Stanford

Michael Bassik

Assistant Professor of Genetics

Bio

ACADEMIC APPOINTMENTS

- Assistant Professor, Genetics
- Member, Bio-X
- Member, Stanford Cancer Institute
- Faculty Fellow, Stanford ChEM-H
- Member, Wu Tsai Neurosciences Institute

PROFESSIONAL EDUCATION

- Postdoctoral Fellow, University of California, San Francisco , Cellular and Molecular Pharmacology (2013)
- Ph.D., Harvard University , Biological and Biomedical Sciences (2005)
- B.S., University of Wisconsin, Madison , Biochemistry and Molecular Biology (1996)

LINKS

- Bassik Lab Website: http://bassiklab.stanford.edu/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Endocytic Pathogens as Tools and Targets

Endocytic pathogens such as protein aggregates, viruses, protein toxins, and bacteria have evolved remarkable ways to enter the cell, disrupt homeostasis, and cause cell death. We use these agents both as probes to understand normal cellular trafficking and signaling events, and to find key targets for therapy.

Stress Signaling to the Cell Death Machinery

Cells have elaborate mechanisms of sensing diverse stresses (oxidative damage, nutrient deprivation, DNA breaks, etc), and must either repair damage or induce cell death. Misregulation of these pathways results in diseases such as cancer and Alzheimer’s. We would like to understand how these signals connect to the death pathway in health and disease in order to improve therapies.

Technology Development and Genetic Interaction Maps

Customized genome-scale gene perturbation libraries: Much of the work we do utilizes genetic screens enabled by novel high-coverage CRISPR/Cas9 libraries (10 sgRNAs/gene) and shRNA libraries (25 shRNAs/gene) we have developed. The high coverage greatly reduces false positive and false negative results. Our platform allows for easy creation of new library designs, and we use a pooled format that can be used to rapidly screen genome-scale libraries in ~1-2 weeks. Libraries can then be analyzed by deep sequencing to quantify changes in sgRNA/shRNA abundance.

Systematic comparison of gene perturbation technologies: We have systematically compared the ability of genome-wide RNAi and CRISPR/Cas9 deletion screens to identify drug targets and essential genes, and have found important differences in their outputs. For example, while both screens perform well in detecting a gold standard set of essential genes, they can identify distinct essential biological processes. Moreover, each technology exhibits its own set of off-target effects and limitations in on-target efficacy.

Using what we have learned about these technologies, we recently created new genome-wide CRISPR libraries that incorporate a number of improved sgRNA features and controls. With a novel statistical framework (casTLE) we can model on- and off-target effects accurately, markedly improve hit detection, and even combine results from screens to improve performance and further limit false positives and false negatives. These studies have demonstrated the utility of parallel screening approaches using complementary technologies to reveal a more complete biological picture.

Systematic genetic interaction maps: We have also developed strategies to systematically knock down/knock out pairs of genes. This has facilitated some of the first systematic genetic interaction maps in mammalian cells. Using these maps, we can understand coordinated gene functions and predict new functions for uncharacterized genes. They also allow us to quickly identify synergistic interactions under stress conditions that we hope to exploit for combination therapies.

Directed evolution using dCas9-targeted somatic hypermutation (CRISPR-X): More recently, we developed a strategy to re-purpose the somatic hypermutation machinery used in antibody diversification to create targeted populations of point mutations. Using dCas9 to recruit a hyperactive variant of the deaminase AID, we can target diverse point mutations within an ~100bp window centered on the sgRNA PAM site. These mutant populations can then be subjected to selection to evolve proteins with improved function or to map the sites of drug-protein interactions. For example, by tiling mutations across PSMB5, we could map known and novel mutations that affect binding to the chemotherapeutic bortezomib.

Teaching

COURSES

2019-20

- Advanced Genetics: GENE 205 (Win)
- Biology and Applications of CRISPR/Cas9: Genome Editing and Epigenome Modifications: BIOS 268 (Spr)
- Current Issues in Genetics: GENE 219 (Aut, Win, Spr)

2018-19

- Advanced Genetics: GENE 205 (Win)
- Biology and Applications of CRISPR/Cas9: Genome Editing and Epigenome Modifications: BIOS 268, GENE 268 (Spr)

2017-18

- Advanced Genetics: GENE 205 (Win)
- Biology and Applications of CRISPR/Cas9: Genome Editing and Epigenome Modifications: BIOS 268 (Spr)

2016-17

- Advanced Genetics: GENE 205 (Win)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Nathan Abell, Roy Ang, Jacob Blum, Tony Boutelle, Gun Woo Byeon, Noori Chai, Shi-An Chen, Ching Pin Cheng, Alex Colville, Robert Coukos, Hannah De Jong, Elbegduuren Erdenee, Alyssa Kaiser, Kyle Kovary, Ragini Phansalkar, Sarah Pierce, John Pluvinage, Andrew Spencley, Theo Susanto, Nikki Teran, Kristen Wells, Robin Yeo, Siming Zhang

Postdoctoral Faculty Sponsor

Asmita Bhattacharya, Kyuho Han, Roarke Kamber, Roni Levin Konigsberg

Doctoral Dissertation Advisor (AC)

Ann Lin, Josh Tycko, David Yao

Doctoral Dissertation Co-Advisor (AC)

Katherine Liu

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biomedical Informatics (Phd Program)
- Cancer Biology (Phd Program)
- Genetics (Phd Program)

Publications

PUBLICATIONS

- **Systematic Identification of Regulators of Oxidative Stress Reveals Non-canonical Roles for Peroxisomal Import and the Pentose Phosphate Pathway.** *Cell reports*
  Dubreuil, M. M., Morgens, D. W., Okumoto, K., Honsho, M., Contrepois, K., Lee-McMullen, B., Traber, G. M., Sood, R. S., Dixon, S. J., Snyder, M. P., Fujiki, Y., Bassik, M. C.
  2020; 30 (5): 1417

- **Lipid-droplet-accumulating microglia represent a dysfunctional and proinflammatory state in the aging brain.** *Nature neuroscience*
  Marschallinger, J., Iram, T., Zardeneta, M., Lee, S. E., Lehallier, B., Haney, M. S., Pluvinage, J. V., Mathur, V., Hahn, O., Morgens, D. W., Kim, J., Tevini, J., Felder, et al
  2020

- **Genome-wide analysis of targets of macrolide antibiotics in mammalian cells.** *The Journal of biological chemistry*
  Gupta, A., Okesli-Armlovich, A., Morgens, D., Bassik, M. C., Khosla, C.
  2020

- **Genome-wide synthetic lethal CRISPR screen identifies FIS1 as a genetic interactor of ALS-linked C9ORF72.** *Brain research*
  Chai, N., Haney, M. S., Couthouis, J., Morgens, D. W., Benjamin, A., Wu, K., Ousey, J., Fang, S., Finer, S., Bassik, M. C., Gitler, A. D.
  2019: 146601

- **Retro-2 protects cells from ricin toxicity by inhibiting ASNA1-mediated ER targeting and insertion of tail-anchored proteins.** *eLife*
  Morgens, D. W., Chan, C., Kane, A. J., Weir, N. R., Li, A., Dubreuil, M. M., Tsui, C. K., Hess, G. T., Lavertu, A., Han, K., Polyakov, N., Zhou, J., Handy, et al
  2019; 8

- **The CoQ oxidoreductase FSP1 acts parallel to GPX4 to inhibit ferroptosis.** *Nature*
  Bersuker, K., Hendricks, J., Li, Z., Magtanong, L., Ford, B., Tang, P. H., Roberts, M. A., Tong, B., Maimone, T. J., Zoncu, R., Bassik, M. C., Nomura, D. K., Dixon, et al
  2019

- **A ZDHHC5-GOLGA7 Protein Acyltransferase Complex Promotes Nonapoptotic Cell Death.** *Cell chemical biology*
  Ko, P., Woodrow, C., Dubreuil, M. M., Martin, B. R., Skouta, R., Bassik, M. C., Dixon, S. J.
  2019
- **Phagolysosome resolution requires contacts with the endoplasmic reticulum and phosphatidylinositol-4-phosphate signalling.** *Nature cell biology*
  Levin-Konigsberg, R., Montano-Rendon, F., Keren-Kaplan, T., Li, R., Ego, B., Mylvaganam, S., DiCiccio, J. E., Trimble, W. S., Bassik, M. C., Bonifacino, J. S., Fairn, G. D., Grinstein, S.
  2019
- **CRISPR-Cas9 Screens Identify the RNA Helicase DDX3X as a Repressor of C9ORF72 (GGGGCC)n Repeat-Associated Non-AUG Translation.** *Neuron*
  Cheng, W., Wang, S., Zhang, Z., Morgens, D. W., Hayes, L. R., Lee, S., Portz, B., Xie, Y., Nguyen, B. V., Haney, M. S., Yan, S., Dong, D., Coyne, et al
  2019
- **Systematic Identification of Host Cell Regulators of Legionella pneumophila Pathogenesis Using a Genome-wide CRISPR Screen.** *Cell host & microbe*
  Jeng, E. E., Bhadkamkar, V., Ibe, N. U., Gause, H., Jiang, L., Chan, J., Jian, R., Jimenez-Morales, D., Stevenson, E., Krogan, N. J., Swaney, D. L., Snyder, M. P., Mukherjee, et al
  2019
- **CRISPR-Cas9 screens identify regulators of antibody-drug conjugate toxicity.** *Nature chemical biology*
  Tsui, C. K., Barfield, R. M., Fischer, C. R., Morgens, D. W., Li, A., Smith, B. A., Gray, M. A., Bertozzi, C. R., Rabuka, D., Bassik, M. C.
  2019
- **Discovery of small molecule inhibitors of human uridine-cytidine kinase 2 by high-throughput screening.** *Bioorganic & medicinal chemistry letters*
  Okesli-Armlovich, A., Gupta, A., Jimenez, M., Auld, D., Liu, Q., Bassik, M. C., Khosla, C.
  2019
- **Astrocyte-to-astrocyte contact and a positive feedback loop of growth factor signaling regulate astrocyte maturation** *GLIA*
  Li, J., Khankan, R. R., Caneda, C., Godoy, M., Haney, M. S., Krawczyk, M. C., Bassik, M. C., Sloan, S. A., Zhan, Y.
  2019; 67 (8): 1571–97
- **Kinetic analysis identifies determinants of sensitivity to MEK inhibitor-induced cell death**
  Inde, Z., Han, K., Bassik, M. C., Dixon, S. J.
  AMER ASSOC CANCER RESEARCH.2019
- **Neuronally Enriched RUFY3 Is Required for Caspase-Mediated Axon Degeneration.** *Neuron*
  Hertz, N. T., Adams, E. L., Weber, R. A., Shen, R. J., O'Rourke, M. K., Simon, D. J., Zebroski, H., Olsen, O., Morgan, C. W., Mileur, T. R., Hitchcock, A. M., Sinnott Armstrong, N. A., Wainberg, et al
  2019
- **SLC19A1 Is an Importer of the Immunotransmitter cGAMP.** *Molecular cell*
  Ritchie, C., Cordova, A. F., Hess, G. T., Bassik, M. C., Li, L.
  2019
- **CD22 blockade restores homeostatic microglial phagocytosis in ageing brains** *NATURE*
  Pluvinage, J. V., Haney, M. S., Smith, B. H., Sun, J., Iram, T., Bonanno, L., Li, L., Lee, D. P., Morgens, D. W., Yang, A. C., Shuken, S. R., Gate, D., Scott, et al
  2019; 568 (7751): 187-+
- **CD22 blockade restores homeostatic microglial phagocytosis in ageing brains.** *Nature*
  Pluvinage, J. V., Haney, M. S., Smith, B. A., Sun, J., Iram, T., Bonanno, L., Li, L., Lee, D. P., Morgens, D. W., Yang, A. C., Shuken, S. R., Gate, D., Scott, et al
  2019
- **Mitigation of off-target toxicity in CRISPR-Cas9 screens for essential non-coding elements.** *Nature communications*
  Tycko, J., Wainberg, M., Marinov, G. K., Ursu, O., Hess, G. T., Ego, B. K., Li, A., Truong, A., Trevino, A. E., Spees, K., Yao, D., Kaplow, I. M., Greenside, et al
  2019; 10 (1): 4063
- **Targeted genomic CRISPR-Cas9 screen identifies MAP4K4 as essential for glioblastoma invasion.** *Scientific reports*
  Prolo, L. M., Li, A., Owen, S. F., Parker, J. J., Foshay, K., Nitta, R. T., Morgens, D. W., Bolin, S., Wilson, C. M., Vega L, J. C., Luo, E. J., Nwagbo, G., Waziri, et al
  2019; 9 (1): 14020

- **Discovery of common and rare genetic risk variants for colorectal cancer** *NATURE GENETICS*
  Huyghe, J. R., Bien, S. A., Harrison, T. A., Kang, H., Chen, S., Schmit, S. L., Conti, D. V., Qu, C., Jeon, J., Edlund, C. K., Greenside, P., Wainberg, M., Schumacher, et al
  2019; 51 (1): 76-+

- **METTL13 Methylation of eEF1A Increases Translational Output to Promote Tumorigenesis.** *Cell*
  Liu, S., Hausmann, S., Carlson, S. M., Fuentes, M. E., Francis, J. W., Pillai, R., Lofgren, S. M., Hulea, L., Tandoc, K., Lu, J., Li, A., Nguyen, N. D., Caporicci, et al
  2018

- **Genome-wide interrogation of extracellular vesicle biology using barcoded miRNAs.** *eLife*
  Lu, A., Wawro, P., Morgens, D. W., Portela, F., Bassik, M. C., Pfeffer, S. R.
  2018; 7

- **Genome-wide CRISPR Analysis Identifies Substrate-Specific Conjugation Modules in ER-Associated Degradation.** *Molecular cell*
  Leto, D. E., Morgens, D. W., Zhang, L., Walczak, C. P., Elias, J. E., Bassik, M. C., Kopito, R. R.
  2018

- **Discovery of common and rare genetic risk variants for colorectal cancer.** *Nature genetics*
  Huyghe, J. R., Bien, S. A., Harrison, T. A., Kang, H. M., Chen, S., Schmit, S. L., Conti, D. V., Qu, C., Jeon, J., Edlund, C. K., Greenside, P., Wainberg, M., Schumacher, et al
  2018

- **Identification of phagocytosis regulators using magnetic genome-wide CRISPR screens.** *Nature genetics*
  Haney, M. S., Bohlen, C. J., Morgens, D. W., Ousey, J. A., Barkal, A. A., Tsui, C. K., Ego, B. K., Levin, R., Kamber, R. A., Collins, H., Tucker, A., Li, A., Vorselen, et al
  2018

- **CBP modulates sensitivity to dasatinib in pre-BCR+ acute lymphoblastic leukemia.** *Cancer research*
  Duque-Afonso, J., Lin, C., Han, K., Morgens, D. W., Jeng, E. E., Weng, Z., Jeong, J., Wong, S. H., Zhu, L., Wei, M. C., Chae, H., Schrappe, M., Cario, et al
  2018

- **KIF15 nanomechanics and kinesin inhibitors, with implications for cancer chemotherapeutics** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Milic, B., Chakraborty, A., Han, K., Bassik, M. C., Block, S. M.
  2018; 115 (20): E4613–E4622

- **A CRISPR-based screen for Hedgehog signaling provides insights into ciliary function and ciliopathies** *Nat. Genet.*
  Breslow, D. K., Hoogendoorn, S., Kopp, A. R., Morgens, D. W., Vu, B. K., Han, K., Li, A., Hess, G. T., Bassik, M. C., Chen, J. K., V, N. M.
  2018; Epub ahead of print: 460–71

- **A CRISPR-based screen for Hedgehog signaling provides insights into ciliary function and ciliopathies.** *Nature genetics*
  Breslow, D. K., Hoogendoorn, S., Kopp, A. R., Morgens, D. W., Vu, B. K., Kennedy, M. C., Han, K., Li, A., Hess, G. T., Bassik, M. C., Chen, J. K., Nachury, M. V.
  2018; 50 (3): 460–71

- **CRISPR-Cas9 screens in human cells and primary neurons identify modifiers of C9ORF72 dipeptide-repeat-protein toxicity.** *Nature genetics*
  Kramer, N. J., Haney, M. S., Morgens, D. W., Jovi#i#, A., Couthouis, J., Li, A., Ousey, J., Ma, R., Bieri, G., Tsui, C. K., Shi, Y., Hertz, N. T., Tessier-Lavigne, et al
  2018

- **CMTM6 maintains the expression of PD-L1 and regulates anti-tumour immunity** *NATURE*
  Burr, M. L., Sparbier, C. E., Chan, Y., Williamson, J. C., Woods, K., Beavis, P. A., Lam, E. N., Henderson, M. A., Bell, C. C., Stolzenburg, S., Gilan, O., Bloor, S., Noori, et al
  2017; 549 (7670): 101–5

- **Genome-scale measurement of off-target activity using Cas9 toxicity in high-throughput screens** *NATURE COMMUNICATIONS*
  Morgens, D. W., Wainberg, M., Boyle, E. A., Ursu, O., Araya, C. L., Tsui, C. K., Haney, M. S., Hess, G. T., Han, K., Jeng, E. E., Li, A., Snyder, M. P., Greenleaf, et al
  2017; 8

- **Population- and individual- specific regulatory variation in Sardinia** *NATURE GENETICS*

Pala, M., Zappala, Z., Marongiu, M., Li, X., Davis, J. R., Cusano, R., Crobu, F., Kukurba, K. R., Gloudemans, M. J., Reinier, F., Berutti, R., Piras, M. G., Mulas, et al
2017; 49 (5): 700-?

- **Synergistic drug combinations for cancer identified in a CRISPR screen for pairwise genetic interactions** *NATURE BIOTECHNOLOGY*
  Han, K., Jeng, E. E., Hess, G. T., Morgens, D. W., Li, A., Bassik, M. C.
  2017; 35 (5): 463-?
- **Human pyrimidine nucleotide biosynthesis as a target for antiviral chemotherapy.** *Current opinion in biotechnology*
  Okesli, A., Khosla, C., Bassik, M. C.
  2017; 48: 127-134
- **Methods and Applications of CRISPR-Mediated Base Editing in Eukaryotic Genomes.** *Molecular cell*
  Hess, G. T., Tycko, J., Yao, D., Bassik, M. C.
  2017; 68 (1): 26–43
- **Static and Dynamic DNA Loops form AP-1-Bound Activation Hubs during Macrophage Development.** *Molecular cell*
  Phanstiel, D. H., Van Bortle, K., Spacek, D., Hess, G. T., Shamim, M. S., Machol, I., Love, M. I., Aiden, E. L., Bassik, M. C., Snyder, M. P.
  2017; 67 (6): 1037–48.e6
- **Finding host targets for HIV therapy.** *Nature genetics*
  Tsui, C. K., Gupta, A., Bassik, M. C.
  2017; 49 (2): 175–76
- **The impact of rare variation on gene expression across tissues.** *Nature*
  Li, X., Kim, Y., Tsang, E. K., Davis, J. R., Damani, F. N., Chiang, C., Hess, G. T., Zappala, Z., Strober, B. J., Scott, A. J., Li, A., Ganna, A., Bassik, et al
  2017; 550 (7675): 239–43
- **Selective silencing of euchromatic L1s revealed by genome-wide screens for L1 regulators.** *Nature*
  Liu, N., Lee, C. H., Swigut, T., Grow, E., Gu, B., Bassik, M., Wysocka, J.
  2017
- **The mTOR Complex Controls HIV Latency** *CELL HOST & MICROBE*
  Besnard, E., Hakre, S., Kampmann, M., Lim, H. W., Hosmane, N. N., Martin, A., Bassik, M. C., Verschueren, E., Battivelli, E., Chan, J., Svensson, J. P., Gramatica, A., Conrad, et al
  2016; 20 (6): 785-797
- **Directed evolution using dCas9-targeted somatic hypermutation in mammalian cells.** *Nature methods*
  Hess, G. T., Frésard, L., Han, K., Lee, C. H., Li, A., Cimprich, K. A., Montgomery, S. B., Bassik, M. C.
  2016
- **E2A-PBX1 remodels oncogenic signaling networks in B-cell precursor acute lymphoid leukemia.** *Cancer research*
  Duque-Afonso, J., Lin, C., Han, K., Wei, M. C., Feng, J., Kurzer, J., Schneidawind, C., Wong, S. H., Bassik, M. C., Cleary, M. L.
  2016
- **Bithionol blocks pathogenicity of bacterial toxins, ricin, and Zika virus** *SCIENTIFIC REPORTS*
  Leonardi, W., Zilbermintz, L., Cheng, L. W., Zozaya, J., Tran, S. H., Elliott, J. H., Polukhina, K., Manasherob, R., Li, A., Chi, X., Gharaibeh, D., Kenny, T., Zamani, et al
  2016; 6
- **Translation readthrough mitigation** *NATURE*
  Arribere, J. A., Cenik, E. S., Jain, N., Hess, G. T., Lee, C. H., Bassik, M. C., Fire, A. Z.
  2016; 534 (7609): 719-?
- **Systematic comparison of CRISPR/Cas9 and RNAi screens for essential genes** *NATURE BIOTECHNOLOGY*
  Morgens, D. W., Deans, R. M., Li, A., Bassik, M. C.
  2016; 34 (6): 634-636
- **Parallel shRNA and CRISPR-Cas9 screens enable antiviral drug target identification** *NATURE CHEMICAL BIOLOGY*
  Deans, R. M., Morgens, D. W., Okesli, A., Pillay, S., Horlbeck, M. A., Kampmann, M., Gilbert, L. A., Li, A., Mateo, R., Smith, M., Glenn, J. S., Carette, J. E., Khosla, et al

2016; 12 (5): 361-?

- **Weak base pairing in both seed and 3' regions reduces RNAi off-targets and enhances si/shRNA designs.** *Nucleic acids research*
  Gu, S., Zhang, Y., Jin, L., Huang, Y., Zhang, F., Bassik, M. C., Kampmann, M., Kay, M. A.
  2014; 42 (19): 12169-12176

- **Functional genomics platform for pooled screening and generation of mammalian genetic interaction maps** *NATURE PROTOCOLS*
  Kampmann, M., Bassik, M. C., Weissman, J. S.
  2014; 9 (8): 1825-1847

- **Next-Generation NAMPT Inhibitors Identified by Sequential High-Throughput Phenotypic Chemical and Functional Genomic Screens.** *Chemistry & biology*
  Matheny, C. J., Wei, M. C., Bassik, M. C., Donnelly, A. J., Kampmann, M., Iwasaki, M., Piloto, O., Solow-Cordero, D. E., Bouley, D. M., Rau, R., Brown, P., McManus, M. T., Weissman, et al
  2013; 20 (11): 1352-1363

- **A systematic mammalian genetic interaction map reveals pathways underlying ricin susceptibility.** *Cell*
  Bassik, M. C., Kampmann, M., Lebbink, R. J., Wang, S., Hein, M. Y., Poser, I., Weibezahn, J., Horlbeck, M. A., Chen, S., Mann, M., Hyman, A. A., Leproust, E. M., McManus, et al
  2013; 152 (4): 909–22

- **Rapid creation and quantitative monitoring of high coverage shRNA libraries.** *Nature methods*
  Bassik, M. C., Lebbink, R. J., Churchman, L. S., Ingolia, N. T., Patena, W., LeProust, E. M., Schuldiner, M., Weissman, J. S., McManus, M. T.
  2009; 6 (6): 443–45