Joel S. Freundlich

Department of Pharmacology, Physiology & Neuroscience
Department of Medicine
Center for Emerging and Reemerging Pathogens
Rutgers University – New Jersey Medical School
Medical Sciences Building, I503
185 South Orange Avenue
Newark, NJ 07103
freundjs@njms.rutgers.edu
(973) 972-7165 (office)
(609)-865-7344 (cell)

RESEARCH INTERESTS

Dr. Freundlich leads a research group of twelve scientists pursuing the development and application of computational, chemical, and biological tools to study infectious diseases, with a specific focus on *Mycobacterium tuberculosis*.

- How may the properties (physiochemical, ADME, biological) of chemical tools be predicted and then evolved via machine learning methodologies?
- How are potent antitubercular agents metabolized by the mammalian host or *M. tuberculosis* in detoxification and/or activation events?
- How do antitubercular small molecules leverage the modulation of more than one target to achieve significant cidality?

PROFESSIONAL EXPERIENCE

RUTGERS UNIVERSITY-NEW JERSEY MEDICAL SCHOOL, Newark, NJ July 2014 to present
Associate professor (Department of Pharmacology & Physiology)
Associate professor (Department of Medicine)
Member (Center for Emerging and Reemerging Pathogens)
Courses taught:
The Chemical Biology of Pathogens GSBS 5160Q – Spring 2015 - 2016
Select Agent Biology MSBS N517Q – Spring 2012 - 2013
Pharmacology PHRM 7206 – Spring 2012 – 2016
Advanced Concepts in I^3 GSBS 5022Q – Spring 2012 – 2013, 2015, 2016
Topics in Pharmacology PHPY-N5030 – Spring 2016
Introduction to Genomics, Proteomics, and Bioinformatics MBGC 5002Q – Spring 2015
University Activities:
Admissions Committee for M.D./Ph.D. candidates (2013–)
Molecular Biology-Genetics-Cancer Track Oversight Committee member (2013–)
Institutional Biosafety Committee member (2013 –)

RUTGERS UNIVERSITY-NEW JERSEY MEDICAL SCHOOL, Newark, NJ May 2011 to June 2014
Assistant professor (Department of Pharmacology & Physiology)
Assistant professor (Department of Medicine)
Member (Center for Emerging and Reemerging Pathogens)

TEXAS A&M UNIVERSITY, College Station, TX March 2006 to April 2011
Senior research scientist (Department of Biochemistry & Biophysics)

- Led research group of 5 – 7 researchers (typically two Ph.D. staff scientists, two post-doctoral associates, and one to three undergraduates) to study the fundamental biology pertinent to *Mycobacterium tuberculosis* and *Plasmodium falciparum*.

RUTGERS UNIVERSITY, Piscataway, NJ March 2009 to May 2011
Visiting professor (Department of Medicinal Chemistry)

- Taught Pharmaceutical Chemistry (30:715:306) in Spring 2010

PRINCETON UNIVERSITY, Princeton, NJ March 2006 to March 2009
Visiting senior research scholar (Department of Chemistry)

- Garnered internal grant support to conduct interdisciplinary research and education programs in infectious diseases through the Grand Challenges Initiative in Global Health. Mentored four undergraduate students in the laboratory and seven students in junior thesis work.

JACOBUS PHARMACEUTICALS, Princeton, NJ November 2003 to March 2006
Senior scientist

- Responsible for project leadership functions, including compound design using molecular modeling tools, management of SAR database, and coordination of biological testing of compounds through academic collaborators.

PROVID PHARMACEUTICALS, Piscataway, NJ May 2003 to October 2003
Consultant

- Investigated design and synthesis of small molecule therapeutics for Huntington's disease.

LOCUS PHARMACEUTICALS, Blue Bell, PA April 2001 to May 2003
Senior Scientist

- Contributed to IND filing of a novel cell cycle inhibitor.
- Utilized rapid design and synthesis approach in the hit generation stage to investigate six biological targets in two years.

PRAECIS PHARMACEUTICALS, Piscataway, NJ June 1998 to March 2001
Scientist II *January 2000 to March 2001*
Scientist I *June 1998 to January 2000*

- Contributed to IND filings for Apan, an Alzheimer's disease therapeutic which inhibits the aggregation of β-amyloid into neurotoxic species, and PPI-2458, an anti-angiogenic therapeutic for non-Hodgkins lymphoma and rheumatoid arthritis.
- Coordinated research efforts of six chemists and biological studies with biochemistry group in Cambridge, MA and CROs.

COLGATE-PALMOLIVE COMPANY, Piscataway, NJ June 1996 to June 1998
Research Scientist - Advanced Technology Group

- Synthesized small organic molecules, modified amino acids, and polyamides and screened for their use in controlling the structure of aluminum and zirconium complexes.

EDUCATION

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Ph.D. in Organic Chemistry, 1996

- Thesis under 2005 Nobel Prize in Chemistry recipient Richard R. Schrock on "Metal-Ligand Multiple Bonds in Organometallic Complexes Featuring Tren-Based Ligand Systems."
- Synthesized triamidoamine ligand complexes of tantalum, niobium, and tungsten as models for olefin and alkyne metathesis catalysts.

CORNELL UNIVERSITY
Master of Engineering (Chemical) with Dean's certificate in Engineering Management, 1992

- Modeled the energetics of pyridine-metal surface interactions by performing Extended Hückel Molecular Orbital Calculations with 1981 Nobel Prize in Chemistry recipient Roald Hoffmann.
- Devised synthetic route towards the DNA lesion product common to spores with Tadhg P. Begley.

Bachelor of Science in Chemical Engineering with Distinction, 1991

- Synthesized imidazole-based molecules to examine the mechanism of β-glucosidase inhibition with Bruce Ganem.
- Utilized the vicinal tricarbonyl moiety in the total synthesis of complex organic molecules with Harry H. Wasserman (Yale University).

PROFESSIONAL ACTIVITIES

NIH Study Section Member
ZRG1 IMST-L (11) B Small Business: Biological Chemistry, Biophysics and Drug Discovery (2012–2013)
NIH Study Section U.S.-South African Program for Collaborative Biomedical Research RFA (2014)
Symposia Chair

- "Tuberculosis: Biology and Emerging Therapeutics," American Chemical Society National Meeting 03/17/2014
- "Advances in Virtual High-Throughput Screening," American Chemical Society National Meeting 04/10/2013

Editorial Board

- Antimicrobial Agents and Chemotherapy (2017 –)

Journal Referee
Antimicrobial Agents and Chemotherapy, Nature Communications, Nature Chemical Biology, ACS Chemical Biology, ACS Infectious Diseases, Journal of Medicinal Chemistry, Bioorganic and Medicinal Chemistry Letters, BMC Bioinformatics, Tetrahedron
Scientific Advisor Board
Hereditary Neuropathy Foundation, Phoenix Nest, Inc., Collaborations Pharmaceuticals
Member

- American Chemical Society
- American Society for Microbiology

PUBLICATIONS

51. Vilchèze, C., Hartman, T., Weinrick, B., Leung, L. W., Freundlich, J.S., Jacobs Jr., W.R., "Enhanced respiration prevents drug tolerance and drug resistance in Mycobacterium tuberculosis," Proceedings of the National Academy of Science USA **2017**, *114*, in press. PMID:

50. Sukheja, P., Kumar, P., Mittal, N., Li, S.-G., Singleton, E., Russo, R., Perryman, A. L., Shrestha, R., Awasthi, D., Husain, S., Soteropoulos, P., Brukh, R., Connell, N., **Freundlich, J.S.**, Alland, D., "A novel small molecule inhibitor of the *Mycobacterium tuberculosis* menaquinone methyltransferase MenG is cidal to both growing and nutritionally-deprived persister cells," mBio **2017**, *8*, e02022. PMID: 28196957

49. Vila-Farres, X., Chu, J., Inoyama, D., Ternei, M.A., Lemetre, C., Cohen, L.J., Cho, W., Reddy, B.V., Zebroski, H.A, **Freundlich, J.S.**, Perlin, D.S., Brady, S.F., "Antimicrobials inspired by nonribosomal peptide synthetase gene cluster," Journal of the American Chemical Society **2017**, *139*, 1404. PMID: 28055186

48. Kumar, P., Kaushik, A., Lloyd, E. P., Li, S.-G., Mattoo, R., Ammerman, N. C., Bell, D. T., Perryman, A. L., Zandi, T. A., Ekins, S., Ginell, S. L., Townsend, C. A., Freundlich, J.S., Lamichhane, G., "Non-classical transpeptidases yield insight into new antibacterials," Nature Chemical Biology **2017***, 13*, 54. PMID: 27820797

49. Chu, J., Vila-Farres, X., Inoyama, D., Ternei, M., Zebroski, H. A., Cohen, L. J., Gordon, E. A., Reddy, B. V. B., Charlop-Powers, Z., Gallardo-Macias, R., Jaskowski, M., Satish, S., Park, S., Perlin, D. S., **Freundlich, J. S.**, and Brady, S., "Syn-BNPs: Discovery of antibiotics using primary sequence data from the human microbiome," Nature Chemical Biology **2016**, *12,* 1004. PMID: 27748750

47. Ekins, S.,* Perryman, A. L., Clark, A. M., Reynolds, R. C., and **Freundlich, J. S.**, "Machine Learning Model Analysis with Small Molecules Tested in a Mouse Model of *Mycobacterium tuberculosis* Infection (2014-2015)," Journal of Chemical Information and Modeling **2016**, *56*, 1332. PMID: 27134728

46. Ekins, S., Mietchen, D., Coffee, M., Stratton, T., **Freundlich, J.**, Freitas-Junior, L., Muratov, E., Siqueira-Neto, J., Williams, A., Andrade, C., "Open drug discovery for the Zika virus," F1000Research **2016**, *5*, 150. PMID: 27134728

45. Ekins, S., **Freundlich, J. S.**, Clark, A. M., Anantpadma, M., Davey, R., and Madrid, P. B., "Machine Learning Models Identify Molecules Active Against the Ebola Virus *In Vitro*," F1000Research **2016**, 1091. PMID: 26834994

44. Perryman, A. L., Stratton, T. P., Ekins, S., and **Freundlich, J. S.,*** "Predicting Mouse Liver Microsomal Stability with "Pruned" Machine Learning Models and Public Data," Pharmaceutical Research **2016**, *33*, 433. PMID: 26415647

43. Ekins, S., Madrid, P. B.[*], Sarker, M., Li, S. -G., Mittal, N., Kumar, P., Wang, X., Stratton, T. P., Zimmerman, M., Talcott, C., Bourbon, P., Travers, M., Yadav, M., and **Freundlich, J. S.**,[*] "Combining Metabolite-Based Pharmacophores with Bayesian Machine Learning Models for *Mycobacterium tuberculosis* Drug Discovery," PloS ONE **2015**, *10*, e0141076. PMID: 26517557

42. Clark, A. M., Dole, K., Coulon-Spektor, A., McNutt, A., Grass, G., **Freundlich, J. S.**, Reynolds, R. C., and Ekins, S., "Open Source Bayesian Models: I. Application to ADME/Tox and Drug Discovery Datasets," Journal of Chemical Information and Modeling **2015**, *55*, 1231. PMID: 25994950

41. Forbes, L., Ebsworth-Mojica, K., DiDone, L., Li, S.-G., **Freundlich, J. S.**, Connell, N., Dunman, P. M., Krysan, D. J., "A high throughput screening assay for anti-mycobacterial small molecules based on adenylate kinase release as a reporter of cell death," PloS ONE **2015**, *10*, e0129234. PMID: 26098625

40. Li, S.-G., Vilchèze, C., Chakraborty, S., Wang, X., Kim, H., Anisetti, M., Ekins, S., Rhee, K. Y., Jacobs Jr., W. R., **Freundlich, J. S.,*** "Evolution of a thienopyrimidine antitubercular relying on medicinal chemistry and metabolomics insights," Tetrahedron Letters **2015**, *56*, 3246. PMID: 26257441

39. Ekins, S., Litterman, N. K., Arnold, R. J., Burgess, R. W., **Freundlich, J. S.**, Gray, S. J., Higgins, J. J., Langley, B., Willis, D. E., Notterpek, L., Pleasure, D., Sereda, M. W., Moore, A., "A brief review of recent Charcot-Marie-Tooth research and priorities," F1000Research **2015**, *4,* 53. PMID: 25901280

38. Perryman, A. L., Yu, W., Wang, X., Ekins, S., Forli, S., Li, S.-G., **Freundlich, J. S.**, Tonge, P. J., Olson, A. J., "A Virtual Screen Discovers Novel, Fragment-Sized Inhibitors of *Mycobacterium tuberculosis* InhA," Journal of Chemical Information and Modeling **2015**, *55*, 645. PMID: 25636146

37. Ekins, S., **Freundlich, J. S.**, Coffee, M., "A common feature pharmacophore for FDA-approved drugs inhibiting the Ebola virus," F1000Research **2014**, *3*, 277. PMID: 25653841

36. Al Olaby, R. R., Cocquerel, L., Zemla, A., Saas, L., Dubuisson, J., Vielmetter, J., Marcotrigiano, J., Khan, A. G., Catalan, F. V., Perryman, A. L., **Freundlich, J. S.**, Forli, S., Levy, S., Balhorn, R., Azzazy, H. M. E., "Identification of a novel drug lead that inhibits HCV infection and cell-to-cell transmission by targeting the HCV E2 glycoprotein," PLoS ONE **2014**, *9*, e111333. PMID: 25357246

35. Stec, J., Vilchèze, C., Lun, S., Perryman, A. L., Wang, X., **Freundlich, J. S.**, Bishai, W., Jacobs, Jr., W. R., Kozikowski, A. P., "Biological Evaluation of Potent Triclosan-Derived Inhibitors of the Enoyl-Acyl

Carrier Protein Reductase InhA in Drug-sensitive and Drug-resistant Strains of *Mycobacterium tuberculosis*," ChemMedChem **2014**, *9*, 2528-37. PMID: 25165007

34. Ekins, S., **Freundlich, J. S.**, Reynolds, R. C., "Are Bigger Datasets Better for Machine Learning? Fusing Single-Point and Dual-Event Dose Response Data for *Mycobacterium tuberculosis*," Journal of Chemical Information and Modeling **2014**, *54*, 2157-65. PMID: 24968215

33. Ekins, S., Nuermberger, E. L., **Freundlich, J. S.**,* "Minding the Gaps in Tuberculosis Research," Drug Discovery Today **2014**, *19*, 1279-82. PMID: 24993157

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31. Ekins, S., Pottorf, R., Reynolds, R. C., Williams, A. J., Clark, A. M., **Freundlich, J. S.**,* "Looking Back To The Future: Predicting In vivo Efficacy of Small Molecules Versus Mycobacterium tuberculosis," Journal of Chemical Information and Modeling **2014**, *54*, 1070-82. PMID: 24665947

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29. Ponder, E. L., **Freundlich, J. S.**, Sarker, M., Ekins, S., "Computational Models For Neglected Diseases: Gaps and Opportunities," Pharmaceutical Research, **2014**, *31*, 271-7. PMID: 23990313

28. Afanador, G.A., Muench, S.P., McPhillie, M., Fomovska, A., Schön, A., Zhou, Y., Cheng, G., Stec, J., **Freundlich, J.S.**, Shieh, H.M., Anderson, J.W., Jacobus, D.P., Fidock, D.A., Kozikowski, A.P., Fishwick C.W., Rice, D.W., Freire, E., McLeod, R., Prigge, S.T., "Discrimination of Potent Inhibitors of Toxoplasma gondii Enoyl-Acyl Carrier Protein Reductase by Thermal Shift Assay." Biochemistry **2013**, *52*, 9155-66. PMID: 24295325

27. Ekins, S., **Freundlich, J. S.**, Reynolds, R. C., "Fusing Dual-Event Datasets for *Mycobacterium tuberculosis* Machine Learning Models and their Evaluation," Journal of Chemical Information and Modeling **2013**, *53*, 3054. PMID: 24144044

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25. Ekins, S., Reynolds, R. C., Franzblau, S. G., Wan, B., **Freundlich, J. S.**, Bunin, B. A., "Enhancing Hit Identification in *Mycobacterium tuberculosis* Drug Discovery Using Validated Dual-Event Bayesian Models," PLoS ONE **2013**, *8*, e63240. PMID: 23667592

24. Ekins, S., **Freundlich, J. S.**, "Computational models for tuberculosis drug discovery," Methods Molecular Biology **2013**, *993*, 245. PMID: 23568475

23. Ekins, S., Reynolds, R. C., Kim, H., Koo, M.-S., Ekonomidis, M., Talaue, M., Paget, S. D., Woolhiser, L. K., Lenaerts, A. J., Bunin, B. A., Connell, N., **Freundlich, J. S.**,* "Novel Bayesian models for drug discovery," Chemistry and Biology **2013**, *20*, 370. PMID: 23521795

22. Anderson, J. W., Terpinski, J., Kumar, T. R. S., Tsai, H.-C., Kuo, M., Ager, A. L., Jacobs Jr., W. R., Schiehser, G. A., Ekins, S., Sacchettini, J. C., Jacobus, D. P., **Freundlich, J. S.**,* "Novel diaryl ureas with efficacy in a mouse model of malaria," Bioorganic and Medicinal Chemistry Letters **2013**, *23*, 1022. PMID: 23313245

21. Krieger, I. V., **Freundlich, J. S.**, Gawandi, V. B., Roberts, J. P., Gawandi, V. B., Sun, Q., Owen, J. L., Fraile, M. T., Huss, S., Duncan, K., Lavandera, J.-L., Ioerger, T. R., Sacchettini, J. C., "Structure-Guided Discovery of Phenyl-diketo Acids as Potent Inhibitors of *M. tuberculosis* Malate Synthase," Chemistry and Biology **2012**, *19*, 1556.

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19. Vilchèze, C., Baughn, A. D., Tufariello, J., Leung, L., Basler, C., Alland, D., Sacchettini, J. C., **Freundlich, J. S.**, and Jacobs Jr., W. R., "Novel Inhibitors of InhA Efficiently kill *Mycobacterium tuberculosis* under Aerobic and Anaerobic Conditions," Antimicrobial Agents and Chemotherapy **2011**, *55*, 3889.

18. Lotesta, S. D., Yates, E. V., Liu, J., Krieger, I., Sacchettini, J. C., **Freundlich, J. S.**, Sorensen, E. J., "Expanding the pleuromutilin class of antibiotics by *de novo* chemical synthesis," Chemical Science **2011**, *2*, 1258.

17. Ekins, S., **Freundlich, J. S.**, "Validating New Tuberculosis Computational Models with Public Whole Cell Screening Aerobic Activity Data Sets, " Pharmaceutical Research **2011**, *28*, 1859.

16. Ekins, S., Williams, A.J., Krasowski, M. D., **Freundlich, J. S.**, "*In Silico* Repositioning of Approved Drugs for Rare and Neglected Diseases," Drug Discovery Today **2011**, *16*, 298.

15. Ekins, S., **Freundlich, J. S.**, Choi, I., Sarker, M., Talcott, C., "Applying Computational Technologies for Tuberculosis Drug Discovery, " *An invited review in* Trends in Microbiology **2011**, *19*, 65.

14. Lamichhane, G., **Freundlich, J. S.**, Ekins, S., Wickramaratne, N., Bishai, W. R., "Essential Metabolites of *M. tuberculosis* and their Molecular Mimics as Therapeutic agents against TB," mBio **2011**, *2*, e00301.

13. **Freundlich, J. S.**,* Lalgondar, M., Wei, J.-R., Swanson, S., Sorensen, E. J., Rubin, E. J., Sacchettini, J. C., "Seeding Antitubercular Drug Discovery through Natural Products: The Abyssomicin C Family as *in vitro* Inhibitors of *Mycobacterium tuberculosis*," Tuberculosis **2010**, *90*, 298.

12. Palaninathan, S. K., Mohamedmohaideen, N. N., Orlandini, E., Ortore, G., Nencetti, S., Lapucci, A., Rossello, A., **Freundlich, J. S.**, and Sacchettini, J. C., "Novel transthyretin amyloid fibril formation inhibitors: Synthesis, biological evaluation, and X-ray structural analysis," PLoS ONE **2009**, *4*, e6290.

11. **Freundlich, J. S.**, Wang, F., Gulten, G., Langley, R.,Vilchèze, C., Jacobs Jr., W. R., and Sacchettini, J. C., "Triclosan derivatives as potent inhibitors of drug-sensitive and drug- resistant *Mycobacterium tuberculosis*," ChemMedChem **2009**, *4*, 241.

10. Yu, M., Kumar, T. R. S., Nkrumah, L. J., Coppi, A., Retzlaff, S., Li, C. D., Kelly, B. J., Moura, P. A., Lakshmanan, V., **Freundlich, J. S.**, Valderramos, J.-C., Vilchèze, C., Siedner, M., Tsai, J. H., Falkard, B., Sidhu, A. B., Purcell, L. A., Gratraud, P., Kremer, L., Water, A. P., Schiehser, G., Jacobus, D. P., Janse, C. J., Ager, A., Jacobs Jr., W. R., Sacchettini, J. C., Heussler, V., Sinnis, P., Fidock, D. A., "The Fatty Acid Biosynthesis Enzyme FabI Plays a Key Role in the Development of Liver Stage Malarial Parasites," Cell Host & Microbe, **2008**, *4*, 567.

9. Sacchettini, J. C., Rubin, E. J., **Freundlich, J. S.**, "Drugs versus bugs: In pursuit of the persistent predator *Mycobacterium tuberculosis,*" *An invited review in* Nature Reviews Microbiology **2008**, *6*, 41.

8. **Freundlich, J. S.**,* Wang, F., Tsai, H.-C., Kuo, M., Shieh, H.-M., Anderson, J. W., Nkrumah, L. J., Valderramos, J. C., Yu, M., Jacobs Jr., W. R., Schiehser, G. A., Jacobus, D. P., Fidock, D. A., Sacchettini, J. C., "X-ray structural analysis of *Plasmodium falciparum* enoyl acyl carrier protein reductase as a pathway

towards the optimization of triclosan antimalarial efficacy," Journal of Biological Chemistry **2007**, *282*, 25436.

7. **Freundlich, J. S.,*** Landis, H., "An Expeditious Aqueous Suzuki Methodology for the Assembly of Aryl-substituted phenols," Tetrahedron Letters **2006**, *47*, 4275.

6. **Freundlich, J. S.,*** Yu, M., Valderramos, J. C., Lucumi, E., Tsai, H-.C., Kuo, M., Jacobs Jr., W. R., Schiehser, G. A., Fidock, D. A., Jacobus, D. P., Sacchettini, J. C., "Synthesis and biological activity of diaryl ether inhibitors of malarial enoyl ACP reductase. Part 2: 2'-Substituted triclosan derivatives," Bioorganic and Medicinal Chemistry Letters **2006**, *16*, 2163.

5. **Freundlich, J. S.,*** Anderson, J. W., Sarantakis, D., Shieh, H.-M., Yu, M., Valderramos, J. C., Lucumi, E., Kuo, M., Jacobs Jr., W. R., Fidock, D. A., Schiehser, G. A., Jacobus, D. P., Sacchettini, J. C., "Synthesis, biological activity, and X-ray crystal structural analysis of diaryl ether inhibitors of malarial enoyl ACP reductase. Part 1: 4'-Substituted triclosan derivatives," Bioorganic and Medicinal Chemistry Letters **2005**, *15*, 5247.

4. **Freundlich, J. S.**, Schrock, R. R., "Synthesis of triamidoamine complexes of niobium," Inorganic Chemistry **1997**, *36*, 7459.

3. **Freundlich, J. S.**, Schrock, R. R., Davis, W. M., "Alkyl and alkylidene complexes of tantalum that contain a triethylsilyl-substituted triamidoamine ligand," Organometallics **1996**, *15*, 2777.

2. **Freundlich, J. S.**, Schrock, R. R., Davis, W. M., "Synthetic and mechanistic investigations of trimethylsilyl-substituted triamidoamine complexes of tantalum that contain metal-ligand multiple bonds," Journal of the American Chemical Society **1996**, *118*, 3643.

1. **Freundlich, J. S.**, Schrock, R. R., Cummins, C. C., Davis, W. M., "Organometallic complexes of tantalum that contain the triamidoamine ligand, $[(Me_3SiNCH_2CH_2)_3N]^{3-}$, including an ethylidene complex formed via a phosphine-catalyzed rearrangement of an ethylene complex," Journal of the American Chemical Society **1994**, *116*, 6476.

PATENTS

U.S. Patent Application Serial No. 12/589,192. "Inhibitors of *Mycobacterium tuberculosis* malate synthase."

U.S. Patent Application Serial No. 60/968,511. "Pyridazinone Prodrugs as Antibacterial Agents."

U.S. Patent Application Serial No. 60/491,278. "Antiviral Aminopyridine Compounds."

U.S. Patent Application Serial No. 60/498,705, "Anti-Cancer Agents and Uses Thereof."

U.S. Patent No. 6,353,076, issued March 5, 2002, "Composition Containing Siloxane Based Polyamides."

U.S. Patent No. 6,051,216, issued April 18, 2000, "Composition Containing Siloxane Based Polyamides."

CURRENT RESEARCH SUPPORT

Joel S. Freundlich (co-PI, 1.2 calendar months) 03/01/17 – 02/28/18
New Jersey Health Foundation
Developing peripherally acting GABAB receptor agonists for pain control
The objective of this program is to explore the rational design of small molecule receptor agonists for GABAB.

Joel S. Freundlich (consortium PI, 1.2 calendar months), Sean Ekins (PI) 08/15/2016 – 07/31/2017
1R41AI122434 NIH/NIAID
Optimization of small molecule triazine antituberculars for *in vivo* efficacy

The objective of this grant is to evolve a triazine antitubercular agent to afford an *in vivo* active through computationally aided medicinal chemistry methods while also probing its mechanism of action.

Joel S. Freundlich (co-investigator, 1.2 calendar months), David Alland (PI) 03/01/2016 – 02/28/2019
R33AI11167 NIH/NIAID
Discovery and validation of drug targets in vulnerable populations
The objective of this grant is to evolve chemical probes and drug discovery hits, modulating essential pathways within the bacterial pathogen, to arrive at *in vivo* active antibacterials with defined protein targets.

Joel S. Freundlich (co-investigator, 1.2 calendar months), Gyanu Lamichhane (PI) 03/01/2016 – 02/28/2019
R33AI111739 NIH/NIAID
Development of oral carbapenem drugs for treatment of drug resistant TB
The objective of this grant is to leverage knowledge of the inhibition of *M. tuberculosis* L,D-transpeptidases by a diverse class of carbapenems, through biochemical, whole-cell, X-ray crystallographic, and cheminformatic methods, to evolve novel *in vivo* efficacious small molecule antituberculars.

Joel S. Freundlich (PI, 5.6 calendar months), David Perlin (PD) 04/25/2014 – 03/31/2019
1U19AI109713 NIH/NIAID
Center to develop therapeutic countermeasures to high-threat bacterial agents
The objective of this grant is to leverage an array of novel computational, chemical, and biological techniques in the discovery and optimization of small molecular antibacterial agents with significant promise to impact next generation therapeutics.

Joel S. Freundlich (co-investigator, 1.65 calendar months), Andrew P. Thomas (PI) 04/16/2012 – 03/31/2017
1R01AI099277 NIH/NIAID
Malaria melatonin receptor signaling as a novel drug target
The objective of this program is to validate a novel antimalarial drug target and mechanism for therapeutic action based on the prior identification of an entirely novel signaling pathway in the malaria parasite.

COMPLETED RESEARCH SUPPORT

Joel S. Freundlich (co-investigator, 0.2 calendar months), Paul Dunman (PI) 09/20/2013 – 08/31/2016
1R01AI103507-01A1 NIH/NIAID
Development of AK-based assays for antimicrobial screening
The objective of this program is to develop and leverage a screening platform to identify novel antimicrobial, including antitubercular, small molecules as the starting points for chemical probe and drug discovery.

Joel S. Freundlich (co-investigator, 0.72 calendar months), Sean Ekins (PI) 08/16/2013 – 07/31/2016
9R44TR000942-02 NIH/NCATS
Biocomputation across distributed private datasets to enhance drug discovery
The objective of this program is to harness machine-learning algorithms to construct predictive models for whole-cell efficacy versus *M. tuberculosis* and select ADMET properties and utilize them in the optimization of promising small molecule antituberculars.

Joel S. Freundlich (co-PI, 0.6 calendar months), David Alland (PI) 03/01/2014 – 02/29/2016
R21AI111647 NIH/NIAID
Discovery and validation of drug targets in vulnerable pathways of Mtb
The objective of this grant is to leverage novel *M. tuberculosis* reporter-based screens to identify chemical probes and drug discovery hits that modulate essential pathways within the bacterial pathogen.

Joel S. Freundlich (co-investigator, 0.36 calendar months), Gyanu Lamichhane (PI) 03/01/2014 – 02/29/2016
R21AI111739 NIH/NIAID
Development of Oral Carbapenem Drugs for Treatment of Drug Resistant TB
The objective of this grant is to study the inhibition of *M. tuberculosis* L,D-transpeptidases by a diverse class of both known and novel carbapenems through biochemical, whole-cell, X-ray crystallographic, and cheminformatic methods.

Joel S. Freundlich (co-investigator, 1.32 calendar months), Gyanu Lamichhane (PI) 11/01/2013 – 10/31/2014
3DP2OD008459-01S1 NIH/OD
New Drug for Treatment of Chronic Bacterial Infection
The objective of this administrative supplement is to leverage novel cheminformatics techniques, based on machine learning methodologies, to design potent inhibitors of *M. tuberculosis* L,D-transpeptidases.

Joel S. Freundlich (co-investigator, 0.48 calendar months), Sean Ekins (PI) 4/25/2012 – 4/30/2014
2R42AI088893 NIH/NIAID
Identification of novel therapeutic for tuberculosis combining cheminformatics, diverse databases and logic-based pathway analysis
The objective of this program is to leverage a novel cheminformatics/systems biology software module in the discovery of chemical probes that modulate *in vivo* essential gene products of *M. tuberculosis*.

Joel S. Freundlich (PI) 04/16/2012–03/31/2013
UMDNJ Foundation
Integrative Studies of Fatty Acid Biosynthesis Modulation by Small Molecules: Mechanism of Action and Potency
The objective of this program is to explore the mechanism of action of a novel small molecule antitubercular agent that targets fatty acid biosynthesis.

Joel S. Freundlich (co-PI), Matthew Neiditch (co-PI), David Alland (co-PI) 05/01/2012–04/30/2013
UMDNJ Foundation
The Structure-Based Evolution of *M. tuberculosis* Inhibitors: An Approach Towards a Novel Tuberculosis Therapeutic
The objective of this program is to leverage a structure-based approach to evolve a set of small molecule modulators of a final step in *Mtb* mycolic acid synthesis.

Joel S. Freundlich (co-PI), Andrew P. Thomas (co-PI) 04/16/2012–03/31/2013
UMDNJ Foundation
Malaria Melatonin Receptor Signaling as a Novel Drug Target
The objective of this program is to validate a novel antimalarial drug target and mechanism for therapeutic action based on the prior identification of an entirely novel signaling pathway in the malaria parasite.

Joel S. Freundlich (co-PI) and Erik Sorensen (co-PI) 04/01/2008–03/31/2010
Princeton University Grand Challenges in Global Health
The Integration of Chemistry and Biology in the Classroom and Laboratory to Seed a Next Generation of Scientists, Policy Leaders, and Therapeutics in the Fight Versus Malaria and Tuberculosis
The objective of this program was to discover novel small organic molecules as potential antitubercular and/or antimalarial agents via their structure-based design, synthesis, and biological study of their efficacy and mechanism of action.

INVITED LECTURES

American Chemical Society Middle Atlantic Regional Meeting – 05/16/07
U.S./Japan Tuberculosis and Leprosy Annual Meeting – 07/10/08
Johns Hopkins University Department of Medicine – 08/18/08
Texas A&M University Department of Biochemistry and Biophysics – 08/26/08
Princeton University Department of Chemistry – 10/21/08
Rutgers University Department of Medicinal Chemistry – 01/06/09

Global Alliance for Tuberculosis Drug Development – 01/13/09
Rider University – 01/30/09
Wyeth Pharmaceuticals – 06/24/09
Schering-Plough Pharmaceuticals – 06/25/09
Harvard University – 02/04/10
University of Medicine and Dentistry of New Jersey Department of Medicine – 05/05/10
US-Japan TB Meeting – 07/15/10
University of Medicine and Dentistry of New Jersey Department of Pharmacology – 10/11/10
Boston University Department of Chemistry – 12/02/10
NIAID/NBIB Science of Microbial Markers in Tuberculosis (SMMarT) – 6/27/11
Columbia University Workshop on Microbial and Host Diagnostics and Discovery – 4/2/12
University of Medicine and Dentistry of New Jersey Dept. of Microbiology & Molecular Genetics – 9/11/12
Gordon Research Conference on TB Drug Discovery – 07/23/13
Global Alliance for Tuberculosis Drug Development – 12/4/13
Rutgers University Department of Chemistry – 12/6/13
Rutgers University Department of Biochemistry and Molecular Biology – 1/9/14
Johns Hopkins University Department of Pharmacology and Molecular Sciences – 1/29/14
Cornell University Department of Chemical and Biomolecular Engineering – 2/3/14
ACS National Meeting Symposium on "Tuberculosis: Biology and Emerging Therapeutics" – 3/17/14
Stony Brook University Tuberculosis Symposium – 9/22/14
UMass Medical School Department of Biochemistry & Molecular Pharmacology – 10/8/14
Princeton University Department of Chemical and Biological Engineering – 11/23/14
UNC-Chapel Hill School of Pharmacy – 12/3/14
Rutgers University Camden Center for Computational and Integrative Biology – 2/3/15
Rutgers University Newark Department of Chemistry – 2/5/15
University of Rochester Medical School Department of Microbiology & Immunology – 2/27/15
World TB Day Conference of TB Biology at the Wadsworth Center – 3/23/15
ACS National Meeting BIOL Young Investigator Symposium – 08/16/2015
Duke University Department of Chemistry – 12/1/15
Rutgers University Center for Integrative Proteomics Research – 12/9/15
St. Jude Children's Research Hospital Department of Chemical Biology and Therapeutics – 1/7/16
Temple University Department of Chemistry – 1/28/16
Princeton University Department of Molecular Biology – 2/19/16
Boston University Department of Medicine – 2/25/16
NJMS Global Tuberculosis Institute World TB Day Symposium – 3/22/16
World TB Day 2016 Symposium – 3/31/16
Rutgers University Department of Chemistry and Chemical Biology Colloquium – 4/12/16
Center of Immunity and Inflammation (CII) at Rutgers University – 5/5/16
University of Maryland Department of Chemistry – 9/15/16
IBM Corporation New Jersey Town Hall Meeting – 11/4/16
Michigan State University Department of Biochemistry and Molecular Biology – 2/9/17