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 evolutionary 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 & Preprints (* 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 in silico directed evolution by a protein language model with EVOLVEpro. *Science*.
   - **Summary:**
     We present EVOLVE-Pro, a state-of-the-art (SOTA) method that uses protein language model to rapidly design protein variants with up to 100-fold higher activity. EVOLVEpro achieves SOTA prediction accuracy across 12 deep mutational scanning datasets and we demonstrate its utility in rapidly engineering monoclonal antibodies, genome editing, and mRNA therapeutics.

[2] Yang, X., Rocks, JW., **Jiang, K.**, Walters, AJ., Rai, K., Liu, J., Nguyen, J., Olson, SD., Mehta, P., Collins, JJ., Daringer, NM., Bashor, CJ. (2025). Engineering synthetic phosphorylation signaling networks in human cells. *Science*.

[3] 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. [Accepted at *Nature Protocols*]

[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 ML Protein Engineering Seminar Series. (Virtual)
- 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.

PROFESSIONAL EXPERIENCE

Graduate Student, Abudayyeh-Gootenberg Lab, MIT & Harvard Medical School   **2021-2025**
- Developed a robust cell state sensor RADARS
- Characterized the first RNA-guided protease (Craspase) and eukaryotic RNA-guided nuclease (Fanzor)
- Developed a robust few-shot protein evolution language model (EVOLVEpro)

Rotational student with Prof. James Collins, MIT   **2021**

Rotational student with Prof. Michael Birnbaum, MIT   **2021**

Undergraduate Research Assistant, Caleb Bashor Lab, Rice University   **2018-2021**
- Engineered a fully synthetic phosphorylation network in mammalian cell

Intern, Regeneron Pharmaceuticals (Therapeutic antibody group)   **2019**
- Elucidated molecular mechanisms driving different humoral responses for adjuvants

Undergraduate Research Assistant, Gang Bao Lab, Rice University   **2017-2021**
- Designed a nanoparticle system for in vivo hyperthermia therapy

AWARDS & HONORS

- **Innovators Under 35** (TR35), MIT Technology Review, Asia-Pacific Region   2024
- **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