

Philip J. Kranzusch

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Dana-Farber Cancer Institute
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Education

- HHMI / LSRF Postdoctoral Fellow 2012 – 2016
University of California–Berkeley, Berkeley, CA
Advisors: Dr. Jennifer A. Doudna and Dr. James M. Berger
- Doctorate in Virology 2007 – 2012
Harvard University, Cambridge, MA
Thesis: Architecture and regulation of the arenavirus polymerase complex
Advisor: Dr. Sean P.J. Whelan
- Bachelors of Science in Molecular Biology 2003 – 2006
University of Wisconsin–Madison, Madison, WI
Comprehensive Honors Degree
GPA: 3.8 / 4.0
Honors Thesis: Generation of a *Tomato spotted wilt virus* pseudo-virion in a yeast vector system

Research Experience

Harvard Medical School, Dana-Farber Cancer Institute
Assistant Professor of Microbiology & Immunobiology

2016 – Present

- My lab studies the cGAS-STING immunity pathway as a paradigm for RNA second messenger signaling, and we use biochemical, structural and cell biology approaches to provide a mechanistic rationale for how the cellular machinery synthesizes and responds to RNA signals. Our work reveals the surprising insight that human cGAS is part of a broad family of largely uncharacterized enzymes, and many RNA second messenger synthases remain to be discovered. In particular we are interested in the following questions:
 - Mechanistically, how do alternative STING conformational states control downstream responses: interferon, inflammation, and autophagy?
 - Can we target specific cGAS-STING signaling events for improved cancer immunotherapies and autoimmune disease treatments?
 - What are the product RNAs synthesized by uncharacterized cGAS-like enzymes, and how do they control innate immunity and developmental signaling?

University of California–Berkeley
HHMI / LSRF Postdoctoral Fellow

2012 – 2016

Advisors: Dr. Jennifer A. Doudna and Dr. James M. Berger

- Using a structural and biochemical approach, I determined the molecular and evolutionary basis of human 2'3' cGAMP signaling in the cGAS-STING response to cytosolic DNA
 - Determined the first structure of human cGAS (**Kranzusch et al., Cell Reports 2013**)
 - Discovered bacterial cGAS-like enzymes, and determined how human cGAS catalyzes formation of a unique 2'–5' phosphodiester bond (**Kranzusch et al., Cell 2014**)
 - Revealed human cGAMP has evolved to achieve universal signaling by exploiting a deeply conserved STING conformational intermediate (**Kranzusch et al., Molecular Cell 2015**)

Harvard Medical School
Virology Ph.D. Student

2007 – 2012

Advisor: Dr. Sean P.J. Whelan

- Developed a system to reconstitute arenavirus RNA synthesis and template interactions *in vitro*, and used single-molecule EM to determine the first low-resolution structural information for this class of viral polymerases (**Kranzusch et al., PNAS 2010**)
- Discovered a new role for the arenavirus matrix protein in regulating RNA synthesis by locking a polymerase–template complex (**Kranzusch et al., PNAS 2012**)

Field Research Assistant , Dzanga-Sangha, Central African Republic Collaboration with Dr. Peter D. Walsh and Dr. Beatrice H. Hahn Noninvasive sampling of pathogen diversity of wild gorilla populations	2008 – 2009
Research Technician , Washington University–St. Louis Advisor: Dr. Andrew Pekosz Investigated role of influenza A virus NS1 cellular localization in effector function	2007
Undergraduate Research Assistant , UW-Madison, Department of Virology and Entomology Advisor: Dr. Thomas L. German	2004 – 2006
Undergraduate Research Assistant , UW-Madison, Department of Genetics / USDA Advisor: Dr. Shelley H. Jansky	2003 – 2006
Independent Honors Research , Estación Biológica, CIEE – Monteverde, Costa Rica Advisor: Dr. Alan Masters	2005

Honors and Funding

- Hood Foundation Childhood Health Research Awards Program** – Fellow, 2017–2019
- Smith Family Awards Program for Excellence in Biomedical Research** – Fellow, 2016–2018
- Claudia Adams Barr Program for Innovative Cancer Research** – DFCI CIV Fellow, 2016–2018
Faculty awards based on independent research proposal
- Life Sciences Research Foundation Fellowship** – HHMI Fellow, 2013 – 2016
Postdoctoral fellowship award based on independent research proposal
- American Cancer Society Postdoctoral Fellowship** – *Declined award to accept LSRF*
- NIH Ruth Kirschstein Postdoctoral Fellowship** – *Declined award to accept LSRF*
- Bernard N. Fields Prize in Microbiology and Molecular Genetics**, 2012
Harvard Medical School research award based on graduate thesis
- Harold M. Weintraub Graduate Student Award Nomination** – Harvard DMS Nominee, 2011
Graduate research award nomination based on Ph.D. studies
- American Society of Microbiology Travel Award**, 2011
- American Society of Virology Travel Award**, 2009
Awards based on research abstract
- Member of the American Society of Virology**, 2008 – Present
- NSF Graduate Research Fellowship Program** – Honorable Mention, 2008 and 2009
Graduate award honorable mention based on research proposal and references
- UW-Madison Senior Honors Thesis Summer Research Grant**, 2006
- UW-Madison Comprehensive Honor's Program** (Letters and Science), 2004, 2005 and 2006
- UW-Madison Dean's List**, 2004, 2005 and 2006
Undergraduate awards based on academic record
- Byrd Scholarship Recipient, Wisconsin State All-Star Scholarship Recipient, Thrivent Scholarship Recipient**, 2003
Undergraduate scholarships based on academic performance and volunteering

Research Publications

21. Lee ASY, **Kranzusch PJ**, Doudna JA, Cate JD.
eIF3d is an mRNA cap-binding protein required for specialized translation initiation.
Nature. 2016; 536(7614), 96–99.
20. Kaya E*, Doxzen KW*, Knoll K, Wilson RC, Strutt SC, **Kranzusch PJ**, Doudna JA.
A bacterial argonate with non-canonical guide RNA specificity.
PNAS. 2016; 113(15), 4057–4062. (*Co-first author)
19. Nuñez JK*, Harrington LB*, **Kranzusch PJ**, Engelman AN, Doudna JA.
Foreign DNA capture during CRISPR–Cas adaptive immunity.
Nature. 2015; 527(7579), 535–538. (*Co-first author)
• Featured in *Nature Reviews Microbiology*
18. **Kranzusch PJ***, Wilson SC*, Lee ASY, Berger JM, Doudna JA, Vance RE.
Ancient origin of cGAS-STING reveals mechanism of universal 2',3' cGAMP signaling.
Molecular Cell. 2015; 59(6), 891–903. (*Co-first author)
• Cover Article

17. Lee ASY, **Kranzusch PJ**, Cate JD.
eIF3 targets cell proliferation mRNAs for translational activation or repression.
Nature. 2015; 522(7554), 111–114.
 - Featured in *Nature Structural & Molecular Biology*
16. **Kranzusch PJ**, Lee ASY, Wilson SC, Solovykh MS, Vance RE, Berger JM, Doudna JA.
Structure-guided reprogramming of human cGAS dinucleotide linkage specificity.
Cell. 2014; 158(5), 1011–1021.
 - Featured in *Chemistry & Biology*
 - Stanford/SSRL Science Highlight
15. Nuñez JK, **Kranzusch PJ**, Noeske J, Wright AV, Davies CW, Doudna JA.
Cas1–Cas2 complex formation mediates spacer acquisition during CRISPR-Cas adaptive immunity.
Nature Structural & Molecular Biology. 2013; 21(6), 528–534.
 - Featured in *Science*
14. Liu W, Li Y, Shaw KS, Learn GH, Plenderleith LJ, Malenke JA, Sundararaman SA, Ramirez MA, Crystal PA, Smith AG, Bibollet-Ruche F, Ayoub A, Locatelli S, Esteban A, Mouacha F, Guichet E, Butel C, Ahuka-Mundede S, Inogwabini BI, Ndjanga JB, Speede S, Sanz CM, Morgan DB, Gonder MK, **Kranzusch PJ**, Walsh PD, Georgiev AV, Muller MN, Piel AK, Stewart FA, Wilson ML, Pusey AE, Cui L, Wang Z, Färnert A, Sutherland CJ, Nolder D, Hart JA, Hart TB, Bertolani P, Gillis A, LeBreton M, Tafon B, Kiyang J, Djoko CF, Schneider BS, Wolfe ND, Mpoudi-Ngole E, Delaporte E, Carter R, Culleton RL, Shaw GM, Rayner JC, Peeters M, Hahn BH, Sharp PM.
African origin of malaria parasite *Plasmodium vivax*.
Nature Communications. 2013; 5, 3346.
13. **Kranzusch PJ**, Vance RE.
cGAS dimerization entangles DNA recognition.
Immunity. 2013; 39(6), 992–994. [Preview]
12. **Kranzusch PJ**, Lee ASY, Berger JM, Doudna JA.
Structure of human cGAS reveals a conserved family of second-messenger enzymes in innate immunity.
Cell Reports. 2013; 3, 1362–1368.
11. Morin B, **Kranzusch PJ**, Rahmeh AA, Whelan SP.
The polymerase of negative-strand RNA viruses.
Current Opinion in Virology. 2013; 3(2), 103–110. [Review]
10. **Kranzusch PJ** and Whelan SP.
Architecture and regulation of negative-strand viral enzymatic machinery.
RNA Biology. 2012; 9(7), 941–948. [Review]
9. **Kranzusch PJ** and Whelan SP.
Arenavirus Z protein controls viral RNA synthesis by locking a polymerase–promoter complex.
PNAS. 2011; 108(49), 19743–19748.
8. Carette JE*, Raaben MR*, Wong AC, Herbert AS, Obernosterer G, Mulherkar N, Kuehne AI, **Kranzusch PJ**, Griffin AM, Ruthel G, Cin PD, Dye JM, Whelan SP, Chandran K, Brummelkamp TR.
Ebola virus entry requires the cholesterol transporter Niemann-Pick C1.
Nature. 2011; 477(7364), 340–3. (*Co-first author)
 - Preview feature in *Nature Reviews Drug Discovery*
7. Radoshitzky SR, Warfield KL, Chi X, Dong L, Kota K, Bradfute SB, Gearhart JD, Retterer C, **Kranzusch PJ**, Misasi JN, Hogenbirk MA, Wahl-Jensen V, Volchkov VE, Cunningham JM, Jahrling PB, Aman MJ, Bavari S, Farzan M, Kuhn JH.
Ebola virus Δ -Peptide Immunoadhesins Inhibit Marburgvirus and Ebola virus Cell Entry.
Journal of Virology. 2011; 85(17), 8502–8513.
6. Rahmeh AA, Schenk AD, Danek EI, **Kranzusch PJ**, Liang B, Walz T, Whelan SP.
Molecular architecture of the vesicular stomatitis virus RNA polymerase.
PNAS. 2010; 107(46), 20075–20080.

5. **Kranzusch PJ**, Schenk AD, Rahmeh AA, Radoshitzky SR, Bavari S, Walz T, Whelan SP. Assembly of a functional Machupo virus polymerase complex. *PNAS*. 2010; 107(46), 20069–20074.
 4. Liu W, Li Y, Learn GH, Rudicell RS, Robertson JD, Keele BF, Ndjango JB, Sanz CM, Morgan DB, Locatelli S, Gonder MK, **Kranzusch PJ**, Walsh PD, Delaporte E, Mpoudi-Ngole E, Georgiev AV, Muller MN, Shaw GM, Peeters M, Sharp PM, Rayner JC, Hahn BH. Origin of the human malaria parasite *Plasmodium falciparum* in gorillas. *Nature*. 2010; 467(7314), 420–425.
 - Cover Article
 - Preview feature in *Nature*
 - Highlighted by BBC News
 3. Radoshitzky SR, Dong L, Chi X, Clester JC, Retterer C, Spurgers K, Kuhn JH, Sandwick S, Ruthel G, Kota K, Boltz D, Warren T, **Kranzusch PJ**, Whelan SP, Bavari S. Infectious Lassa virus, but not filoviruses, is restricted by BST-2/tetherin. *Journal of Virology*. 2010; 84(20), 10569–10580.
 2. Neel C, Etienne L, Li Y, Takehisa J, Rudicell RS, Bass IN, Moudindo J, Mebenga A, Esteban A, Van Heuverswyn F, Liegeois F, **Kranzusch PJ**, Walsh PD, Sanz CM, Morgan DB, Ndjango JB, Plantier JC, Locatelli S, Gonder MK, Leendertz FH, Boesch C, Todd A, Delaporte E, Mpoudi-Ngole E, Hahn BH, Peeters M. Molecular epidemiology of simian immunodeficiency virus infection in wild-living gorillas. *Journal of Virology*. 2009; 84(3), 1464–1476.
 1. Rahmeh AA, Li J, **Kranzusch PJ**, Whelan SP. Ribose 2'-O methylation of the vesicular stomatitis virus mRNA cap precedes and facilitates subsequent guanine-N-7 methylation by the large polymerase protein. *Journal of Virology*. 2009; 83(21), 11043–11050.
- Book: Kuhn JH (Co-editor and Contributor **Kranzusch PJ**). Filoviruses, A compendium of 40 years of epidemiological, clinical, and laboratory studies. *Archives of Virology, Supplement*. 2008; 20, 12–360.

Invited Research Talks (Excluding Faculty Interviews)

Nucleic Acid Sensing Pathways, Keystone Symposia, Dresden, Germany 2016

"Ancient cGAS-STING pathways reveal evolution of human innate immunity"

Harvard Medical School Special Seminar, Boston, MA 2015

"Ancient cGAS homologs reveal evolution of innate immune signaling"

USC-Keck School of Medicine, MMI Young Investigator Seminar Series, Pasadena, CA 2015

"Ancient cGAS homologs reveal evolution of innate immune signaling"

Center for RNA Systems Biology Meeting, Berkeley, CA 2014

"Structural and mechanistic homology between bacterial signaling and mammalian innate immunity"

Structure Supergroup Seminar, Berkeley, CA 2014

"Twisted evolution in cyclic dinucleotide specificity"

American Society of Virology Meeting, Madison, WI 2012

"Z controls arenavirus RNA synthesis by locking a polymerase-promoter complex"

This Week in Virology, Ep. 148, 2011

Virology podcast with Vincent Racaniello (<http://www.microbe.tv/twiv/twiv-148-retreating-into-harvard-virology/>)

American Society of Microbiology Conference on Viral Genome Replication, Banff, Canada 2011

"Architecture and assembly of a functional Machupo virus polymerase complex reveals new insight into arenavirus RNA synthesis"

National Research Centers of Excellence Meeting, Las Vegas, NV 2010

"An *in vitro* assay for promoter recognition in Machupo virus reveals the requirements for replication complex formation"

American Society of Virology Meeting, Vancouver, Canada 2009

"*In vitro* reconstitution of Ebola virus RNA modifying activities"

Teaching and Service

Harvard Medical School Cancer Immunology Course – Lecturer, 2016 (1 session)

Harvard Medical School Virology 200 – Discussion Leader, 2016 (3 sessions)

DFCI Cancer Immunology & Virology Retreat – Co-organizer 2017

Harvard Medical School Ph.D. Program in Virology Admissions Committee – Member, 2016–2017

DFCI Cancer Immunology Seminar Series – Co-Organizer 2016–2017

Harvard Medical School Ph.D. Program in Virology Preliminary Qualifying Exam – Examiner, 2016