtricitabine triphosphate concentrations in blood cells compared with isolated peripheral blood mononuclear cells: a new measure of antiretroviral adherence?. J Acquir Immune Defic Syndr. 2013 Mar 1;62(3):260-6. PubMed Central PMCID: PMC4042836.

c. Barry JA, Robichaud G, Bokhart MT, Thompson C, Sykes C, Kashuba AD, Muddiman DC. Mapping antiretroviral drugs in tissue by IR-MALDESI MSI coupled to the Q Exactive and comparison with LC- MS/MS SRM assay. J Am Soc Mass Spectrom. 2014 Dec;25(12):2038-47. PubMed Central PMCID: PMC4201889.
d. Thompson CG, Bokhart MT, Sykes C, Adamson L, Fedoriw Y, Luciw PA, Muddiman DC, Kashuba AD, Rosen EP. Mass Spectrometry Imaging Reveals Heterogeneous Efavirenz Distribution within Putative HIV Reservoirs. Antimicrob Agents Chemother. 2015 May;59(5):2944-8. PubMed Central PMCID: PMC4394831.

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.

a. Nicol MR, Fedoriw Y, Mathews M, Prince HM, Patterson KB, Geller E, Mollan K, Mathews S, Kroetz DL, Kashuba AD. Expression of six drug transporters in vaginal, cervical, and colorectal tissues: Implications for drug disposition in HIV prevention. J Clin Pharmacol. 2014 May;54(5):574-83. PubMed PubMed Central PMCID: PMC4061289.
b. Thompson CG, Sedykh A, Nicol MR, Muratov E, Fourches D, Tropsha A, Kashuba AD. Short communication: cheminformatics analysis to identify predictors of antiviral drug penetration into the female genital tract. AIDS Res Hum Retroviruses. 2014 Nov;30(11):1058-64. PubMed Central PMCID: PMC4208595.
c. Nicol MR, Emerson CW, Prince HM, Nelson JA, Fedoriw Y, Sykes C, Geller EJ, Patterson KB, Cohen MS, Kashuba AD. Models for predicting effective HIV chemoprevention in women. J Acquir Immune Defic Syndr. 2015 Apr 1;68(4):369-76. PubMed Central PMCID: PMC4334725.

Complete list of published work in NCBI Collections:
http://www.ncbi.nlm.nih.gov/sites/myncbi/angela.kashuba.1/bibliography/43851578/public/?sort=date&direc tion=ascending

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.

5R01AI122319-02 01/01/2016-12/312020
NIH/NIAID (PI: Kashuba)
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.

1UM1AI126619-01 7/14/2016 – 6/30/2021
NIH (PI: Margolis); Role: Project Leader 3.2
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.

NHMRC ID: 1101836 11/28/2016 – 12/31/2019
NHMRC/University of Melbourne (PI: Lewin); Role: Consortium PI
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.