Joel S. Freundlich

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RESEARCH INTERESTS

The design and synthesis of chemical tools and their use in conjunction with biological methods to study infectious diseases (currently tuberculosis and malaria)

- How does the pathogen adapt to life within the host?
- How does the host respond to the infection?

PROFESSIONAL EXPERIENCE

RUTGERS UNIVERSITY-NEW JERSEY MEDICAL SCHOOL, Newark, NJ May 2011 to present
Assistant professor (Department of Pharmacology & Physiology)
Assistant professor (Department of Medicine)
Member (Center for Emerging and Reemerging Pathogens)
Courses taught:
Select Agent Biology MSBS N517Q – Spring 2012, Spring 2013
Pharmacology PHRM 7206 – Spring 2012, Spring 2013
Advanced Concepts in I^3 GSBS 5022Q – Spring 2012, Spring 2013
University Activities:
Admissions Committee for M.D./Ph.D. candidates (2013–)
Molecular Biology-Genetics-Cancer Track Oversight Committee member (2013–)

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 (2013–)
Symposia Chair

- "Advances in Virtual High-Throughput Screening," American Chemical Society National Meeting 04/2013

Journal Referee
Nature Communications, Nature Chemical Biology, ACS Chemical Biology, Journal of Medicinal Chemistry, Bioorganic and Medicinal Chemistry Letters, BMC Bioinformatics, Tetrahedron
Member

- American Chemical Society, American Association of Immunologists

PUBLICATIONS

32. Nixon, M. R., Saoinz, K. W., Koo, M.-S., Szymonifka, M. J., Jung, H., Roberts, J. P., Nandakumar, M, Kumar, A., Liao, R., Rustad, T., Sacchettini, J. C., Rhee, K. Y., **Freundlich, J. S.**, Sherman, D. R., "Folate Pathway Disruption Leads to Critical Disruption of Methionine Derivatives in *Mycobacterium tuberculosis*," Chem. Biol. **2014**, *21*, in press.

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," J. of Chem. Inf. Model. **2014**, *54*, 1070-82. PMID: 24665947

30. Ekins, S., **Freundlich, J. S.**, Hobrath, J. V., White, E. L., Reynolds, R. C., "Combining Computational Methods for Hit to Lead Optimization in *Mycobacterium tuberculosis* Drug Discovery," Pharm. Res. **2014**, *31*, 414-35. PMID: 24132686

29. Ponder, E. L., **Freundlich, J. S.**, Sarker, M., Ekins, S., "Computational Models For Neglected Diseases: Gaps and Opportunities," Pharm. Res., **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," J. Chem. Inf. Model. **2013**, *53*, 3054. PMID: 24144044

26. Wilson, R., Kumar, P., Parashar, V., Vilchèze, C., Veyron-Churlet, R., **Freundlich, J. S.**, Barnes, S. W., Walker, J. R., Szymonifka, M. J., Marchiano, E., Shenai, S., Colangeli, R., Jacobs Jr., W. R., Neiditch, M. B., Kremer, L., Alland, D., "Antituberculosis thiophenes define a requirement for Pks13 in mycolic acid biosynthesis," Nat. Chem. Biol. **2013**, *9*, 499. PMID: 23770708

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 Mol. Bio. **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.

20. Sarker, M., Talcott, C., Madrid, P., Chopra, S., Bunin, B. A., Lamichhane, G., **Freundlich, J. S.**, and Ekins, S., "Combining Cheminformatics Methods and Pathway Analysis To Identify Molecules with Whole-Cell Activity Against Mycobacterium tuberculosis," Pharmaceutical Research **2012**, *29*, 2115.

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 (PI, 4.2 calendar months), David Perlin (PD) 04/25/2014 – 03/31/2019
1U19AI109713 NIH/NIAID
Center to develop therapeutic countermeasures to high-threat bacterial agents

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

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

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

Joel S. Freundlich (co-investigator, 0.6 calendar months), Paul Dunman (PI) 09/20/2013 – 08/31/2016
1R01AI103507-01A1 NIH/NIAID
Development of AK-based assays for antimicrobial screening

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

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

COMPLETED RESEARCH SUPPORT

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

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

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

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

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

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” – 3/17/2014