RICHARD L. FROCK, PhD

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THE FROCK LAB DA BREAKPOINT MAPPING website: <u>frocklab.stanford.edu</u> social media: <u>twitter.com/FrockLab</u>

EDUCATIONAL BACKGROUND

12/18/2009 - Ph.D. in Biochemistry, University of Washington 05/20/2001 - B.A. in Biochemistry, Vassar College

PROFESSIONAL APPOINTMENTS

01/01/2018- Assistant Professor

present Stanford University School of Medicine, Stanford, CA Department of Radiation Oncology, Division of Radiation and Cancer Biology

02/01/2010- Research Fellow

12/15/2017 Harvard Medical School, Department of Genetics, Boston, MA
 Boston Children's Hospital, Program in Cellular and Molecular Medicine, Boston, MA
 Mentor: Frederick W. Alt
 Research Focus: Mechanisms of DSB repair and chromosomal translocations during V(D)J
 and Class Switch Recombination using Linear Amplification-Mediated High-Throughput
 Genome-wide Translocation Sequencing (LAM-HTGTS)

2001-2009 Predoctoral Research Associate
 University of Washington, Department of Biochemistry, Seattle, WA
 Mentors: Brian K. Kennedy & Steve D. Hauschka
 Committee members: Richard D. Palmiter, David R. Morris, Stephen J. Tapscott, Edith
 H. Wang, Stephen M. Schwartz
 Dissertation: A Role for A-Type Nuclear Lamins in the Homeostasis of Striated Muscle and the Immune System

HONORS AND AWARDS

- 2019 V Scholar, V Foundation for Cancer Research
- 2019 Early Career Investigator Travel Award, RRS
- 2019 Radiation Research Foundation Career Development Award
- 2014 Allergic and Immunologic Disease Postdoctoral National Research Service Award
- 2014 Boston Children's Hospital PCMM Scientific Retreat Poster Award
- 2011 Northwest Genomic Engineering Consortium Travel Award
- 2011 Immune Disease Institute Scientific Retreat Poster Award
- 2010 Cancer Immunology Postdoctoral National Research Service Award
- 2008 North American Vascular Biology Organization Vasculata Poster Award
- 2006 Cardiovascular and Pathology Predoctoral National Research Service Award
- 2006 Schultz Cancer Biology Travel Award

PUBLICATIONS

PEER-REVIEWED ORIGINAL RESEARCH PUBLICATIONS (20 total)

20. Lattanzi A, Camarena J, Lahiri P, Segal H, Srifa W, Vakulskas CA, *Frock RL, Kenrick J, Lee C, Talbott N, Skowronski J, Cromer MK, Charlesworth CT, Bak RO, Mantri S, Bao G, DiGiusto D, Tisdale J, Wright JF, Bhatia N, Roncarolo MG, Dever DP, Porteus MH. Development of β-globin gene correction in human hematopoietic stem cells as a potential durable treatment for sickle cell disease. <u>Science Translational Medicine</u>. 2021 Jun 16;13(598):eabf2444. DOI: 10.1126/scitranslmed.abf2444.

*Conception and design, data acquisition, data analysis and interpretation, supervision, funding, commented on manuscript

- 19. Liang Z, Kumar V, Le Bouteiller M, Zurita J, Kenrick J, Lin SG, Lou J, Hu J, Ye AY, Boboila C
 ◆Alt FW, ◆Frock RL. Ku70 suppresses alternative end-joining in G1-arrested progenitor B cells.
 <u>Proc. Natl. Acad. Sci. USA.</u> 2021 May 25;118 (21):e2103630118. PMC8166026.
 Featured as Publication of the Week in <u>SCIENCE IN THE CITY</u>
- Wang Q, Liu J, Janssen JM, Le Bouteiller M, *Frock RL, Gonçalves MAFV. Precise and broad scope genome editing based on high-specificity Cas9 nickases. <u>Nucleic Acids Research</u>. 2021 Jan 25;49(2):1173-1198. PMC7826261.

*Conception and design, data interpretation, supervision, commented on manuscript and revision

 Chen X, Tasca F, Wang Q, Liu J, Janssen, Brescia MD, Bellin M, Szuhai K, Kenrick J, *Frock RL, Gonçalves MAFV. Expanding the editable genome and CRISPR-Cas9 versatility using DNA cutting-free gene targeting based on in trans paired nicking. <u>Nucleic Acids Research</u>. 2020 Jan 24;48(2):974-995. PMC6954423.

*Conception and design, data acquisition, data analysis and interpretation, supervision, commented on manuscript and revision

 Layer JV, Cleary J, Brown AJ, Stevenson KE, Morrow SN, Scoyk AV, Blasco RB, Karaca E, Meng F, *Frock RL, Tivey T, Kim SS, Fuchs H, Chiarle R, Alt FW, Roberts SA, Weinstock DM, Day TA. Parp3 promotes long-range end-joining in murine cells. *Proc Natl Acad Sci U S A*. 2018 Oct 2;115(40):10076-10081. PMC6176633.

*Designed and performed experiments, analyzed sequencing data, commented on manuscript

 Willis NA, *Frock RL, Menghi F, Duffey EE, Panday A, Camacho V, Hasty EP, Liu ET, Alt FW, Scully R. Mechanism of tandem duplication formation in BRCA1-mutant cells. *Nature*. 2017 Nov 30;551(7682):590-595. PMC5728692.

*Designed and performed experiments, analyzed sequencing data, commented on manuscript

14. Paulsen BS, Mandal PK, *Frock RL, Boyraz B, Yadav R, Gutierrez-Martinez P, Ebina W, Fasth A, Talkowski ME, Agarwal S, Alt FW, Rossi, DJ. Ectopic expression of RAD52 and dn53BP1 improves homology-directed repair during CRISPR/Cas9-mediated genome editing. <u>Nature Biomedical</u> <u>Engineering</u>. 2017 Nov;1(11):878-888. PMC6918705. Featured in Nature Biomedical Engineering.

*Designed and performed experiments, analyzed sequencing data, commented on manuscript

+Kumar V, Alt FW, +Frock RL. PAXX and XLF DNA repair factors are functionally redundant in joining DNA breaks in a G1-arrested progenitor B-cell line. *Proc Natl Acad Sci U S A.* 2016 Sep 20;113(38):10619-24. PMC5035843. Briefly highlighted in *Cell Reports* Facebook post 10/6/2016

 +Zhao L, +Frock RL, Du Z, Hu J, Chen L, Krangel MS, Alt FW. Orientation-specific RAG activity in chromosomal loop domains contributes to Tcrd V(D)J recombination during T cell development. *Journal of Experimental Medicine*. 2016 Aug 22;213(9):1921-1936. PMC4995090.

- Hu J, Meyers RM, Dong J, Panchakshari RA, ♦Alt FW, ♦Frock RL. Detecting DNA double- stranded breaks in mammalian genomes by linear amplification-mediated high-throughput genome-wide translocation sequencing. <u>Nature Protocols</u>. 2016 May;11(5):853-71. PMC4895203
- Hu J, Zhang, Y, Zhao L, Frock RL, Du Z, Meyers RM, Meng FL, Schatz DG, Alt FW. Chromosomal loop domains direct the recombination of antigen receptor genes. <u>*Cell.*</u> 2015 Nov 5;163(4):947-59. PMC4660266 Featured in *Trends in Molecular Medicine*
- Frock RL, +Hu J, Meyers RM, Ho YJ, Kii E, Alt FW. Genome-wide detection of DNA doublestranded breaks induced by engineered nucleases. <u>Nature Biotechnology</u>. 2015 Feb;33(2):179-86. PMC4320661 Featured in Nature Biotechnology and Molecular Cell
- Frock RL, + Chen SC, Dai DF, Pak DN, Frett E, Lau C, Brown C, Wang Y, Rabinovitch PS, Santana LS, Ladiges WC, Worman HJ, Kennedy BK. Cardiomyocyte-specific expression of lamin A improves cardiac function in *Lmna-/-* mice. <u>PLoS One.</u> 2012 7(8):e42918. PMC3419749.
- *Chiarle R, *Zhang Y, *Frock RL, *Lewis SM, Molinie B, Ho YJ, Myers DR, Choi VW, Compagno M, Malkin DJ, Neuberg D, Monti S, Giallourakis CC, Gostissa M, Alt FW. Genome-wide Translocation Sequencing Reveals Mechanisms of Chromosome Breaks and Rearrangements in B Cells. <u>Cell.</u> 2011 Sep 30;147(1):107-19. PMC3186939 Featured in *Cell* and *Nature Reviews Genetics*
- 6. +Hale JS, +Frock RL, Mamman SA, Fink PJ, Kennedy BK. Cell-extrinsic defective lymphocyte development in *Lmna-/-* mice. <u>*PLoS One.*</u> 2010 5(4):e10127. PMC2853576.
- #Frock RL, Kudlow BA, Evans AM, Jameson SA, Hauschka SD, Kennedy BK. Lamin A/C and emerin are critical for skeletal muscle satellite cell differentiation. <u>*Genes Dev.*</u> 2006 20(4): 486-500. PMC1369050.
- Johnson BR, Nitta RT, Frock RL, Mounkes L, Barbie DA, Stewart CL, Harlow E, Kennedy BK. Atype lamins regulate retinoblastoma protein function by promoting subnuclear localization and preventing proteasomal degradation. <u>Proc Natl Acad Sci U S A</u>. 2004 101(26): 9677-9682. PMC470734.
- Barbie DA, Kudlow BA, Frock R, Zhao J, Johnson BR, Dyson N, Harlow E, Kennedy BK. Nuclear reorganization of mammalian DNA synthesis prior to cell cycle exit. <u>Mol Cell Biol.</u> 2004 24(2): 595-607. PMC343811.
- #Deng WM, Schneider M, Frock R, Castillejo-Lopez C, Gaman EA, Baumgartner S, Ruohola-Baker H. Dystroglycan is required for polarizing the epithelial cells and the oocyte in Drosophila. <u>Development.</u> 2003 130(1): 173-184.
- 1. Pfennig BW and **Frock RL**. The use of molecular modeling and VESPR theory in the undergraduate curriculum to predict the three-dimensional structure of molecules. *J Chem Ed* 1999 7: 1018- 1022.

✦Co-first author; **♦**Co-corresponding author; #Journal cover

PEER-REVIEWED ARTICLES (OTHER - 2 total)

- Frock RL, Sadeghi C, Meng J, Wang JL. DNA End Joining: G0-ing to the Core. <u>Biomolecules</u> 2021 Oct 9;11(10):1487. PMC8533500 (corresponding author)
- 1. Smith ED, Kudlow BA, **Frock RL**, Kennedy BK. A-type nuclear lamins, progerias and other degenerative disorders. <u>Mech Ageing Dev.</u> 2005 126(4): 447-460. DOI: 10.1016/j.mad.2004.10.006

BOOK CHAPTERS (1 total)

 + Frock RL, + Hu J, Alt FW. Mechanisms of recurrent chromosomal translocations. In Janet Rowley, Terence Rabbitts, & Michelle LeBeau (Eds.) <u>Chromosomal Translocations and</u> <u>Genome Rearrangements in Cancer</u>. Switzerland: Springer International Publishing, 2015. Pp. 27-51. DOI: 10.1007/978-3-319-19983-2

+Co-first author

PUBLISHED MEETING ABSTRACTS (5 total)

- Barghouth PG, Ollivier J, Montay-Gruel P, Loo BW, Vozenin M, Limoli C, Frock RL. 2021. Ultra-high dose rate (FLASH) irradiation does not alter microhomology mediated recombination under varying oxygen tension when compared to standard clinical dose rates. *Clin Cancer Res* 27:8s PO-012. DOI: <u>10.1158/1557-3265.RADSCI21-PO-012</u>
- Frock RL, Kumar V, Liang Z, Zurita J, Du Z, Lin SG, Boboila C, Alt FW. 2019 Ku70 suppresses alternative end-joining in G1-arrested progenitor B cells. *Cancer Res* 79:13s 1745. DOI: <u>10.1158/1538-7445.AM2019-1745</u>
- Vanoli F, Ito S, Frock RL, Alt FW, Moynahan M, Jasin M, 2017. PARP inhibitor Olaparib induces genomic instability in normal mammalian cells. *Mol Cancer Res* 15:4s B37. DOI: <u>10.1158/1557-3125.DNAREPAIR16-B37</u>
- Mandal PK, Paulsen BS, Frock RL, Gutierrez-Martinez P, Ebina W, Agarwal S, Alt FW, Rossi DJ. 2016. Transient Manipulation of DNA Damage Repair Pathway Choice Improves Homology-Directed Repair During CRISPR/Cas9-Mediated Genome Editing. *Mol Ther* 24:1s pS227 568. DOI: <u>10.1016/S1525-0016(16)33376-7</u>
- Hu J, Zhang Y, Zhao L, Frock RL, Du Z, Meyers RM, Meng FL, Schatz DG, Alt FW. 2016. Topologically associated domains genome-wide restrict the off-target activity of recombination activating gene 1/2 endonuclease. *Cancer Immunol Res* 4:1s A180. DOI: <u>10.1158/2326-6074.CRICIMTEATIAACR15-A180</u>

EDITORIAL SERVICE

- <u>Review Editor (2021-present</u>)
 - o Genome Editing in Blood Disorders, Frontiers in Genome Editing
 - o Genome Organization and Dynamics, Frontiers in Molecular Biosciences
- <u>Ad hoc Reviewer (2018-present):</u>
 - Nature Structural & Molecular Biology, Nature Protocols, Nucleic Acids Research, Nature Communications, PLoS ONE, Trends in Cancer
 - Frontiers in Genetics (Public Reviewer): Libri A, Marton T, Deriano L. The (lack of) DNA double-strand break repair pathway choice during V(D)J recombination. 2022 doi: 10.3389/fgene.2021.823943
- <u>Review Editor, B cell Biology, Frontiers in Immunology (2018-present; Public Reviewer below):</u>
 - Corcoran AE, Rogers CH, Mielczarek O. Dynamic 3D locus organisation and its drivers underpin immunoglobulin recombination. 2020 <u>doi: 10.3389/fimmu.2020.633705</u>
 - Smith AL, Scott JNF, Boyes J. The ESC: The Dangerous By-Product of V(D)J. 2020 <u>doi:</u> <u>10.3389/fimmu.2019.01572</u>
 - Safonova Y and Pevzner PA. De novo inference of diversity genes and analysis of noncanonical V(DD)J recombination in immunoglobulins. 2019 <u>doi:</u> <u>10.3389/fimmu.2019.00987</u>

PATENTS

"Methods relating to the detection of recurrent and non-specific double strand breaks in the genome" Alt FW, **Frock RL**, Hu J, Meyers RM WO2016081798, USPTO 15/527,790 Patent No.10640820 (5/5/2020).

UNIVERSITY ADMINISTRATIVE SERVICE

PhD Thesis Committee

2020	Defense Chair, Tony Gao (Qi)
2019-present	Member, Maxim Markovic (Nolan)
2019	Defense Chair, Michael Debreuil (Bassik)
2019	Defense Chair, Zintis Inde (Dixon)

Department Radical Seminar Speaker Series (Virtual)2021-presentSpeaker organizer and host

SERVICE TO PROFESSIONAL ORGANIZATIONS

MEMBERSHIPS

- Radiation Research Society (2019-present)
- American Association for Cancer Research (2018-present)
- American Association for the Advancement of Science (2010-present)
- Society for Developmental Biology (2009-present)
- American Society for Cell Biology (2002-present)

COMMITTEE SERVICE

- <u>AACR Annual Meeting 2021</u>. April 9-14, 2021, Virtual— Chair, DNA Damage and Repair Section, Molecular and Cellular Biology, Genetics Subcommittee.
- <u>Gordon Research Conference: DNA Damage, Mutation and Cancer.</u> March 1-6, 2020, Ventura, CA—Academia Career Mentoring Dinner
- <u>FASEB SRC: Genetic Recombination and Genome Rearrangements Conference</u>. July14-19, 2019, Steamboat Springs, CO—Discussion Session Leader; Career Workshop Panelist
- <u>Northeast Regional Life Sciences Core Directors Meeting</u>, October 13-15, 2016, Boston, MA— Breakout Session Organizer for CRISPR off-targets

CERTIFICATIONS

• MCHRI Eureka Translational Medicine, February 9-13, 2020, Monterey, CA

PRESENTATIONS

INVITED ORAL PRESENTATIONS (National; 23 total)

- 1. "Cutting and pasting: DNA repair artistry in non-cycling cells" University of the Pacific Biological Sciences Seminar, **April 8, 2022**, Stockton, CA
- 2. "Aberrant DNA end joining mechanisms in non-cycling cells" Stanford Radiation Oncology Department Retreat, November 18-19, 2021, Stanford, CA
- 3. "DNA end joining in quiescent progenitor B cells" University of California, Davis, Seminar in Molecular Genetics. November 15, 2021, Davis CA
- 4. "Functional genomics of DNA repair processes" 44th Annual Stanford Cancer Biology Program Scientific Conference, November 12-13, 2021, Woodside, CA
- 5. "Identifying the rules of engagement: DNA end-joining in G1/G0-phase" Stanford Radiation Oncology Faculty Seminar Series, **February 5, 2021**, Stanford, CA
- 6. "Mind the Gap: Breaking new ground on G1-phase end-joining" Tulane University, Department of Biochemistry and Molecular Biology Seminar Series. April 20, 2020, Webinar (COVID-19)
- 7. "Repair Fate Mapping of Broken Ends in Non-Dividing Cells" <u>Gordon Research Conference</u>: <u>DNA Damage, Mutation and Cancer.</u> March 1-6, 2020, Ventura, CA
- 8. "Elucidating DNA DSB repair pathway choice in G1-phase progenitor B cells" <u>65th Annual</u> <u>Radiation Research Society Meeting</u>, November 3-6, 2019, San Diego, CA

- 9. "Elucidating mechanisms of chromosome translocations and double strand break repair" 41st Annual Stanford Cancer Biology Program Scientific Conference, **September 14-15, 2018**, San Jose, CA
- "New Insights into Non-Homologous End-Joining Mechanisms of Recurrent DNA Double-Stranded Breaks in Progenitor B cells" <u>2nd Annual Genome Editing USA Congress</u>, May 10-11, 2018, Boston, MA
- 11. "Assessing Endonuclease Off-Target Activity and Genome-wide Collateral Damage" <u>Northeast</u> <u>Regional Life Sciences Core Directors Meeting</u>, October 13-15, 2016, Boston, MA.
- "Breaking Bad: Genome-wide Detection of Designer Nuclease Targeting and its Ensuing Collateral Damage" <u>Precision Medicine Symposia-2016 on RNAi/Genome Editing</u>, May 4-5, 2016, Burlington, MA.
- 13. "Breaking Bad: Genome-wide Detection of Designer Nuclease Targeting and its Ensuing Collateral Damage" *Clinical Immunology Society Annual Meeting*, April 14-17, 2016, Boston, MA.
- "Genome-wide Detection of DNA Double-Stranded Breaks Induced by Engineered Nucleases" <u>Information Gathering Meeting on Human Editing</u>, October 5, 2015, National Academy of Sciences, Washington, D.C.
- 15. "Genome-wide Detection of DNA Double-stranded Breaks Induced by Engineered Nucleases" <u>HHMI Scientific Meeting</u>, February 10-12, 2015, Chevy Chase, MD
- "Genome-wide Detection of DNA Double-Stranded Breaks Induced by Engineered Nucleases" <u>Genome Engineering: The CRISPR/Cas Revolution</u>, September 24-27, 2015, Cold Spring Harbor, NY
- "Genome-wide Assessment of Custom Nuclease-mediated On and Off-target Breaks and Translocations in Human Cells" Harvard Medical School, Division of Immunology Trainee Forum, April 11, 2014, Boston, MA.
- 18. "Principles of Translocations in Human Cells Using Engineered Nucleases Targeting the RAG1 Locus" Harvard Medical School, DNA Replication and Repair Series, August 1, 2013, Boston, MA.
- 19. "Principles of Translocations in Human Cells Using Engineered Nucleases Targeting the RAG1 Locus" Boston Children's Hospital Program in Cellular and Molecular Medicine Open Forums, **March 22, 2013**, Boston, MA.
- 20. "Genome-wide Translocation Sequencing Reveals Mechanisms of Chromosome Breaks and Rearrangements in B cells" 4th Annual Northwest Genome Engineering Consortium workshop on Genome Engineering, Nov 8, 2011, Seattle, WA.
- 21. "Elucidating the Mouse B Lymphocyte Translocatome" Harvard Medical School Immune Disease Institute Open Forums, **March 18, 2011**, Boston, MA.
- 22. "Delayed Muscle Differentiation Kinetics in *Lmna*[⊥] Myoblasts" *3rd Seattle Muscular Dystrophy Conference*, **June 14-15**, **2007**, Seattle, WA.
- 23. "Lamin A/C and Emerin are Critical for Normal Adult Skeletal Myogenesis" *Northwest Developmental Biology Conference*, March 16-19, 2005, Friday Harbor, WA.

INVITED ORAL PRESENTATIONS (International; 3 total)

- "High-Throughput Methods to Study V(D)J Recombination, IgH Class Switch Recombination, Chromosomal Translocations, and DNA End-Joining" 19th International Summer School on Immunology - FEBS advanced lecture course Immune System: Genes, Receptors and Regulation, September 23-30, 2017, Hvar Island, Croatia.
- 2. "Genome-wide Analysis of Designer Nuclease Targeting" 9th Stem Cell Clonality and Genome

Stability Retreat, October 17-18, 2016, Florence, Italy.

3. "Gene Editing Tools and Assessing their Genome-wide Collateral Damage" Precision Genome Engineering Training Day, **January 27, 2016**, Ghent, Belgium.

TEACHING

Fall 2021	Lecturer Stanford University, CBIO 240: Molecular and Genetic Basis of Cancer Role: Lecture on DNA end joining mechanisms and chromosome translocations, V(D)J recombination and hematologic malignancies.
Spring 2019-2022	Lecturer Stanford University, RADO 202: The Basic Science of Radiation and Cancer Biology Role: Single lecture on the DNA damage response, DNA repair pathways, and Genome Instability Syndromes for medical students.
Fall 2018-2020	Lecturer Stanford University, CBIO 280: Cancer Biology Journal Club Role: Lecture on chromosome translocations, DNA repair outcomes and other laboratory research topics.
Fall 2018	Discussion Section Leader Stanford University, CBIO 240: Molecular and Genetic Basis of Cancer Role: Facilitated journal club style discussions on papers related to the lecturer's weekly topic for graduate students
Sept. 2017	Lecturer, FEBS International Summer School on Immunology, Hvar Island, Croatia
Spring 2003	Teaching Assistant, Univ. Washington, BIOC 442: Molecular and Cellular Biology
Winter 2003	Teaching Assistant, Univ. Washington, HUBIO 524: Biochemistry and Metabolism
Fall 2002	Teaching Assistant, Univ. Washington, BIOC 426: Basic Techniques in Biochemistry
Spring 1999	Teaching Assistant, Vassar College, CHEM 245: Organic Chemistry Laboratory
Spring 1998	Teaching Assistant, Vassar College, CHEM 110/111: General Chemistry Laboratory

MENTORING (PI)

Postdoctoral Fellows:

- Jinglong Wang (2020-present) Postdoctoral Scholar, Stanford University, Stanford, CA
- Carlos Origel (2020-2021) Postdoctoral Fellow, Oregon Health & Science University, Portland, OR
- Marie Le Bouteiller (2019-2021) Homemaker
- Paul Barghouth (2019-2021) Researcher, Nucleix, San Diego, CA

Masters/Doctoral/Medical/Veterinary Students:

- Kristin Conner (2022-present) Veterinary Medicine Candidate, UC Davis, CA
- Cheyenne Sadeghi (2021-present) Computer Science Masters Student, Stanford University, Stanford, CA

Research Technicians/Bioinformaticians:

- Josefin Kenrick (2018-2021) Graduate Student, KTH Royal Institute of Technology, Stockholm, Sweden
- Micah Kelly (2018-2019) Project Manager, Twist Bioscience, South San Francisco, CA

Undergraduate Research Students:

• Anushka Edlabadkar (2022-present) – Undergraduate, UC San Diego, CA

- Long Le (2022-present) Undergraduate, UC Berkeley, CA
- Jodie Meng (2021-2022) Undergraduate, Stanford University, Stanford, CA
- Anita Taft (2021) Undergraduate, Stanford University, Stanford, CA

High School Summer Students:

• Finn Maniscalco (2019) – Undergraduate, University of Pennsylvania, Philadelphia, PA