

Ralph Elliot Kleiner
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EDUCATION

May 2011 Harvard University, Cambridge, MA
Ph.D. in Chemistry

June 2005 Princeton University, Princeton, NJ
A.B. in Chemistry, *Cum Laude*
Certificate in Applied and Computational Mathematics

APPOINTMENTS

2017-present Associated Faculty in Molecular Biology, Princeton University
2016-present Assistant Professor of Chemistry, Princeton University
2014-2016 Revson Foundation Biomedical Fellow, The Rockefeller University
2011-2014 Damon Runyon Postdoctoral Fellow, The Rockefeller University

TRAINING

2011-2016
(Postdoctoral) The Rockefeller University, Laboratory of Chemistry and Cell Biology
Principal Investigator: Professor Tarun M. Kapoor
Investigated 'readers' of DNA-damage-associated histone 'mark' γ H2AX using chemical proteomics, biochemistry, and cell biology; developed methods for generating site-specifically modified tubulin and microtubules

2005-2011
(Ph.D.) Harvard University, Department of Chemistry and Chemical Biology
Principal Investigator: Professor David R. Liu
Developed strategies for the synthesis and selection of DNA-templated synthetic polymers and small molecules; discovered highly selective Src kinase inhibitors and the first physiologically active inhibitor of Insulin-Degrading Enzyme (IDE) from a DNA-templated macrocycle library

2002-2005
(A.B.) Princeton University, Department of Chemistry and Department of Chemical Engineering
Principal Investigators: Professor Michael H. Hecht, Professor Christodoulos Floudas
Conducted research on the design and biophysical analysis of *de novo* four-helix bundle proteins.

AWARDS

2019 NSF CAREER Award
2019 Alfred P. Sloan Foundation Research Fellowship
2017 Sidney Kimmel Foundation Scholar Award
2016 Damon Runyon Dale F. Frey Award for Breakthrough Scientists
2014 Revson Foundation Fellowship in Biomedical Science
2012 Damon Runyon Cancer Research Foundation Postdoctoral Fellowship
2001 National Merit Scholar

PUBLICATIONS

1. "Profiling dynamic RNA-protein interactions using small molecule-induced RNA editing" Seo, K.W.; **Kleiner, R.E.** *bioRxiv* (2022) <https://doi.org/10.1101/2022.06.30.498348>.
2. "Live-cell RNA imaging with metabolically incorporated fluorescent nucleosides" Wang, D.; Shalamberidze, A.; Arguello, A.E.; Purse, B.; **Kleiner, R. E.** *J. Am. Chem. Soc.* **144**, 14647-14656 (2022).
3. "Reactivity-dependent profiling of RNA 5-methylcytidine dioxygenases" Arguello, A.E.; Li, A.; Sun, X.; Eggert, T.W.; Mairhofer, E.; **Kleiner, R.E.** *Nat. Commun.* **13**, 4176 (2022).
4. "Chemical Method to Sequence 5-Formylcytosine on RNA" Li, A.; Sun, X.; Arguello, A.E.; **Kleiner, R.E.** *ACS Chem. Biol.* **17**, 3, 503-508 (2022).
5. "Interrogating the Transcriptome with Metabolically Incorporated Ribonucleosides" **Kleiner, R.E.** *Mol. Omics.* **17**, 833-41 (2021).
6. "Activity-based RNA-modifying enzyme probing reveals DUS3L-mediated dihydrouridylation" Dai, W.; Li, A.; Yu, N.J.; Nguyen, T.; Leach, T.W.; Wuhr, M.; **Kleiner, R.E.** *Nat. Chem. Biol.* **17**, 1178-1187 (2021).
7. "A neural m6AYthdf pathway is required for learning and memory in Drosophila" Kan, L.; Ott, S.; Joseph, B.; Park, E.S.; Dai, W.; **Kleiner, R.E.**; Claridge-Chang, A.; Lai, E.C. *Nat. Commun.* **12**, 1458 (2021).
8. "Mechanisms of Epitranscriptomic Gene Regulation" Seo, K.W.; **Kleiner, R.E.** *Biopolymers* doi: 10.1002/bip.23403 (2020).
9. "Cell- and Polymerase-Selective Metabolic Labeling of Cellular RNA with 2'-Azidocytidine" Wang, D.; Zhang, Y.; **Kleiner, R. E.** *J. Am. Chem. Soc.* **142**, 14417-14421 (2020).
10. "YTHDF2 Recognition of N¹-methyladenosine (m¹A)-modified RNA Is Associated with Transcript Destabilization" Seo, K. W.; **Kleiner, R. E.** *ACS Chem. Biol.* **15**, 132-139 (2020).
11. "High-throughput approaches to profile protein-RNA interactions" Nechay, M.; **Kleiner, R. E.** *Curr. Opin. Chem. Biol.* **54**, 37-44 (2019).
12. "In vitro selection with a site-specifically modified RNA library reveals the binding preferences of N⁶-methyladenosine (m⁶A) reader proteins" Arguello, A. E.; Leach, R. W.; **Kleiner, R. E.** *Biochemistry* **58**, 3386-3395 (2019).
13. "A Metabolic Engineering Approach to Incorporate Modified Pyrimidine Nucleosides into Cellular RNA" Zhang, Y.; **Kleiner, R. E.** *J. Am. Chem. Soc.* **141**, 3347-3351 (2019).
14. "A Photocrosslinking-Based RNA Chemical Proteomics Approach to Profile m⁶A-Regulated Protein-RNA Interactions" Arguello, A. E.; Srikumar, T.; **Kleiner, R. E.** *Curr. Protoc. Nucleic Acid Chem.* **75**, e69 (2018).
15. "Reading the RNA Code" **Kleiner, R. E.** *Biochemistry* **57**, 11-12 (2018).
16. "RNA Chemical Proteomics Reveals the N⁶-Methyladenosine (m⁶A)-Regulated Protein-RNA Interactome" Arguello, A. E.; DeLiberto, A. N.; **Kleiner, R. E.** *J. Am. Chem. Soc.* **139**, 17249-17252 (2017).

Publications before Princeton:

17. "A Chemical Proteomics Approach to Reveal Direct Protein-Protein Interactions in Living Cells" **Kleiner, R. E.**; Hang, L. E.; Molloy, K. R.; Chait, B. T.; Kapoor, T. M. *Cell Chem. Biol.* **25**, 110-120.e3 (2018).
18. "Structural and Biochemical Basis for Intracellular Kinase Inhibition by Src-specific Peptidic Macrocycles" Aleem, S. U.*; Georghiou, G.*; **Kleiner, R. E.***; Guja, K. E.; Craddock, B. P.; Lyczek, A.; Chan, A. I.; Garcia-Diaz, M.; Miller, W. T.; Liu, D. R.; Seeliger, M. A. *Cell Chem. Biol.* **23**, 1103-1112 (2016).
19. "Mutations in Human Tubulin Proximal to the Kinesin-Binding Site Alter Dynamic Instability at Microtubule Plus- and Minus-Ends" Ti, S. C.; Pamula, M. C.; Howes, S. C.; Duellberg, C.; Cade,

- N. I.; **Kleiner, R. E.**; Forth, S.; Surrey, T.; Nogales, E.; Kapoor, T. M. *Dev. Cell* **4**, 72-84 (2016).
20. "Chemical Proteomics Reveals a γ H2AX-53BP1 Interaction in the DNA Damage Response" **Kleiner, R. E.**; Verma, P.; Molloy, K. R.; Chait, B. T.; Kapoor, T. M. *Nat. Chem. Biol.* **10**, 807-814 (2015).
21. "Anti-Diabetic Activity of Insulin-Degrading Enzyme Inhibitors Mediated by Multiple Hormones" Maianti, J. P.; McFedries, A.; Foda, Z. H.; **Kleiner, R. E.**; Du, X.; Lessring, M.; Tang, W.; Charron, M. J.; Seeliger, M. A.; Saghatelian, A.; Liu, D. R.; *Nature* **511**, 94-98 (2014).
22. "Bumping Up Kinase Activity with an ATP-Derived Neo-Substrate" **Kleiner, R. E.**; Kapoor, T. M. *Cell* **154**, 716-718 (2013).
23. "Site-Specific Chemistry on the Microtubule Polymer" **Kleiner, R. E.**; Ti, S. C.; Kapoor, T. M. *J. Am. Chem. Soc.* **135**, 12520-12523 (2013).
24. "Highly specific, bisubstrate-competitive Src inhibitors from DNA-templated macrocycles" Georghiou, G.*; **Kleiner, R. E.***; Pulkoski-Gross, M.; Liu, D. R.; Seeliger, M. A. *Nat. Chem. Biol.* **8**, 366-374 (2012).
25. "Small-Molecule Discovery from DNA-Encoded Chemical Libraries" **Kleiner, R. E.***; Dumelin, C. E.*; Liu, D. R. *Chem. Soc. Rev.* **40**, 5707-5717 (2011).
26. "In Vitro Selection of a DNA-Templated Small-Molecule Library Reveals a Class of Macrocyclic Kinase Inhibitors" **Kleiner, R. E.**; Dumelin, C. E.; Tiu, G. C.; Sakurai, K.; Liu, D. R. *J. Am. Chem. Soc.* **132**, 11779-11791 (2010).
27. "An In Vitro Translation, Selection and Amplification System for Peptide Nucleic Acid" Brudno, Y.; Birnbaum, M. E.; **Kleiner, R. E.**; Liu, D. R. *Nat. Chem. Biol.* **6**, 148-155 (2010).
28. "DNA-Templated Polymerization of Side-Chain-Functionalized Peptide Nucleic Acid Aldehydes" **Kleiner, R. E.**; Brudno, Y.; Birnbaum, M. E.; Liu, D. R. *J. Am. Chem. Soc.* **130**, 4646-4659 (2008).
29. "An Intein-Based Genetic Selection Enables Construction of a High-Quality Library of Binary Patterned De Novo Sequences" Bradley, L. H.; **Kleiner, R. E.**; Wang, A. F.; Hecht, M. H.; Wood, D.W. *Protein Eng. Des. Sel.* **18**, 201-207 (2005).

INVITED SEMINARS

1. Department of Chemistry, Yale University, April 2023, New Haven, CT.
2. Department of Chemistry, University of California, Davis, April 2023, Davis, CA
3. Department of Chemistry, University of California, Berkeley, February 2023, Berkeley, CA.
4. Department of Chemistry, University of Chicago, January 2023, Chicago, IL.
5. Department of Chemistry, University of Pennsylvania, January 2023, Philadelphia, PA.
6. Department of Chemistry, Columbia University, December 2022, New York, NY.
7. Chemical Biology Program, Memorial Sloan Kettering Cancer Center, December 2022, New York, NY.
8. Department of Chemistry, Stanford University, November 2022, Palo Alto, CA
9. Molecular Discovery Seminar Series, National Cancer Institute, November 2022, Frederick, MD.
10. Department of Biochemistry, University of Colorado, Boulder, November 2022, Boulder, CO.
11. Department of Chemistry, Harvard University, October 2022, Cambridge, MA.
12. Department of Pharmacological Sciences, Stony Brook University, October 2022, Stony Brook, NY.
13. Department of Chemistry, The Scripps Research Institute, October 2022, San Diego, CA.
14. Department of Chemistry and Biochemistry, University of California, San Diego, October 2022, San Diego, CA.
15. Department of Chemistry, Boston College, September 2022, Chestnut Hill, MA
16. Department of Chemistry, New York University, September 2022, New York, NY
17. Department of Chemistry, Cornell University, May 2022, Ithaca, NY
18. Department of Chemistry, University of California, Irvine, April 2022, Irvine, CA

19. Department of Materials Science and Chemical Engineering, State University of New York, Stony Brook, March 2022, virtual seminar
20. Department of Chemistry, University of Michigan, February 2022, Ann Arbor, MI
21. RNA Institute, University of Albany, February 2022, virtual seminar
22. Epigenetics Consortium, University of Minnesota, April 2021, virtual seminar
23. Department of Chemistry, University of the Sciences, January 2021, virtual seminar
24. Emerging Science and Innovation, Pfizer, January 2021, virtual seminar
25. Department of Pharmacology, Physiology and Neuroscience, Rutgers New Jersey Medical School, May 2020 (rescheduled), Newark, NJ
26. Cancer Pharmacology Research Program, Rutgers Cancer Institute of New Jersey, November 2019, New Brunswick, NJ
27. Chemical Biology Interface Summer Retreat, Perelman School of Medicine, University of Pennsylvania, July 2019, Philadelphia, PA
28. Center for Advanced Biotechnology and Medicine, Rutgers University, December 2018, Piscataway, NJ

CONFERENCE PRESENTATIONS

1. Oral Presentation. *Telluride Science Research Center Workshop on Nucleic Acid Chemistry*, July 2022, Telluride, CO.
2. Oral Presentation. *Gordon Research Conference on Bioorganic Chemistry*, June 2022, Andover, NH
3. Oral Presentation. *Symposium on Chemistry of Nucleic Acid Components*, June 2022, Cesky Krumlov, Czech Republic.
4. Oral Presentation. *American Society for Biochemistry and Molecular Biology*, April 2022, Philadelphia, PA.
5. Oral Presentation. *American Chemical Society National Meeting*, March 2022, Hybrid Meeting
6. Oral Presentation. *Pacificchem*, December 2021, Virtual Meeting
7. Oral Presentation. *Discovery on Target*, September 2021, Boston, MA
8. Oral Presentation. *Discovery on Target*, September 2020, Virtual Meeting
9. Oral Presentation. *American Chemical Society National Meeting*, August 2020, Virtual Meeting
10. Oral Presentation. *Symposium on Chemistry of Nucleic Acid Components*, June 2020 (rescheduled), Cesky Krumlov, Czech Republic.
11. Oral Presentation. *Gordon Research Conference on Bioorganic Chemistry*, June 2020 (rescheduled), Andover, NH
12. Oral Presentation. *American Chemical Society National Meeting*, August 2019, San Diego, CA
13. Oral Presentation. *Gordon Research Conference on Nucleosides, Nucleotides and Oligonucleotides*, June 2019, Newport, RI.
14. Oral Presentation. *Annual Meeting of the RNA Society*, June 2019, Krakow, Poland.
15. Oral Presentation. *Gordon Research Conference on RNA Editing*, March 2019, Lucca, Italy.
16. Oral Presentation. *American Chemical Society National Meeting*, August 2018, Boston, MA.

ISSUED U.S. PATENTS

1. "Macrocyclic kinase inhibitors and uses thereof" Liu, D. R.; **Kleiner, R. E.** U.S. Patent No. 8,975,232
2. "Macrocyclic insulin-degrading enzyme (IDE) inhibitors and uses thereof" Liu, D. R.; Maianti, J. P.; Saghatelian, A.; **Kleiner, R. E.** U.S. Patent No. 9,610,322

TEACHING EXPERIENCE

Spring 2022 Instructor, CHM 541: Chemical Biology II, Princeton University

Curriculum Vitae, Ralph E. Kleiner

Fall 2021 Instructor, CHM 538: Topics in Biological Chemistry, Princeton University
Fall 2020 Instructor, CHM 538: Topics in Biological Chemistry, Princeton University
Spring 2020 Instructor, CHM 541: Chemical Biology II, Princeton University
Fall 2019 Instructor, CHM 538: Topics in Biological Chemistry, Princeton University
Spring 2019 Instructor, CHM 541: Chemical Biology II, Princeton University
Fall 2018 Instructor, CHM 538: Topics in Biological Chemistry, Princeton University
Spring 2018 Instructor, CHM 541: Chemical Biology II, Princeton University
Fall 2017 Instructor, CHM 538: Topics in Biological Chemistry, Princeton University
Spring 2017 Instructor, CHM 541: Chemical Biology II, Princeton University
Fall 2015 Teaching Fellow, TPCB Principles of Chemical Biology, The Rockefeller University
Spring 2006 Teaching Fellow, Chem 27: Organic Chemistry of Life, Harvard University
Fall 2006 Teaching Fellow, Chem 280: Macromolecular Structure and Function, Harvard University

SERVICE ACTIVITIES

2022 *Ad hoc* member, NIH Synthetic and Biological Chemistry A (SBCA) Study Section
2021-2022 Bioengineering Initiative Faculty Search Committee, Princeton University
2020- Graduate Studies Committee, Department of Chemistry, Princeton University
2019- Committee on Examinations and Standing, Princeton University
2012 Planning Committee for Anderson Cancer Symposium, The Rockefeller University
2004-2005 Committee on the Course of Study, Princeton University
2004-2005 President's Award for Distinguished Teaching Selection Committee, Princeton University

CURRENT SUPPORT

Rutgers Cancer Institute-Princeton Ludwig Branch Pilot award

Kleiner (PI) 6/14/2022-6/13/2023

"Cancer-associated epitranscriptomic reprogramming through RNA dihydrouridine modification"

National Science Foundation CAREER MCB-1942565

Kleiner (PI) 12/15/2019-11/30/2024

"CAREER: A Chemoproteomic Strategy to Decipher Epitranscriptomic Pyrimidine Modifications"

The goal of this proposal is to study epitranscriptomic pyrimidine modifications using metabolic labeling and chemoproteomics.

National Institutes of Health R01 GM132189

Kleiner (PI) 4/1/2019-3/31/2024

"Chemical Approaches to Illuminate the Epitranscriptome"

The goal is to study post-transcriptional RNA methylation and its link to the cellular stress response.

Gordon and Betty Moore Foundation

Kleiner (Co-PI) 1/1/2019-12/31/2022

"Electron Transfer Through Entrained DNA Strands"

The goal is to study charge transfer in DNA in cells and to develop ways to attain vibrational synchronization through passive and activating locking of the key vibrations along a chromophore chain.

COMPLETED SUPPORT

Princeton Catalysis Initiative

Kleiner (Co-PI) 7/1/2020-6/30/2022

Curriculum Vitae, Ralph E. Kleiner

“Profiling the RNA modification landscape of SARS-CoV-2”

The goal is to analyze post-transcriptional RNA modifications in the SARS-CoV-2 genome and study the role of these modifications in the viral life cycle.

Sloan Foundation Research Fellowship

Kleiner (PI) 9/15/2019-9/14/2021

“Chemical Approaches to Illuminate Nucleic Acid Biology”

Princeton Catalysis Initiative

Kleiner (Co-PI) 7/1/2019-6/30/2021

“Mapping the RNA epitranscriptome using nanopore sequencing and machine learning”

The goal is to develop a direct strategy for RNA modification sequencing using biological nanopores, synthetic RNA libraries, and machine learning.

Princeton Catalysis Initiative

Kleiner (Co-PI) 7/1/2018-6/30/2020

The goals are to develop modified trans-splicing ribozyme constructs for the site-specific installation of post-transcriptional modifications into viral RNA genomes and apply this methodology to study the role of RNA modifications in the viral life cycle.

Princeton University Innovation Fund for New Ideas in the Natural Sciences

Kleiner (PI) 04/01/2018-3/31/2020

“A ‘turn-on’ fluorescent probe to visualize interactions of the anti-cancer drug cisplatin with cellular RNA”

The goal is to examine platinum-modified RNA in living cells using reaction-sensitive fluorescent Pt probes compounds.

Sidney Kimmel Foundation Scholar Award

Kleiner (PI) 07/01/2017-06/30/2019

“Chemical Approaches to Investigate RNA Modifications in Cancer Progression and Therapy”

Damon Runyon Cancer Research Foundation Dale F. Frey Award for Breakthrough Scientists

Kleiner (PI) 09/01/2016-08/31/2018

“Using Chemistry to Illuminate DNA and RNA Damage Processes in Cells”