OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 01/31/2026)

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

My career spans more than 35 years in translational infectious disease research, with a strong emphasis on elucidating mechanisms of pathogenicity and developing countermeasures against high-threat agents that cause acute and chronic disease, particularly in patients with cancer. I have led multiple biomarker and rapid molecular diagnostic programs supported by R01 and U19 mechanisms. In addition, I have directed five highly successful national drug accelerator programs sponsored by the NIH and/or the Department of Defense, each involving close partnerships with industry. My current work focuses on advancing novel anti-infective strategies, including the development of therapeutics targeting high-threat viral, bacterial, and fungal pathogens. Notably, I serve as co-PI, together with Nobel Laureate Dr. Charles Rice (Rockefeller University), on the NIH Antiviral Drug Discovery (AViDD) program. Our consortium, the Metropolitan Antiviral Drug Accelerator (MAVDA), has advanced four antiviral candidates, including one that progressed to Phase II clinical trials. I also lead an NIH-designated national Center of Excellence in Translational Research (CETR) focused on discovering novel antibiotics to combat drug-resistant bacterial infections and co-lead a second CETR with National Academy of Sciences member Dr. Arturo Casadevall to develop transformative therapeutic and diagnostic solutions for drug-resistant fungal diseases. My translational team, which integrates experienced investigators from academia and industry, has supported the development of both small-molecule and biologic therapeutics, including four FDA-approved drugs and several additional candidates in late-stage clinical development. With a publication record exceeding 365 peer-reviewed papers, reviews, and book chapters, I have demonstrated a sustained commitment to advancing translational biomedical research.

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

1U19AI189168-01 Perlin (PI) 6/20/25- 6/19/2030
NIH/NIAID
Center for accelerated development of drug candidates targeting high threat bacterial infections

1U19AI1714010 Perlin (co-PI), Rice (co-PI) 05/17/2022 – 4/30/2026
NIH/NIAID
Metropolitan AntiViral Drug Accelerator

1U19AI189183-01 Casadevall (PI) Perlin (PI) 8/01/25 -7/31/2030
Accelerator for the rapid development of countermeasures targeting drug resistant fungal pathogens

2 R01 AI109025-11 Perlin (PI) 07/01/2023 - 06/30/2028
NIH/NIAID
Critical Factors Influencing Echinocandin Resistance in *Candida glabrata*

Recently Completed Related Grants

1U19AI142731-01 Perlin (PI) 4/01/2019 – 3/31/2025
NIH/NIAID
Center to develop innovative therapeutics to multidrug resistant high-threat bacterial agents

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-coronaviruses

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 - 11/30/2023
NIH/NIAID
Novel bi-specific immunotherapeutic against high-threat Gram-negative pathogens

U19 AI109713-01 Perlin (PI) 3/01/2014 – 2/28/2019
NIH/NIAID
Center to develop therapeutic countermeasures to high-threat bacterial agents

Citations

a. Meyer C, Garzia A, Miller MW, Huggins DJ, Myers RW, Hoffmann HH, Ashbrook AW, Jannath SY, Liverton N, Kargman S, Zimmerman M, Nelson AM, Sharma V, Dolgov E, Cangialosi J, Penalva-Lopez S, Alvarez N, Chang CW, Oswal N, Gonzalez I, Rasheed R, Goldgirsh K, Davis JA, Ramos-Espiritu L, Menezes MR, Larson C, Nitsche J, Ganichkin O, Alwaseem H, Molina H, Steinbacher S, Glickman JF, **Perlin DS**, Rice CM, Meinke PT, Tuschl T. Small-molecule inhibition of SARS-CoV-2 NSP14 RNA cap methyltransferase. *Nature* 2025. Jan 637(8048):1178-1185. doi: 10.1038/s41586-024-08320-0.

b. Alvarez N, Adam GC, Howe JA, Sharma V, Zimmerman MD, Dolgov E, Rasheed R, Nizar F, Sahay K, Nelson AM, Park S, Zhou X, Burlein C, Fay JF, Iwamoto DV, Bahnck-Teets CM, Getty KL, Lin Goh S, Salhab I, Smith K, Boyce CW, Cabalu TD, Murgolo N, Fox NG, Mayhood TW, Shurtleff VW, Layton ME, Parish CA, McCauley JA, Olsen DB, **Perlin DS**. 2024. Novel Pan-Coronavirus 3CL Protease Inhibitor MK-7845: Biological and Pharmacological Profiling. Viruses. 2024 Jul 18;16(7):1158. doi: 10.3390/v16071158.

c. Shurtleff VW, Layton ME, Parish CA, Perkins JJ, Schreier JD, Wang Y, Adam GC, Alvarez N, SBahmanjah S, Bahnck-Teets CM, Boyce CW, Burlein C, Cabalu TD, Campbell BT, Carroll SS, Chang W, de Lera Ruiz M, Dolgov E, Fay JF, Fox NG, Shih Lin Goh SL, Hartingh TJ, Hurzy DM, Kelly III MJ, Klein DJ, KlinglereF-M, Krishnamurthy H, Kudalkar SN, Mayhood TW, McKenna PM, Murray EM, Nahas D, Nawrat CC, Park S, Qian D, Roeckera AJ, Sharma c, Shipe WD, Su J, Taggart RV, Truong Q, Wu Y, Zhou X, Zhuang N, **Perlin DS**, Olsen DB, Howe JA, and McCauley JA 2024 Invention of MK-7845, a SARS-CoV-2 3CL protease inhibitor employing a novel difluorinated glutamine mimic. J Med Chem. 2024 Mar 14;67(5):3935-3958. doi: 10.1021/acs.jmedchem.3c02248.

d. Chang CW, Oswal N, Murugan M, Goldgirsh K, Tsao W, Park S, Perlin DS. A novel cellular tool for screening human pan-coronavirus antivirals. Antiviral Res. 2025 Jun 10;240:106212. doi: 10.1016/j.antiviral.2025.106212. PMID: 40505777

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022- Deputy Director Consortium Integration and Strategic Initiatives for Research, Lombardi Comprehensive Cancer Center Consortium

2019- Professor, Dept. of Microbiol & Immunol, Georgetown Univ Sch. of Med, Washington,

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

Honors

2025	Fellow, Infectious Diseases Society of America
2023	Dr. Sol J. Barer Award for Vision, Innovation and Leadership
2022	Notable Health Care Leader- Crain's New York Business
2021, 2024	Named top 25 national innovator by Modern Healthcare
2020, 2021	EJI, honored as top Scientist in New Jersey
2021	NJBIZ, Healthcare Hero award for COVID-19 response
2019, 2020	Named top 10 Health Care Influencer in New Jersey- RO1-NJ
2018	Fellow, American Academy of Microbiology
2017- 2021	Chair, Audit Committee, American Society for Microbiology (ASM)
2017	Named inaugural Editor-in-Chief for Journal of Fungi
2012-	Executive Committee, Board of Directors, Aaron Diamond AIDS Research Center
2009-2012	Distinguished Visiting Professor, University of Manchester, United Kingdom
2005	Fellow, The New York Academy of Sciences

Contributions to Science

1. Drug discovery targeting 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 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. Meyer C, Garzia A, Miller MW, Huggins DJ, Myers RW, Hoffmann HH, Ashbrook AW, Jannath SY, Liverton N, Kargman S, Zimmerman M, Nelson AM, Sharma V, Dolgov E, Cangialosi J, Penalva-Lopez S, Alvarez N, Chang CW, Oswal N, Gonzalez I, Rasheed R, Goldgirsh K, Davis JA, Ramos-Espiritu L, Menezes MR, Larson C, Nitsche J, Ganichkin O, Alwaseem H, Molina H, Steinbacher S, Glickman JF, **Perlin DS**, Rice CM, Meinke PT, Tuschl T. Small-molecule inhibition of SARS-CoV-2 NSP14 RNA cap methyltransferase. *Nature* 2025. Jan;637(8048):1178-1185. doi: 10.1038/s41586-024-08320-0.
b. Alvarez N, Adam GC, Howe JA, Sharma V, Zimmerman MD, Dolgov E, Rasheed R, Nizar F, Sahay K, Nelson AM, Park S, Zhou X, Burlein C, Fay JF, Iwamoto DV, Bahnck-Teets CM, Getty KL, Lin Goh S, Salhab I, Smith K, Boyce CW, Cabalu TD, Murgolo N, Fox NG, Mayhood TW, Shurtleff VW, Layton ME, Parish CA, McCauley JA, Olsen DB, **Perlin DS**. 2024. Novel Pan-Coronavirus 3CL Protease Inhibitor MK-7845: Biological and Pharmacological Profiling. Viruses. 2024 Jul 18;16(7):1158. doi: 10.3390/v16071158.

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. 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.

2. Drug resistance and tolerance 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 drug tolerance leading to emergence of echinocandin and multidrug resistance in *Candida species* including *Candida auris* and *Aspergillus* species.

a. 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-
b. Arastehfar A, Daneshnia F, Hovhannisyan H, Fuentes D, Cabrera N, Quinteros C, Ilkit M, Ünal N, Hilmioğlu-Polat S, Jabeen K, Zaka S, Desai JV, Lass-Flörl C, Shor E, Gabaldon T, **Perlin DS.** Overlooked *Candida glabrata* petites are echinocandin tolerant, induce host inflammatory responses, and display poor *in vivo* fitness. mBio. 2023 Oct 31;14(5):e0118023. doi: 10.1128/mbio.01180-23.
c. 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.
d. 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.

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, viral 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

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. My research group has been using novel technology to image and quantify the level of drugs in life-threatening diseases resulting from intra-abdominal 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.

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