SPANDAN CHENNAMADHAVUNI, PhD

Principal Scientist & Head of Discovery | Medicinal Chemistry | Drug Discovery
Boston, MA | 662-801-3628 | schennam@gmail.com
scholar.google.com/Spandan-Chennamadhavuni | US Permanent Resident (EB-1A — Extraordinary Ability)

PROFESSIONAL SUMMARY

18+ years drug discovery expertise spanning antiviral, oncology, and CNS programs. Proven track record in SBDD/LBDD/CADD, hit-to-lead, lead optimization, IND-enabling studies, cross-functional team leadership, CRO management, and IP creation across small molecules and macrocycles. 1,169 citations | h-index 10 | i10-index 11 | 4 patents | 2 NIH grants.

CORE COMPETENCIES

Medicinal Chemistry | Organic Synthesis | Asymmetric and Chiral Synthesis | Macrocyclic Drug Design | Peptidomimetic Chemistry | Nucleoside Analog Design | Covalent Inhibitor Design | Fragment-Based Drug Design (FBDD) | Rhodium (II)-Carbenoid C–H Functionalization | Natural Product Synthesis

Structure-based design (SBDD) | Ligand-based design (LBDD) | Computer-aided drug design (CADD) | Molecular docking | Virtual screening | Pharmacophore modeling | Hit-to-lead advancement | Lead optimization | Multiparameter optimization | SAR/SPR analysis | PK/PD modeling | ADMET optimization | IND-enabling studies | Beyond Rule-of-Five (bRo5)

RdRp inhibitor programs (RSV, SARS-CoV-2, dengue) | Viral protease inhibitors | MALT1 paracaspase | TAK1 kinase inhibitors | APE1 (BER) | Protein-protein interactions (PPI) | NF-κB/REL | Antimicrobial resistance (AMR/colistin) | Therapeutic areas: antiviral, oncology, and CNS (SNRI/5HT2A)

Project Team Leadership | Cross-Functional Team Management | CRO/FTE Management | NIH Grant Administration | IP Strategy & Patent Filing | Preclinical Candidate Selection | IND Application | cGMP/GMP Manufacturing

PROFESSIONAL EXPERIENCE

Principal Scientist & Head of Discovery — 2022 – 2026

Atea Pharmaceuticals, Inc. | Boston, MA

- **RSV RdRp Program Lead:** Tasked with building Atea's RSV antiviral pipeline from scratch, directed cross-functional team of chemists, CADD scientists, PK, and biologists; advanced program to preclinical candidate stage.
- **Synthetic Route Architecture:** Faced with no existing synthetic access to lead scaffolds, designed de novo multi-step routes to 4 distinct RSV inhibitor series, enabling parallel SAR/MPO optimization campaigns across 200+ analogs.
- **SBDD Portfolio Strategy:** Assigned as sole chemistry leader across all Atea discovery programs; applied structure-based design to dengue (AT-752 franchise), RSV, and broad-spectrum antiviral series, accelerating candidate selection timelines.
- **IP Generation:** Identified novel antiviral chemotype with favorable IP landscape; designed and synthesized diaryl hydantoin series, resulting in composition-of-matter patent filing (2024).
- **Peptidomimetic Protease Inhibitors:** Tasked with expanding antiviral portfolio to protease targets; executed full SBDD-guided SAR campaign across broad-spectrum viral protease series; manuscript in preparation (2025).
- **CRO Oversight:** Managed external chemistry FTEs across global CROs; implemented real-time project monitoring systems, maintaining milestone delivery and compound quality standards across 3 concurrent programs.

Senior Staff Scientist & Group Leader — 2015 – 2022

Emory University, Department of Chemistry (Prof. Dennis Liotta Group) | Atlanta, GA

- **COVID-19 / Molnupiravir — Key Contributor:** Tasked with rationalizing antiviral mechanisms during the pandemic emergency; constructed bio structural models of SARS-CoV-2 RdRp pre-catalytic complex, providing mechanistic basis for EIDD-2801 (Molnupiravir/Lagevrio™), which received FDA Emergency Use Authorization as a first-in-class oral COVID-19 antiviral; published in J. Chem. Inf. Model. (2021).
- **Next-Generation SARS-CoV-2 Antivirals:** Following Remdesivir EUA, tasked with developing improved RdRp and protease inhibitors; designed and synthesized novel nucleoside analog and peptidomimetic series using SBDD, achieving improved selectivity over approved agents.

- **HBV Drug Repurposing Program:** Challenged to rescue clinically failed nucleoside drugs for hepatitis B; modulated PK/ADMET profiles through systematic analog synthesis, restoring antiviral efficacy in cellular models;.
- **Antibiotic Resistance (AMR/Colistin) — NIH-R33:** Responding to colistin-resistant A. baumannii crisis, collaborated with microbiologists to identify NaxD as adjuvant target; synthesized hit-to-lead small molecule series re-sensitizing resistant bacteria; secured NIH-R33 grant; published ACS Infectious Diseases (2023).
- **Pancreatic Cancer — Curcumin Analog Program:** Tasked with developing novel antitumor agents for pancreatic/breast cancer; synthesized 20+ monocarbonyl curcumin analog (MAC/UBS109) series with in vitro potency; demonstrated tumor xenograft reduction in vivo; published Oncotarget (2018); secured $50,000 in non-profit funding.
- **Team & Grant Leadership:** Managed group of 5–6 scientists across synthesis, CADD, and pharmacology; administered 2 funded NIH grants (R01, R33); led external CRO collaborations, maintaining on-time delivery for all preclinical milestones.

Scientific Consultant **2019 – 2025**

Migra Therapeutics (2019) | Rixoma Therapeutics (2020–2022) | Suneco Therapeutics (2023–2025)

- **Nanoparticle Drug Delivery IP Evaluation (Migra):** Led 4-member consulting team to assess targeted nanoparticle cancer platform; evaluated freedom-to-operate, GMP manufacturing path, and clinical trial strategy; pitched to venture capitalists, facilitating seed funding discussions.
- **cGMP Manufacturing & CRO Management (Rixoma):** Engaged as primary consultant for nutraceutical API manufacturing; established cGMP production protocols, managed offshore CROs, and delivered quarterly progress reports, ensuring regulatory compliance.

Scientist **2014 – 2015**

Harvard Medical School / Dana-Farber Cancer Institute (Nathanael Gray & Scott Labs) | Boston, MA

- **MALT1 Covalent Inhibitor Program (NIH-R01CA182736):** Tasked with developing first selective covalent MALT1 paracaspase inhibitors for chemoresistant ABC-DLBCL; synthesized ~100 tri/tetrapeptide substrate-mimetic inhibitors; achieved cellular potency and in vivo tumor suppression; published J. Clin. Invest. (2018, 67 citations) and Bioorg. Med. Chem. Lett. (2019, 17 citations).
- **Janssen Pharmaceuticals In-Licensing:** Developed MALT1 inhibitor IP portfolio through systematic SAR and warhead optimization; resulted in comprehensive patent (WO/2017/040304) in-licensed to Janssen Pharmaceuticals, translating academic discoveries to industry pipeline.

Postdoctoral Associate **2011 – 2014**

Boston University, Department of Chemistry (John Porco Jr. Group) | Boston, MA

- **Macrocycle Drug-Likeness Rules — Nature Chemical Biology:** Tasked with establishing first predictive framework for macrocycle oral bioavailability and target-binding; synthesized 100+ structurally diverse macrocycles, co-developed computational FTMap analysis; landmark publication in Nature Chemical Biology (2014, 471 citations) established bRo5 drug-likeness rules analogous to Lipinski's Ro5.
- **APE1 Macrocyclic Inhibitor Discovery:** Assigned to identify first macrocyclic inhibitors of APE1 (base excision repair target upregulated in resistant tumors); applied SBDD hot-spot mapping to guide macrocycle design; published J. Med. Chem. (2019, 20 citations).
- **NF-κB/REL Inhibitor (Oncology):** Developed calafianin monomer derivatives as selective REL/NF-κB inhibitors; demonstrated proliferation arrest and apoptosis in B-lymphoma cell lines; published Molecules (2015).
- **Novel Macrocyclization Methodology:** Developed diastereodivergent one-pot intramolecular aza-Michael/lactamization sequence providing stereochemical control over chiral macrocyclic scaffolds; published J. Org. Chem. (2018); one provisional patent filed.

Doctoral Student — Organic/Medicinal Chemistry **2006 – 2011**

Emory University, Department of Chemistry (Prof. Huw Davies Group) | Atlanta, GA

- **Cyclopropane-Based SNRI Analogs (Neuropathic Pain):** Charged with accessing structurally novel SNRI scaffolds for neuropathic pain lacking effective therapies; synthesized ~40 chiral cyclopropane analogs via Rh(II)-catalyzed

enantioselective C–H functionalization; demonstrated SERT/NET activity; resulted in issued US patent and Tetrahedron (2013, 29 citations).

- **5HT2A Antagonists (Cocaine Addiction):** Tasked with providing CNS tool compounds to evaluate 5HT2A as cocaine addiction target; synthesized ~100 antagonists, applied computational docking to rationalize SAR; validated efficacy in vitro, in vivo, and in non-human primate studies.
- **TAK1 Kinase Inhibitor Program (Oncology):** Assigned to develop selective TAK1 kinase inhibitors (NF-κB/TGFβ signaling in cancer); synthesized ~50 inhibitors, established potency, and selectivity profile; resulted in funded NIH-R01 grant and issued US patent (9,751,825, 2017).
- **Enantioselective Cyclopropanation Methodology:** Developed comprehensive guide to dirhodium(II)-catalyzed enantioselective cyclopropanation; established substrate scope and stereochemical models; published Synfacts (2013) and Organic Syntheses (2010).

Doctoral Student — Organic Chemistry **2003 – 2006**

University of Mississippi (Jon C Antilla Group) | Oxford, MS

- **Organocatalytic Imine Amidation (JACS):** Challenged to develop metal-free enantioselective imine functionalization during early organocatalysis era; pioneered chiral phosphoric acid-catalyzed imine amidation achieving high ee without transition metals; published J. Am. Chem. Soc. (2005, 290+ citations), supported by NIH-R01 grant.

EDUCATION

Ph.D., Organic/Medicinal Chemistry 2011

Emory University, Atlanta, GA (Adviser: Prof. Huw M.L. Davies)

Ph.D. coursework, Organic Chemistry (transferred) 2003–2006

University of Mississippi, Oxford, MS (Adviser: Prof. Jon C Antilla)

SELECTED PEER-REVIEWED PUBLICATIONS (15 TOTAL | 1,169 CITATIONS | H-INDEX 10 | I10-INDEX 11)

- Crispell E, Chennamadhavuni S, et al. Antibiotic adjuvant inhibits NaxD to reverse colistin resistance. ACS Infect. Dis. (2023) [NIH-R33]
- Prussia AJ, Chennamadhavuni S. Biostructural models for nucleoside analogs binding to SARS-CoV-2 RdRp. J. Chem. Inf. Model. 61, 1402 (2021) [10 citations]
- Trilles R, Chennamadhavuni S, et al. Discovery of macrocyclic APE1 inhibitors. J. Med. Chem. 62, 1971 (2019) [20 citations]
- Hatcher JM, Chennamadhavuni S, et al. Peptide-based covalent MALT1 inhibitors. Bioorg. Med. Chem. Lett. 29, 1336 (2019) [17 citations]
- Fontán L, Chennamadhavuni S, et al. Covalent MALT1 inhibition suppresses B cell lymphoma. J. Clin. Invest. 128, 4397 (2018) [67 citations]
- Shoji M, Chennamadhavuni S, et al. Inhibition of breast cancer metastasis with UBS109. Oncotarget 9, 36102 (2018) [12 citations]
- Chennamadhavuni S, et al. Diastereodivergent synthesis of chiral pyrrolodiazepinediones. J. Org. Chem. 83, 15449 (2018)
- Villar EA, Chennamadhavuni S, et al. How proteins bind macrocycles. Nat. Chem. Biol. 10, 723 (2014) [471 citations] ★ Landmark bRo5 rules paper
- Rowland GB, Chennamadhavuni S, et al. Brønsted acid-catalyzed imine amidation. J. Am. Chem. Soc. 127, 15696 (2005) [290+ citations] ★ Seminal organocatalysis paper

Full list: Google Scholar

PATENTS

- Diaryl hydantoin compounds and uses thereof — Composition of matter patent filed (2024) [Atea Pharmaceuticals]
- Gray NS, Scott DA, Chennamadhavuni S, et al. MALT1 inhibitors. US Patent 10,711,036 / WO/2017/040304 (2020) [In-licensed: Janssen Pharmaceuticals]
- Davies HML, Chennamadhavuni S, Bakin A. TAK1 kinase inhibitors. US Patent 9,751,825 & 10,093,609 (2017–2018)
- Davies HML, Chennamadhavuni S, et al. Cyclopropyl derivatives and methods of use. US Patent 10,207,984 (2019)

HONORS & RECOGNITION

- USCIS EB-1A Permanent Residency — Extraordinary Ability in Sciences (2020s) — one of the highest evidentiary standards in U.S. immigration law, reserved for those in the top percentile of their field.
- Key contributor to FDA Emergency Use Authorization of Molnupiravir (Lagevrio™) for COVID-19 — structural modeling work published 2021.
- Nature Chemical Biology macrocycle paper (2014) cited 471+ times — among most-cited papers in macrocycle drug design field.
- JACS organocatalysis paper (2005) cited 290+ times — seminal contribution to asymmetric synthesis.
- Two funded NIH grants as principal investigator/co-investigator (R01, R33)
- Technology in-licensed to Janssen Pharmaceuticals (J&J) MALT1 inhibitor patent
- $50,000 non-profit research grant from "It's the Journey" organization for pancreatic cancer research.

TECHNICAL SKILLS

Synthesis: Multi-step organic synthesis, chiral synthesis, asymmetric catalysis, Rh(II) carbenoid C–H functionalization, macrocyclization, peptide/peptidomimetic synthesis, nucleoside chemistry, heterocyclic synthesis

Design & Modeling: Schrödinger Suite, MOE, AutoDock, Glide, FTMap, pharmacophore modeling, molecular dynamics, free-energy perturbation (FEP), virtual screening, QSAR/QSPR

Analysis: NMR (1H, 13C, 2D), HPLC, LC-MS, HRMS, chiral HPLC, PK/PD data analysis, ADMET profiling, in vitro/in vivo data interpretation

Leadership: Cross-functional team management, CRO oversight, NIH grant writing & administration, patent preparation, IND strategy, preclinical candidate selection, project management (Agile/Waterfall)