BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **David S. Perlin**

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

POSITION TITLE: Executive Director and Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

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 successfully perform this innovative research 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 leading a NIH/NIAID Center of Excellence in Translational Research (CETR). My experience also derives from a 13-year role leading the Public Health Research Institute (PHRI), a translational infectious diseases research group (www.phri.org) that has prominent research programs (20 PI-directed labs) in drug discovery, diagnostics and drug resistance, and has generated significant intellectual property (>300 patents) and licensed technology resulting in FDA-approved clinical products. It is also derived from my role as Director for the Rutgers Regional Biocontainment Laboratory (RBL), an NIH designated national laboratory for the study of high threat agents. In my career, I have studied detailed biochemical and genetic mechanisms in drug resistant bacteria and fungi, and have helped develop countermeasures in the form of novel therapeutics and diagnostics, some of which have been developed as commercial products. As current CETR director for development of antibiotics against multidrug resistant pathogens, I help direct compound discovery and lead compound optimization for 6 programs, and oversee 6 different support cores. I also integrated support for evaluation of compounds from 12 companies in this period. 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; our group logged more than 1.7 million animal day trials of BSL3 agents. Currently, I am an advisor to numerous Pharma and biotech companies for development of novel therapeutics, including The Medicines Company for the development of newly approved Vabormere. I also serve as a member of the CLSI assessing clinical breakpoints for drug resistance. I have published extensively (240+ 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 directing a current CETR are strong assets to help lead this program.

1. **Perlin DS**, Rautemaa-Richardson R, Alastruey-Izquierdo A. The global problem of antifungal resistance: prevalence, mechanisms, and management. Lancet Infect Dis. 2017 Jul 31. pii: S1473-3099
2. 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. Antimicrobials Inspired by Nonribosomal Peptide Synthetase Gene Clusters. J Am Chem Soc. 2017 Feb 1;139(4):1404-1407.
3. Karl S. Drlica and **David S. Perlin** Antibiotic Resistance: Understanding and responding to an emerging crisis. Upper Saddle River, New Jersey, Pearson Education, January 201

B. Positions and Honors

Positions and Employment

1984-1985	Research Assistant Professor, Department of Biochemistry, University of Rochester School of Medicine and dentistry, Rochester, NY
1985-1988	Assistant Member, Public Health Research Institute, New York, NY
1986-1991	Adjunct Assistant Professor, New York University School of Medicine, 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
2002-2013*	Professor, Department of Microbiology and Molecular Genetics, UMDNJ, Newark, NJ
2005-2006	President, Public Health Research Institute, Newark, NJ
2006-	Executive Director, Public Health Research Institute, Rutgers (formerly UMDNJ), Newark, NJ
2009-	Director, Rutgers Regional Biocontainment Laboratory
2013-	Professor, Department of Microbiology, Biochemistry and Molecular Genetics, Rutgers Biomedical and Health Sciences, 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
2005-	Board of Directors, Aaron Diamond AIDS Research Center (ADARC)
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 (founding), 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

Honors

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	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 bacteria and fungi. An epidemic of multidrug (MDR) 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. My group has evaluated novel compounds from Pharma (Merck, Pfizer, Astellas, Astra-Zeneca, Celgene) and more than two dozen biotechs for in vitro potency and spectrum, mechanism of action, resistance potential and efficacy in a range of animal models. We have been involved mostly with small molecule development programs but most recently, the development of novel antibody drug conjugates. We have helped develop two preclinical development candidates (PDC) that are entering optimization and pre-IND-enabling studies directed at CRE-based wound infections and *Neisseria gonorrhea* vaginal infections, respectively. I currently serve as Principal Investigator for an NIH/NIAID Center of Excellence in Translational Research (CETR) to develop a new generation of antibiotics against known MDR bacteria. The CETR, a collaborative public-private partnership involving Rutgers University, Rockefeller University and Merck (Cubist) Pharmaceuticals, serves to jump-start the discovery of novel antibiotics by linking highly creative senior researchers and providing critical core resources to turn highly promising early concept molecules into potential therapeutics suitable for clinical evaluation.

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. 2018 Feb 12. 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 3(1). pii: e00528-17. doi: 10.1128/mSphere.00528-17
c. 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 Microbiol18(9):1308-16.
d. Chu J, Vila-Farres X, Inoyama D, Ternei M, Cohen LJ, Gordon EA, Reddy BV, Charlop-Powers Z, Zebroski HA, Gallardo-Macias R, Jaskowski M, Satish S, Park S, **Perlin DS**, Freundlich JS, Brady SF. Discovery of MRSA active antibiotics using primary sequence from the human microbiome. Nat Chem Biol. 2016 (12):1004-1006
e. Jimenez-Ortigosa C, Paderu P, Motyl MR, **Perlin DS**. 2014. Enfumafungin derivative MK-3118 shows increased in vitro potency against clinical echinocandin-resistant *Candida* Species and Aspergillus species isolates. Antimicrobial agents and chemotherapy 58:1248-1251.

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, enzyme kinetic inhibition, MIC, pharmacodynamics and clinical outcome. This multifactorial approach was critical to the development of revised CLSI breakpoints. Established in 2008 as the Astellas (initially Pfizer) global clinical Reference Center for molecular evaluation of echinocandin resistance from patients failing therapy, we have evaluated the *FKS* mechanism in hundreds of clinical isolates from patients failing therapy. We have examined the relationship between resistance and virulence, and we have used PK-PD studies to understand the importance of specific mutations and potential therapeutic response. Finally, we have helped define genetic factors that contribute to emergence of echinocandin and multidrug resistance in *Candida* and *Aspergillus* species.

a. 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
b. 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.

c. Garcia-Effron G, Lee S, Park S, Cleary JD, **Perlin DS**. 2009. Effect of *Candida glabrata* FKS1 and FKS2 mutations on echinocandin sensitivity and kinetics of 1,3-beta-D-glucan synthase: implication for the existing susceptibility breakpoint. Antimicrobial agents and chemotherapy 53:3690-3699.
d. Park, S, Kelly, R., Nielsen-Kahn, J, Robles, J, Hsu,M-J, Register, E, Li, W, Vyas, V, Fan, H, Abruzzo, G, Flattery, A, Gill, C, Chrebet, G, Parent, S, Kurtz, M, Teppler, H, Douglas, CM and **Perlin, DS.** 2005 Specific substitutions in the echinocandin target Fks1p account for reduced susceptibility of rare laboratory and clinical *Candida* isolates. Antimicrob. Agents Chemother. 49(8):3264-73.

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 period 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. 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
b. 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 Chemoth60(11):6573-6577.
c. Zhao Y, Garnaud C, Brenier-Pinchart MP, Thiébaut-Bertrand A, Saint-Raymond C, Camara B, Hamidfar R, Cognet O, Maubon D, Cornet M, **Perlin DS. 2016.** Direct molecular diagnosis of aspergillosis and CYP51A profiling from respiratory samples of French patients. Front Microbiol. 7:1164.
d. Zhao, Y, Park, S, Kreiswirth, BM, Ginocchio, CC and **Perlin, DS**. (2009) Rapid real-time nucleic Acid sequence-based amplification-molecular beacon platform to detect fungal and bacterial bloodstream infections. Journal of Clincial Microbiology. 47(7): 2067–2078.
e. Denning, DW, Park, S, Lass-Florl, C, Fraczek, MG, Kirwan, M, Gore, R, Smith, J, Bueid, A, Moore, CB, Bowyer, P and **Perlin, DS.** (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. Animal models of infection. We are actively engaged in developing and running BSL2/BSL3 small animal infection models for fungal, ESKAPE, M.tb and select agent bacterial pathogens to evaluate emerging candidate vaccines, diagnostics and lead compounds, as well as to learn novel insights into pathogenicity. I am fully committed to this vital research support program as Director of the Rutgers Regional Biocontainment Laboratory (RBL), one of thirteen NIH designated national centers for the study of highly transmissible pathogen. The animal model program supports a wide range of internal and regional research programs. The models include skin and soft tissue, pneumonia and systemic models. For more than a decade, my group served as the Small Animal Core for the Region II, NIH Regional Centers of Excellence in Biodefense and Emerging Infectious Diseases. An important part of the ongoing RBL function is to maintain small animal models of select agents, MDR/XDR M.tb, other bacteria and pandemic flu. In the past nine years, our group has logged >1.6 million animal days of BSL3 infection agents and we have performed more than 20 vaccine studies with these agents during this period.

a. Zhao Y, Prideaux B, Nagasaki Y, Lee MH, Chen PY, Blanc L, Ho H, Clancy CJ, Nguyen MH, Dartois V, **Perlin DS**. Unraveling Drug Penetration of Echinocandin Antifungals at the Site of Infection in an Intra-abdominal Abscess Model. Antimicrob Agents Chemother. 61(10). pii: e01009-17.
b. Zhao, Y, Paderu, P, Delmas, G, Park, S, Leivers, S, and **Perlin, DS** (2015). CHD-FA is a highly promising topical broad-spectrum antimicrobial for drug-resistant wound infections. Journal of Trauma and Acute Care Surgery. 79(4 Suppl 2), S121-9.
c. Boyer, J.L., Sofer-Podesta, C., Ang, J., Hackett, N.R., Chiuchiolo, M.J., Senina, S., **Perlin, D**., Crystal**,** R.G. (2010) Protective immunity against a lethal respiratory *Yersinia pestis* challenge induced by V antigen or the F1 capsular antigen incorporated into adenovirus capsid. Hum Gene Ther. 21:891-901
d. Do, Y., Koh, H., Park, C.G., Dudziak, D., Seo, P., Mehandru, S., Choi, J.H., Cheong, C., Park, S., **Perlin, D.S.**, Powell, B.S. and Steinman, R.M. (2010) Targeting of LcrV virulence protein from *Yersinia pestis* to dendritic cells protects mice against pneumonic plague. European Journal of Immunology 40:2791-6

D. Research Support

Current Research Support

U19 AI109713-01 Perlin (PI) 3/01/14 – 2/28/19
Center to develop therapeutic countermeasures to high-threat bacterial agents
This program will develop and evaluate new antibacterial agents against ESKAPE and other high-threat pathogens.
Role: PI

R01 AI109025 Perlin (PI) 7/01/14-6/30/18
Critical factors influencing echinocandin resistance in *Candida glabrata*.
The aim of this project is to determine cellular factors contributing to emergence of FKS-mediated drug resistance in Candida glabrata
Role: PI

CDC Perlin (PI) 9/30/16-9/29/18
A comprehensive study of multidrug resistance determinants and drivers in the major fungal pathogen *Candida glabrata*

CDC Perlin (PI) 9/30/17-9/29/18
Rapid identification and analysis of transmission of the emerging pathogen *Candida auris*

R21 AI121555 Clancy (PI) 01/1/16-12/31/18
NIH-NIAID
Imaging and PK/PD of micafungin at sites of Candida glabrata infection in vivo

QNRF Saad Taj-Aldeen (PI) 10/01/16 –9/30/18
Molecular assessment of drug resistance among bloodstream *Candida* infections in high-risk patients

AMPLYX Pharmaceuticals Perlin (PI) 6/15/16-7/14/18
In vitro antifungal properties of APC001A; Evaluation of APX001 in a murine candidiasis model

Astellas Pharma US, Inc Perlin (PI) 10/01/14-1/15/19
Echinocandin Resistance Reference Center
Global reference/referral center for drug resistance

<u>Pending Research Support- (Awaiting final Council approval)</u>

1 R01 AI138986-01 Perlin (PI) 06/01/2018 - 5/31/2023
NIH/NIAID
Novel bi-specific immunoprophylactics against multi-drug resistant Gram-negative bacterial infections.
Reviewed: 2/12/18; RFA raw score 24 (no percentile); funding anticipated

2 R01 AI109025-05 Perlin (PI) 07/01/2018 - 06/30/23
NIH/NIAID
Critical Factors Influencing Echinocandin Resistance in *Candida glabrata*
Reviewed: 2/26/18; Score: 3rd percentile; funding anticipated