

Wyatt Miller, M.S.

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Research Interests

How cells detect synthetic mRNA, and how choices in mRNA design and manufacturing (nucleoside modification, capping, dsRNA byproducts) change that response. Self-amplifying RNA and RNA sensing, with the long-term aim of building mRNA therapeutics for rare diseases.

Education

M.S., Chemistry, Department of Chemistry & Biochemistry, University of California San Diego Jun 2021 – Dec 2023
GPA 3.85. Thesis: *Production and Purification of Fructose 2,6-Bisphosphate and Its Activity as the Cofactor of Polynucleotide Kinase 3'-Phosphatase* (2023). Advisor: Gourisankar Ghosh, Ph.D.

B.S., Biochemistry, California State University San Marcos Aug 2017 – Dec 2020
GPA 3.50. Upper-division GPA 3.72. Dean's List, four semesters.

Publications

1. Chakraborty A, Sreenivasmurthy SG, **Miller W**, Huai W, Biswas T, Mandal SM, Boscá L, Krishnan B, Ghosh G, Hazra T. Fructose-2,6-bisphosphate restores DNA repair activity of PNKP and ameliorates neurodegenerative symptoms in Huntington's disease. *Proc Natl Acad Sci U S A*. 2024;121(39):e2406308121. doi:10.1073/pnas.2406308121
2. Liu MA, Shahabi S, Jati S, Tang K, Gao H, Jin Z, **Miller W**, Meunier FA, Ying W, van den Bogaart G, Ghosh G, Mahata SK. Gut microbial DNA and immune checkpoint gene Vsig4/CRIg are key antagonistic players in healthy aging and age-associated development of hypertension and diabetes. *Front Endocrinol*. 2022;13:1037465. doi:10.3389/fendo.2022.1037465

Patent Applications (U.S. Provisional, assigned to Arcturus Therapeutics; lead inventor)

1. Methods and Compositions for In Vitro Transcription of RNA (pyrophosphate-mediated magnesium control in IVT). No. 63/856,160, filed Aug 2025.
2. Self-Amplifying RNA Compositions and Methods of Use (modified nucleosides in saRNA). No. 63/903,022, filed Oct 2025.
3. Methods and Compositions for In Vitro Transcription of RNA (co-transcriptional capping). No. 64/134,351, filed Aug 2026.

Research Experience

Research Associate II, RNA Innovation & Process Development, Arcturus Therapeutics, San Diego, CA Jan 2024 – present

Supervisors: Maher Alayyoubi, Ph.D.; Daiki Matsuda, Ph.D. (Executive Director, RNA Innovation)

- **Co-transcriptional capping.** Asked which IVT conditions control how much cap analog ends up on the transcript. Built an HPLC method that separates capped from uncapped RNA and gives same-day results; the standard approach relies on mass spectrometry, where the analysis alone takes days. Used it to map IVT conditions against capping efficiency and found conditions that keep capping high while using less cap analog. Basis of provisional application 64/134,351.
- **Modified nucleosides in self-amplifying RNA.** Tested whether N1-methylpseudouridine is compatible with saRNA replication. Modified saRNA gave higher protein expression and lower innate immune activation, measured with A549-Dual reporter cells (NF- κ B and IRF pathway readouts) and by cytokine levels in mice. Basis of provisional application 63/903,022.
- **dsRNA and degradation during IVT.** Standard chelators improve purity but cannot be used in a therapeutic process. Raised pyrophosphate, a natural IVT byproduct, so it acts as a weak built-in magnesium chelator. This cut dsRNA and truncated products and made long transcripts more stable. Basis of provisional application 63/856,160.
- **Translation and immunogenicity.** Developed a translation-enhancement strategy and screened mRNA constructs, giving 2-fold higher protein expression (Hep3B and A549 cells, mice) and 2-fold higher IgG titers (mice) than our clinical-stage benchmarks.
- Automated high-throughput mRNA synthesis and potency testing on Hamilton and Integra liquid handlers.

- Trained an intern and managed junior scientists who repeated these results.

Graduate Student Researcher, Ghosh Lab, Department of Chemistry & Biochemistry, UC San Diego Jun 2021 – Dec 2023

- **PNKP regulation by a glycolytic metabolite.** The lab had seen that the DNA repair enzyme PNKP associates with the glycolytic enzyme PFKFB3. Reproduced that result and followed it up to ask whether PFKFB3's product, fructose-2,6-bisphosphate (F2,6BP), acts on PNKP directly. Produced and purified F2,6BP, purified recombinant PNKP, and built a fluorescence-based phosphatase assay. F2,6BP increased PNKP 3'-phosphatase activity about 1.5-fold. This work became the M.S. thesis and contributed to the PNAS 2024 paper, where collaborators showed F2,6BP reduced DNA damage in Huntington's disease models.
- Mentored three undergraduate researchers in molecular biology methods and data analysis.
- Funded summer research appointment, Ghosh Lab, summers 2022 and 2023.

Presentations

Poster. Improving integrity of self-amplifying mRNA vaccine to increase shelf life. Arcturus Therapeutics Board of Directors Scientific Review, San Diego, CA, 2025. Selected to present.

Teaching and Mentoring

- **Teaching Assistant**, Department of Chemistry & Biochemistry, UC San Diego, five quarters, 2021–2023: General Chemistry Lab (2 quarters), Organic Chemistry Lab (2 quarters), Biochemistry Lab (1 quarter). About 150 students in total.
- **Research mentoring:** three undergraduates (UC San Diego, 2021–2023); an intern and junior scientists (Arcturus, 2024–present).
- **Student mentoring:** mentored visiting students from Mexico in a seven-week summer research program at UC San Diego, summer 2023.

Honors and Activities

All-Conference Scholar-Athlete, Southwestern Lacrosse Conference, UC San Diego. Collegiate lacrosse, CSU San Marcos (2017–2020) and UC San Diego (2021–2023). Eagle Scout, Boy Scouts of America.

Technical Skills

- **RNA:** IVT optimization, co-transcriptional capping, saRNA, nucleoside modification, mRNA purification and characterization, dsRNA analysis
- **Biochemistry:** recombinant protein expression and purification (E. coli), enzyme assay development, ÄKTA and Bio-Rad FPLC, HPLC, tangential flow filtration, HPLC-based capping analysis
- **Cell biology:** mammalian cell culture, transfection, luciferase reporter assays, immunoblotting, in-cell western, RT-qPCR, molecular cloning
- **Automation and data:** Hamilton and Integra liquid handlers, Python, GraphPad Prism, JMP, Benchling, SnapGene