

Qiangqiang Shi, Ph.D.

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RESEARCH EXPERIENCE

Postdoctoral Fellow

University of Pennsylvania, Philadelphia, PA

04/2023 – Present

Advisor: Michael J. Mitchell, Ph.D.

Research Focus: *Development of novel mRNA lipid nanoparticles (LNPs) for Immunotherapy and Early Life (Embryos) Engineering*

- ❖ **Designed the prodrug LNP (pLNPs) library** embedding an intracellularly cleavable drug for codelivery of mRNA and small-molecule drug.
- ❖ Demonstrated **tumor control, T cell response** in tumor microenvironment, and **immunological memory** in a colon adenocarcinoma model via pLNP, **supporting an *in situ* vaccination paradigm** and systemic responses.
- ❖ **Led cross-disciplinary collaboration** (chemistry and immunology), and drafted an NIH R01 grant aligning with PI.
- ❖ **Created the novel IL library via Sulfur(VI) Fluoride Exchange (SuFEx) click chemistry** and discovered lung-tropic LNP, leading a platform for ***i.v.* lung-targeted mRNA vaccination**.
- ❖ Achieved predominant pulmonary transfection with LNPs, **enabling on-site antigen presenting cell (APC) cross-presentation**.
- ❖ Applied the lead **lung-targeted mRNA-LNP vaccine for potent lung cancer treatment**.
- ❖ Engineered **novel LNP formulations** for preimplantation **embryos** and **embryonic stem cells (ESCs)**.
- ❖ Enabled delivery of functional Cas9 mRNA and gRNA into **embryos and ESCs by optimized LNP for gene editing**.
- ❖ **Published first and co-first author** research articles in *Nature Nanotechnology*, *Nature*, and *PNAS*.

Graduate Researcher

09/2016 – 12/2022

University of Science and Technology of China (USTC), Hefei, Anhui

Advisor: Shiyong Liu, Ph.D.

Research Focus: *Innovation and Functional Exploration of Precise Encoded Polymeric Amphiphiles with Direct Sequence Readout*

- ❖ **Engineered “digital micelles”** with spherical and rod-like structures from **precise sequence-defined amphiphilic oligourethanes (SDOs)**.
- ❖ **Enabled direct sequence readout of SDOs** by tandem mass spectrometry and **label-free *ex vivo* quantification and Imaging** across cells, organs, and tissue slices **in the same animal**.
- ❖ Assembled SDOs to nanorods possessing different surface chemical groups such as methoxy (OMe), hydroxyl (OH), and maleimide (MI) moieties, **revealing surface-chemistry dependent protein coronas and reduced liver/spleen accumulation for MI-bearing nanorods**.
- ❖ **Invented dendritic quaternary-encoded oligourethanes** with a photoresponsive trigger and self-immolative backbones; undecodable by primary/tandem MS due to dendritic conformation, generating 2772-bit 2D keys ($\sim 1.98 \times 10^{87}$ permutations) for **high-strength encryption**.
- ❖ **Published 5 first author** research articles in *Nature Chemistry*, *Journal of the American Chemical Society*, and *Angewandte Chemie International Edition*.

- ❖ **Published 3 first and co-first author** review articles in *Progress in Polymer Science (invited)* and *Angewandte Chemie International Edition (invited)*, and *Nature Review Cancer*.
- ❖ **Mentored** three graduate students and two master students.

Undergraduate Researcher

09/2014 – 07/2016

Anhui Normal University, Wuhu, Anhui

Advisor: Xiaojun Zhang, Ph.D.

Research Focus: Hierarchical core-shell nanorod arrays for high-performance supercapacitor electrodes

- ❖ Fabricated ZnO@MnO₂@PPy ternary core-shell nanorod arrays (NRAs) via a layer-by-layer route to obtain self-supported electrodes.
- ❖ Improved charge-transfer kinetics (lower R_s by EIS) and delivered 1281 F g⁻¹ at 2.5 A g⁻¹ with areal capacitance 1.793 F cm⁻²; showed 90% retention after 5000 cycles.
- ❖ Outperformed ZnO@MnO₂ controls with ~1.6× higher areal capacitance and better rate capability, validating the conductive PPy shell strategy.
- ❖ **Published** one research article in *RSC Advances*.

EDUCATION

Doctor of Philosophy, Chemistry (polymer chemistry)

09/2016 – 12/2022

University of Science and Technology of China (USTC), Hefei, Anhui

Won Chinese Academy of Science (CAS) Presidential Scholarship **Special Prize (1%)**

Bachelor of Science, Chemistry

09/2012 – 06/2016

Anhui Normal University, Wuhu, Anhui

Won outstanding Undergraduate of Anhui Province **(5%)**

PUBLICATIONS

*Denotes equal contribution

h-index: 13

Citations: https://scholar.google.com/citations?user=eaDh_GwAAAAJ&hl=en

i10-index: 15

First and co-first author (13 papers)

25. **Q. Shi**, N. Gong, J. Wang, R. Palanki, M. Alameh, J. Melamed, J. Xu, C. Figueroa-Espada, L. Xue, Y. Zeng, X. Han, Q. Chen, H. Yamagata, R. E. Mayta, I. Yoon, D. Weissman, & M. J. Mitchell. Prodrug-tethered lipid nanoparticles for synergistic mRNA cancer immunotherapy. *Nature Nanotechnology* (2025), *in press*.
24. **Q. Shi**, H. Yin, R. Song, J. Xu, J. Tan, X. Zhou, J. Cen, Z. Deng, H. Tong, C. Cui, Y. Zhang, X. Li, Z. Zhang, & S. Liu. Digital micelles of encoded polymeric amphiphiles for direct sequence reading and ex vivo label-free quantification. *Nature Chemistry* 15, 257-270 (2023).
23. M. Chen*, J. Cen*, **Q. Shi***, J. Tan*, H. Geisler, Z. Lu, J. Zhao, B. Shao, C. You, Y. Liu, K. Jiang, G. Zhang, J. Hu, M. J. Mitchell, & S. Liu. Precision PEG lipids mitigate immunogenicity and enable repeatable mRNA therapeutics. *Nature* (2025), *in revision*.
22. C. Liu*, **Q. Shi***, X. Huang, S. Koo, N. Kong, & W. Tao. mRNA-based cancer therapeutics. *Nature Review Cancer* 23, 526-543 (2023).
21. J. Wang*, X. Huang*, **Q. Shi***, K. L. Swingle, A. G. Hamilton, N. Gong, & M. J. Mitchell. Drug-loaded bispecific T cell nanoengager overcomes T cell exhaustion for potent cancer immunotherapy. *Proceedings of the National Academy of Sciences* 122, (45), e2409564122 (2025)
20. **Q. Shi**, Z. Luo, Q. Zheng, A. Thatte, & M. J. Mitchell. Lung-targeted mRNA lipid nanoparticle vaccine against lung cancer. *In preparation*.

- 19 **Q. Shi**, C. Song, M. Chen, J. Xu, S. Zheng, J. Tan, J. Zhang, N. Wang, J. Hu, & S. Liu. Label-Free Quantification of Digital Nanorods Assembled from Discrete Oligourethane Amphiphiles. *Journal of the American Chemical Society*, 145, 23176-23187 (2023).
- 18 **Q. Shi**, X. Zhou, J. Xu, J. Zhang, N. Wang, G. Zhang, J. Hu, & S. Liu. Dendric Digital Oligourethanes for Quaternary Data Encryption. *Angewandte Chemie International Edition* 62, e202214695 (2023).
- 17 **Q. Shi**, Z. Zhang, & S. Liu. Precision Sequence-Defined Polymers: from Sequencing to Biological Functions *Angewandte Chemie International Edition* 62, e202313370 (2023).
- 16 **Q. Shi**, Z. Deng, M. Hou, X. Hu, & S. Liu. Engineering precise sequence-defined polymers for advanced functions. *Progress in Polymer Science*, 141, 101677 (2023).
- 15 **Q. Shi**, Y. Yu, L. Guo, J. Zhang, J. Tan, J. Zhang, J. Hu, & S. Liu. Controlled Fabrication of Distinct Nanostructures from Discrete Oligourethanes via Thermal Annealing. *ACS Macro Letters* 13, 1456-1462 (2024).
- 14 **Q. Shi**, X. Zhou, J. Xu, N. Wang, J. Zhang, X. Hu, & S. Liu. Controlled Fabrication of Uniform Digital Nanorods from Precise Sequence-Defined Amphiphilic Polymers in Aqueous Media. *Chinese Journal of Polymer Science* 41, 768-777 (2023).
- 13 M. Chen*, J. Cen*, **Q. Shi***, B. Shao, J. Tan, X. Ye, Z. He, Y. Liu, G. Zhang, J. Hu, & S. Liu. Ultrasound-Enhanced Spleen-Targeted mRNA Delivery via Fluorinated PEGylated Lipid Nanoparticles for Immunotherapy. *Angewandte Chemie International Edition* 64, e202500878 (2025).

Co-author (12 papers)

- 12 J. Cen, M. Chen, S. Shi, R. Song, **Q. Shi**, Z. Lu, J. Zhao, L. Shen, R. Tan, C. Song, Y. Zhang, L. Wang, J. Hu, M. J. Mitchell, Z. Zhang, & S. Liu. Molecular Fishing of Discrete PEG Derivatives for Precision Bioconjugates and Liposomal Delivery. *Nature Biomedical Engineering* (2025), *under review*.
- 11 Y. Zeng, J. Xu, J. Wang, L. Xue, H. Giesler, J. R. Melamed, **Q. Shi**, M. S. Padilla, J. Liu, Z. Luo, J. Zhu, A. S. Thatte, C. G. Figueroa-Espada, M. Ang, A. M. Murray, H. M. Yamagata, A. E. Metzloff, D. Weissman & M. J. Mitchell. mRNA lipid nanoparticle cancer vaccine platform co-delivering STING agonists for enhanced antitumor activity. *Proceedings of the National Academy of Sciences* (2025), *in revision*,
- 10 J. Xu, X. Han, H. Zhao, J. Zhu, Y. Zeng, Z. Luo, K. Swingle, A. G. Hamilton, C. Yi, L. Xue, G. Dwivedi, **Q. Shi**, R. Whitaker, N. Gong, B. Hymms, J. Wang, Q. Chen, I. C. Yoon, Y. Gong, Y. Fan, D. Weissman, & M. J. Mitchell. Therapeutic RNA delivery to the infarcted heart promotes angiogenesis and reverses endothelial plasticity. *Nature* (2025), *in revision*.
- 9 D. Kim, N. Gong, M. G. Alameh, E. L. Han, H. Wang, J. Wang, E. Feng, I. C. Yoon, A. M. Murray, **Q. Shi**, S. J. Moon, K. Mrksich, D. Weissman, & M. J. Mitchell. Crosslinked ionizable lipids reprogram dendritic cell metabolism for potent mRNA vaccination. *Nature Materials* (2025), *in press*.
- 8 Z. Deng, **Q. Shi**, J. Tan, J. Hu, & S. Liu. Sequence-Defined Synthetic Polymer for New-Generation Functional Biomaterials. *ACS Materials Letters* 3, 1339-1356 (2021).
- 7 W. Tao, W. He, X. Feng, G. Liu, **Q. Shi**, J. Tan, J. Hu, S. Yang, G. Liu, & R. H. Yang. Cationic Single-Unit Monomer Insertion (cSUMI): From Discrete Oligomers to the α -/ ω -End and In-Chain Sequence-Regulated Polymers. *Journal of the American Chemical Society* 145, 3636-3646 (2023).
- 6 J. Xu, C. Z. Lv, **Q. Shi**, J. L. Zhang, N. Wang, G. Y. Zhang, J. Hu, & S. Liu. Controlled Self-Assembly of Discrete Amphiphilic Oligourethanes with a Cascade Self-Immolative. *Angewandte Chemie International Edition* 62, e20230611 (2023).
- 5 L. Xue, X. Xiong, G. Zhao, W. Molina-Arocho, R. Palanki, Z. Xiao, X. Han, I. Yoon, C. G. Figueroa-Espada, J. Xu, N. Gong, **Q. Shi**, Q. Chen, M. Alameh, A. Vaughan, M. Haldar, K. Wang, D. Weissman, & M. J. Mitchell. Multiarm-Assisted Design of Dendron-like Degradable Ionizable Lipids Facilitates Systemic mRNA Delivery to the Spleen. *Journal of the American Chemical Society* 147, 1542-1552 (2025).

4. X. Han, M. Alameh, Y. Xu, R. Palanki, R. El-Mayta, G. Dwivedi, K. Swingle, J. Xu, N. Gong, L. Xue, **Q. Shi**, I. Yoon, C. Warzecha, J. Wilson, D. Weissman, & M. J. Mitchell. Optimization of the activity and biodegradability of ionizable lipids for mRNA delivery via directed chemical evolution. *Nature Biomedical Engineering* 8, 1412–1424 (2024).
3. I. Yoon, L. Xue, Q. Chen, J. Liu, J. Xu, Z. Siddiqui, D. Kim, B. Chen, **Q. Shi**, E. Han, M. Ruiz, K. Vining, & M. J. Mitchell. Piperazine-Derived Bisphosphonate-Based Ionizable Lipid Nanoparticles Enhance mRNA Delivery to the Bone Microenvironment. *Angewandte Chemie International Edition* 64, e202415389 (2025).
2. N. Gong, D. Kim, M. G. Alameh, R. E. Mayta, E. L. Han, G. Dwivedi, R. Palanki, **Q. Shi**, X. Han, L. Xue, J. Xu, Z. Meng, T. Luo, C. G. Figueroa-Espada, D. Weissman, J. Li, & M. J. Mitchell. Mannich reaction-based combinatorial libraries identify antioxidant ionizable lipids for mRNA delivery with reduced immunogenicity. *Nature Biomedical Engineering* (2025). DOI: <https://doi.org/10.1038/s41551-025-01422-8>.
1. W. Ma, **Q. Shi**, H. Nan, Q. Hu, X. Zheng, B. Geng, & X. Zhang. Hierarchical ZnO@MnO₂@PPy ternary core-shell nanorod arrays: an efficient integration of active materials for energy storage. *RSC Advances* 5, 39864-39869 (2015).

AWARDS

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| 10. | Chinese Academy of Science (CAS) Presidential Scholarship Special Prize (1%) | 2022 |
| 9. | Chinese Academy of Science (CAS) Excellent Doctoral Dissertation Award (3%) | 2024 |
| 8. | Anhui Province Excellent Doctoral Dissertation Award (5%) | 2023 |
| 7. | Guanghua scholarship at USTC | 2021 |
| 6. | Graduate Excellent Academic Scholarship at USTC | 2016-2022 |
| 5. | Outstanding Undergraduate of Anhui Province (5%) | 2016 |
| 4. | Outstanding Undergraduate at Anhui Normal University | 2016 |
| 3. | Outstanding Academic Scholarship at Anhui Normal University | 2015-2016 |
| 2. | National Inspiration Scholarship | 2015 |
| 1. | National Inspiration Scholarship | 2015 |

ORAL PRESENTATIONS

4. **Q. Shi**, M. J. Mitchell. *Prodrug-tethered lipid nanoparticles for synergistic mRNA cancer immunotherapy*. - Society for Biomaterials (SFB) 2025 Annual Meeting, Chicago, IL (2025).
3. **Q. Shi**, M. J. Mitchell. *Prodrug-tethered lipid nanoparticles for synergistic mRNA cancer immunotherapy*. - Biomedical Engineering Society (BMES) 2024 Annual Meeting, Baltimore, MD (2024).
2. **Q. Shi**, M. J. Mitchell. *Prodrug-tethered lipid nanoparticles for synergistic mRNA cancer immunotherapy*. - Center for cellular Immunotherapies Research in Progress (CCI-RIP), Philadelphia, PA (2024).
1. **Q. Shi**, S. Liu. *Innovation and Functional Exploration of Precise Encoded Polymeric Amphiphiles with Direct Sequence Readout*. - Annual Academic Conference for Graduate Students of USTC, Hefei, Anhui (2021).

PATENT APPLICATIONS

2. **Q. Shi**, & M. J. Mitchell. *Ionizable Lipid Prodrug Compounds and Lipid Nanoparticles (LNPs) Comprising Same*. U.S. Provisional Patent Appl. No. 63/7 10, 328, filed October 22, 2024.
1. **Q. Shi**, & S. Liu. *Barcode micelles and their preparation methods, detection methods and applications*. Patent No. ZL 2022 1 0271139.4.

MENTORSHIP

University of Science and Technology of China (USTC)

5. Xin Zhou, Master's Student, Department of Polymer Science and Engineering, USTC 2018 – 2021
Project –*Synthesis and Application of Self-immolative Polymers.*
4. Jie Xu, Graduate Student, Department of Polymer Science and Engineering, USTC 2018 – 2020
Project –*Controlled Self-Assembly of Discrete Amphiphilic Oligourethanes with a Cascade Self-Immolative Motif.*
3. Yong Yu, Master's Student, Department of Polymer Science and Engineering, USTC 2019 – 2022
Project –*Controlled Fabrication of Distinct Nanostructures from Discrete Oligourethanes via Thermal Annealing.*
2. Jialin Zhang, Graduate Student, Department of Polymer Science and Engineering, USTC 2020 – 2022
Project –*Solid phase synthesis for Fabricating Novel precision Self-immolative Polymers.*
1. Lingxiao Guo, Graduate Student, Department of Polymer Science and Engineering, USTC 2020 – 2022
Project –*Sequence-defined Polymers for Data Encryption.*

PROFESSIONAL EXPERIENCE

Journal Reviewer

Guest editor for special issue of *Molecular Therapy Methods & Clinical Development* (Lipid nanoparticles for cell and gene therapy)
Biomaterials
Chemistry of Materials
PloS One
Heliyon

RESEARCH SUPPORT

AIRFoundry Seed Grants (Upenn)

Current stage: Submitted

Amount: \$10,000 / 1 year

Role: PI

2026 University Research Foundation Grants Program

Current stage: Submitted

Amount: \$75,000 / 1 year

Role: Co-wrote with PI (M. J. Mitchell, and A. J. Modzelewski)

Melanoma Research Foundation Breakthrough Consortium (MRFBC) Team Award

03/2025 – 03/2027

Current stage: Funded

Amount: \$125,000 / 1 year for 2 years

Role: Co-wrote with PI (R. Amaravadi, and M. J. Mitchell)

TEACHING

University of Science and technology of China (USTC)

CHEM6019P Functional Polymer Materials

TA

1 Semester

REFERENCES

Prof. Michael Mitchell

Associate Professor of Bioengineering, University of Pennsylvania

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Address: 1 uCity Square, Room 1010, 25 N 38th St, Philadelphia, PA 19104

Prof. Andrew J. Modzelewski

Assistant Professor of Molecular Biology, University of Pennsylvania

Official Email: amodz@vet.upenn.edu

Address: School of Veterinary Medicine, 3800 Spruce Street, Philadelphia, PA 19104

Prof. Ravi Amaravadi

Professor of Medicine, Associate Director of Translational Research, Scientific Director of the Tara Miller Melanoma Center, University of Pennsylvania Perelman

Official Email: Ravi.Amaravadi@pennmedicine.upenn.edu

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