

BIOGRAPHICAL SKETCH

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NAME: Andrew Mehle

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

POSITION TITLE: Assistant Professor

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
Villanova University, Villanova PA	BS	June 1998	Biology
Villanova University, Villanova PA	BA	June 1998	Honors
Harvard University, Cambridge MA mentor – Dana Gabuzda, MD	PhD	Dec. 2004	Virology
University of California Berkeley, Berkeley CA mentor – Jennifer Doudna, PhD		2005-2011	Postdoctoral training

A. Personal Statement

Influenza virus is a serious public health threat causing significant morbidity, mortality and socioeconomic consequences. Seasonal outbreaks are punctuated by the emergence of novel pandemic isolates that have even more potential for widespread infection and disease. This risk is amplified as there are only two main classes of approved antivirals, and only the neuraminidase inhibitors are efficacious against currently circulating strains. There is a clear need for the development of new antiviral therapies and the identification of novel antiviral targets. Given the critical role of the polymerase during viral replication, and its attractiveness as a drug target, it is essential to clearly understand the impact changes in polymerase activity will have on species tropism and disease progression. My lab is addressing this knowledge gap by studying the basic mechanisms of influenza virus polymerase activity and regulation. With support from my R00 award, our studies of the polymerase have identified an important interaction between the viral polymerase and the host that regulates cross-species transmission. We have exploited biochemical and genetic approaches to define host factors that regulate influenza virus replication and identified the presence of a species-specific “restriction factor” that blocks polymerase function and have defined its mode of action. These experiments also revealed that post-translational modifications regulate the influenza polymerase as it transitions from transcription to replication during the viral life cycle. Our published data show that dynamic and tightly controlled regulatory events modulate assembly of the viral replication machinery. We are well-suited to investigate these regulatory mechanisms, bringing almost 20 years of experience studying how post-translational modifications of viral proteins by host enzymes modifies their activity, beginning with my graduate work defining the regulation of the HIV-1 Vif protein by phosphorylation and ubiquitination. This experience has extended to my role as a New Investigator where my lab has published two papers describing important interaction sites in the viral polymerase and how they engage the host cell environment, two high-profile manuscripts demonstrating that phosphorylation by host kinases regulates assembly of the viral replication machinery, further evidence that another post-translation modification, ubiquitin, impacts polymerase function, as well as five papers detailing a highly sensitive influenza reporter virus that enables rapid analysis of viral replication *in vivo*. Thus, the Mehle lab is highly motivated with the experience and new tools to define the mechanisms of regulated polymerase activity and their linkage to virus replication and pathology. Moreover, we have established strong collaborations that bring expertise in studying the regulatory post-translational modifications we have identified. Given the obvious public health implications of influenza viruses and the specter of a highly pathogenic influenza outbreak, our results will offer significant impact towards understanding the host and viral mediators of disease pathology and suggest potential therapeutic strategies to control infection.

B. Positions and Honors

Positions and Employment

- 1998-2004 **Graduate student**, Laboratory of Dana Gabuzda, MD, Division of Medical Science, Harvard University. Ph.D. thesis title: "HIV-1 Vif: a novel SOCS-box protein that targets APOBEC3G for proteasomal degradation"
- 1999 **Teaching Assistant**, Harvard University, Division of Medical Science – Molecular Biology. Coordinated by Steve Buratowski, PhD.
- 2004-2005 **Postdoctoral fellow**, Laboratory of Dana Gabuzda, MD, Dana Farber Cancer Institute
- 2005-2011 **Postdoctoral fellow**, Laboratory of Jennifer Doudna, PhD, University of California, Berkeley
- 2011-2018 **Assistant Professor**, Department of Medical Microbiology & Immunology, University of Wisconsin-Madison
- 2018- **Associate Professor**, Department of Medical Microbiology & Immunology, University of Wisconsin-Madison

Honors

- 1994-1998 Presidential Scholar, Villanova University
- 1998 Phi Beta Kappa Honor Society Induction
- 1998 John McClain Award for outstanding academic performance in biology (highest rank in major), Villanova University
- 1998 Gregor Mendel Award for academic excellence in the sciences (highest rank in sciences), Villanova University
- 1998 *Summa cum laude*, Villanova University
- 1998 National Science Foundation Predoctoral Fellowship
- 2006 Kirschstein National Research Service Award Postdoctoral Fellowship – NIGMS
- 2009 K99/R00 NIH Pathways to Independence Award – NIGMS
- 2012 Shaw Scientist Awardee, James D. and Dorothy Shaw Fund, Greater Milwaukee Foundation
- 2012 New Investigator Awardee, Wisconsin Partnership Education and Research Committee
- 2016 State-of-the-Art Lecturer, American Society for Virology annual meeting
- 2016 Invited keynote speaker, 5th International Influenza Meeting (Munster, DEU)
- 2017 Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Disease
- 2017 Invited Instructor, 14th Hong Kong University – Pasteur Virology Course
- 2018 Invited speaker, University of California Berkeley 10th Anniversary CEND Symposia

Editorial Boards and service

- 2010- *Frontiers in Virology*, editorial board member
- 2015- *Viruses*, Associate Editor
- 2015-2017 *Journal of Virology*, editorial board member
- 2015 *Ad hoc* reviewer for the Medical Research Council (MRC, UK)
- 2015- *Virology*, editorial board member
- 2016-2018 American Society for Virology Program Committee
- 2016 *Ad hoc* reviewer for the Wellcome Trust and Wellcome Trust DBT India Alliance
- 2016 *Ad hoc* reviewer for NIH Study Section - Virology A
- 2017 *Ad hoc* reviewer for the Wellcome Trust, Agence Nationale de la Recherche (ANR), Department of Defense Congressionally Directed Medical Research Programs
- 2018 *Ad hoc* reviewer for NIH Topics in Virology – ZRG1 IDM-W (02)

Selected speaker, session chair and invited seminars

2009: Gordon Research Conference: Viruses and Cells; **2010**: XIV International Conference on Negative Strand Viruses, Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis; **2011**: Bay Area Symposia on Viruses; University of Wisconsin Madison Virology Seminar Series; **2012**: Loyola University Stritch School of Medicine; Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis session chair; Great Lakes Regional Center of Excellence annual meeting; **2013**: Promega Corporation; Montana State; University of Wisconsin Raper Symposium; University of Wisconsin Madison Virology Seminar Series; **2014**: Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis speaker and session chair; Society of Nuclear Medicine & Molecular Imaging national meeting; Ichan School of Medicine at

Mount Sinai; **2015**: University of Wisconsin La Crosse; Stanford University School of Medicine; XVI International Conference on Negative Strand Viruses; 34th American Society for Virology annual meeting speaker and session convener; **2016**: Viruses2016, Basel CHE; 35th American Society for Virology annual meeting State-of-the-Art Lecturer; 5th International Influenza Meeting, Munster, DEU (keynote lecturer); Merck (West Point, PA), Options IX (Chicago, IL); **2017**: University of Georgia, UT Austin, Harvard Medical School, Gordon Research Conference: Viruses and Cells, 36th American Society for Virology annual meeting session convener, 14th Hong Kong University – Pasteur Virology Course (Hong Kong, invited instructor), Montana State University, Duke; **2018**: University of California Berkeley 10th CEND Symposia, University of Michigan, University of Texas Southwestern, University of Arkansas for Medical Sciences, University of Illinois, Dalhousie University, University of Vermont

C. Contribution to Science

Regulation of the influenza virus replication machinery. Influenza virus assembles large ribonucleoprotein (RNP) complexes that direct replication and transcription of the viral genome. These RNPs contain the polymerase, genomic RNA and oligomeric copies of nucleoprotein (NP). RNP formation and polymerase activity are essential for successful infection, and as such are prime targets for antiviral interventions. It is therefore critical to understand how these massive RNPs assemble and their activities are regulated. *We identified key features of both the viral polymerase and NP that are required for RNP assembly. We elucidated a critical phospho-regulatory mechanism whereby NP oligomerization, and resultant RNP assembly, is specifically controlled by host kinases.* Our data show that dynamic phosphorylation of NP is a major regulator of RNP assembly and modulates progression through the viral life cycle. The evolutionary conservation of these phospho-sites suggests that our results are broadly applicable across viral strains and genera and reveal a global regulatory strategy for *Orthomyxoviridae*. By identifying host kinases as essential partners in RNP assembly, we have dramatically expanded the target space for antiviral intervention.

- Kirui J, Bucci MD, Poole DS and **Mehle A**. 2014. Conserved features of the PB2 627 domain impact influenza virus polymerase function and replication. *J Virol.* **88**:5977-5986. PMID:PMC24623411.
- Mondal A, Potts GK, Dawson AR, Coon JJ, **Mehle A**. 2015. Phosphorylation at the homotypic interface regulates nucleoprotein oligomerization and assembly of the influenza virus replication machinery. *PLOS Pathogens.* **11**:e1004826. doi: 10.1371/journal.ppat.1004826. PMID: PMC4395114.
- Kirui J, Mondal A, **Mehle A**. 2016 Ubiquitination up-regulates influenza virus polymerase function. *J Virol.* **90**:10906-10914. doi:10.1128/JVI.01829-16. PMID5110180. *selected as an "Article of Significant Interest"*
- Mondal A, Dawson AR, Potts GK, Freiburger EC, Baker SF, Moser LA, Bernard KA, Coon JJ, **Mehle A**. 2017. Influenza virus recruits host protein kinase C to control assembly and activity of its replication machinery. *eLife.* **6**:e26910. doi:10.7554/eLife.26910.

Seeing is believing: in vivo imaging tools to quantify influenza virus replication. Animal models have proven invaluable in understanding the *in vivo* replication of influenza virus and immune responses by the host. Existing methods for infections in animals relied on indirect measures of viral levels, or used laborious assays, and in most cases required the sacrifice of the animal, and hence the end of the experiment. There was no capacity to monitor viral dynamics in real time, severely limiting the ability to quickly screen the efficacy of antiviral treatments, the pathogenicity of emerging influenza virus, or the protection afforded by new vaccine formulations. *We have overcome these limitations by developing an influenza reporter virus suitable for in vivo imaging in the mouse and ferret models.* For the first time, our newly developed tool permits non-invasive, longitudinal measures of viral load and dissemination within the same animal over the entire course of infection. The papers below describe our development of this powerful new technology and highlight unexpected findings in replication dynamics, transmission and vaccination that would not have been possible using traditional approaches.

- Tran V, Moser LA, Poole DS and **Mehle A**. 2013. Highly sensitive real-time in vivo imaging of an influenza reporter virus reveals dynamics of replication and spread. *J Virol.* **87**:13321-13329. PMID3838222.
- Karlsson EA*, Meliopoulos VA*, Savage C, Livingston B, **Mehle A**#, Schultz-Cherry S#. 2015. Visualizing Real-Time Influenza Virus Infection, Transmission and Protection in Ferrets. *Nature Communications.* **6**:6378. # = co-corresponding. PMID4366512.

- Tran V, Poole DS, Jeffery JJ, Sheahan TP, Creech D, Yevtodiyyenko A, Peat AJ, Francis KP, You S, **Mehle A**. 2015. Multi-modal imaging with a toolbox of influenza A reporter viruses. *Viruses*. **7**:5319-5327. PMC4632381.
- Czako R, Vogel L, Lamirande EW, Bock KW, Moore IN, Ellebedy AH, Ahmed R, **Mehle A**, Subbarao K. 2017. *In Vivo* Imaging of Influenza Virus Infection in Immunized Mice. *mBio*. **8**:3 e00714-17. PMC5449660.

Crossing species barriers. Influenza viruses circulating in avian reservoirs represent a significant public health threat as a potential source of human pandemic viruses. Transmission of influenza viruses into the human population requires surmounting barriers to cross-species infection that involve a complex interplay between the virus and host. Understanding the mechanisms by which influenza viruses acquire the ability to infect multiple species is thus imperative to controlling future outbreaks. *We have shown that the influenza virus polymerase is a major determinant of viral tropism.* Our work suggested that mammals express a potent and selective restriction factor that inhibits viral polymerases derived from avian influenza viruses, thus blocking cross-species transmission. We further defined the molecular consequences of restriction and identified multiple adaptive strategies exploited by influenza virus as it evolves in new hosts. Moreover, our results provide the foundation to focus prevention efforts on the viruses most likely to establish infections in humans, and possibly exploit naturally occurring inhibitory mechanisms for general antiviral therapy.

- Mehle A** and Doudna JA. 2008. An inhibitory activity in human cells restricts the function of an avian-like influenza virus polymerase. *Cell Host Microbe*. **4**:111-122. PMC2597520. *a "Featured Article"*
- Mehle A** and Doudna JA. 2009. Adaptive strategies of the influenza virus polymerase for replication in humans. *Proc Natl Acad Sci U S A*. **106**:21312-21316. PMC2789757. *a "Top Story" for PNAS*
- Poole D, Yú S, Cai Y, Dinis JM, Müller MA, Jordan I, Friedrich TC, Kuhn JH, **Mehle A**. 2014. Influenza A virus polymerase is a hot spot for adaptive changes during experimental evolution in bat cells. *J Virol*. **88**:12572-85. PMC4248895
- Baker SF, Ledwith MP, **Mehle A**. 2018. Differential splicing of ANP32A in birds alters its ability to stimulate RNA synthesis by restricted influenza polymerase. *Cell Reports*. in press.

Virus:host interactions. During viral infection, a struggle exists between the host and the virus. Cells contain antiviral factors that selectively target and inhibit viral proteins and nucleic acids, whereas viruses neutralize these inhibitors and co-opt other cellular factors necessary for their replication. The balance between these opposing forces influences the outcome of a viral infection, which ranges from abortive infections and rapid clearance, to systematic subversion of the host cell and chronic viral infection, to highly pathogenic acute infections with occasional lethality. We characterized this nexus between the HIV-1 Vif protein, the cellular antiviral protein APOBEC3G, and the host ubiquitin machinery. We identified the E3 ubiquitin ligase exploited by Vif to degrade APOBEC3G and neutralize its antiviral activity. Subsequent analysis characterized the protein interfaces within these complexes, how interactions are regulated by phosphorylation, and discovered a highly unusual zinc-binding domain within Vif essential for its function. These results laid the foundation for rational drug discovery, for which we provided proof-of-principle. Elucidating the function of Vif and APOBEC3G, by our work and that of others, dramatically expanded our knowledge of virus:host interactions and the battle that occurs as retroviruses attempt to infect an unwilling host.

- Mehle A**, Goncalves J, Santa-Marta M, McPike M and Gabuzda D. 2004. Phosphorylation of a novel SOCS-box regulates assembly of the HIV-1 Vif-Cul5 complex that promotes APOBEC3G degradation. *Genes Dev*. **18**:2861-2866. PMC534646. *highlighted on the cover*
- Mehle A**, Strack B, Ancuta P, Zhang C, McPike M and Gabuzda D. 2004. Vif overcomes the innate antiviral activity of APOBEC3G by promoting its degradation in the ubiquitin-proteasome pathway. *J Biol Chem*. **279**:7792-7798.
- Mehle A**, Thomas ER, Rajendran KS and Gabuzda D. 2006. A zinc-binding region in Vif binds Cul5 and determines cullin selection. *J Biol Chem*. **281**:17259-17265.
- Mehle A**, Wilson H, Zhang C, Brazier AJ, McPike M, Pery E and Gabuzda D. 2007. Identification of an APOBEC3G binding site in human immunodeficiency virus type 1 Vif and inhibitors of Vif-APOBEC3G binding. *J Virol*. **81**:13235-13241. PMC2169136.

Full bibliography available here: <https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40317733>. Citation metrics are available at <http://scholar.google.com/citations?user=zi6ekpQAAAAJ&hl>.

D. Research Support

NIH NIAID R01 AI125271

PI = Andrew Mehle

07/01/2016-06/30/2021

“Regulation of the influenza virus polymerase”

Here we use biochemical approaches to understand how post-translational modifications control the influenza replication machinery.

NIH NIAID R01 AI125392

co-PI = Andrew Mehle

04/01/2017-03/31/2022

“Mechanisms of influenza transmission bottlenecks: impact on viral evolution”

This proposal defines intra- and interhost viral evolution and its impact on disease pathogenicity and transmission.

Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Disease

PI= Andrew Mehle

07/01/2017-08/30/2022

“Defining the functional landscape between intracellular pathogens and the host”

The award funds research into understanding how canonical anti-viral proteins can be subverted to function as pro-viral effectors during infection.

NIH NIAID R21 AI125897

PI = Andrew Mehle

07/01/2016-06/30/2018 (no cost extension to 5/31/2019)

“Identifying host factors and the mechanisms used to control influenza virus replication”

This exploratory grant funds studies to determine the mechanisms by which influenza virus exploits anti-viral factors and apoptosis to maximize viral replication.

Shaw Scientist Award

PI=Andrew Mehle

07/01/2012-06/30/2032

“Catching the flu: regulating and restricting the influenza virus polymerase”

The early career award supports our structural and genomic studies of influenza polymerase function.

Completed Research Support (last 3 years)

UW2020 Initiative

PI = Andrew Mehle

“Genomic Approaches to Identify Host Factors and Mechanisms that Modulate Pathogen Infections”

This project develops new genetic approaches to identify critical host factors exploited by pathogens during infection.

Roche Postdoctoral Fellowship

PI/Mentor=Andrew Mehle “Functional characterization of host factors controlling influenza polymerase activity”

American Lung Association Basic Research Grant RG-310016

PI=Andrew Mehle “Understanding the role of inflammation during influenza virus-mediated lung damage”

Mehle CV extended honors, awards, service and full bibliography

amehle@wisc.edu • mehlelab.com • [@mehlelab](https://twitter.com/mehlelab)

Positions and Honors

Positions

- 1998-2004 **Graduate student**, Laboratory of Dana Gabuzda, MD, Division of Medical Science, Harvard University. Ph.D. thesis title: "HIV-1 Vif: a novel SOCS-box protein that targets APOBEC3G for proteasomal degradation"
- 1999 **Teaching Assistant**, Harvard University, Division of Medical Science – Molecular Biology. Coordinated by Steve Buratowski, PhD.
- 2004-2005 **Postdoctoral fellow**, Laboratory of Dana Gabuzda, MD, Dana Farber Cancer Institute
- 2005-2011 **Postdoctoral fellow**, Laboratory of Jennifer Doudna, PhD, University of California, Berkeley
- 2011-current **Assistant Professor**, Department of Medical Microbiology & Immunology, University of Wisconsin-Madison

Honors

- 1993 Villanova University-NSF-HHMI Young Scholar
- 1996 HHMI Summer Undergraduate Research Program at the University of Pittsburgh
- 1994-1998 Presidential Scholar, Villanova University
- 1998 Phi Beta Kappa Honor Society Induction
- 1998 John McClain Award for outstanding academic performance in biology (highest rank in major), Villanova University
- 1998 Gregor Mendel Award for academic excellence in the sciences (highest rank in sciences), Villanova University
- 1998 *Summa cum laude*, Villanova University
- 1998-2001 National Science Foundation Predoctoral Fellowship
- 2004 Travel fellowship, 11th Conference on Retroviruses and Opportunistic Infections
- 2005 Travel fellowship, 12th Conference on Retroviruses and Opportunistic Infections
- 2006 Kirschstein National Research Service Award Postdoctoral Fellowship - NIGMS
- 2008 Travel fellowship, Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis
- 2009 Selected speaker, Gordon Research Conference: Viruses and Cells
- 2009 K99/R00 NIH Pathways to Independence Award – NIGMS
- 2010 Selected speaker, XIV International Conference on Negative Strand Viruses
- 2010 Selected speaker, Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis
- 2011 Invited speaker, Bay Area Symposia on Viruses
- 2011 Mirus Bio Research Award
- 2012 Shaw Scientist Awardee, James D. and Dorothy Shaw Fund, Greater Milwaukee Foundation
- 2012 New Investigator Awardee, Wisconsin Partnership Education and Research Committee
- 2012 Session Chair, Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis
- 2014 Selected speaker, Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis
- 2014 Session Chair, Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis
- 2014 Invited speaker, Society of Nuclear Medicine & Molecular Imaging national meeting
- 2015 Selected speaker, XVI International Conference on Negative Strand Viruses
- 2015 Session Convener and speaker, 34th American Society for Virology annual meeting
- 2016 Selected speaker, Viruses 2016, (Basel, CHE)
- 2016 "State of the Art" Lecturer, 35th American Society for Virology annual meeting
- 2016 Invited keynote speaker, 5th International Influenza Meeting (Munster, DEU)
- 2017 Selected speaker, Gordon Research Conference: Viruses and Cells
- 2017 Invited Lecturer, 14th Hong Kong University – Pasteur Virology Course (Hong Kong)
- 2017 Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Disease
- 2018 Invited Speaker, 10th Center of Emerging and Neglected Diseases Symposia, University of California Berkeley

Seminars and Presentations

- 2008: 27th American Society for Virology annual meeting
- 2009: Gordon Research Conference: Viruses and Cells
28th American Society for Virology annual meeting
- 2010: XIV International Conference on Negative Strand Viruses
Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis
29th American Society for Virology annual meeting
- 2011: Bay Area Symposia on Viruses
University of Wisconsin Madison Virology Seminar Series
- 2012: Loyola University Stritch School of Medicine
Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis session chair
Great Lakes Regional Center of Excellence annual meeting
- 2013: Promega Corporation
Montana State University
University of Wisconsin Raper Symposium
University of Wisconsin Madison Virology Seminar Series
- 2014: Keystone Symposia: Cell Biology of Virus Entry, Replication, & Pathogenesis (and session chair)
Society of Nuclear Medicine & Molecular Imaging national meeting
Ichan School of Medicine at Mount Sinai
- 2015: Stanford University School of Medicine
XVI International Conference on Negative Strand Viruses
University of Wisconsin La Crosse
34th American Society for Virology annual meeting
- 2016: Viruses 2016, (Basel, CHE)
“State of the Art” Lecturer at 35th American Society for Virology annual meeting
Invited keynote speaker, 5th International Influenza Meeting (Munster, DEU)
Merck (West Point, PA)
Options IX (Chicago, IL)
- 2017: University of Georgia
University of Texas Austin
Harvard Medical School
36th American Society for Virology annual meeting (session convener)
Invited Lecturer, 14th Hong Kong University – Pasteur Virology Course (Hong Kong)
Gordon Research Conference: Viruses and Cells
Montana State University
Duke University
- 2018: 10th Center of Emerging and Neglected Diseases Symposia, University of California Berkeley
University of Michigan
University of Texas Southwestern
University of Arkansas for Medical Sciences
University of Illinois
Dalhousie University
University of Vermont
17th Negative Strand Virus meeting (Verona, Italy)
37th American Society for Virology annual meeting (session convener)

Editorial Boards and service

- 2010- *Frontiers in Virology*, editorial board
- 2012 *Ad hoc* reviewer for ICTR
- 2013 *Ad hoc* reviewer for ICTR
- 2014 *Ad hoc* reviewer for ICTR
- 2015- *Viruses*, Associate Editor
- 2015-2017 *Journal of Virology*, editorial board
- 2015 *Ad hoc* reviewer for the Medical Research Council (MRC, UK)
- 2015 Selection committee for international 2016 *Viruses* travel award

- 2015 *Virology*, editorial board
 2016-2018 American Society for Virology Program Committee
 2016 *Ad hoc* reviewer for the Wellcome Trust (UK) and Wellcome Trust DBT India Alliance
 2016 *Ad hoc* reviewer for NIH Study Section – Virology A
 2017 *Ad hoc* reviewer for the Wellcome Trust (UK)
 2017 *Ad hoc* reviewer for the Agence Nationale de la Recherche (France)
 2017 *Ad hoc* reviewer for the Department of Defense Congressionally Directed Medical Research Programs
 2018 *Ad hoc* reviewer for NIH Topics in Virology – ZRG1 IDM-W (02)

Ad hoc reviewer for *ACS Chemical Biology, ACS Infectious Diseases, Bioessays, Cell Host and Microbe, Cell Reports, eLife, Frontiers in Virology, Journal of General Virology, Journal of Virology, Nature, Nature Communications, Nature Structure and Molecular Biology, PLOS One, PLOS Pathogens, PNAS, Scientific Reports, Virology, Viruses*

Full Bibliography—Publications since starting in Madison listed below beginning at #11 and available here: <https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40317733> and here scholar.google.com/citations?user=zi6ekpQAAAAJ&hl.

1. Gorry PR, Taylor J, Holm GH, **Mehle A**, Morgan T, Cayabyab M, Farzan M, Wang H, Bell JE, Kunstman K, Moore JP, Wolinsky SM and Gabuzda D. (2002) Increased CCR5 affinity and reduced CCR5/CD4 dependence of a neurovirulent primary human immunodeficiency virus type 1 isolate. *J Virol.* **76**:6277-6292. PMID:136234.
2. Ancuta P, Rao R, Moses A, **Mehle A**, Shaw SK, Luscinskas FW and Gabuzda D. (2003) Fractalkine preferentially mediates arrest and migration of CD16+ monocytes. *J Exp Med.* **197**:1701-1707. PMID: PMC2193954.
3. **Mehle A**, Goncalves J, Santa-Marta M, McPike M and Gabuzda D. (2004) Phosphorylation of a novel SOCS-box regulates assembly of the HIV-1 Vif-Cul5 complex that promotes APOBEC3G degradation. *Genes Dev.* **18**:2861-2866. PMID:534646.
- highlighted on the cover
4. **Mehle A**, Strack B, Ancuta P, Zhang C, McPike M and Gabuzda D. (2004) Vif overcomes the innate antiviral activity of APOBEC3G by promoting its degradation in the ubiquitin-proteasome pathway. *J Biol Chem.* **279**:7792-7798.
5. **Mehle A**, Thomas ER, Rajendran KS and Gabuzda D. (2006) A zinc-binding region in Vif binds Cul5 and determines cullin selection. *J Biol Chem.* **281**:17259-17265.
6. Gorry PR, Dunfee RL, Mefford ME, Kunstman K, Morgan T, Moore JP, Mascola JR, Agopian K, Holm GH, **Mehle A**, Taylor J, Farzan M, Wang H, Ellery P, Willey SJ, Clapham PR, Wolinsky SM, Crowe SM and Gabuzda D. (2007) Changes in the V3 region of gp120 contribute to unusually broad coreceptor usage of an HIV-1 isolate from a CCR5 Δ 32 heterozygote. *Virology.* **362**:163-178. PMID: PMC1973138.
7. **Mehle A**, Wilson H, Zhang C, Brazier AJ, McPike M, Pery E and Gabuzda D. (2007) Identification of an APOBEC3G binding site in human immunodeficiency virus type 1 Vif and inhibitors of Vif-APOBEC3G binding. *J Virol.* **81**:13235-13241. PMID: PMC2169136.
8. **Mehle A** and Doudna JA. (2008) An inhibitory activity in human cells restricts the function of an avian-like influenza virus polymerase. *Cell Host Microbe.* **4**:111-122. PMID: PMC2597520.
- selected as the "Featured Article"
9. **Mehle A** and Doudna JA. (2009) Adaptive strategies of the influenza virus polymerase for replication in humans. *Proc Natl Acad Sci U S A.* **106**:21312-21316. PMID: PMC2789757.
- a "Top Story" for *PNAS in the News*
10. **Mehle A** and Doudna JA. (2010) A host of factors regulating influenza virus replication. *Viruses.* **2**:566-573. PMID: PMC3185602.
11. Bhattacharya D, Ansari IH, **Mehle A** and Striker R. (2012) Fluorescence resonance energy transfer-based intracellular assay for the conformation of hepatitis C virus drug target NS5A. *J Virol.* **86**:8277-8286. PMID: PMC3421644.

12. **Mehle A**, Dugan VG, Taubenberger JK and Doudna JA. (2012) Reassortment and mutation of the avian influenza virus polymerase PA subunit overcome species barriers. *J Virol.* **86**:1750-1757. PMID: PMC3264373.
- selected as an "Article of Significant Interest"
13. **Mehle A** and McCullers JA. (2013) Structure and function of the influenza virus replication machinery and PB1-F2. 133-145. *Textbook of Influenza*, (eds. R Webster, A Monto, T Braciale, R Lamb). John Wiley & Sons, Ltd,
14. Tran V, Moser LA, Poole DS and **Mehle A**. (2013) Highly sensitive real-time in vivo imaging of an influenza reporter virus reveals dynamics of replication and spread. *J Virol.* **87**:13321-13329. PMID: PMC3838222.
15. Kirui J, Bucci MD, Poole DS and **Mehle A**. (2014) Conserved features of the PB2 627 domain impact influenza virus polymerase function and replication. *J Virol.* **88**:5977-5986. PMID: PMC4093881.
16. **Mehle A**. (2014) Unusual influenza A viruses in bats. *Viruses.* **6**:3438-3449. PMID: PMC4189031.
17. Poole DS, Yu S, Cai Y, Dinis JM, Muller MA, Jordan I, Friedrich TC, Kuhn JH and **Mehle A**. (2014) Influenza A virus polymerase is a site for adaptive changes during experimental evolution in bat cells. *J Virol.* **88**:12572-12585. PMID: PMC4248895.
18. Striker R and **Mehle A**. (2014) Inhibitors of peptidyl proline isomerases as antivirals in hepatitis C and other viruses. *PLoS Pathog.* **10**:e1004428. PMID:4223064.
19. Bhattacharya D, **Mehle A**, Kamp TJ and RC Balijepalli. (2015) Intramolecular ex vivo Fluorescence Resonance Energy Transfer (FRET) of Dihydropyridine Receptor (DHPR) β_{1a} Subunit Reveals Conformational Change Induced by RYR1 in Mouse Skeletal Myotubes. *PLoS One.* **10**:e0131399. PMID: PMC4482598.
20. Karlsson EA[#], Meliopoulos VA[#], Savage C, Livingston B, **Mehle A*** and Schultz-Cherry S*. (2015) Visualizing real-time influenza virus infection, transmission and protection in ferrets. *Nat Commun.* **6**:6378. PMID: PMC4366512. *co-corresponding authors
21. **Mehle A**. (2015) Fiat Luc: Bioluminescence Imaging Reveals In Vivo Viral Replication Dynamics. *PLoS Pathog.* **11**:e1005081. PMID: PMC4565549.
22. Mondal A, Potts GK, Dawson AR, Coon JJ and **Mehle A**. (2015) Phosphorylation at the homotypic interface regulates nucleoprotein oligomerization and assembly of the influenza virus replication machinery. *PLoS Pathog.* **11**:e1004826. PMID: 4395114.
23. Tran V, Poole DS, Jeffery JJ, Sheahan TP, Creech D, Yevtodiyeenko A, Peat AJ, Francis KP, You S and **Mehle A**. (2015) Multi-Modal Imaging with a Toolbox of Influenza A Reporter Viruses. *Viruses.* **7**:5319-5327. PMID: PMC4632381.
25. **Mehle A**. (2016) The Avian Influenza Virus Polymerase Brings ANP32A Home to Roost. *Cell Host and Microbe.* **19**:137-138.
26. Kirui J*, Tran V* and **Mehle A**. (2016) Host factors regulating the influenza virus replication machinery. *Influenza: Current Research*, Y. Tao and Q. Wang (ed.). Caister Academic Press, Norfolk, UK, pp. 77–100. *co-first authors
27. Kirui J, Mondal A, **Mehle A**. 2016 Ubiquitination up-regulates influenza virus polymerase function. *J Virol.* **90**:10906-10914. doi:10.1128/JVI.01829-16. PMID: PMC5110180.
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28. Karlsson EA, Hertz T, Johnson C, **Mehle A**, Krammer F, Schultz-Cherry S. (2016) Obesity Outweighs Protection Conferred by Adjuvanted Influenza. *mBio* **7**(4):e01144-16. PMID:4981723.
29. Czakó R, Vogel L, Lamirande EW, Bock KW, Moore IN, Ellebedy AH, Ahmed R, **Mehle A**, Subbarao K. 2017. *In Vivo* Imaging of Influenza Virus Infection in Immunized Mice. *mBio.* **8**:3 e00714-17. PMID: PMC5449660.
30. Karlsson EA[#], Meliopoulos VA[#], Tran Vy[#], Savage C, Livingston B, Schultz-Cherry S*, **Mehle A***. 2017. Measuring influenza virus infection using bioluminescent reporter viruses for *in vivo* imaging and *in vitro* replication assays. *Methods in Molecular Biology.* in press
31. Mondal A, Dawson AR, Potts GK, Freiburger EC, Baker SF, Moser LA, Bernard KA, Coon JJ, **Mehle A**. 2017. Influenza virus recruits host protein kinase C to control assembly and activity of its replication machinery. *eLife.* **6**:e26910. doi:10.7554/eLife.26910.
32. Baker SF, Ledwith MP, **Mehle A**. 2018. Differential splicing of ANP32A in birds alters its ability to stimulate RNA synthesis by restricted influenza polymerase. *Cell Reports.* in press.
33. Dawson AR, **Mehle A**. 2018. Flu's Cues: exploiting host post-translational modifications to direct the influenza virus replication cycle. *PLoS Pathog.* in press.

Full Research Support History

Current

NIH NIAID R01 AI125271

PI = Andrew Mehle

07/01/2016-06/30/2021

“Regulation of the influenza virus polymerase”

Here we use biochemical approaches to understand how post-translational modifications control the influenza replication machinery.

NIH NIAID R01AI125392

co-PI = Andrew Mehle

04/01/2017-03/31/2022

“Mechanisms of influenza transmission bottlenecks: impact on viral evolution”

This proposal defines intra- and interhost viral evolution and its impact on disease pathogenicity and transmission.

Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Disease

PI= Andrew Mehle

07/01/2017-08/30/2022

“Defining the functional landscape between intracellular pathogens and the host”

The award funds research into understanding how canonical anti-viral proteins can be subverted to function as pro-viral effectors during infection.

NIH NIAID R21 AI125897

PI = Andrew Mehle

07/01/2016-06/30/2018 (NCE until 5/31/2019)

“Identifying host factors and the mechanisms used to control influenza virus replication”

This exploratory grant funds studies to determine the mechanisms by which influenza virus exploits anti-viral factors and apoptosis to maximize viral replication.

Shaw Scientist Award

PI=Andrew Mehle

07/01/2012-06/30/2032

“Catching the flu: regulating and restricting the influenza virus polymerase”

The early career award supports our structural and genomic studies of influenza polymerase function.

Completed Research Support

UW2020 Initiative

PI = Andrew Mehle

“Genomic Approaches to Identify Host Factors and Mechanisms that Modulate Pathogen Infections”

This project develops new genetic approaches to identify critical host factors exploited by pathogens during infection.

ended 03/31/2017

Roche Postdoctoral Fellowship

PI/Mentor = Andrew Mehle

“Functional characterization of host factors the control influenza polymerase activity”

This award provides funds for a joint postdoctoral research in the lab of Dr. Mehle and Roche.

ended 1/14/17

American Lung Association Basic Research Grant RG-310016

PI=Andrew Mehle

“Understanding the role of inflammation during influenza virus-mediated lung damage”

ended 5/31/2016

K99GM88484/R00GM088484 Pathways to Independence + Administrative Supplement to Promote Diversity

PI=Andrew Mehle

“Regulating Influenza Polymerase Structure and Function by Phosphorylation”

ended 12/31/2015

New Investigator Program – Wisconsin Partnership Education and Research Committee (#2563)

PI =Andrew Mehle

“Dissecting Cross-Species Transmission of Influenza Virus”

ended 12/31/2014

Kirschstein National Research Service Award Postdoctoral Fellowship F32GM077931

PI=Andrew Mehle

“Structure And Activity Of A Cellular IRES Element”

ended 4/6/2009

Trainees

Lab Member	Position ^a	Dates	Degree (if applicable)
James Kirui	graduate student (CMB)	2011-2016	PhD
Daniel S. Poole	lab manager	2011-2015	
Cait Hamele	undergraduate research	2012-2014	BS
Chris Andrews	undergraduate research	Summer 2012, 2013	BS
Vy Tran	graduate student (MDTP) MBTG Trainee ^b	2013-2016	PhD
	Postdoctoral Fellow	2016-2017	
Arindam Mondal	Postdoctoral Fellow	2013-2016	
Katie Welsh	student hourly	2013-2014	BS
Michael Donohue	undergraduate research	Summer 2013	
Danielle Marie Smith	student hourly	2014-2015	BS
	undergraduate research	2015-2016	
Olivia Cottrell	undergraduate research	2014-2015	BS
Gloria Larson	graduate student (MDTP) VTG Trainee ^c	2014-current	in progress
Anthony Dawson	graduate student (CMB) VTG Trainee ^c	2014-current	in progress
Steven Baker	Postdoctoral Fellow MHD Trainee ^d	2015-current	
Jonathan Divito	student hourly	2016-2017	BS
	undergraduate research	2017-2018	
Grace Schaack	rotating student (MSTP)	Summer 2016	in progress
	MD/PhD Student (MSTP) ^e	2018-	
Katie Amato	graduate student (MDTP) MBTG Trainee ^b	2016-current	in progress
Mitch Ledwith	graduate student (CMB)	2016-current	in progress
Arianna Domek	student hourly	2017-2018	in progress
Christina Higgins	lab manager	2017-current	
Kaitlin Davis	Postdoctoral Fellow	2018-	
Cason King	Postdoctoral Fellow	2018-	
Collin Mowbray	student hourly	2018-	in progress

^aMDTP = Microbiology Doctoral Training Program; MSTP = Medical Scientist Training Program; CMB = Cell and Molecular Biology Graduate Program, ^bMolecular Biology Training Grant (T32GM07215), ^cVirology Training Grant (T32AI078985), ^dMicrobes in Health and Disease (T32AI055397), ^eRath 4-year Fellowship

Presentations by lab members

2012: James Kirui* (graduate student) – talk at the American Society for Virology annual meeting

2013: James Kirui (graduate student) and Vy Tran (graduate student) – posters at the American Society for Virology annual meeting

Vy Tran (graduate student) – talk in the University of Wisconsin Madison Virology Seminar Series

2014: Vy Tran (graduate student), Arindam Mondal (postdoc), Daniel Poole[#] (research scientist) – talks at the American Society for Virology annual meeting

James Kirui (graduate student) – University of Wisconsin Madison Virology Seminar Series

2015: Vy Tran (graduate student) – talk in the MDTP seminar series

Arindam Mondal (postdoc) – poster at the Gordon Research Conference: Viruses and Cells, University of Wisconsin Madison Virology Seminar Series, job interview for a faculty position at the India Institute of Technology

2016: Arindam Mondal (postdoc), Steve Baker (postdoc), Gloria Larson* (graduate student) and Tony Dawson* (graduate student) – talks at the American Society for Virology annual meeting; Gloria Larson (graduate student) gave a talk at the annual Wisc-e-sota UW/UMN virology symposia; Tony Dawson (graduate student) received the “best poster” prize at the Wisc-e-sota meeting

2017: Steve Baker* (postdoc), Gloria Larson (graduate student) and Tony Dawson (graduate student) – talks at the American Society for Virology annual meeting

Gloria Larson (graduate student) – Cell Symposia: Emerging and re-emerging viruses, poster

Steven Baker* – talk at 6th European Science Working group on Influenza (Latvia)

2018: Gloria Larson* (graduate student), Mitch Ledwith* and Tony Dawson* (graduate student) – talks at the American Society for Virology annual meeting

Steven Baker* – Keystone Symposia: Cells vs. Pathogens: Intrinsic Defenses and Counterdefenses (poster)

* travel award recipient, # UW Madison career development grant