BIOGRAPHICAL SKETCH

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NAME: Adamson, Brittany

eRA COMMONS USER NAME (credential, e.g., agency login): bsadamson

POSITION TITLE: Assistant Professor, Richard B. Fisher Preceptor in Integrative Genomics, Lewis-Sigler Institute for Integrative Genomics & the Department of Molecular Biology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology, Cambridge, MA	BS	06/2005	Biology
Harvard University, Cambridge, MA	PHD	03/2013	Genetics and Genomics
University of California, San Francisco, CA	Postdoctoral Fellow	07/2018	Cell Biology

A. Personal Statement

My lab uses and develops innovative genomics technologies to study gene function in human cells, with particular interest in understanding (a) how cells leverage genetic pathways to respond to stimuli, stress, and/or damage and (b) how these pathways, or defects in these pathways, contribute to disease and/or impact medical therapies. My expertise in genetics, cell biology, genome engineering, systems biology, and functional genomics makes me well-suited to carry out this research. Indeed, throughout my career, I have developed and co-developed tools used widely for such work, including platforms for performing CRISPR/Cas-based genetic screens with high-content, molecular phenotypes (e.g., Perturb-seq). I also have a proven track record of using functional genomics to achieve my research goals. For example, a long-standing focus of my research has been to elucidate mechanisms of DNA repair in human cells. As a graduate student, I performed genetic screens to identify DNA damage response genes. More recently, I combined this interest with my technical expertise to co-develop a technology for systematically mapping cellular processes that control DNA repair (i.e., Repair-seq). Applications of this technology have since generated deep mechanistic insights. Finally, I am committed to mentoring students and postdocs. Our group currently includes two postdocs, seven graduate students, and undergraduate students, some with co-mentors to support highly interdisciplinary projects. Three of my trainees have independent fellowships, including a Damon Runyon Postdoctoral Research Fellowship and an NSF Graduate Research Fellowship.

Ongoing and recently completed projects that I would like to highlight include:

Princeton Catalysis Initiative Fund, MacMillan (PI), Adamson Role: Co-Investigator
07/01/2019-06/30/2022
Investigating biophysical interactions in DNA repair

Searle Scholars Program, SSP-2020-101, Adamson (PI)
07/01/2020-06/30/2023
Mapping the processes of genome editing in human cells

NIH/NIGMS, R35 GM138167, Adamson (PI)
08/25/2020-07/31/2025
Mapping the DNA damage response in human cells with high-resolution functional genomics

NIH/NCI/RBHS-Cancer Institute of NJ, Libutti (PI), Adamson Role: Co-Investigator
01/16/2020-02/28/2021
New Investigator Award

Citations:

1. Hussmann JA, Ling J, Ravisankar P, Yan J, Cirincione A, Xu A, Simpson D, Yang D, Bothmer A, Cotta-Ramusino C, Weissman JS, Adamson B. Mapping the genetic landscape of DNA double-strand break repair. Cell. 2021 Oct 28;184(22):5653-5669.e25. PubMed Central PMCID: PMC9074467.
2. Replogle JM, Norman TM, Xu A, Hussmann JA, Chen J, Cogan JZ, Meer EJ, Terry JM, Riordan DP, Srinivas N, Fiddes IT, Arthur JG, Alvarado LJ, Pfeiffer KA, Mikkelsen TS, Weissman JS, Adamson B. Combinatorial single-cell CRISPR screens by direct guide RNA capture and targeted sequencing. Nat Biotechnol. 2020 Aug;38(8):954-961. PubMed Central PMCID: PMC7416462.
3. Adamson B, Norman TM, Jost M, Cho MY, Nuñez JK, Chen Y, Villalta JE, Gilbert LA, Horlbeck MA, Hein MY, Pak RA, Gray AN, Gross CA, Dixit A, Parnas O, Regev A, Weissman JS. A Multiplexed Single-Cell CRISPR Screening Platform Enables Systematic Dissection of the Unfolded Protein Response. Cell. 2016 Dec 15;167(7):1867-1882.e21. PubMed Central PMCID: PMC5315571.
4. Adamson B, Smogorzewska A, Sigoillot FD, King RW, Elledge SJ. A genome-wide homologous recombination screen identifies the RNA-binding protein RBMX as a component of the DNA-damage response. Nat Cell Biol. 2012 Feb 19;14(3):318-28. PubMed Central PMCID: PMC3290715.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2022 -	Scientific Advisory Board member, Arbor Biotechnologies, Inc., Cambridge, MA
2020 -	General Member and Advisor in the Academy of Mentors, New Jersey Alliance for Clinical and Translational Science, New Brunswick, NJ
2019 -	Full Member, Genomic Instability and Cancer Genetics Program, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
2019 - 2021	ThinkLab Advisory Board member, Single-cell Genomics, Celsius Therapeutics, Cambridge, MA
2018 -	Assistant Professor, Richard B. Fisher Preceptor in Integrative Genomics, Lewis-Sigler Institute for Integrative Genomics & the Department of Molecular Biology, Princeton University, Princeton, NJ
2013 - 2018	Postdoctoral Research with Jonathan S. Weissman, Ph.D., University of California, San Francisco, San Francisco, CA
2013 - 2013	Research Fellow in Medicine with Stephen J. Elledge, Ph.D., Harvard Medical School & Brigham and Women's Hospital, Boston, MA
2007 - 2012	Doctoral Research with Stephen J. Elledge, Ph.D., Harvard Medical School, Boston, MA
2005 - 2006	Research Technician I with Angelika Amon, Ph.D., Howard Hughes Medical Institute, Massachusetts Institute of Technology, Cambridge, MA
2004 - 2005	Undergraduate Research with Angelika Amon, Ph.D., Massachusetts Institute of Technology, Cambridge, MA

Honors

2020 - 2025	Maximizing Investigators' Research Award for Early Stage Investigators, NIH/NIGMS
2020 - 2023	Searle Scholars Award, Searle Scholars Program
2014 - 2017	Postdoctoral Research Fellowship, Damon Runyon Cancer Research Foundation
2020	New Investigator Award, NIH/NCI/Rutgers Cancer Institute of New Jersey
2010	Future of Science Fund Scholarship, Keystone Symposia

C. Contribution to Science

1. Prior to the advent of engineered CRISPR/Cas systems, there were few methods available for systematic analysis of gene function in human cells—and those that we had were fraught with technical problems. Despite these challenges, I used one such method (i.e., RNAi) to perform an important genetic screen during my graduate studies. This screen, which is now a highly-cited resource, identified human genes involved in homologous recombination, a major form of DNA repair. Additionally, by supporting the development of methods for identifying and circumventing off-target effects, data from my screen helped improve RNAi screening procedures. Since the completion of this project, I have worked on CRISPR/Cas-based approaches, which now enable dramatically improved genetics-based inquiry in human cells (notable examples included and described below).

    a. Horlbeck MA, Gilbert LA, Villalta JE, Adamson B, Pak RA, Chen Y, Fields AP, Park CY, Corn JE, Kampmann M, Weissman JS. Compact and highly active next-generation libraries for CRISPR-mediated gene repression and activation. Elife. 2016 Sep 23;5 PubMed Central PMCID: PMC5094855.
    b. Gilbert LA, Horlbeck MA, Adamson B, Villalta JE, Chen Y, Whitehead EH, Guimaraes C, Panning B, Ploegh HL, Bassik MC, Qi LS, Kampmann M, Weissman JS. Genome-Scale CRISPR-Mediated Control of Gene Repression and Activation. Cell. 2014 Oct 23;159(3):647-61. PubMed Central PMCID: PMC4253859.
    c. Adamson B, Smogorzewska A, Sigoillot FD, King RW, Elledge SJ. A genome-wide homologous recombination screen identifies the RNA-binding protein RBMX as a component of the DNA-damage response. Nat Cell Biol. 2012 Feb 19;14(3):318-28. PubMed Central PMCID: PMC3290715.
    d. Sigoillot FD, Lyman S, Huckins JF, Adamson B, Chung E, Quattrochi B, King RW. A bioinformatics method identifies prominent off-targeted transcripts in RNAi screens. Nat Methods. 2012 Feb 19;9(4):363-6. PubMed Central PMCID: PMC3482495.

2. Among my most notable technical achievements is Perturb-seq, a platform I co-developed to generate rich transcriptome-level phenotypes for tens of thousands to millions of separately perturbed cells in single pooled experiments. The ability to collect such phenotypes from multiplexed experiments was, at the time, groundbreaking, and we showed that, with these phenotypes, we could infer functional relationships between genes, decouple transcriptional circuits, and identify cell-to-cell heterogeneities. Consistent with my long-standing interest in cellular stress responses, we applied Perturb-seq to study the unfolded protein response (UPR). The UPR is a stress response network associated with the endoplasmic reticulum (ER). Using Perturb-seq, we showed how different UPR programs respond to different stresses in human cells. We also nominated a mechanism for maintaining ER homeostasis through activation of an isolated part of the UPR. Broadly, this work showcased the complexity of one cellular stress response and demonstrated how ‘high-resolution’ functional genomics approaches can be used to map the organization of complex cellular systems to reveal mechanistic insights. Recently, building on efforts to enable screens with programmed combinations of perturbations, we further expanded the capabilities of Perturb-seq.

    a. Replogle JM, Norman TM, Xu A, Hussmann JA, Chen J, Cogan JZ, Meer EJ, Terry JM, Riordan DP, Srinivas N, Fiddes IT, Arthur JG, Alvarado LJ, Pfeiffer KA, Mikkelsen TS, Weissman JS, Adamson B. Combinatorial single-cell CRISPR screens by direct guide RNA capture and targeted sequencing. Nat Biotechnol. 2020 Aug;38(8):954-961. PubMed Central PMCID: PMC7416462.
    b. Horlbeck MA, Xu A, Wang M, Bennett NK, Park CY, Bogdanoff D, Adamson B, Chow ED, Kampmann M, Peterson TR, Nakamura K, Fischbach MA, Weissman JS, Gilbert LA. Mapping the Genetic Landscape of Human Cells. Cell. 2018 Aug 9;174(4):953-967.e22. PubMed Central PMCID: PMC6426455.
    c. Dixit A, Parnas O, Li B, Chen J, Fulco CP, Jerby-Arnon L, Marjanovic ND, Dionne D, Burks T, Raychowdhury R, Adamson B, Norman TM, Lander ES, Weissman JS, Friedman N, Regev A. Perturb-Seq: Dissecting Molecular Circuits with Scalable Single-Cell RNA Profiling of Pooled Genetic Screens. Cell. 2016 Dec 15;167(7):1853-1866.e17. PubMed Central PMCID: PMC5181115.
    d. Adamson B, Norman TM, Jost M, Cho MY, Nuñez JK, Chen Y, Villalta JE, Gilbert LA, Horlbeck MA, Hein MY, Pak RA, Gray AN, Gross CA, Dixit A, Parnas O, Regev A, Weissman JS. A Multiplexed

Single-Cell CRISPR Screening Platform Enables Systematic Dissection of the Unfolded Protein Response. Cell. 2016 Dec 15;167(7):1867-1882.e21. PubMed Central PMCID: PMC5315571.

3. Human cells use a sophisticated set of DNA repair mechanisms to safeguard their genomes. Understanding how these mechanisms work—and, in particular, how they ensure response flexibility across conditions—is an overarching goal of my research. As a graduate student, I contributed to the characterization of important DNA repair factors and I identified many other genes and proteins with interesting DNA repair phenotypes or features. More recently, I co-developed a high-throughput genomics approach to study DNA repair at the systems-level. This approach, called Repair-seq, measures the effects of thousands of genetic perturbations on mutations introduced at targeted DNA lesions, producing 'high-resolution' molecular phenotypes containing detailed information about DNA repair gene function. Similar to our work with Perturb-seq, collecting rich phenotypes for many genes enabled principled analysis of a complex cellular system. Using this approach, we uncovered unexpected relationships among DNA repair genes and isolated incompletely characterized repair processes.

    a. Hussmann JA, Ling J, Ravisankar P, Yan J, Cirincione A, Xu A, Simpson D, Yang D, Bothmer A, Cotta-Ramusino C, Weissman JS, Adamson B. Mapping the genetic landscape of DNA double-strand break repair. Cell. 2021 Oct 28;184(22):5653-5669.e25. PubMed Central PMCID: PMC9074467.
    b. Izhar L, Adamson B, Ciccia A, Lewis J, Pontano-Vaites L, Leng Y, Liang AC, Westbrook TF, Harper JW, Elledge SJ. A Systematic Analysis of Factors Localized to Damaged Chromatin Reveals PARP-Dependent Recruitment of Transcription Factors. Cell Rep. 2015 Jun 9;11(9):1486-500. PubMed Central PMCID: PMC4464939.
    c. Ciccia A, Nimonkar AV, Hu Y, Hajdu I, Achar YJ, Izhar L, Petit SA, Adamson B, Yoon JC, Kowalczykowski SC, Livingston DM, Haracska L, Elledge SJ. Polyubiquitinated PCNA recruits the ZRANB3 translocase to maintain genomic integrity after replication stress. Mol Cell. 2012 Aug 10;47(3):396-409. PubMed Central PMCID: PMC3613862.
    d. O'Connell BC, Adamson B, Lydeard JR, Sowa ME, Ciccia A, Bredemeyer AL, Schlabach M, Gygi SP, Elledge SJ, Harper JW. A genome-wide camptothecin sensitivity screen identifies a mammalian MMS22L-NFKBIL2 complex required for genomic stability. Mol Cell. 2010 Nov 24;40(4):645-57. PubMed Central PMCID: PMC3006237.

4. Genome editing, which allows DNA sequence changes to be made to the genomes of living cells, has become a ubiquitous part of biomedical research, and therapeutic genome editing holds promise for addressing a host of unmet medical needs. However, control over installation of targeted sequence changes—specifying 'edit' frequency and type—remains a key challenge. Central to efforts to address this challenge is understanding the processes by which genome editing technologies work. Generally, a programmable enzyme cuts or damages DNA at a specific site in the genome. Then, a cell's own mechanisms of DNA repair permanently install a sequence change at that site. Using our screening technologies, we have collaboratively 'mapped' the cellular processes responsible for these steps across three different editing approaches: DNA double-strand break (DSB)-induced editing, base editing, and prime editing. We have also applied insights from this work to develop improved genome editing tools.

    a. Koblan LW, Arbab M, Shen MW, Hussmann JA, Anzalone AV, Doman JL, Newby GA, Yang D, Mok B, Replogle JM, Xu A, Sisley TA, Weissman JS, Adamson B, Liu DR. Efficient C•G-to-G•C base editors developed using CRISPRi screens, target-library analysis, and machine learning. Nat Biotechnol. 2021 Nov;39(11):1414-1425. PubMed Central PMCID: PMC8985520.
    b. Chen PJ, Hussmann JA, Yan J, Knipping F, Ravisankar P, Chen PF, Chen C, Nelson JW, Newby GA, Sahin M, Osborn MJ, Weissman JS, Adamson B, Liu DR. Enhanced prime editing systems by manipulating cellular determinants of editing outcomes. Cell. 2021 Oct 28;184(22):5635-5652.e29. PubMed Central PMCID: PMC8584034.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1jgAfRgKeBNks/bibliography/public/