

BIOGRAPHICAL SKETCH

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NAME: Ritola, Kimberly

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

POSITION TITLE: Associate Professor, Department of Pharmacology

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 North Carolina-Chapel Hill	B.S.	05/1998	Biology
University of North Carolina-Chapel Hill	Ph.D.	07/2005	Genetics and Microbiology
Rockefeller University, New York	Postdoctoral	08/2010	Hepatitis C Viral Fitness

A. Personal Statement

My early career was spent investigating viral diversity and fitness starting with pseudorabies (enveloped DNA virus) as an undergraduate, lentivirus (enveloped, retrovirus) as a graduate student at UNC-Chapel Hill and Hepatitis C (enveloped, RNA) as a post-doc in the Nobel prize winning lab of Charlie Rice at Rockefeller University. My work focused on viral diversity with-in infected individuals and more specifically, how viral genetic and population diversity affect viral fitness. This training provided a thorough understanding of how genetic changes can impact different stages of the virus life cycle. During my time at HHMI-Janelia, I integrated my strong virology background with newly gained experience in how viral vectors are leveraged in the neurosciences to mark, map and modulate neurons to improve viral construct design and production for adeno-associated virus (AAV), rabies virus, and lentivirus vectors. We have pioneered small scale, high throughput, high quality virus production allowing investigators to use multiple viral payloads with unparalleled reproducibility and efficacy. I developed the Janelia-Viral Tools Shared Resource from a subdivision of the Molecular Biology Shared Resource into its own department providing state of the art viral tools for the entire HHMI community and their collaborators, more than doubling our yearly vector output. This feat was in no small part due to implementation of the philosophy that viral tools should be customized to match the goals of the end experiment. The high quality of our viral tools has been recognized internationally and we have trained and shared our protocols with groups setting up their own viral vector cores such as the Champaulmad, Sainsbury Wellcome, Addgene and Max Planck. At the time of my departure, Janelia-Viral Tools was producing over 900 AAV vectors per year to be used in different classes of neurons, cardiac and muscle cells. Strong relationships with our user base (HHMI funded labs and their collaborators) have allowed me to gain a deep understanding of the current limitations and strengths for each of these viral vectors when applied in vivo. The following references reflect projects for which I contributed significantly to experimental viral vector design beyond providing a reagent.

1. Xiao X, Deng H, Furlan A, Yang T, Zhang X, Hwang GR, Tucciarone J, Wu P, He M, Palaniswamy R, Ramakrishnan C, **Ritola K**, Hantman A, Deisseroth K, Osten P, Huang ZJ, Li B. A Genetically Defined Compartmentalized Striatal Direct Pathway for Negative Reinforcement. *Cell*. 2020 Oct 1;183(1):211-227.e20. doi: 10.1016/j.cell.2020.08.032. Epub 2020 Sep 15. PMID: 32937106.

2. François A, Low SA, Sypek EI, Christensen AJ, Sotoudeh C, Beier KT, Ramakrishnan C, **Ritola KD**, Sharif-Naeini R, Deisseroth K, Delp SL, Malenka RC, Luo L, Hantman AW, Scherrer G. 2017. A Brainstem-Spinal Cord Inhibitory Circuit for Mechanical Pain Modulation by GABA and Enkephalins. *Neuron* 22;93(4):822-839.
3. Tervo DG, Hwang BY, Viswanathan S, Gaj T, Lavzin M, **Ritola KD**, Lindo S, Michael S, Kuleshova E, Ojala D, Huang CC, Gerfen CR, Schiller J, Dudman JT, Hantman AW, Looger LL, Schaffer DV, Karpova AY. 2016. A Designer AAV Variant Permits Efficient Retrograde Access to Projection Neurons. *Neuron* 19;92(2):372-382.
4. Betley JN, Cao ZF, **Ritola KD**, Sternson SM. 2013. Parallel, redundant circuit organization for homeostatic control of feeding behavior. *Cell* 5;155(6):1337-50.

B. Positions and Honors

Positions and Employment

2010-2011	Senior Scientific Reviewer, Department of Medical Devices, Office of In vitro Diagnostics, Center for Devices and Radiological Health, Food and Drug Administration, Silver Spring, MD.
2011-2014	Research Specialist III, HHMI-Janelia Research Campus, Ashburn, VA.
2014-2021	Scientific Operations Manager-Viral Tools, HHMI-Janelia Research Campus, Ashburn, VA.
2021-Current	Associate Professor, Department of Pharmacology, UNC-Chapel Hill
2021-Current	Member, UNC Neuroscience Center

Other Experience and Professional Memberships

2012-2021	Member, Internal Biosafety Committee, HHMI-Janelia Research Campus
2019-Current	Member, American Society for Gene and Cell Therapy

Honors

1995	Howard Hughes Summer Research Grant
1995	Howard Hughes Outstanding Undergraduate Research Award
2000	Trainee NIH Training Grant T32-AI007419: "Molecular Biology of Viral Diseases"
2002	9 th Conference on Retroviruses and Opportunistic Infections Travel Grant
2004	11 th Conference on Retroviruses and Opportunistic Infections Travel Grant
2007	Ruth L. Kirschstein National Research Service Award (NRSA), DK080650

C. Contributions to Science

<https://www.ncbi.nlm.nih.gov/myncbi/kimberly.ritola.1/bibliography/public/>

1. *Characterized transmission and disease dynamics during HIV-1 infection*. Determined complexity of transmitted viral population to identify determinants allowing for infection with multiple viral variants. Investigated the viral quasi-species in the periphery and central nervous system and their role in the development of HIV-1-associated dementia. Co-inventor on patent application for HIV-1 vaccine candidate.
 - a. Harrington PR, Schnell G, Letendre SL, **Ritola K**, Robertson K, Hall C, Burch C, Jabara C, Moore DT, Ellis RJ, Price RW, and Swanstrom R. 2009. HIV-1 env Compartmentalization in Cerebrospinal Fluid is a Biological Marker of Dementia. *AIDS* 23:907-15.
 - b. **Ritola K**, Robertson K, Fiscus S, Hall C, and Swanstrom R. 2005. Increased Human immunodeficiency virus-1 (HIV-1) env compartmentalization in the presence of HIV-1 associated dementia (HAD). *J. Virol.* 79:10830-4
 - c. Harrington PR, Hass DW, **Ritola K**, Swanstrom R. 2005. Compartmentalized human immunodeficiency virus type 1 present in cerebrospinal fluid is produced by short-lived cells. *J. Virol.* 79:7959-66.
 - d. Ngrengramlert W, Kwiek JJ, Kamwendo DD, **Ritola K**, Swanstrom R, Wongsrichanalai C, Mill RS, Ittarat W, and Meshnick SR. 2005. Measuring allelic heterogeneity in plasmodium falciparum by heteroduplex tracking assay. *Am J Trop Med Hyg.* 72:694-701.

- e. **Ritola K**, Pilcher CD, Fiscus SA, Hoffman NG, Nelson JA, Kitrinis KM, Hicks CB, Eron JJ Jr, Swanstrom R. 2004. Multiple V1/V2 env variants are frequently present during primary infection with human immunodeficiency virus type 1. *J Virol.* 78:11208-18.
 - f. Gorry PR, Bristol G, Zack JA, **Ritola K**, Swanstrom R, Birch CJ, Bell JE, Bannert N, Crawford K, Wang H, Schols D, De Clercq E, Kunstman K, Wolinsky SM, Gabuzda D. 2001. Macrophage Tropism of Human Immunodeficiency Virus Type 1 Isolates from Brain and Lymphoid Tissues Predicts Neurotropism Independent of Coreceptor Specificity. *J Virol.* 75:10073-89.
2. *Determined host and virus interactions during HCV infection and treatment with novel HCV inhibitors.* I studied the emergence of HCV drug resistance mutations during treatment with novel HCV specific protease and polymerase inhibitors. I developed a direct competition assay to illustrate the ability of wild type virus to compensate for fitness losses in the resistant population. Building off my previous work, I developed assays to assess HCV population complexity within various biological compartments as well as developing cell culture conditions for isolating replicating HCV variants from patient blood samples.
- a. Charles ED, Brunetti C, Marukian S, Ritola KD, Talal AH, Marks K, Jacobson IM, Rice CM, Dustin LB. 2011. Clonal B cells in patients with hepatitis C virus-associated mixed cryoglobulinemia contain an expanded anergic CD21low B-cell subset. *Blood* 19;117(20):5425-37.
 - b. Ploss A, Khetani SR, Jones CT, Syder AJ, Trehan K, Gaysinskaya VA, Mu K, **Ritola K**, Rice CM, Bhatia SN. 2010. Persistent hepatitis C virus infection in microscale primary human hepatocyte cultures. *PNAS* 107:3141-5.
 - c. Marukian S, Christopher T. J, Andrus L, **Ritola K**, Charles ED, Rice CM, Dustin LB. 2008. Cell culture-produced hepatitis C virus does not infect peripheral blood mononuclear cells. *Hepatology* 48: 1843-50
3. *Create best-in-class viral tools for the HHMI community.* For the last ten years, I have applied my strong virology training to create viral tools for basic science research. I have systematically optimized viral production protocols for adeno-associated virus (AAV), rabies and lentiviruses. Under my direction, Janelia Viral Tools has garnered a reputation for being the best-in-class for not only viral tool production, but also virus tool specialization to specific investigator needs. I give support from viral construct design, customized viral vector production, all the way through to experimental design and trouble-shooting. I integrate information from our wide user base (ranging from neuroscience to cardiac research) to help investigators stream-line efforts and shorten time to experimental success. Our improvements in vector production and design have allowed us to successfully package longer than wild-type AAV constructs with reliable biologically relevant activity in vivo—a first in the AAV field. We also helped identify a novel AAV capsid with improved retrograde tracing capabilities (Tervo et al). We have created new rabies packaging cell lines to improve titer and in-vivo activity. My integration of virology with user feedback has been critical for successful fine-tuning of viral vectors to investigator specific experimental needs and the resulting peer-reviewed published papers.
- a. Xiao X, Deng H, Furlan A, Yang T, Zhang X, Hwang GR, Tucciarone J, Wu P, He M, Palaniswamy R, Ramakrishnan C, **Ritola K**, Hantman A, Deisseroth K, Osten P, Huang ZJ, Li B. A Genetically Defined Compartmentalized Striatal Direct Pathway for Negative Reinforcement. *Cell.* 2020 Oct 1;183(1):211-227.e20. doi: 10.1016/j.cell.2020.08.032. Epub 2020 Sep 15. PMID: 32937106.
 - b. François A, Low SA, Sypek EI, Christensen AJ, Sotoudeh C, Beier KT, Ramakrishnan C, **Ritola KD**, Sharif-Naeini R, Deisseroth K, Delp SL, Malenka RC, Luo L, Hantman AW, Scherrer G. 2017. A Brainstem-Spinal Cord Inhibitory Circuit for Mechanical Pain Modulation by GABA and Enkephalins. *Neuron* 22;93(4):822-839.
 - c. Tervo DG, Hwang BY, Viswanathan S, Gaj T, Lavzin M, **Ritola KD**, Lindo S, Michael S, Kuleshova E, Ojala D, Huang CC, Gerfen CR, Schiller J, Dudman JT, Hantman AW, Looger LL, Schaffer DV, Karpova AY. 2016. A Designer AAV Variant Permits Efficient Retrograde Access to Projection Neurons. *Neuron* 19;92(2):372-382.
 - d. Betley JN, Cao ZF, **Ritola KD**, Sternson SM. 2013. Parallel, redundant circuit organization for homeostatic control of feeding behavior. *Cell* 5;155(6):1337-50.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

PI:

09/2021-08/2026 U24NS124025 BRAIN Viral Vector Services and Distribution Core

9/2021-08/2024 R01FD007476 Nanopore Methods for Determining Capsid Viability

Co-PI:

09/2021-09/2024 RF1MH126706 AnteroTag, a Novel Method for Trans-Synaptic Delivery of Active Agents to Map and Modify Anterograde Populations

09/2021-08/2024 R01FD007481 Platform for Rapid Expression, Purification, and Analysis of Patient-Specific Gene Therapy Products

01/2022-12/2026 R01NS125843 Enhancement, mapping, and validation of viral vectors for primate optogenetics

Completed Research Support

2014-2021 Howard Hughes Medical Institute-Janelia Research Campus, Scientific Operations Manager

2007-2010 Ruth L. Kirschstein National Research Service Award (NRSA), DK080650

2000-2005 Trainee NIH Training Grant T32-AI007419: "Molecular Biology of Viral Diseases"