Stanford

Richard Frock

Assistant Professor of Radiation Oncology (Radiation and Cancer Biology)

Radiation Oncology - Radiation and Cancer Biology

Curriculum Vitae available Online

CONTACT INFORMATION

- **Administrative Contact**

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Bio

ACADEMIC APPOINTMENTS

- Assistant Professor, Radiation Oncology - Radiation and Cancer Biology
- Member, Bio-X
- Member, SPARK at Stanford
- Member, Maternal & Child Health Research Institute (MCHRI)
- Member, Stanford Cancer Institute

HONORS AND AWARDS

- Research Scholar, American Cancer Society - Lisa Dean Moseley Foundation Stem Cell Consortium
- V Scholar, V Foundation for Cancer Research
- Career Development Award, Radiation Research Foundation

PROFESSIONAL EDUCATION

- Research Fellow, Boston Children's Hospital , Program in Cellular and Molecular Medicine
- PhD, University of Washington , Biochemistry (2009)
- BA, Vassar College , Biochemistry (2001)

PATENTS

- Frederick W Alt, Richard L Frock, Jiazhi Hu, Robin M Meyers. " Patent WO2016081798 Methods relating to the detection of recurrent and non-specific double strand breaks in the genome", Nov 20, 2015

LINKS

- Website - Frocklab: https://frocklab.stanford.edu
- Twitter - FrockLab: https://twitter.com/FrockLab

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

We are a functional genomics laboratory interested in elucidating mechanisms of DNA repair pathway choice and genome instability. We use genome-wide repair fate maps of targeted DNA double strand breaks (DSBs) to develop pathway-specific models and combinatorial therapies. Our expertise overlaps many different fields including: genome editing, ionizing radiation, cancer therapeutics, V(D)J and IgH class switch recombination, repair during transcription and replication, and meiosis.

We are specifically interested in secondary repair mechanisms, their collaboration with the epigenetic DNA Damage Response (DDR), and how they can be promoted over nonhomologous end joining (NHEJ) or homologous recombination (HR) in cancers.

Our recent work in quiescent cells revealed a robust bona fide alternative end joining (A-EJ) mechanism, completely independent of NHEJ, comprising the Parp1-XRCC1/Lig III axis and dependent on 53BP1 and the ATM-initiated DDR. This pathway is distinguished from an NHEJ-variant A-EJ mechanism we describe that leverages the first half of NHEJ (i.e. DNA-PK) to resect ends and form joints that are enriched with microhomology. Curiously, these activities do not require polymerase theta, suggesting additional mechanisms that leverage microhomology-mediated end-joining (MMEJ) may contribute to the COSMIC (v3.4) indel ID6 and ID8 signatures found in many cancer genomes.

Teaching

STANFORD ADVISEES

Postdoctoral Faculty Sponsor

Garima Chaturvedi

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)

Publications

PUBLICATIONS

- **Polymerase theta repairs persistent G1-induced DNA breaks in S-phase during class switch recombination.** *Nature communications*
  Marton, T., Wang, J., Vaysse, A., Yu, W., Commere, P. H., Holleville, Q., Espie-Caullet, T., Frock, R., Deriano, L.
  2025; 16 (1): 10536
- **ATM and 53BP1 regulate alternative end joining-mediated V(D)J recombination.** *Science advances*
  Wang, J., Sadeghi, C. A., Le, L. V., Le Bouteiller, M., Frock, R. L.
  2024; 10 (31): eadn4682
- **DNA-PKcs suppresses illegitimate chromosome rearrangements.** *Nucleic acids research*
  Wang, J., Sadeghi, C. A., Frock, R. L.
  2024
- **Shifted PAMs generate DNA overhangs and enhance SpCas9 post-catalytic complex dissociation.** *Nature structural & molecular biology*
  Wang, J., Le Gall, J., Frock, R. L., Strick, T. R.
  2023
- **FLASH-RT does not affect chromosome translocations and junction structures beyond that of CONV-RT dose-rates.** *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*
  Barghouth, P. G., Melemenidis, S., Montay-Gruel, P., Ollivier, J., Viswanathan, V., Jorge, P. G., Soto, L. A., Lau, B. C., Sadeghi, C., Edlabadkar, A., Zhang, R., Ru, N., Baulch, et al

2023: 109906

- **Development of beta-globin gene correction in human hematopoietic stem cells as a potential durable treatment for sickle cell disease.** *Science translational medicine*
  Lattanzi, A., Camarena, J., Lahiri, P., Segal, H., Srifa, W., Vakulskas, C. A., Frock, R. L., Kenrick, J., Lee, C., Talbott, N., Skowronski, J., Cromer, M. K., Charlesworth, et al
  2021; 13 (598)

- **Ku70 suppresses alternative end joining in G1-arrested B cells** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Liang, Z., Kumar, V., Bouteiller, M., Zurita, J., Kenrick, J., Lin, S. G., Lou, J., Hu, J., Ye, A., Boboila, C., Alt, F. W., Frock, R. L.
  2021; 118 (21)

- **Mechanism of tandem duplication formation in BRCA1-mutant cells.** *Nature*
  Willis, N. A., Frock, R. L., Menghi, F. n., Duffey, E. E., Panday, A. n., Camacho, V. n., Hasty, E. P., Liu, E. T., Alt, F. W., Scully, R. n.
  2017; 551 (7682): 590–95

- **Detecting DNA double-stranded breaks in mammalian genomes by linear amplification-mediated high-throughput genome-wide translocation sequencing** *NATURE PROTOCOLS*
  Hu, J., Meyers, R. M., Dong, J., Panchakshari, R. A., Alt, F. W., Frock, R. L.
  2016; 11 (5): 853-871

- **Genome-wide detection of DNA double-stranded breaks induced by engineered nucleases** *NATURE BIOTECHNOLOGY*
  Frock, R. L., Hu, J., Meyers, R. M., Ho, Y., Kii, E., Alt, F. W.
  2015; 33 (2): 179-186

- **Genome-wide Translocation Sequencing Reveals Mechanisms of Chromosome Breaks and Rearrangements in B Cells** *CELL*
  Chiarle, R., Zhang, Y., Frock, R. L., Lewis, S. M., Molinie, B., Ho, Y., Myers, D. R., Choi, V. W., Compagno, M., Malkin, D. J., Neuberg, D., Monti, S., Giallourakis, et al
  2011; 147 (1): 107-119

- **High throughput mutational characterization of the GPCR ligand C5a using yeast display and deep sequencing.** *Structure (London, England : 1993)*
  Xu, Y., Thakkar, K., Guan, L., Miao, Y., Mehibel, M., Lee, R. B., Marciano, D., Viswanathan, V., Wang, Z., Wang, J., Ji, L., Cao, H., Petrakian, et al
  2025

- **Senataxin promotes recombination fidelity during antigen receptor gene diversification.** *Science signaling*
  Libri, A. B., Wang, J., Marton, T., Yu, W., Dossin, F., Balmus, G., Reina-San-Martin, B., Frock, R., Lescale, C., Deriano, L.
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- **FTO inhibition enhances the therapeutic index of radiation therapy in head and neck cancer.** *JCI insight*
  Ji, L., Pu, L., Wang, J., Cao, H., Melemenidis, S., Sinha, S., Guan, L., Laseinde, E. E., von Eyben, R., Richter, S. A., Nam, J. M., Kong, C., Casey, et al
  2025; 10 (11)

- **Alternative End Joining and the ATM-Initiated DNA Damage Response Suppress MH-Mediated V(D)J Recombination and Translocation**
  Wang, J., Sadeghi, C., Le, L., Le Bouteiller, M., Frock, R. L.
  WILEY.2024: 56-57

- **Increased AID results in mutations at the CRLF2 locus implicated in Latin American ALL health disparities.** *Nature communications*
  Rangel, V., Sterrenberg, J. N., Garawi, A., Mezcord, V., Folkerts, M. L., Calderon, S. E., Garcia, Y. E., Wang, J., Soyfer, E. M., Eng, O. S., Valerin, J. B., Tanjasiri, S. P., Quintero-Rivera, et al
  2024; 15 (1): 6331

- **Tert-expressing cells contribute to salivary gland homeostasis and tissue regeneration after radiation therapy.** *Genes & development*
  Guan, L., Viswanathan, V., Jiang, Y., Vijayakumar, S., Cao, H., Zhao, J., Colburg, D. R., Neuhöfer, P., Zhang, Y., Wang, J., Xu, Y., Laseinde, E. E., Hildebrand, et al
  2024

- **Author Correction: Shifted PAMs generate DNA overhangs and enhance SpCas9 post-catalytic complex dissociation.** *Nature structural & molecular biology*
  Wang, J., Le Gall, J., Frock, R. L., Strick, T. R.

2024

- **Increased AID Results in Mutations at the CRLF2 Locus Implicated in Latin American ALL Health Disparities.** *Research square*
  Pannunzio, N., Rangel, V., Sterrenberg, J., Garawi, A., Mezcord, V., Folkerts, M., Caulderon, S., Wang, J., Soyfer, E., Eng, O., Valerin, J., Tanjasiri, S., Quintero-Rivera, et al
  2023

- **FLASH-RT does not affect chromosome translocations and junction structures beyond that of CONV-RT dose-rates.** *bioRxiv : the preprint server for biology*
  Barghouth, P. G., Melemenidis, S., Montay-Gruel, P., Ollivier, J., Viswanathan, V., Jorge, P. G., Soto, L. A., Lau, B. C., Sadeghi, C., Edlabadkar, A., Manjappa, R., Wang, J., Bouteiller, et al
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- **DNA End Joining: G0-ing to the Core.** *Biomolecules*
  Frock, R. L., Sadeghi, C., Meng, J., Wang, J. L.
  2021; 11 (10)

- **Ku70 suppresses alternative end joining in G1-arrested progenitor B cells.** *Proceedings of the National Academy of Sciences of the United States of America*
  Liang, Z., Kumar, V., Le Bouteiller, M., Zurita, J., Kenrick, J., Lin, S. G., Lou, J., Hu, J., Ye, A. Y., Boboila, C., Alt, F. W., Frock, R. L.
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- **Ultra-high dose rate (FLASH) irradiation does not alter microhomology mediated recombination under varying oxygen tension when compared to standard clinical dose rates.**
  Barghouth, P., Ollivier, J., Montay-Gruel, P., Loo, B. W., Vozenin, M., Limoli, C., Frock, R.
  AMER ASSOC CANCER RESEARCH.2021

- **Precise and broad scope genome editing based on high-specificity Cas9 nickases.** *Nucleic acids research*
  Wang, Q., Liu, J., Janssen, J. M., Le Bouteiller, M., Frock, R. L., Goncalves, M. A.
  2021

- **Ku70 suppresses alternative end-joining in G1-arrested progenitor B cells**
  Frock, R. L., Kumar, V., Liang, Z., Zurita, J., Du, Z., Lin, S. G., Boboila, C., Alt, F. W.
  AMER ASSOC CANCER RESEARCH.2019

- **Expanding the editable genome and CRISPR-Cas9 versatility using DNA cutting-free gene targeting based on in trans paired nicking.** *Nucleic acids research*
  Chen, X. n., Tasca, F. n., Wang, Q. n., Liu, J. n., Janssen, J. M., Brescia, M. D., Bellin, M. n., Szuhai, K. n., Kenrick, J. n., Frock, R. L., Gonçalves, M. A.
  2019

- **Parp3 promotes long-range end joining in murine cells** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Layer, J., Cleary, J., Brown, A. J., Stevenson, K. E., Morrow, S. N., Van Scoyk, A., Blasco, R. B., Karaca, E., Meng, F., Frock, R. L., Tivey, T., Kim, S., Fuchs, et al
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- **Ectopic expression of RAD52 and dn53BP1 improves homology-directed repair during CRISPR-Cas9 genome editing.** *Nature biomedical engineering*
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- **PAXX and XLF DNA repair factors are functionally redundant in joining DNA breaks in a G1-arrested progenitor B-cell line** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Kumar, V., Alt, F. W., Frock, R. L.
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- **Orientation-specific RAG activity in chromosomal loop domains contributes to Tcrd V(D)J recombination during T cell development.** *journal of experimental medicine*
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- **Chromosomal Loop Domains Direct the Recombination of Antigen Receptor Genes** *CELL*
  Hu, J., Zhang, Y., Zhao, L., Frock, R. L., Du, Z., Meyers, R. M., Meng, F., Schatz, D. G., Alt, F. W.
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- **Mechanisms of Recurrent Chromosomal Translocations** *Chromosomal Translocations and Genome Rearrangements in Cancer*
  Frock, R. L., Hu, J., Alt, F. W.
  Springer International Publishing.2015; 1: 27–51
- **Cardiomyocyte-Specific Expression of Lamin A Improves Cardiac Function in Lmna(-/-) Mice** *PLOS ONE*
  Frock, R. L., Chen, S. C., Da, D., Frett, E., Lau, C., Brown, C., Pak, D. N., Wang, Y., Muchir, A., Worman, H. J., Santana, L. F., Ladiges, W. C., Rabinovitch, et al
  2012; 7 (8)
- **Cell-Extrinsic Defective Lymphocyte Development in Lmna(-/-) Mice** *PLOS ONE*
  Hale, J. S., Frock, R. L., Mamman, S. A., Fink, P. J., Kennedy, B. K.
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- **Lamin A/C and emerin are critical for skeletal muscle satellite cell differentiation** *GENES & DEVELOPMENT*
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  Smith, E. D., Kudlow, B. A., Flock, R. L., Kennedy, B. K.
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- **A-type lamins regulate retinoblastoma protein function by promoting subnuclear localization and preventing proteasomal degradation** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
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- **Nuclear reorganization of mammalian DNA synthesis prior to cell cycle exit** *MOLECULAR AND CELLULAR BIOLOGY*
  Barbie, D. A., Kudlow, B. A., Frock, R., Zhao, J. Y., Johnson, B. R., Dyson, N., Harlow, E., Kennedy, B. K.
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- **Dystroglycan is required for polarizing the epithelial cells and the oocyte in Drosophila** *DEVELOPMENT*
  Deng, W. M., Schneider, M., Frock, R., Castillejo-Lopez, C., Baumgartner, S., Ruohola-Baker, H.
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