Philip J. Kranzusch

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Assistant Professor
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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 — GPA: 3.8 / 4.0
  Comprehensive Honors Degree
  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 2008 – 2009
Collaboration with Dr. Peter D. Walsh and Dr. Beatrice H. Hahn
Noninvasive sampling of pathogen diversity of wild gorilla populations

Research Technician, Washington University–St. Louis 2007
Advisor: Dr. Andrew Pekosz
Investigated role of influenza A virus NS1 cellular localization in effector function

Undergraduate Research Assistant, UW-Madison, Department of Virology and Entomology 2004 – 2006
Advisor: Dr. Thomas L. German

Undergraduate Research Assistant, UW-Madison, Department of Genetics / USDA 2003 – 2006
Advisor: Dr. Shelley H. Jansky

Independent Honors Research, Estación Biológica, CIEE – Monteverde, Costa Rica 2005
Advisor: Dr. Alan Masters

Honors and Funding

Cancer Research Institute Clinic and Laboratory Integration Program Award – 2017–2019
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 Kirschtein 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
Byrd Scholarship Recipient, **Wisconsin State All-Star Scholarship Recipient**, **Thrivent Scholarship Recipient**, 2003
Undergraduate scholarships based on academic performance and volunteer service

Research Publications

20. Brejc K*, Bian Q*, Uzawa S, Wheeler BS, Anderson EC, King DS, **Kranzusch PJ**, Preston CG, Meyer BJ. Dynamic control of X-chromosome conformation and repression by a histone H4K20 demethylase. ***Cell***. 2017; *Advance Online Publication*, doi:10.1016/j.cell.2017.07.041. (*Co-first author)

19. Harrington LB*, Doxzen KW*, Ma E, Liu J, Knott GJ, Edraki A, Garcia B, Amrani N, Chen JS, Cofsky JC, **Kranzusch PJ**, Sontheimer EJ, Davidson AR, Maxwell KL, Doudna JA. A broad-spectrum inhibitor of CRISPR-Cas9. ***Cell***. 2017; *Advance Online Publication*, doi:10.1016/j.cell.2017.07.037. (*Co-first author)

18. 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.

17. Kaya E*, Doxzen KW*, Knoll K, Wilson RC, Strutt SC, **Kranzusch PJ**, Doudna JA. A bacterial argonaute with non-canonical guide RNA specificity. ***PNAS***. 2016; 113(15), 4057–4062. (*Co-first author)

16. 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*

15. **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

14. 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*

13. **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

12. 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*

11. Liu W, Li Y, Shaw KS, Learn GH, Plenderleith LJ, Malenke JA, Sundararaman SA, Ramirez MA, Crystal PA, Smith AG, Bibollet-Ruche F, Ayouba A, Locatelli S, Esteban A, Mouacha F, Guichet E, Butel C, Ahuka-Mundeke S, Inogwabini BI, Ndjango 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.

10. **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(5), 1362-1368.

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.
Ebolavirus Δ-Peptide Immunoadhesins Inhibit Marburgvirus and Ebolavirus 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.

Reviews and Commentaries

4. de Oliveira Mann CC, **Kranzusch PJ**.
cGAS conducts micronuclei DNA surveillance.
Trends in Cell Biology. 2017; *Advance Online Publication*, doi:10.1016/j.tcb.2017.08.007 [Preview]

3. **Kranzusch PJ**, Vance RE.
cGAS dimerization entangles DNA recognition.
Immunity. 2013; 39(6), 992–994. [Preview]

2. 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]

1. **Kranzusch PJ** and Whelan SP.
Architecture and regulation of negative-strand viral enzymatic machinery.
RNA Biology. 2012; 9(7), 941–948. [Review]

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)

Beth Israel Deaconess Medical Center – CVVR Seminar Series, Boston, MA 2017
American Society of Microbiology Meeting, New Orleans, LA 2017 – Invited Speaker
Brandeis University Biochemistry Department Seminar Series, Waltham, MA 2017
Nucleic Acid Sensing Pathways, Keystone Symposia, Dresden, Germany 2016
Harvard Medical School Microbiology & Immunobiology Special Seminar, Boston, MA 2015
USC-Keck School of Medicine, MMI Young Investigator Seminar Series, Pasadena, CA 2015
Center for RNA Systems Biology Meeting, Berkeley, CA 2014
Structure Supergroup Seminar, Berkeley, CA 2014
American Society of Virology Meeting, Madison, WI 2012
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
National Research Centers of Excellence Meeting, Las Vegas, NV 2010
American Society of Virology Meeting, Vancouver, Canada 2009

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