ANDREY FEKLISTOV, PhD

San Francisco Bay Area | U.S. Citizen | andreyf@stanford.edu | Google Scholar

STRUCTURAL BIOLOGY & BIOCHEMISTRY | SMALL-MOLECULE DRUG DISCOVERY **andreyfeklistov.com**

PROFESSIONAL SUMMARY

Structural biologist, biochemist, and drug discovery program leader with 20+ years of experience connecting protein structure to regulatory mechanisms in transcription biology and structure-guided small-molecule design.

- Integrates structural, biochemical, assay, computational, and functional evidence to build falsifiable mechanistic models of protein function and regulation.
- Since 2019, drug discovery work has involved leadership in computationally guided small-molecule programs across immuno-oncology, broader oncology, and inflammation. Key contributions include target tractability assessment, assay design and data interpretation, scaffold/chemotype strategy, compound prioritization, and program-level discovery decisions.
- Contributions to transcription mechanisms and antibiotic inhibition of bacterial RNA polymerase have been recognized by a Blavatnik Award for Young Scientists and a Merck Foundation Postdoctoral Fellowship, with lead-author work in *Science* and *Cell* (cover story).
- Current Stanford work focuses on mechanisms of human transcriptional regulation using AI-enabled structural bioinformatics, structure prediction, and mechanistic modeling.

CORE EXPERTISE

Computational chemistry & structure-based drug design: Schrödinger Suite; docking and IFD-MD; MD and ensemble analysis; FEP+; WaterMap; RDKit; Biopython; binding-site and ligandability analysis; custom cheminformatics workflows for chemical-space exploration and scaffold hopping; active learning; multiparameter optimization in LiveDesign; covalent inhibitor design

Structural & experimental biology: X-ray crystallography; single-particle cryo-EM; protein expression and purification; protein-ligand, protein-protein, and protein-nucleic-acid analysis; SELEX; biochemical assay design and development; stopped-flow kinetics; mechanism-driven experimental design

Discovery strategy & program leadership: target enablement and tractability assessment; scaffold/chemotype strategy; hit-to-lead reasoning; compound triage and prioritization; SAR interpretation; assay-informed chemistry decisions; medicinal chemistry-facing design strategy; CRO/vendor coordination; consultant management; cross-functional scientific communication

AI & scientific computing: Python; AI-assisted coding and data analysis; hierarchical multi-agent research system design; biomolecular structure prediction and complex co-folding (AlphaFold 3, Chai-1, Boltz); HPC cluster computing and batch-job execution; literature, sequence, structure, and functional-data mining; MSA-based evolutionary covariance analysis; reproducible scientific workflows; mechanistic model building

PROFESSIONAL EXPERIENCE

STANFORD UNIVERSITY SCHOOL OF MEDICINE | Palo Alto, CA **2021-Present**

Senior Research Engineer (2022-Present) | Visiting Scholar (2021-2022), Roger D. Kornberg Laboratory

- Published a single-author Trends in Biochemical Sciences perspective (2024) synthesizing promoter-melting dynamics into a unified mechanistic framework.
- Formulated a mechanistic hypothesis addressing a central unresolved question in eukaryotic transcription: how activator binding to human Mediator is transmitted to RNA polymerase II, and published a concise version of the model. An expanded manuscript is in preparation.
- Developed an end-to-end computational pipeline for large-scale AlphaFold co-folding ensemble analysis integrating cryo-EM, sequence/biophysical evidence, and functional datasets to refine testable models of human transcription regulation.
- Built Claude Code/Codex-assisted AI reasoning infrastructure for Mediator biology, combining an Obsidian-based structured project knowledge system with a hierarchical division of agent roles across code development, result review, and adversarial hypothesis testing.
- Built a modular JavaScript automation system for lab-wide procurement, organizing thousands of records and automating reminder workflows.

INTERX / NEOTX, LAB DIVISION | Menlo Park, CA **2019-Present**

Scientific Director & Head of Biology (2019-2022) | Scientific Director / Consultant, part-time (2022-present)

- Led structure-guided chemical strategy for PD-L1-centered preclinical small-molecule discovery (manuscript in preparation), with additional work developing small-molecule approaches for PARP and TNF-alpha.
- Advanced PD-L1 chemistry from a fragment hit into a differentiated lead series, establishing a novel chemotype in a patent-crowded inhibitor landscape and extending the series toward sp3-enriched ligand space through custom cheminformatics scripting.
- Set compound-prioritization and follow-up design priorities by weighing structural models, SAR, and biochemical/cellular assay data.
- Worked with Robert Dow (BioPharmaWorks; Pfizer veteran) and Stevan Djuric (former AbbVie VP, Discovery Chemistry) as senior medicinal chemistry advisors, contributing independent structure-guided chemical judgment to design choices.
- Led a five-person MS/PhD discovery team, coordinated external consultants and CROs, and contributed to target selection, senior scientific hiring, IP strategy, and provisional patent preparation.

ROCKEFELLER UNIVERSITY | New York, NY **2006-2019**

Research Associate/ Independent Project Lead (2011-2019) | Postdoctoral Fellow (2006-2011), Seth A. Darst Laboratory

- Designed and executed structural and mechanistic studies of bacterial transcription, integrating high-resolution X-ray crystallography, single-particle cryo-EM, reconstituted transcription biochemistry, molecular biology, and stopped-flow fluorescence assay development.
- Defined key structural and kinetic principles of a central mechanism in molecular biology: how bacterial RNA polymerase recognizes promoter DNA and melts the transcription bubble; work culminated in a Cell cover article (first/co-corresponding author) and a Science paper (first/corresponding author).

ADDITIONAL DRUG DISCOVERY & TARGET-STRATEGY PROGRAMS

PARP: Formulated an early structure-based strategy focused on the adenine pocket and evaluated structural evidence, known chemical matter, assay logic, and tractability before a portfolio pivot to PD-L1.

TNF-alpha: Designed an early small-molecule strategy for TNF-alpha that integrated structural analysis, disease rationale, assay logic, and tractability. Contributed to a successful Israel Innovation Authority grant application.

AHR / inflammatory bowel disease (IBD): Advised an early-stage startup on target evaluation and initial strategy for the human aryl hydrocarbon receptor (AHR) in chronic IBD and integrated receptor structure/function, ligand selectivity, disease biology, and small-molecule tractability.

ADDITIONAL RESEARCH EXPERIENCE

UNIVERSITY OF WISCONSIN-MADISON | Madison, WI **2014**
Honorary Fellow, Robert C. Landick Laboratory

- Used stopped-flow fluorescence kinetics to resolve RNA polymerase structural dynamics during promoter opening.

PUBLIC HEALTH RESEARCH INSTITUTE | Newark, NJ **2004-2006**
Research Scientist, Alexander D. Goldfarb Laboratory

- Clarified a key mechanistic question in the action of rifampicin, a clinically important first-line tuberculosis antibiotic; published as first author in PNAS.

INSTITUTE OF MOLECULAR GENETICS / MOSCOW STATE UNIVERSITY | Moscow, Russia **2002-2006**
Graduate Researcher, Andrey V. Kulbachinskiy Laboratory

- Used SELEX and mechanistic biochemistry to identify high-affinity RNA polymerase aptamers and discover a previously unrecognized bacterial promoter element that determines holoenzyme promoter recognition (first author, Molecular Cell).

SELECTED WORK

*Author key: underlined name = first author; * = corresponding author.*

In preparation

- Feklistov A*, Kornberg RD. A Structural Model of Transcription Activation by Mediator.
- Feklistov A*, et al. Structure-guided scaffold diversification of small-molecule PD-L1 dimerization inducers from phenyl-benzothiophene cores to sp3-enriched spirocyclic ligands.

Published

- Kornberg RD, Feklistov A*. In Defense of Biochemistry: Studies of Transcriptional Regulation. Journal of Molecular Biology. 2025;437(22):169299.
- Feklistov A*. Dynamics and logic of promoter melting. Trends in Biochemical Sciences. 2024;49:8-11.
- Feklistov A*, et al. RNA polymerase motions during promoter melting. Science. 2017;356:863-866.
- Bae B, Feklistov A, et al. Structure of a bacterial RNA polymerase holoenzyme open promoter complex. eLife. 2015;4:e08504. **Equal contribution.**
- Feklistov A*, Darst SA. Structural basis for promoter -10 element recognition by the bacterial RNA polymerase sigma subunit. Cell. 2011;147:1257-1269. **Cover story.**
- Feklistov A, et al. Rifamycins do not function by allosteric modulation of Mg2+ binding to the RNA polymerase active center. PNAS. 2008;105:14820-14825.
- Feklistov A, et al. A basal promoter element recognized by free RNA polymerase sigma subunit determines promoter recognition by RNA polymerase holoenzyme. Molecular Cell. 2006;23:97-107.

Full publication record: Google Scholar

SELECTED TALKS

- **Invited seminars:** Karolinska Institute (2018); University of Birmingham (2018); Hong Kong University of Science and Technology (2014).
- **Selected conference talks:** Harden Conference, "Machines on Genes IV" (2016); FASEB SRC Mechanism and Regulation of Prokaryotic Transcription (2015, 2011); Gordon Research Conference, Nucleic Acids (2015).

EDUCATION & SELECTED TRAINING

PhD, Molecular Biology | Moscow State University, 2006
BSc/MS, Biochemistry, summa cum laude | Moscow State University, 2002

Selected training: Medicinal Chemistry in Drug Discovery (Drew University); High-Throughput Virtual Screening (Schrödinger); X-Ray Methods in Structural Biology (CSHL); RapiData X-Ray Crystallography (NSLS/Brookhaven); CCP4 Crystallography School (APS/Argonne); stopped-flow kinetics workshop (UT Austin); Stanford AI training.

SELECTED HONORS & PROFESSIONAL SERVICE

- **Blavatnik Award for Young Scientists** (2012)
- **Merck Foundation Postdoctoral Fellowship** (2009-2011)
- **Evrogen JSC Award for Young Scientists** (2002)
- **International Biology Olympiad Silver Medal** (1997)

Ad hoc reviewer: Science, Nature Reviews Microbiology, Genes & Development, Cell Reports, Biochemistry, BMC Biology, and Journal of Molecular Biology.