BIOGRAPHICAL SKETCH

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NAME: Judd F. Hultquist

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

POSITION TITLE: Assistant Professor of Medicine

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
Marquette University, Milwaukee, WI, USA	B.S.	05/2008	Biochemistry
University of Minnesota, Minneapolis, MN, USA	Ph.D.	12/2012	Molecular Biology
University of Minnesota, Minneapolis, MN, USA	Post Doc	11/2013	Virology
Gladstone Institutes, San Francisco, CA, USA	Post Doc	07/2018	Systems Biology

A. Personal Statement

Viruses are specialized molecular machines selected over millions of years of co-evolution to exploit the cellular networks of their hosts for replication and survival. This reliance on and manipulation of the host manifests itself in thousands of molecular changes that influence cellular function and may result in disease. A systematic, quantitative understanding of these changes is essential for the understanding of these disease states and for the development of next-generation therapeutics. Only recently, however, have technological advances in molecular measurement and manipulation allowed for the precise, high-throughput determination of mammalian cell architecture. The goal of my research program is to adapt and advance these systems-based approaches to primary cell models of disease in order to map the host-pathogen relationship as it unfolds within its cellular environment. To realize this goal, my group leverages diverse expertise in primary cell models, proteomic profiling, and functional genomics to study the changing landscape of protein-protein interactions, post-translational modifications, and gene expression profiles during the course of viral infection. The result of these efforts has been a body of work at the intersection of systems biology and molecular virology, defining host-pathogen interactions and their consequences to viral replication and pathogenesis. Through these efforts, I ultimately hope to strengthen the bridge from big data to targeted discovery to clinical application for the development of personalized, host-driven therapies and the advancement of human health. Current projects in the lab are focused on understanding the proteomic and genetic landscapes dictating human cell interactions with a variety of clinically relevant pathogens including Respiratory Syncytial Virus (RSV), Influenza A Virus (IAV), Human Immunodeficiency Virus (HIV), SARS Coronavirus 2 (SARS-CoV-2), *P. aeruginosa*, etc.

Dr. Judd F. Hultquist is an Assistant Professor in the Division of Infectious Diseases in the Feinberg School of Medicine at Northwestern University. The Hultquist laboratory is located in the Fred and A. Norman Drucker Laboratory for Virology Research on the medical research campus in downtown Chicago, Illinois, United States. The Hultquist lab consists of 1500 sq. ft. of dedicated BSL2 research space, including two fully equipped BSL2 tissue culture suites and one BSL2+ tissue culture suite. The floor additionally hosts the laboratories of established medical researchers Dr. Steven Wolinsky and Dr. Richard D'Aquila, and contains all necessary equipment for virologic research. The Hultquist lab has full access to all cores and institutes affiliated with the Feinberg School of Medicine, including the Northwestern University Center for Advanced Technologies (NUCATS), the Third Coast Center for AIDS Research (TC-CFAR), the Northwestern University Sequencing Core (NUSeq), etc. In collaboration with colleagues at the neighboring Northwestern Memorial and Lurie's Children's Hospitals, the Hultquist lab has the ability to perform observational and translational research with access to patient cohort data and clinical samples.

B. Positions and Honors

Positions and Employment

07/18 – present Assistant Professor, Department of Medicine, Division of Infectious Diseases, Northwestern University Feinberg School of Medicine

Academic and Professional Honors

2019 Gilead Sciences Research Scholars Program in HIV Award
2018 Gladstone Institute of Virology and Immunology Postdoctoral Award of Excellence in Science
2018 NIH K22 Career Transition Award
2016 American Foundation for AIDS Research (amFAR) Mathilde Krim Fellowship
2016 Roche Pharmaceuticals Postdoctoral Fellowship
2016 Gladstone Institutes Convergence Zone Postdoctoral Award of Excellence in Science
2016 UCSF Center for AIDS Research (CFAR) Mentored Science Award
2015 L. Kirschstein National Research Service Award (T32 Training Grant)
2015 Program for Breakthrough Biomedical Research Postdoctoral Independent Research Award
2013 University of Minnesota Best Dissertation Award in Biological and Life Sciences
2013 Uta von Schwedler Prize for Outstanding Thesis Research in Retrovirology
2012 Beatrice Z. Milne and Theodore Brandenburg Award for Exceptional Thesis Research
2009 National Science Foundation Graduate Research Fellowship
2008 Marquette University College of Arts and Sciences Gold Medal Award for Highest GPA
2008 Marquette University Honors Award for Superior Academic Achievement
2008 Biological Sciences Academic Achievement Award
2008 Gammex Undergraduate Research Award
2008 University of Minnesota Graduate Student Fellowship
2007 Undergraduate Research Award in Biological Sciences
2007 Barry M. Goldwater Scholarship
2004 Marquette University Ignatius Scholarship for Academic Excellence

Professional Membership and Service

2020 Inclusion, Diversity, Equity and Accessibility (IDEA) Committee, Driskill Graduate Program
2020 Admissions Committee, Driskill Graduate Program
2019 Data Insight Group, Third Coast Center for AIDS Research Viral Pathogenesis Core
2019 External Scientific Advisory Board member, RADAR cohort
2019 Ad hoc referee, *Scientific Reports, PloS One*
2018 Ad hoc referee, *PLoS Pathogens*
2016 Ad hoc referee, *AIDS Research & Human Retroviruses*, *Bio-protocols*, *Microbial Pathogenesis*

C. Contributions to Science

C.1. *Primary Cell Gene Editing for the Discovery of Host-Pathogen Interactions*. Understanding the molecular basis of viral pathogenesis is essential for the development of next-generation therapeutics. This includes determining how viral pathogens interact with and utilize the specialized niches of their hosts for replication as well as understanding how this results in pathogenesis and disease. CRISPR-Cas9 genome editing tools have now made it possible to specifically and efficiently mediate the expression of target host genes in many different model systems, opening up dramatic new avenues in many areas of study. I have been at the forefront of developing novel ways to use this technology to study host-pathogen interactions, from the application of genome-wide CRISPR screens to the development of a novel primary T cell gene-editing platform to the discovery of the first anti-Cas9 proteins in bacteriophages.

1. **Hultquist J.F.**, Hiatt J., Schumann K., McGregor M.J., Roth T.L., Haas P., Doudna J., Marson A., & Krogan, N.J. (2019). CRISPR-Cas9 genome engineering of primary CD4+ T cells for the interrogation of HIV-host factor interactions. *Nature Protocols*. 14: 1-27. PMID: 30559373.
2. Rauch B.J., Silvis M.R., **Hultquist J.F.**, Waters C.S., McGregor M.J., Krogan N.J., & Bondy-Demony J. (2017). Inhibition of CRISPR-Cas9 with Bacteriophage Proteins. *Cell*. 168: 150-158. PMID: 28041849.

3. Park R.*, Wang T.*, Koundakjian D., **Hultquist J.F.**, LaMothe-Molina P., Monel B., Schumann K., Yu H., Krupzcak K.M., Garcia-Beltran W., Piechocka-Trocha A., Krogan N.J., Marson A., Sabatini D., Lander E., Hacohen N., & Walker, B.D. (2017). A genome-wide CRISPR screen identifies a restricted set of HIV host dependency factors. *Nature Genetics*. 49: 193-203. PMID: 27992415.
4. **Hultquist J.F.***, Schumann K.*, Woo J.M., Manganaro L., McGregor M.J., Doudna J., Simon V., Krogan N.J., & Marson, A. (2016). A Cas9 Ribonucleoprotein Platform for Functional Genetic Studies of HIV-Host Interactions in Primary Human T Cells. *Cell Reports*. 17: 1438-1452. PMID:27783955.

C.2. *Proteomic Profiling of Viral Infection*. In addition to genetic approaches, proteomic methods can provide rich functional and mechanistic insight into the processes driving viral replication and pathogenesis. Protein-protein interactions are among the first physical handles that mediate viral hijacking of a host cell. In addition, the manipulation of protein post-translational modifications by both the virus and host response assist in setting up environments that either promote or are hostile to infection. Moving from a transcriptomic to a proteomic understanding of disease is therefore critical to better understand the interplay between host and pathogen, between replication and pathogenesis, and between biomarkers and patient outcome. Towards this end, I have strived to apply and adapt proteomic approaches to primary models of disease.

1. Batra J.*, **Hultquist J.F.***, Liu D., Shtanko O., Von Dollen J., Satkamp L., Jang G.M., Luthra P., Schwarz T.M., Small G.I., Arnett E., Anantpadma M., Reyes A., Leung D.W., Kaake R., Haas P., Schmidt C.B., Schlesinger L.S., LaCount D.J., Davey R.A., Amarasinghe G.K., Basler C.F., & Krogan N.J. (2018). Protein interaction mapping identifies RBBP6 as a negative regulator of Ebola virus replication. *Cell*. 175: 1917-1930. PMID: 30550789.
2. Zhao N., Sebastiano V., Moshkina N., Mena N., **Hultquist J.F.**, Jimenez-Morales D., Ma Y., Rialdi A., Albrecht R., Fenouil R., Sanchez-Aparicio M., Ayllon J., Ravisankar S., Haddad B., Ho J.S.Y., Low D., Jin J., Yurchenko V., Prinja R.K., Tarakhovsky A., Squatrito M., Pinto D., Allette K., Byun M., Smith M.L., Sebra R., Guccione E., Tumpey T., Krogan N.J., Greenbaum B., van Bakel H., Garcia-Sastre A., & Marazzi, I. (2018). Influenza virus infection causes global RNAPII termination defects. *Nature Structural & Molecular Biology*. 25: 885–893. PMID: 30177761.
3. Rialdi A., **Hultquist J.F.**, Jimenez-Morales D., Peralta Z., Campisi L., Fenouil R., Moshkina N., Wang Z.Z., Laffleur B., Kaake R.M., McGregor M.J., Haas K., Pefanis E., Albrecht R.A., Pache L., Chanda S., Jen J., Ochando J., Byun M., Basu U., Garcia-Sastre A., Krogan N.J., van Bakel H., & Marazzi, I. (2017). The RNA Exosome Syncs IAV-RNAPII Transcription to Promote Viral Ribogenesis and Infectivity. *Cell*. 169: 679-692. PMID: 28475896.
4. Heaton N.S., Moshkina N., Fenouil R., Gardner T.J., Aguirre S., Shah P.S., Zhao N., Manganaro L., **Hultquist J.F.**, Noel J., Sachs D.H., Hamilton J., Leon P.E., Chawdury A., Tripathi S., Melegari C., Campisi L., Hai R., Metreveli G., Gamarnik A.V., García-Sastre A., Greenbaum B., Simon V., Fernandez-Sesma A., Krogan N.J., Mulder L.C., van Bakel H., Tortorella D., Taunton J., Palese P., & Marazzi I. (2016). Targeting Viral Proteostasis Limits Influenza Virus, HIV, and Dengue Virus Infection. *Immunity*. 44: 46-58. PMID: 26789921.

C.3. *APOBEC3 Biology*. The rapid ability of viruses to evolve resistance to drugs that target viral proteins has encouraged a push to discover small molecules that act through inhibition of host proteins that are essential for virus replication, but not cellular function. One promising set of human genes that may be leveraged for the treatment of retrovirus infections, like HIV, are the APOBEC3 family of antiviral enzymes. All seven members of this gene family have been implicated in viral restriction, but a systematic study of these genes was lacking. This series of papers, among others, chronicles some of my work defining the restrictive repertoire of APOBEC3 proteins and their mechanism-of-action against HIV infection in human T cells. These studies draw on a diverse array of techniques and strategies in cell lines and primary cell models to define the restrictive repertoire including viral resistance studies, evolutionary analysis, gene knockout/knockdown/overexpression, mutational analysis, polymorphism analysis, and expression profiling.

1. Refsland E.W., **Hultquist J.F.**, Luengas E.M., Ikeda T., Shaban N.M., Law E.K., Brown W.L., Reilly C., Emerman M., & Harris, R.S. (2014). Natural polymorphisms in human APOBEC3H and HIV-1 Vif combine in primary T lymphocytes to affect viral G-to-A mutation levels and infectivity. *PLoS Genetics*. 10: e1004761. PMID: 25411794.
2. Refsland E.W., **Hultquist J.F.**, & Harris R.S. (2012). Endogenous origins of HIV-1 G-to-A hypermutation and restriction in the nonpermissive T cell line CEM2n. *PLoS Pathogens*. 8: e1002800. PMID: 22807680.

3. **Hultquist J.F.**, Lengyel J.A., Refsland E.W., LaRue R.S., Lackey L., Brown W.L., & Harris R.S. (2011). Human and rhesus APOBEC3D, APOBEC3F, APOBEC3G, and APOBEC3H demonstrate a conserved capacity to restrict Vif-deficient HIV-1. *Journal of Virology*. 85: 11220-11234. PMID: 21835787.
4. Albin J.S., Hache G., **Hultquist J.F.**, Brown W.L., & Harris R.S. (2010). Long-term restriction by APOBEC3F selects Human Immunodeficiency Virus type 1 variants with restored Vif function. *Journal of Virology*. 84: 10209-10219. PMID: 20686027.

C.4. *HIV Vif E3 Ligase Biology*. While my earlier studies definitively defined the restrictive repertoire of APOBEC3 proteins against HIV, a major block to leveraging these proteins as a therapeutic target is the ability of HIV to defend against APOBEC3 attack through the function of the viral Vif protein. Vif was known to recruit a Cullin E3 ligase complex to degrade the APOBEC3 proteins, but efforts to inhibit this viral defense complex failed, in part because the Vif E3 ligase could not be reconstituted *in vitro* nor was it amenable to structural study. Using proteomic profiling and other systems techniques, we identified a missing member of the E3 ligase complex, the transcription factor CBFbeta. When supplied *in vitro*, this protein allowed for full reconstitution of the Vif E3 ligase complex and quickly led to solution of the Vif crystal structure. This has stimulated a push across the field to search for inhibitors of this unique and essential viral complex. Furthermore, evolutionary analysis has demonstrated that CBFbeta is required for the Vif E3 ligase complexes of all primate-infecting lentiviruses, but dispensable for non-primate lentiviruses. Thus, this virus family is divergent in its requirement for non-canonical E3 ligase components to form a functional complex. One theory for this divergence is the necessity for 'dual-hijacking' in primates, where these viruses require not only APOBEC3 neutralization, but gain extra benefit from disturbing CBFbeta-mediated transcription.

1. Binning J.M., Smith A.M., **Hultquist J.F.**, Craik C.S., Caretta N., Campbell M.G., Burton L., La Greca F., McGregor M.J., Ta H.M., Bartholomeeusen K., Peterlin B.M., Krogan N.J., Sevillano N., Cheng Y., & Gross J.D. (2018). Fab-based inhibitors reveal ubiquitin independent functions for HIV Vif neutralization of APOBEC3 restriction factors. *PLoS Pathogens*. 14: e1006830. PMID: 29304101.
2. **Hultquist J.F.**, McDougle R.M., Anderson B.A., & Harris R.S. (2012). HIV type 1 viral infectivity factor and the RUNX transcription factors interact with core binding factor β on genetically distinct surfaces. *AIDS Research & Human Retroviruses*. 28: 1543-1551. PMID: 22725134.
3. **Hultquist J.F.**, Binka M., LaRue R.S., Simon V., & Harris R.S. (2012). Vif proteins of human and simian immunodeficiency viruses require cellular CBFβ to degrade APOBEC3 restriction factors. *Journal of Virology*. 86: 2874-2877. PMID: 22205746.
4. Jäger S.*, Kim D.Y.*, **Hultquist J.F.***, Shindo K., LaRue R.S., Kwon E., Li M., Anderson B.D., Yen L., Stanley D., Mahon C., Kane J., Franks-Skiba K., Cimermancic P., Burlingame A., Sali A., Craik C.S., Harris R.S., Gross J.D., & Krogan N.J. (2011). Vif hijacks CBFβ to degrade APOBEC3G and promote HIV-1 infection. *Nature*. 481: 371-375. PMID: 22190037.

**** Complete list of published work is available online at Pubmed ****
https://www.ncbi.nlm.nih.gov/pubmed/?term=Hultquist+JF

D. Research Support

Ongoing

UL1 TR002389-04S2 Soloway (PI) 07/13/20 – 06/30/21
University of Chicago, Chicago, IL. (Prime: CTSA NCATS UL1 TR002389)
Supplement: *Epidemiological and clinical characterization of genomic variation in SARS-CoV-2*
Parent: *ITM 2.0: Advancing Translational Science in Metropolitan Chicago*
This collaborative proposal between CTSA centers at Northwestern University and the University of Chicago seeks to use Bayesian modeling to identify clinical, demographic, and virological predictors of COVID-19 disease severity for use in clinical settings.
Role: Multiple Principal Investigator

Dixon Translational Research Grant Hultquist/Ozer (co-PI) 04/01/20 – 04/01/21
Northwestern University, Chicago, IL. (Prime: CTSA NUCATS UL1 TR001422)
Epidemiological, clinical, and functional characterization of genomic variation in SARS-CoV-2
This translational science research award administered by the Northwestern University Clinical and Translational Sciences (NUCATS) Institute is made possible by a generous donation from the Dixon family. This proposal

seeks to perform whole genome sequencing of SARS-CoV-2 isolates from COVID-19 patients at Northwestern Memorial Hospital to better understand the epidemiological history of the pandemic in Chicago, identify clade-defining mutations, and determine the impact of viral variation on clinical outcomes and biochemical function.
Role: co-Principal Investigator

Third Coast CFAR Supplemental Award D'Aquila (PI) 08/01/20 – 07/31/21
Northwestern University, Chicago, IL. (Prime: Third Coast CFAR, P30 AI117943)
Exploring Small Molecule Regulators of the Super Elongation Complex as Novel HIV Latency Reversal Agents
This Center for AIDS Research (CFAR) supplement will test the efficacy of small molecule regulators of the Super Elongation Complex (SEC) to reactivate latent HIV viruses and to determine their mechanism-of-action with the ultimate goal of developing new strategies to combat HIV persistence in future curative strategies.
Role: Principal Investigator

Cancer Center Supplemental Award Platanias (PI) 06/01/20 – 05/31/21
Northwestern University, Chicago, IL. (Prime: NIH/NCI P30 CA060553)
COVID19: Production of protein array for serum antibody screening
This collaborative award with the Center for Structural Genomics of Infectious Diseases proposes to determine the functional, structural, and serological consequences of SARS-CoV-2 genetic variation.
Role: *co-Investigator*

Third Coast CFAR Supplemental Award Hultquist (PI) 07/01/18 – 03/31/20
Northwestern University, Chicago, IL. (Prime: Third Coast CFAR, P30 AI117943)
Determining the Role of N6-Methyladenosine during HIV Replication in Primary T Cells
This Center for AIDS Research (CFAR) supplement provides funding to knock-out the m6A pathway in primary T cells and quantify the impacts on active replication and m6A modification to the HIV genome.
Role: Principal Investigator

HARC Center Collaborative Opportunity Fund Hultquist (PI) 09/15/18 – 08/31/20
Northwestern University, Chicago, IL. (Prime: HARC Center, P50 GM082250)
Understanding the Structural/Functional Basis of HIV Replication in Macrophages
This renewal application for a HARC Center collaborative award would provide funding to perform systematic AP-MS studies on macrophage-tropic strains of HIV proteins in THP-1 cells and quantify the impacts of genetic ablation on high priority targets in primary macrophages.
Role: Principal Investigator

K22 AI136691 Hultquist (PI) 07/01/18 – 07/01/20
Northwestern University, Chicago, IL. (Prime: NIH NIAID AI136691)
The Influence of Early Integration Events on HIV Latency and Reactivation Potential
This career transition award tests the hypothesis that the molecular pathway used by HIV to integrate into the host genome fundamentally influences not only the probability of establishing latency, but also its maintenance and the effectiveness of reactivation drugs.
Role: Principal Investigator

Gilead Sciences Research Scholars Program in HIV Hultquist (PI) 06/01/19 – 06/01/21
Northwestern University, Chicago, IL. (Prime: Gilead Sciences, Inc.)
Exploring the Genetic Determinants Underlying HIV Replication and Latency
This early investigator award explores the role of protein-protein interactions in the establishment of HIV latency and looks to adapt single-cell RNA-sequencing approaches for use in identifying CRISPR-edited cells.
Role: Principal Investigator

R01 AI150998 Hope/Bieniasz (co-PI) 12/01/19 – 11/30/24
Northwestern University, Chicago, IL. (Prime: Northwestern University)
Functionally Defining HIV-Host Interactions During the Early HIV-1 Lifecycle
This large-format R01 tests the hypothesis that the early phase of HIV infection is defined by a sequence of steps with kinetics, dynamics, and host contributions varying by virus strain, cell type, and cellular environment. We will leverage a series of new technologies (imaging, cryo-EM, CRISPR-Cas9, etc.) to define the sequence of events during early HIV-1 replication that result in productive infection in different primary cell types.
Role: co-Investigator