BIOGRAPHICAL SKETCH

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NAME: Angela Kashuba

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POSITION TITLE: John A. and Margaret P. McNeill, Sr. Distinguished Professor and Dean

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, Canada	BS	05/1990	Pharmacy
Women's College Hospital, Toronto, Canada	Resident	06/1991	Hospital Pharmacy
State University of New York, Amherst, NY	PHMD	05/1995	Clinical Pharmacy
Bassett Research Center, Cooperstown, NY	Postdoctoral Fellow	06/1997	Clinical Pharmacology

A. Personal Statement

I have been Director of the Clinical Pharmacology and Analytical Chemistry Core for the UNC Center for AIDS Research for 20 years, and our Core facility works with up to 80 investigators per year on preclinical and clinical pharmacology projects. I am the John A. and Margaret P. McNeill Sr. Distinguished Professor and Dean of the Eshelman School of Pharmacy at the University of North Carolina at Chapel Hill and Director of the University of North Carolina (UNC) Center for AIDS Research (CFAR) Clinical Pharmacology and Analytical Chemistry Core. I am an Adjunct Professor of Medicine in the Division of Infectious Diseases at the UNC School of Medicine, am board-certified by the American Board of Clinical Pharmacology, and am part of the UNC HIV Cure Center. My laboratory also works with the ACTG and IMPAACT networks to provide bioanalytical support for clinical trials and is part of the CPQA Cross-Network Clinical Pharmacology Laboratory Forum. I oversee a multidisciplinary and translational research program focused on optimizing antiretroviral pharmacology in HIV treatment, prevention, and cure. My laboratory is CLIA- (#34D1022136) and CAP- (LAP#7521077;AU-ID#1589458) accredited. My research group has significant expertise in designing and conducting clinical investigations involving compounds under IND, and providing data reports to regulatory bodies as part of NDAs, or for changes to the product label for dosing considerations. Along with traditional pharmacology techniques, my laboratory is developing methods for mass spectrometry imaging of small molecules in tissues and hair, and a hollow fiber model system to conduct more rigorous PK/PD in cell systems for HIV cure. Given our extensive experience with the CFAR, and with running a Core facility, we are aware of the importance of communication, collaboration, constructing realistic research plans, timelines, and budgets that are crucial for the success of the current application. I will apply my expertise in bioanalytical chemistry, pharmacokinetic and pharmacodynamic analysis to provide guidance regarding study design, data analyses, and data interpretation/reporting to our CFAR users. I am also delighted that Mackenzie Cottrell serves as co-Director for this Core, and I will continue to work closely with her to serve our UNC CFAR investigators with a Clinical Pharmacology and Analytical Chemistry Core.

Ongoing and recently completed research funding I'd like to highlight include:

Ongoing Research Support

5P30AI050410 Swanstrom (PI) 8/21–5/26
National Institutes of Health
University of North Carolina Center for AIDS Research
The UNC CFAR is a consortium of three complementary institutions, UNC, RTI International, and FHI 360 with particular strengths in HIV/AIDS basic, clinical, and social/behavioral research and social health advocacy. Its 8

cores, Scientific Working Groups, Research Interest Groups, and Strategic Community Engagement Education Dissemination Office provide extensive resources for research, training, and career development, as well as pilot funding, to advance the worldwide fight to prevent, treat, and cure HIV/AIDS and its comorbidities.
Role: Director, Clinical Pharmacology and Analytical Chemistry Core

1U01HL146194 Floris-Moore (PI) 04/19-03/26
National Heart, Lung, and Blood Institute
UNC MACS/WIHS Combined Cohort Study Clinical Research Site
The Multicenter AIDS Cohort Study(MACS)/Women's Interagency HIV Study (WIHS) Combined Cohort Study (CCS) is a longitudinal, observational cohort study of persons with HIV and a demographically matched cohort of men and women at risk for HIV infection. The CCS supports basic, clinical, and contextual research on HIV disease across the lifespan, including HIV-related chronic comorbidities and health disparities.
Role: Co-Investigator

MISP # 59493 Kashuba (PI) 06/20-06/25
Merck
Single Dose Pharmacokinetics of Doravirine in HIV-infected Pregnant Women
Clinical study to perform PK analysis to obtain dosing information in HIV+ pregnant women

None White-Harris (PI) 10/22 – 10/25
McKesson Fdn
McKesson LEAD Program: Leading in Excellence, Advancing Diversity
The McKesson LEAD program will develop health care professionals who will have the perspective of Diversity, Equity and Inclusion (DEI) training, along with the breadth and depth of knowledge to care for the world through practice, research, and community engagement.

R01AI152713 Johnson (PI) 04/20 – 02/25
NIH/Research Triangle Institute (RTI International)
Long-Acting Prevention Implantable System (LAPIS)
Evaluate safety and PK profiles of five implant designs (3 single agent, 2 co-formulated) through depletion
Role: Consortium PI

Completed Research Support

1UL1TR002489 Buse (PI) 03/18-02/23
National Center for Advancing Translational Sciences
Clinical and Translational Science Award
A national consortium of medical research institutions is working together and shares a common vision: to improve the way biomedical research is conducted across the country, reduce the time it takes for laboratory discoveries to become treatments for patients, engage communities in clinical research efforts, and train the next generation of clinical and translational researchers. UNC, RTI International, NC State University and NC A&T State University are partners in this effort.
Role: Mentor, KL2 Scholars, Education Program

B. Positions and Honors

Positions and Employment

2019-present Dean, UNC Eshelman School of Pharmacy - John A and Margaret P McNeill, Sr. Distinguished Professorship, UNC, Chapel Hill, NC
2015-2019 Chair, Division of Pharmacotherapy and Experimental Therapeutics, UNC Eshelman School of Pharmacy, UNC, Chapel Hill, NC
2013-2019 John A. and Deborah S. McNeill, Jr. Distinguished Professor, UNC Eshelman School of Pharmacy, UNC, Chapel Hill, NC
2012-present Adjunct Professor, Infectious Diseases, Department of Medicine, School of Medicine, UNC, Chapel Hill, NC
2011-present Professor of Pharmacy, with Tenure, Eshelman School of Pharmacy, UNC, Chapel Hill, NC
2011-2019 Co-Director, Clinical Pharmacology Fellowship Program (T32 National Institute of General Medical Sciences and National Institute of Child Health and Human Development), UNC

and Duke University, Chapel Hill and Durham, NC
2011-2017 Director, Preclinical and Clinical Pharmacology Core, Martin Delaney Collaboratory to Eradicate HIV-1 Infection (CARE; U19 NIAID), UNC, Chapel Hill, NC
2011-2015 Vice Chair for Research and Graduate Education, Division of Pharmacotherapy and Experimental Therapeutics, Eshelman School of Pharmacy, UNC, Chapel Hill, NC
2004-present Director, Clinical Pharmacology and Analytical Chemistry Core, University of North Carolina at Chapel Hill (UNC) Center for AIDS Research (CFAR), Chapel Hill, NC

Other Experience and Professional Memberships

2013-2017 Invited Member, Advisory Committee on Research on Women's Health, NIH Office of Research on Women's Health
2011-2017 Chair, Clinical Pharmacology Best Practices Working Group, NIH/Division of AIDS
2010-2014 Member, AIDS Discovery and Development of Therapeutics Study Section, NIH/National Institute of Allergy and Infectious Diseases
2008-2010 Member, Publications Committee, American Society for Clinical Pharmacology and Therapeutics
2006-2020 Member, Organizing Committee, International Workshop on Clinical Pharmacology of HIV Therapy
2004-2018 Member, Plan for HIV-Related Research on Women and Girls, NIH/Office of AIDS Research Planning Committee
2001-present Diplomat, American Board of Clinical Pharmacology
2000-2014 Member, Organizing Committee, International Workshop on HIV In Women
1999-2006 Pharmacology Committee Member, Vice-Chair, Pharmacology Lab Director, AIDS Clinical Trials Group

Honors

2024 Faculty Service Award, Carolina Alumni Association
2021 Charles Boucher Memorial Lecture (Inaugural Lecture), Virology Education
2020 Rawls-Palmer Progress in Medicine Award, American Society for Clinical Pharmacology & Therapeutics
2017 Fellow, American College of Clinical Pharmacology
2017 American College of Clinical Pharmacy Therapeutic Frontiers Award
2016 Society of Infectious Diseases Pharmacists' Pharmacotherapy Paper of the Year
2013 Academic Leadership Fellow, UNC Chapel Hill Institute for the Arts and Humanities
2009 Leon I Goldberg Young Investigator Award, American Society for Clinical Pharmacology and Therapeutics
2007 Pam Herriott Award for Outstanding Service, UNC Department of Infectious Diseases

C. Contributions to Science

1. **Novel analytic approaches to measure antiretrovirals**. 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 and in hair samples. This technology allows us insight into pharmacokinetics and pharmacodynamics of small molecules in unperturbed tissue, and also into noninvasive longitudinal objective daily drug adherence, respectively.
   a. 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.
   b. 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.
   c. Thompson CG, Rosen EP, Prince HMA, White N, Sykes C, de la Cruz G, Mathews M, Deleage C, Estes JD, Charlins P, Mulder LR, Kovarova M, Adamson L, Arora S, Dellon ES, Peery AF, Shaheen

NJ, Gay C, Muddiman DC, Akkina R, Garcia JV, Luciw P, **Kashuba ADM**. Heterogeneous antiretroviral drug distribution and HIV/SHIV detection in the gut of three species. Sci Transl Med. 2019 Jul 3;11(499). PMCID: PMC8273920.

d. Rosen EP, White N, Gilliland WM Jr, Gerona RR, Gandhi M, Amico KR, Mayer KH, Gulick RM, **Kashuba ADM**. Mass spectrometry imaging of hair identifies daily maraviroc adherence in HPTN 069/ACTG A5305. PLoS One. 2023 Jun 23;18(6):e0287449. PMID: 37352285; PMCID: PMC10289441.

2. **Measuring 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. **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.
   b. 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.
   c. Scholz EMB, Mwangi JN, De la Cruz G, Nekorchuk M, Chan CN, Busman-Sahay K, Adamson L, Luciw P, Fedoriw Y, Estes JD, Rosen EP, **Kashuba ADM**. Quantitative Imaging Analysis of the Spatial Relationship between Antiretrovirals, Reverse Transcriptase Simian-Human Immunodeficiency Virus RNA, and Collagen in the Mesenteric Lymph Nodes of Nonhuman Primates. Antimicrob Agents Chemother. 2021 May 18;65(6):e00019-21. PMCID: PMC8315948.
   d. Devanathan AS, White NR, Desyaterik Y, De la Cruz G, Nekorchuk M, Terry M, Busman-Sahay K, Adamson L, Luciw P, Fedoriw Y, Estes JD, Rosen EP, **Kashuba ADM**. Quantitative Imaging Analysis of the Spatial Relationship between Antiretrovirals, Reverse Transcriptase Simian-Human Immunodeficiency Virus RNA, and Fibrosis in the Spleens of Nonhuman Primates. Antimicrob Agents Chemother. 2022 Aug 16;66(8):e0060922. PMID: 35856680; PMCID: PMC9380553.
3. **Clinical pharmacokinetic studies.** I have developed a research group that is proficient in the design and execution of clinical pharmacokinetics studies under IND. We are currently conducting a study of doravirine pharmacokinetics in HIV-infected pregnant women.
   a. Brown KC, Patterson KB, Malone SA, Shaheen NJ, Prince HM, Dumond JB, Spacek MB, Heidt PE, Cohen MS, **Kashuba AD**.Single and multiple dose pharmacokinetics of maraviroc in saliva, semen, and rectal tissue of healthy HIV-negative men.J Infect Dis. 2011 May 15;203(10):1484-90. PubMed Central PMCID: PMC3080897
   b. Patterson KB, Dumond JB, Prince HA, Jenkins AJ, Scarsi KK, Wang R, Malone S, Hudgens MG, **Kashuba AD**. Protein binding of lopinavir and ritonavir during 4 phases of pregnancy: implications for treatment guidelines.J Acquir Immune Defic Syndr. 2013 May 1;63(1):51-8. PubMed Central PMCID: PMC3625477
   c. Adams JL, Patterson KB, Prince HM, Sykes C, Greener BN, Dumond JB, **Kashuba AD**. Single and multiple dose pharmacokinetics of dolutegravir in the genital tract of HIV-negative women. Antivir Ther. 2013;18(8):1005-13. PubMed Central PMCID: PMC4038682.
   d. Leung E, Cottrell ML, Sykes C, White N, **Kashuba ADM**, Dumond JB. A multicompartment population PK model to predict tenofovir and emtricitabine mucosal tissue concentrations for HIV prevention. CPT Pharmacometrics Syst Pharmacol. 2023 Dec;12(12):1922-1930. doi: 10.1002/psp4.13042. Epub 2023 Oct 9. PMID: 37814498; PMCID: PMC10725258.

Complete list of published work in NCBI Collections:
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