Kaiyi Jiang

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EDUCATION

Massachusetts Institute of Technology, Cambridge, MA — Expected May 2025
Doctor of Philosophy (Ph.D.) in Biological Engineering
GPA: 5.0 out of 5.0
Thesis title: Harnessing biological diversity and machine learning to develop a cell engineering toolbox
Advisors: Omar Abudayyeh, Jonathan Gootenberg, and Michael Birnbaum

Rice University, Houston, TX
Bachelor of Engineering in Biomedical Engineering — May 2021
GPA: 4.0 out of 4.0 (**Summa cum laude**)
Thesis title: Engineering synthetic phosphorylation signaling networks in mammalian cells
Advisors: Caleb Bashor, Pankaj Mehta, and Gang Bao

RESEARCH INTERESTS

- Harnessing biological diversity to discover novel reprogrammable systems
- AI/ML models to engineer RNA and proteins
- Synthetic biology for *in vivo* recording and lineage tracing
- Gene/cell therapy for autoimmune disease and cancer

PUBLICATIONS (* denotes co-first author)

[1] **Jiang, K.*,** Yan, Z.*, Bernardo, MD., Sgrizzi, S.R., Villiger, L., Kayabolen, A., Kim, B., Carscadden, J.K., Hiraizumi, M., Nishimasu, H., Gootebnerg, J.S., Abudayyeh, O.O. (2024). Rapid protein evolution by few-shot learning with a protein language model ***bioRxiv.*** [Under Review]

- **Summary:**
  We present EVOLVE-Pro, a state-of-the-art (SOTA) ensemble protein language model that can rapidly design protein variants with up to 100-fold higher activity than wild-type. We showed superior of EVOLVE-Pro's performance across 12 DMS datasets. We used it to evolve a SOTA T7 RNA polymerase and miniature CRIPSR nucleases and demonstrate efficient in vivo gene therapy and mRNA therapeutics with these engineered enzymes.

[2] Koob, J.*, **Jiang, K.***, Sgrizzi, S.R.*, Chen, F., Abudayyeh, O.O., Gootenberg, J.S. (2024). Sensing and perturbing mammalian cell states with reprogrammable ADAR sensors. [AIP at ***Nature Protocols***]

[3] Yang, X., Rocks, JW., **Jiang, K.**, Walters, AJ., Rai, K., Liu, J., Nguyen, J., Olson, SD., Mehta, P., Collins, JJ., Daringer, NM., Bashor, CJ. (2024). Engineering synthetic phosphorylation signaling networks in human cells. [AIP at ***Science***]

[4] **Jiang, K.*,** Koob, J.*, Chen, X.D.*, Krajeski, R.N.*, Zhang, Y., Volf, V., Zhou, W., Sgrizzi, S.R., Villiger, L., Gootenberg, J.S., Chen, F., Abudayyeh, O.O. (2023). Programmable eukaryotic protein synthesis with RNA sensors by harnessing ADAR. ***Nature Biotechnology***.

- **Summary:**
  We engineered the first robust mammalian RNA-sensor based on ADAR called RADARS. The sensor can be reprogrammed to track any RNA species inside eukaryotic cells and allow conditional cargo expression based on the presence/expression of target mRNA(s). We demonstrate that the system can be readily integrated into AAV, lentivirus, and synthetic mRNA to selectively turn on an arbitrary protein of interest. We showcase the use of this system in cell specific killing, lineage tracing and *in vivo* recording for reprogrammable cell control.
- **Highlight:**
  This work was highlighted in Derek Lowe's IN THE PIPELINE. (2022), Ono et al, RNA Biology. (2023) and Twist Bioscience's Top Moments in Biotech (2022)

[5] **Jiang, K.***, Lim, J.*, Sgrizzi, S.R., Trinh, M., Kayabolen, A., Yutin, N., Bao, W., Kato, K., Koonin, E., Gootenberg, J.S., Abudayyeh, O.O. (2023). Programmable RNA-guided DNA endonucleases are widespread in eukaryotes. ***Science Advances.***

- **Summary:**
  We discovered a novel group of RNA-guided DNA endonucleases widespread in eukaryotes and their viruses named Fanzor. This was the first evidence of reprogrammable RNA-guided DNA nucleases in eukaryotes, and we characterized Fanzors' (eukaryotic homologs of TnpB) adaptations into the eukaryotic world with nuclear localization signal (NLS), introns and association with diverse transposons. This work established the presence of RNA-guided DNA nucleases in all three kingdoms of life and the diversity of RNA-guided reprogrammable systems.
- **Highlight:**
  This work was highlighted in Patinios et al, Mol. Cell. (2023) & Karvelis et al, The CRISPR Journal. (2023)

[6] Kato, K.*, Okazaki, S.*, Schmitt-Ulms, C.*, **Jiang, K.***, Zhou, W., Ishikawa, J., Isayama, Y., Adachi, S., Nishizawa, T., Makarova, K.S., et al. (2022). RNA-triggered protein cleavage and cell death by the RNA-guided type III-E CRISPR-Cas nuclease-protease complex. ***Science***.

- **Summary:**
  We discovered the first RNA-guided protease systems in prokaryotic antiviral defense systems. We biochemically characterized the Cas7-11/Csx29/Csx30 systems in the context of abortive infection module against phage invasion. We then engineered the system and adapted it as an RNA-sensor system in mammalian cell.
- **Highlight:**
  This work was highlighted in Burgess et al, Nature Reviews Genetics. (2023), Chen et al, Trends in microbiology. (2023), and Wang et al, Nucleic Acids Research. (2022).

[7] Yarnall, M.T.N.*, Ioannidi, E.I.*, Schmitt-Ulms, C.*, Krajeski, R.N.*, Lim, J., Villiger, L., Zhou, W., **Jiang, K.**, Roberts, N., Zhang, L., et al. (2022). Drag-and-drop genome insertion without DNA cleavage with CRISPR-directed integrases. ***Nature Biotechnology***.

[8] Sebesta, C., Torres Hinojosa, D., Wang, B., Asfouri, J., Li, Z., Duret, G., **Jiang, K.**, Xiao, Z., Zhang, L., Zhang, Q., et al. (2022). Subsecond multichannel magnetic control of select neural circuits in freely moving flies. ***Nature Materials***.

[9] Zhang, L., Zhang, Q., Hinojosa, D.T., **Jiang, K.**, Pham, Q.K., Xiao, Z., Colvin, V.L., Bao, G. (2022) Multifunctional Magnetic Nanoclusters Can Induce Immunogenic Cell Death and Suppress Tumor Recurrence and Metastasis. ***ACS Nano***.

[10] **Jiang, K.**, Zhang, Q., Hinojosa, D.T., Zhang, L., Xiao, Z., Yin, Y., Tong, S., Colvin, V.L., Bao, G. (2021) Controlled oxidation and surface modification increase heating capacity of magnetic iron oxide nanoparticles. ***Applied Physics Reviews.***

[11] **Jiang, K.**, Zhang, L., Bao, G. (2021) Magnetic iron oxide nanoparticles for biomedical applications. ***Current Opinion in Biomedical Engineering***.

INVITED TALKS & PRESENTATIONS

- 2024 Cradle Bio invited seminar on machine learning for protein engineering. (Virtual)
- 2024 Harvard Medical School Machine learning to accelerate biology journal club, Boston, MA.
- 2024 SynBYSS, Rising star junior speaker. (Virtual)
- 2024 Bunker Hill community college, STEM Seminar, Boston, MA.
- 2024 Tufts BME162 Molecular Biotech invited lecture, Boston, MA.
- 2023 Bioengineering and Toxicology Seminar, Boston, MA.
- 2023 Harvard Medical School Genome Engineering Symposium, Boston, MA.
- 2023 Broad Gene regulation observatory seminar, Boston, MA.
- 2023 Mammalian Synthetic Biology Workshop (Poster presentation), Stanford, CA.
- 2023 Broad Institute Cell Circuits and Epigenetics Seminar, Boston, MA.
- 2022 Harvard Medical School Genome Engineering Seminar Series, Boston, MA. (Virtual)
- 2022 Boston Mammalian Synthetic Biology Symposium, Boston, MA.
- 2022 Single Cell Genomics Day, NYC, NY. (Virtual)
- 2019 Annual meeting of Biomedical Engineering Society (BMES), Philadelphia, PA.

RESEARCH EXPERIENCE

Graduate Student, AbuGoot Lab, Massachusetts Institute of Technology **2021-Now**
Advisors: Jonathan Gootenberg & Omar Abudayyeh

- Developed the first robust mammalian cell RNA sensor, reprogrammable ADAR sensors (RADARS), that senses endogenous RNA transcripts down to 13 TPM and release arbitrary payload upon ADAR mediated stop codon editing. Deployed this technology for cell state-specific apoptosis, molecular recording (lineage tracing), in vivo detection of tissue markers with live bioluminescence imaging, and RNA gated synthetic mRNA cytokine therapies for RNA immunotherapy in solid tumor.
- Built a few-shot AI protein engineering model comprising large protein langue model (ESM) and domain specific top layer regression model for rapid evolution of enzymatic function. This model achieved SOTA performance on DMS datasets. I deployed this model on a novel miniature CRISPR nuclease (PsaCas12f) and rapidly evolved a 10-fold more active epPsaCas12f for *in vivo* genome editing. Using this model, I evolved a SOTA T7 RNA polymerase that produces mRNA with near zero immunogenicity and 10-fold higher translation for in vivo mRNA therapeutics.
- Discovered the first RNA-guided protease in type III-E CRISPR systems (Craspase Cas7-11/Csx29/Csx30). I characterized the role of Csx29 in abortive infection module in bacterial antiviral defense systems, using post-translational protein cleavage upon RNA detection. I reprogrammed the system to function as an RNA sensor system in mammalian cell and demonstrated the potential for mammalian cell RNA diagnostic and therapy.
- Discovered a novel group of eukaryotic RNA-guided DNA endonucleases (Fanzor). This is the first example of RNA-guided DNA nuclease mechanism in eukaryotes and demonstrated the evolution of RNA-guided nuclease TnpB's adaptation into the eukaryotic world as they gradually acquired NLS and introns. Bioinformatic mining revealed more than 3,000 novel clusters in the eukaryotic genomes and Fanzors serve as a rich resource for future nucleases.

Undergraduate Research Assistant, Bashor Lab, Rice University **2018-2021**
Advisors: Caleb Bashor & Pankaj Mehta

- Developed a comprehensive engineering framework for post-translational protein circuits in mammalian cells based on phosphorylation. By exploiting the natural diversity of kinase, phosphatase, and SH2/SH3 domains, we designed a highly tunable phosphorylation-based protein circuits that allow fast time scale response to extracellular stimuli. We built a biophysical model to characterize each modular protein part for prediction of large design space and deployed the circuit for tuning of T cell activities through sensing cytokines.

Undergraduate Research Assistant, Bao Lab, Rice University **2017-2021**
Advisor: Gang Bao

- Designed a novel magnetic nanoparticle platform for *in vivo* hyperthermia therapy and conditional drug release. I developed novel synthesis methods that enable more than 50% heat generation under clinically applicable magnetic field and demonstrated the potential for free radical immunotherapy in solid tumor.

Intern, Regeneron Pharmaceuticals (Therapeutic antibody group) **2019**
Advisor: Sang-Ryul Lee

- Identified the role of different adjuvants in eliciting immune repones of mice to foreign antigens. Through understanding of molecular differences between adjuvants in terms of germinal centers and plasma cell formation, we formulated the antigen with an optimal adjuvant for enhanced production of therapeutic antibodies for triple negative breast cancer.

AWARDS & HONORS

- **30 under 30,** All-America Chinese Youth Federation, The Log Angeles Post 2024
- The Wishnok Prize, Massachusetts Institute of Technology 2024
- MiraclePlus (Former Y Combinator China) Fellow 2024
- Distinction in Research and Creative Works 2021
- Outstanding Junior in Bioengineering 2020
- Tau Beta Pi Member 2019
- Louis J. Walsh Scholarships 2019-2021
- Best Oral Presentation Award, Rice University Research Symposium 2019
- President's Honor Roll 2017-2021

PATENTS

1. Abudayyeh, O., Gootenberg, J., Nishimasu, H., Kazuki, K., Okazaki, S., Schmitt-Ulms, C., and **Jiang, K.** (2024). RNA-triggered protein cleavage and applications by the CRISPR Cas7-11-Csx29 complex. US Patent App. 18/234,690
2. **Jiang, K.**, Krajeski, R.N., Abudayyeh, O.O., Gootenberg, J.S., Zhang, Y., Chen, F., Chen, X., and Koob, J.G. (2023). Deaminase-based rna sensors. US Patent App. 17/806,879
3. Abudayyeh, O., Gootenberg, J., Villiger, L., and **Jiang, K.** (2023). Programmable insertion approaches via reverse transcriptase recruitment. US Patent App. 18/067,214
4. Abudayyeh, O., Gootenberg, J., and **Jiang, K**. (2023). Site specific genetic engineering utilizing trans-template rnas. US Patent App. 18/303,533
5. **Jiang, K.,** Villiger, L., Abudayyeh, O., and Gootenberg, J. (2023) Systems, methods, and compositions comprising miniature CRISPR nucleases for gene editing and programmable gene activation and inhibition. US Patent App. 63/211,610
6. Abudayyeh, O., Gootenberg, J., **Jiang, K**, and Lim, J. (2023). Fanzors are rna-guided nucleases encoded in eukaryotic genomes. US Patent App. 18/406,066

TEACHING EXPERIENCE

- Fall 2022 **20.110J: Thermodynamics of Biomolecular Systems,** Massachusetts Institute of Technology
  Graduate Teaching Assistant for Prof. Christopher Voigt, Prof. Linda Griffith & Prof. Eric Alm
- Fall 2020 **BIOE252: Bioengineering Fundamentals,** Rice University
  Undergraduate Teaching Assistant for Prof. Renata Ramos
- Fall 2019 **MATH211: ODEs and Linear Algebra,** Rice University
  Undergraduate Teaching Assistant for Prof. Milivoje Lukic

MENTORSHIP

- **For research associate Josephine Carscadden** May 2024-Now
  Josephine worked with me on evolving antibodies with machine learning models.
- **For high school intern Katrina Yang** May 2024-Aug 2024
  Katrina worked with me on optimizing circular RNA production.
- **For undergraduate intern Rahul Rajendran** May 2024-Aug 2024
  Rahul worked with me on optimizing large cargo gene insertion technology
- **For rotational student Jett Liu (MIT Microbiology)** Jan-March2024
  Jett worked with me on using large protein language model to optimize Rubisco's catalytic activity.
- **For rotational student Kai Wang (Harvard BBS)** Jan- March2024
  Kai worked with me on exploring RNA gated expression of cytokines and optimized the production of RADARS synthetic mRNA for in vivo delivery.
- **For research associate Samantha Sgrizzi** 2022-2024
  Sam worked with me on using machine learning models to in silico evolve higher activity proteins including polymerases, CRISPR/Cas nucleases, and carbonic anhydrases. She developed high throughput cell free expression systems for testing mutants. Sam is now a PhD student in University of Washington, Seattle.
- **For undergraduate student Michael Trinh (University of Toronto)** Jan-Dec2023
  Michael worked with me discovery of eukaryotic RNA-guided nucleases. He also designed RADARS constructs that selectively turn on OSKM in senescent cells. With this work, Michael won the time initiative aging research fellowship. Michael is now a PhD student in McGill University.
- **For high school student Rayya Reda Frayn** June-August 2023
  Rayya is learning basic molecular biology skills and looking into cost-effective high throughput multi-part Gibson assembly.

- **For rotational student Benyapa Khowpinitchai (Harvard BBS)** Feb- June2023
  Ben worked with me on engineering miniature CRISPR/Cas12f nucleases for *in vivo* gene regulation.
- **For rotational student Shuchen Luo (MIT Chemistry)** Aug- Dec2022
  Shuchen worked with me on optimization of RADARS platform for cancer cell specific killing and detection.
- **For rotational student Kathrin Kajderowicz (MIT BCS)** Jan- March2024
  Kat worked with me on using RADARS to perform RNA gated genome editing that can be used for *in vivo* lineage tracing. Kat is now a PD Soros Ph.D. Fellow at Whitehead Institute.

Professional Societies

- Biomedical Engineering Society (BMES) 2020-Now
- American Institute of Chemical Engineers (AIChE) 2023-Now

Journal Reviewer

*PLOS ONE *Frontiers in Neuroscience *Science of the Total Environment