
BIOGRAPHICAL SKETCH

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NAME: **David S. Perlin**

eRA COMMONS USER NAME (credential, e.g., agency login): perlin

POSITION TITLE: Chief Scientific Officer, SVP and Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Brandeis University, Waltham, MA	A.B.	1976	Biology
Cornell University, Ithaca, NY	Ph.D.	1980	Plant Physiology
Yale University School of Medicine, New Haven, CT	Postdoc.	1980-83	Biochemistry, Genetics
University of Rochester School of Medicine and Dentistry, Rochester, NY	Postdoc.	1983-85	Biochemistry

A. Personal Statement

I have the proven experience necessary to advise this program. It is derived from 30+ years as a Principal Investigator (PI) for major government (NIH, DOD, CDC), foundation (Gates), and commercial (Pharma and biotech) grants/contracts for drug resistance, diagnostics, and drug discovery including a current role as PI/PD leading an NIH Center of Excellence in Translational Research (CETR). My experience also derives from a 13-year role leading the Public Health Research Institute (PHRI)(Rutgers University-New Jersey Medical School), a translational infectious diseases research group with prominent research programs in drug discovery, diagnostics and drug resistance. In my career, I have studied molecular mechanisms responsible for drug resistant bacteria and fungi, and have helped develop novel therapeutics and diagnostics, some of which are now commercial products. My group has developed molecular diagnostics and biomarkers for sepsis involving bacterial and fungal infections in high risk patients. Some products are licensed and were developed in partnerships with prominent diagnostic companies. We have also developed a range of molecular diagnostic products for the CDC and local hospitals for outbreak pathogens including drug resistance determinants. I have participated in diagnostic development meetings on behalf of device manufacturers and Pharma with the FDA and EMA. As a current CETR director for development of antibiotics against multidrug resistant pathogens, I help direct compound discovery and lead compound optimization for 5 programs, and oversee multiple support cores. As an Executive Committee member and director (2003-2014) for the small animal core of the Region II NIH Regional Center of Excellence in Biodefense and Emerging Infectious Diseases, I led more than three dozen studies of novel vaccines, therapeutics and diagnostics against select agents, TB and other high-threat pathogens. Currently, I am an advisor to numerous Pharma, biotech and diagnostic companies for development of novel therapeutics and diagnostics. I have published extensively (250+ papers, chapters and reviews), especially on drug resistance, drug evaluation and diagnostics (see <https://www.ncbi.nlm.nih.gov/pubmed/?term=perlin+d>). Overall, I believe that my research and administrative experience, and leadership are strong assets to support the development goals of this program.

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- Perlin DS**, Rautemaa-Richardson R, Alastruey-Izquierdo A. 2017. The global problem of antifungal resistance: prevalence, mechanisms, and management. *Lancet Infect Dis*. pii: S1473-3099. doi: 10.1016/S1473-3099(17)30316
 - Perlin DS**. 2015. Echinocandin Resistance in *Candida*. *Clin Infect Dis*. 2015 Dec 1;61 Suppl 6:S612-7.
 - Shor E, **Perlin DS**. 2015. Coping with stress and the emergence of multidrug resistance in fungi. *PLoS Pathogens* 11:e1004668.
 - Perlin DS**. 2015. Antifungals: From Genomics to Resistance and the Development of Novel Agents. *Clin Infect Dis* 61:1213-1214.
 - Cowen LE, Sanglard D, Howard SJ, Rogers PD, **Perlin DS**. 2014. Mechanisms of Antifungal Drug Resistance. *Cold Spring Harbor Perspective Med*. 5(7):a019752.
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B. Positions and Honors

Positions and Employment

1985-1988 Assistant Member, Public Health Research Institute, New York, NY
1989- 1991 Associate Member, Public Health Research Institute, New York, NY
1992- Member, Public Health Research Institute, New York, NY
1992-2002 Adjunct Associate Professor, New York University School of Medicine, New York, NY
2005-2006 President, Public Health Research Institute, Newark, NJ
2006-2018 Executive Director, Public Health Research Institute, NJ Med Sch-UMDNJ, Newark, NJ
2009-2018 Director, Rutgers Regional Biocontainment Laboratory
2002-2018 Professor, Department of Microbiology, Biochemistry and Molecular Genetics, New Jersey Medical School, Rutgers Biomedical and Health Sciences, Newark, NJ
2019- Chief Scientific Officer, Hackensack Meridian Health Center for Discovery and Innovation, Nutley, NJ
2019- Professor, Dept. of Medical Sciences, Hackensack Meridian Health School of Medicine at Seton Hall
2019- Professor Emeritus, Infectious Diseases, Rutgers University, Newark, NJ

Other Experience and Professional Memberships

1987- American Society for Biochemistry and Molecular Biology
1997- American Society for Microbiology
1990- Genetics Society of America
1998- Medical Mycology Society of New York
2015- Infectious Diseases Society of America
1991- Editorial Board Member, Journal Bioenergetics and Biomembranes
2000 Editorial Board Member, Microbial Drug Resistance
1997 Editorial Board Member, Electronic Journal of Biotechnology
2008 Editorial Board Member, Open Access Emergency Medicine
2007 Editorial Board Member, Global Health Governance
2014 Editor-in-Chief (inaugural), Journal of Fungi
2015 Editorial Board Member, mSphere

Government

1996 Physical Biochemistry Study Section
2002 NIH Physical Biochemistry Study Section
2002 NIH NIAID Special Emphasis Panel Fungal Drug Testing Contract Review
2002 NIH NIAID Special Emphasis Panel New Animal Models for Invasive Aspergillosis
2003 NIH NIAID NBL/RBL Special Core Facility Review
2004 NIH NIAID ZRG1 Bacterial and Fungal Pathogenesis
2004 NIH Physiological Chemistry (PC1) Study Section
2006 NIH-NIAID SEP UC7 National Biocontainment Laboratory Ops Cooperative Agreement.
2007 NIH ZRG1 BCMB-B Special emphasis panel meeting
2008 NIH Biological Chemistry and Macromolecular Biophysics Study Section
2008 NIH DDR-Drug Discovery and Mechanisms of Antimicrobial Resistance
2008 NIH Infectious Diseases and Microbiology IRG, Special Emphasis Panel
2010 NIH Director's Opportunity for Research in Five Thematic Areas (RC4)
2011 NIH-NIAID Microbiology and Infectious Diseases B Sub-Committee (MID-B)
2016 NIH-NIAID Topics in Drug Discovery and Mechanisms of Antimicrobial Resistance
2017 NIH-NIAID, ZRG1 IDM S (02) Special emphasis panel
2018 NIH0NIAID, ZRG1-IDM-R07, Special emphasis panel on drug resistance

Honors (Recent)

2005 Fellow, The New York Academy of Sciences
2009-2012 Distinguished Visiting Professor, University of Manchester, United Kingdom
2012- Executive Committee, Board of Directors, Aaron Diamond AIDS Research Center (ADARC)
2015 Foundation lecturer, British Society of Medical Mycology, Aberdeen, Scotland
2016 Perlman Symposium Principal Lecturer, University of Wisconsin, Madison, WI
2017 Appointed Audit Chair, American Society for Microbiology (ASM)
2017 Keynote lecturer, Israel Society of Medical Mycology, Tel Aviv, Israel
2018 Fellow, American Academy of Microbiology

C. Contributions to Science

1. Drug discovery against multidrug resistant fungi and bacteria. Multidrug-resistance plagues global and U.S. healthcare and with few new antibiotics making it to market from a diminished pipeline, there is an unmet medical need for new therapeutics to treat drug-resistant infections. The Perlin Lab has been involved in developing new targets and novel chemical scaffolds against high-threat fungal and bacterial pathogens. They are interested in developing both narrow- and broad-spectrum agents against high-threat multi-drug resistant bacterial and fungal pathogens commonly associated with systemic infections among immunosuppressed patients. For the past 4 years, Dr. Perlin has led an NIH designated Center of Excellence in Translational Research (CETR) that is developing a new generation of antibiotics against known MDR bacteria. The CETR, a collaborative public-private partnership involving Rutgers University, Rockefeller University and Merck Pharmaceuticals, serves to jump-start the discovery of novel antibiotics by joining together highly creative senior researchers and providing critical core resources to turn highly promising early concept molecules into potential therapeutics suitable for clinical evaluation. In addition to antibiotic development, the Perlin lab has been active in supporting drug development efforts for numerous companies engaged in antifungal drug development.

- a. Hover BM, Kim SH, Katz M, Charlop-Powers Z, Owen JG, Ternei MA, Maniko J, Estrela AB, Molina H, Park S, **Perlin DS**, Brady SF. 2018. Culture-independent discovery of the malacidins as calcium-dependent antibiotics with activity against multidrug-resistant Gram-positive pathogens. *Nat Microbiol.* 3(4):415-422. doi: 10.1038/s41564-018-0110-1.
- b. Vila-Farres X, Chu J, Ternei MA, Lemetre C, Park S, **Perlin DS**, Brady SF. 2018. An Optimized Synthetic-Bioinformatic Natural Product Antibiotic Sterilizes Multidrug-Resistant *Acinetobacter baumannii*-Infected Wounds. *mSphere.* 2018 Jan 24;3(1). pii: e00528-17. doi: 10.1128/mSphere.00528-17.
- c. Vila-Farres X, Chu J, Inoyama D, Ternei MA, Lemetre C, Cohen LJ, Cho W, Reddy BV, Zebroski HA, Freundlich JS, **Perlin DS**, Brady SF. (2017) Antimicrobials Inspired by Nonribosomal Peptide Synthetase Gene Clusters. *J Am Chem Soc.* 1;139(4):1404-1407
- d. Zhao Y, Perez WB, Jiménez-Ortigosa C, Hough G, Locke JB, Ong V, Bartizal K, **Perlin DS**. 2016 CD101: a novel long-acting echinocandin. *Cell Microbiol*18(9):1308-16

2. Drug resistance mechanisms in fungi. I have had a longstanding interest in antifungal drug resistance, which continues to be an emerging problem in medical mycology. We first reported the mechanism of clinical resistance to echinocandin class antifungal drugs in 2005 and have provided a comprehensive molecular and clinical assessment of the resistance mechanism resulting in 75 papers and reviews. Our work has been instrumental in moving the field forward and has emphasized correlations between resistance mutations, genetics, enzyme kinetic inhibition, MIC, pharmacodynamics, resistance factors and clinical outcome. This multifactorial approach was critical to the development of revised CLSI breakpoints. My lab was established (by Pfizer and Astellas) in 2008 as a Global Clinical Reference Center for molecular evaluation of echinocandin resistant strains from patients failing therapy. In this period, we have evaluated the *FKS* mechanism in nearly one thousand clinical isolates. We have examined the relationship between resistance, virulence, and strain lineage, and we have used PK-PD studies to understand the importance of specific mutations and potential therapeutic response. Finally, in recent years, we have helped define underlying genetic and host factors that contribute to emergence of echinocandin and multidrug resistance in *Candida* and *Aspergillus* species.

- a. Shor E, Schuyler J and **Perlin DS** 2019. A novel, drug resistance-independent, fluorescence-based approach to measure mutation rates in microbial pathogens. *mBio*, 10(1). pii: e00120-19. doi: 10.1128/mBio.00120-19
- b. Kordalewska M, Lee A, Park S, Berrio I, Chowdhary A, Zhao Y, **Perlin DS**. 2018. Understanding Echinocandin resistance in the emerging pathogen *Candida auris*. *Antimicrob Agents Chemother.* 62(6). pii: e00238-18. doi: 10.1128/AAC.00238-18.
- c. Healey KR, Nagasaki Y, Zimmerman M, Kordalewska M, Park S, Zhao Y and **Perlin DS** 2017. The gastrointestinal tract is a major source of echinocandin drug resistance in a murine model of *Candida glabrata* colonization and systemic dissemination. *Antimicrobial Agents and Chemotherapy.* 22;61(12). pii: e01412-17. doi: 10.1128/AAC.01412-17.
- d. Healey KR, Zhao Y, Perez WB, Lockhart SR, Sobel JD, Farmakiotis D, Kontoyiannis DP, Sanglard D, Taj-Aldeen SJ, Alexander BD, Jimenez-Ortigosa C, Shor E, **Perlin DS**. 2016. Prevalent mutator genotype identified in fungal pathogen *Candida glabrata* promotes multi-drug resistance. *Nat Commun.* 7:11128.

- e. **Perlin DS**, Rautemaa-Richardson R, Alastruey-Izquierdo A. 2017. The global problem of antifungal resistance: prevalence, mechanisms, and management. *Lancet Infect Dis.* 17(12):e383-e392. doi: 10.1016/S1473-3099(17)30316.

3. Rapid detection of respiratory and bloodstream infections (BSIs) and associated resistance markers.

Early and appropriate antimicrobial therapy is critical to a favorable outcome for patients with respiratory and BSIs. Current diagnostic methods are inadequate and reducing the time from specimen collection to species identification and antimicrobial susceptibility is essential for improving patient outcome. For the past decade and one-half, my group has been involved in developing next-generation nucleic acid PCR- and RNA-based molecular beacon platforms for rapid identification of bacterial and fungal pathogens, and associated drug resistance in high threat bacterial and fungal pathogens.

- a. Hou X, Lee A, Jiménez-Ortigosa C, Kordalewska M, **Perlin DS**, Zhao Y. 2018. Rapid detection of *ERG11*-associated azole resistance and *FKS*-Associated echinocandin resistance in *Candida auris*. *Antimicrob Agents Chemother.* 63(1). pii: e01811-18. doi: 10.1128/AAC.01811-18.
- b. Zhao Y, Nagasaki Y, Paderu P, Sugrue MW, Leather HL, Wingard JR, **Perlin DS**. 2018. Applying host disease status biomarkers to therapeutic response monitoring in invasive aspergillosis patients. *Med Mycol.* 2019 Jan 1;57(1):38-44. doi: 10.1093/mmy/myx164.
- c. Kordalewska M, Zhao Y, Lockhart SR, Chowdhary A, Berrio I, **Perlin DS**. (2017) Rapid and accurate molecular identification of the emerging multidrug resistant pathogen *Candida auris*. *J Clin Microbiol.* May 24. pii: JCM.00630-17. doi: 10.1128/JCM.00630-17
- d. Zhao Y, Nagasaki Y, Kordalewska M, Press EG, Shields RK, Nguyen MH, Clancy CJ, **Perlin DS**. (2016) Rapid Detection of *FKS*-Associated Echinocandin Resistance in *Candida glabrata*. *Antimicrob Agents Chemother*60(11):6573-6577.
- e. Denning, D.W., Park, S., Lass-Flörl, C., Fraczek, M.G., Kirwan, M., Gore, R., Smith, J., Bueid, A., Moore, C.B., Bowyer, P. and **Perlin, D.S.** (2011) High-frequency triazole resistance found in nonculturable *Aspergillus fumigatus* from lungs of patients with chronic fungal disease. *Clin. Infect Dis* 52(9):1123-9.

4. Improving existing drug therapy.

A key factor for successful therapy is whether a drug get to the site of infection at the desired level for efficacy. Our group, led by Dr. Nancy Zhao, has been using novel technology to image and quantify the level of drugs in life-threatening diseases resulting from intraabdominal abscesses and pulmonary lesions. This work provides insights into more effective therapy by increasing exposure levels and reducing the emergence of drug resistance resulting from suboptimal dosing. In addition to drug access, drug response is often limited factors such as an individual's metabolism, which effect the whether a drug is present at the desired concentration over the course of therapy. Classically, therapeutic drug monitoring (TDM) has been used to assess drug levels in patients. This is often a laboratory-intensive process that can take several days. We are developing novel technology to rapidly assess drug levels of first-line antimicrobial agents in blood in real-time at the bedside.

- a. Zhao Y, Prideaux B, Nagasaki Y, Lee MH, Chen PY, Blanc L, Ho H, Clancy CJ, Nguyen MH, Dartois V, **Perlin DS**. 2017 Unraveling Drug Penetration of Echinocandin Antifungals at the Site of Infection in an Intra-Abdominal Abscess Model. *Antimicrob Agents Chemother.* AAC.01009-17. doi: 10.1128/AAC.01009-17.
- b. Healey KR, Nagasaki Y, Zimmerman M, Kordalewska M, Park S, Zhao Y and **Perlin DS** 2017. The gastrointestinal tract is a major source of echinocandin drug resistance in a murine model of *Candida glabrata* colonization and systemic dissemination. *Antimicrobial Agents and Chemotherapy.* AAC.01412-17. doi: 10.1128/AAC.01412-17
- c. Wiedman GR, Zhao Y, **Perlin DS**. 2018. A Novel, Rapid, and Low-Volume Assay for Therapeutic Drug Monitoring of Posaconazole and Other Long-Chain Azole-Class Antifungal Drugs. *mSphere.* 2018 Dec 19;3(6). pii: e00623-18. Doi 10.1128/mSphere.00623-18.
- d. Wiedman GR, Zhao Y, Mustaev A, Ping J, Vishnubhotla R, Johnson ATC, **Perlin DS**. 2017. An Aptamer-Based Biosensor for the Azole Class of Antifungal Drugs. *mSphere.* 2017 Aug 23;2(4). pii: e00274-17. doi: 10.1128/mSphere.00274-17.

D. Research Support

Current Research Support

2 R01 AI109025-05 NIH/NIAID Critical Factors Influencing Echinocandin Resistance in <i>Candida glabrata</i> .	Perlin (PI)	07/01/2018 -6/30/23
U19 AI109713-01 Center to develop therapeutic countermeasures to high-threat bacterial agents This CETR program is developing new antibacterial agents against ESKAPE and other high-threat pathogens.	Perlin (PI)	3/01/14 – 2/28/20
1 R01 AI138986-01 NIH/NIAID Novel bi-specific immunoprophylactics against multi-drug resistant Gram negative bacterial infections.	Perlin (PI)	05/01/2018 - 5/31/23
1 R01 AI141183-01 NIH/NIAID Novel bi-specific immunotherapeutic against high-threat Gram-negative pathogens	Perlin (PI)	12/01/2018 - 11/30/23
1U19AI142731-01 Center to develop innovative therapeutics to multidrug resistant high-threat bacterial agents	Perlin (PI)	5/01/19 – 4/30/24
Astellas Pharma US, Inc Echinocandin Resistance Reference Center Global reference/referral center for drug resistance	Perlin (PI)	10/01/14-1/15/20

Recently Completed Related Grants

CDC A comprehensive study of multidrug resistance determinants and drivers in the major fungal pathogen <i>Candida glabrata</i>	Perlin (PI)	9/30/16-9/29/18
CDC Rapid identification and analysis of transmission of the emerging pathogen <i>Candida auris</i>	Perlin (PI)	9/30/17-9/29/18
DoD 110303 Evaluation of Carbohydrate Derived Fulvic Acid (CHD-FA) as a topical broad-spectrum antimicrobial for drug resistant wound infections	Perlin (PI)	9/30/12-4/29/17
U01 AI066561 A rapid and expendable nucleic acid platform to detect bacterial bloodstream infections.	Perlin (PI)	7/01/2005-3/31/12
U54 AI0571580 NIH-NIAID Small Animal Core, Region II Regional Center of Excellence, Biodefense and Emerging Infectious Diseases	Perlin (PI)	9/01/03-2/28/15
QNRF Molecular assessment of drug resistance among bloodstream <i>Candida</i> infections in high-risk patients	Saad Taj-Aldeen (PI)	10/01/16 –9/30/18
R01AI069397 NIH-NIAID Mechanism of clinical resistance to echinocandin antifungal drugs	Perlin (PI)	12/01/06-11/30/12
U54 AI0571580 Small Animal Core, Region II RCE Biodefense and Emerging Infectious Diseases	Lipkin (PI)	9/01/03-2/28/15