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 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 am well qualified to lead this program. I am a Professor of Microbiology and Immunology and have worked over the past 30+ years to advance novel approaches to overcome infections from high-threat pathogens, especially in cancer patients. In my career, I have led numerous discovery programs as a Principal Investigator (PI) for major government (NIH, DOD, CDC), foundation (Gates), and commercial (Pharma and biotech) grants/contracts for drug discovery programs including my current role leading two NIH Centers of Excellence in Translational Research. I have studied molecular mechanisms responsible for drug resistant bacteria and fungi, and I have helped develop novel therapeutics and diagnostics against high-threat bacteria, viruses and fungi. I have worked closely with Pharma and Biotech over the years to advance new products, and I have participated in development meetings on behalf of device manufacturers and Pharma with the FDA and EMA. I am actively engaged in drug discovery and serve as PI for an NIH CETR for development of anti-infectives against multidrug resistant bacterial pathogens. I am also co-PI for one of nine national NIH AViDD programs to develop antiviral drugs against SARS- CoV-2 and other pandemic viruses. Furthermore, I am an advisor to numerous Pharma, biotech and diagnostic companies for development of novel therapeutics and diagnostics, and I have contributed to the development of 4 FDA approved drugs and other drugs in late-stage clinical trials. I have published extensively including 340+ papers, chapters and reviews. Overall, I believe that my research and administrative experience, and leadership are strong assets to support the discovery goals of this program

Ongoing and recently completed projects that I would like to highlight include:

2 R01 AI109025-05 Perlin (PI) 07/01/2018 - 06/30/23
NIH/NIAID
Critical Factors Influencing Echinocandin Resistance in *Candida glabrata.*

1U19AI1714010 Perlin (co-PI), Rice (co-PI) 05/17/2022 – 5/16/2027
NIH/NIAID
Metropolitan AntiViral Drug Accelerator

1U19AI142731-01 Perlin (PI) 4/01/19 – 3/31/24
NIH/NIAID
Center to develop innovative therapeutics to multidrug resistant high-threat bacterial agents

1 R01 AI138986-01 Perlin (PI) 05/01/2018 - 5/31/2024
NIH/NIAID
Novel bi-specific immunoprophylactics against multi-drug resistant Gram-negative bacterial infections.

1 R01 AI141183-01 Perlin (PI) 12/01/2018 - 11/30/23
NIH/NIAID
Novel bi-specific immunotherapeutic against high-threat Gram-negative pathogens

3U19AI142731-02S1 Perlin (PI) 08/25/2020 – 04/30/2024
NIH/NIAID
A CETR-based partnership accelerator for rapid drug development targeting SARS-CoV-2 and pan-CoVs

Recently Completed Related Grants

U19 AI109713-01 Perlin (PI) 3/01/14 – 2/28/20
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.

Citations

a. Gow NAR, Johnson C, Berman J, Coste AT, Cuomo CA, **Perlin DS**, Bicanic T, Harrison TS, Wiederhold N, Bromley M, Chiller T, Edgar K 2022l The importance of antimicrobial resistance in medical mycology. Nat Commun. 2022 Sep 12;13(1):5352.
b. Wang Z, Koirala B, Hernandez Y, Zimmerman M, Park S, **Perlin DS**, Brady SF. 2022. A naturally inspired antibiotic to target multidrug-resistant pathogens. Nature. 601(7894):606-611.
c. Wang Z, Koirala B, Hernandez Y, Zimmerman M, Park S, **Perlin DS**, Brady SF. 2022. A naturally inspired antibiotic to target multidrug-resistant pathogens. Nature. 2022 Jan 5. doi: 10.1038/s41586-021- 04264-x
d. Arastehfar A, Daneshnia F, Cabrera N, Penalva-Lopez S, Sarathy J, Zimmerman M, Shor E, **Perlin DS** Macrophage internalization creates a multidrug-tolerant fungal persister reservoir and facilitates the emergence of drug resistance. Nat Commun. 2023 Mar 2;14(1):1183. doi: 10.1038/s41467-023-36882-6.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

1985-1988 Assistant Member, Public Health Research Institute, New York, NY
1989-1991 Associate Member, Public Health Research Institute, New York, NY
1992-2018 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- CSO, Hackensack Meridian Health Center for Discovery and Innovation, Nutley, NJ
2019- Professor, Dept. of Medical Sciences, Hackensack Meridian School of Medicine
2019- Professor, Dept. of Microbiol & Immunol, Georgetown Univ Sch. of Med, Washington, D.C.
2022- Deputy Director Consortium Integration and Strategic Initiatives for Research, Lombardi Comprehensive Cancer Center Consortium

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)
2017 Named inaugural Editor-in-Chief for *Journal of Fungi*

2017; 2021 Chair, Audit Committee, American Society for Microbiology (ASM); Named to Finance Comm.
2018 Fellow, American Academy of Microbiology
2019, 2020 Named top 10 Health Care Influencer in New Jersey- RO1-NJ
2021 NJBIZ, Healthcare Hero award for COVID-19 response
2020, 2021 EJI, honored as top Scientist in New Jersey
2021 Named top 25 national innovator by Modern Healthcare
2022 Notable Health Care Leader- *Crain's New York Business*
2023 Dr. Sol J. Barer Award for Vision, Innovation and Leadership

Contributions to Science

1. **Drug discovery against high-threat bacteria, fungi and viruses.** 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. I lead an NIH designated Center of Excellence in Translational Research (CETR) and an Antiviral Drug Discovery accelerator (AViDD) that is developing a new generation of antibiotics against high-threat bacteria and viruses like SARS- CoV-2. These programs are collaborative public-private partnerships that accelerate the discovery and development of novel antibiotics and antivirals by joining together academic and industry researchers and providing critical core resources to turn highly promising early concept molecules into potential therapeutics suitable for clinical evaluation.
   a. Wang Z, Koirala B, Hernandez Y, Zimmerman M, Park S, **Perlin DS**, Brady SF. 2022. A naturally inspired antibiotic to target multidrug-resistant pathogens. Nature. 2022 Jan 5. doi: 10.1038/s41586-021- 04264-x
   b. Park S, Russo R, Westfall L, Shrestha R, Zimmerman M, Dartois V, Kurepina N, Kreiswirth B, Singleton E, Li SG, Mittal N, Ahn YM, Bilotta J, Connolly KL, Jerse AE, Freundlich JS, **Perlin DS.** A Novel Oral GyrB/ParE Dual Binding Inhibitor Effective against Multidrug-Resistant *Neisseria gonorrhoeae* and Other High-Threat Pathogens. Antimicrob Agents Chemother. 2022 Aug 16:e0041422. doi: 10.1128/aac.00414-22.
   c. Lovey A, Krel M, Borchardt A, Brady T, Cole JN, Do QQ, Fortier J, Hough G, Jiang W, Noncovich A, Tari L, Zhao Q, Balkovec JM, Zhao Y, **Perlin DS**. Development of novel immunoprophylactic agents against multidrug resistant Gram-negative bacterial infections. Antimicrob Agents Chemother. 2021 Aug 9:AAC0098521. doi: 10.1128/AAC.00985-21
   d. 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.

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 150 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 (Pfizer then Astellas) as a Global Clinical Reference Center for molecular evaluation of echinocandin resistant strains from patients failing therapy. 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 species* including *Candida auris* and *Aspergillus* species.
   a. Garcia-Rubio R, Jimenez-Ortigosa C, DeGregorio L, Quinteros C, Shor E, **Perlin DS.** Multifactorial role of mitochondria in echinocandin tolerance revealed by transcriptome analysis of drug-tolerant cells. mBio. 2021 12(4):e0195921. doi: 10.1128/mBio.01959-21

b. Shor E, **Perlin DS**. DNA damage response of major fungal pathogen Candida glabrata offers clues to explain its genetic diversity. Curr Genet. 2021 Jun;67(3):439-445. doi: 10.1007/s00294-021-01162-7.
c. Satish S, Jiménez-Ortigosa C, Zhao Y, Lee MH, Dolgov E, Krüger T, Park S, Denning DW, Kniemeyer O, Brakhage AA, **Perlin DS**. Stress-Induced Changes in the Lipid Microenvironment of β-(1,3)-d-Glucan Synthase Cause Clinically Important Echinocandin Resistance in Aspergillus fumigatus. MBio. 2019 10(3). pii: e00779-19. doi: 10.1128/mBio.00779-19.
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.

3. **Rapid detection of respiratory, GI tract and bloodstream infections, 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 viral, bacterial and fungal pathogens, and associated drug resistance in high threat bacterial and fungal pathogens.

a. Kordalewska M, Perlin DS. 2022. Detection and Identification of Candida auris from Clinical Skin Swabs. Methods Mol Biol. 2022;2542:245-256. doi: 10.1007/978-1-0716-2549-1_18.
b. Zhao Y, Lee A, Composto K, Cunningham MH, Mediavilla JR, Fennessey S, Corvelo A, Chow KF, Zody M, Chen L, Kreiswirth BN, Perlin DS. 2021 A novel diagnostic test to screen SARS-CoV-2 variants containing E484K and N501Y mutations. Emerg Microbes Infect. 2021 Dec;10(1):994-997. doi: 10.1080/22221751.2021.1929504.
c. Zhao Y, Cunningham MH, Mediavilla JR, Park [S], Fitzgerald S, Ahn HS, Li X, Zhan C, Hong T, Munk G, Chow KF, **Perlin DS**. 2021. An observational study of COVID-19 from a large healthcare system in Northern New Jersey: Diagnosis, clinical characteristics, and outcomes. Sci Rep Feb 23;11(1):4389. doi: 10.1038/s41598-021-83959-7.
d. 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. 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 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. Lee A, Wang N, Carter CL, Zimmerman M, Dartois V, Shaw KJ, Perlin DS, Zhao Y. Therapeutic Potential of Fosmanogepix (APX001) for Intra-abdominal Candidiasis: from Lesion Penetration to Efficacy in a Mouse Model. Antimicrob Agents Chemother. 2021 Mar 18;65(4):e02476-20. doi: 10.1128/AAC.02476-20.
b. Lee A, Prideaux B, Lee MH, Zimmerman M, Dolgov E, Perlin DS, Zhao Y. 2019. Tissue Distribution and Penetration of Isavuconazole at the Site of Infection in Experimental Invasive Aspergillosis in Mice with Underlying Chronic Granulomatous Disease. Antimicrob Agents Chemother 63(6). pii: e00524-19. doi: 10.1128/AAC.00524-19.
c. 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.
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.00274-1

Complete List of Published Work in MyBibliography:
(see: https://pubmed.ncbi.nlm.nih.gov/?term=perlin%2Bds&sort=date)