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: Milena Ewa Kordalewska

eRA COMMONS USER NAME (credential, e.g., agency login): mk1521

POSITION TITLE: Research Assistant Member and Assistant 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
Gdansk University of Technology, Gdansk, Poland	MSc Eng	07/2009	Biotechnology
Gdansk University of Technology, Gdansk, Poland	PhD	07/2016	Biotechnology
Public Health Research Institute, Rutgers Biomedical and Health Sciences, Newark, NJ, USA	Postdoc	01/2019	Molecular Microbiology

A. Personal Statement

My research program addresses the rising threat of fungal diseases by improving our understanding of how certain fungi avoid drug action and developing tools to quickly identify and fight them. My expertise lies in translational research bridging molecular microbiology, genetic epidemiology and mechanisms of drug resistance, diagnostics development, and drug discovery. I run a research program focused on Candida auris, a recently emerged and rapidly expanding nosocomial pathogen. I have a proven track record of developing and validating molecular diagnostic assays for human-pathogenic filamentous fungi and yeasts. I developed the first molecular tests for rapid and accurate detection and identification of C. auris and its molecular markers of antifungal drug resistance, which were later validated for culture-independent/direct use on clinical swabs. Furthermore, I have defined factors contributing to echinocandin drug resistance in C. auris, and laid foundations for better understanding of C. auris response to azole and amphotericin B drug treatment. Additionally, I have been investigating factors contributing to drug resistance development in Candida species with special emphasis on 1) frequencies of mutations leading to resistance in vitro and in vivo; 2) correlations between gene mutations, enzyme kinetic inhibition, minimal inhibitory concentration (MIC) values, pharmacodynamic resistance, and clinical outcomes. I have direct and ample experience working with our murine models of neutropenic invasive candidiasis and Candida gastrointestinal (GI) colonization. I have worked closely with numerous academic, clinical, and public health collaborators, as well as commercial partners. Recently, I have been awarded two research grants from the New Jersey Health Foundation. I conceived and coordinated a C. auris diagnostics project sponsored by the CDC and served as a co-PI in a Merck-sponsored project "Drug resistance profiles of bacterial and fungal isolates from superinfections in hospitalized COVID-19 patients". I also curated our large laboratory collection of fungi and coordinated the Reference center for molecular evaluation of drug resistance to echinocandin and triazole antifungal drugs funded by Astellas Pharma. Overall, my training and experience uniquely position me to lead research projects in the field of medical mycology.

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

New Jersey Health Foundation Kordalewska **(PI)** 02/17/2025 - 02/16/2026 Impact of sphingolipid biosynthesis inhibition on *Candida auris* echinocandin susceptibility

New Jersey Health Foundation Kordalewska **(PI)** 02/15/2024 - 02/14/2026 Enhanced diagnostic assays for *Candida auris* bloodstream infections Merck Investigator Studies Program (MISP) #60453 Kordalewska (**co-PI** with Kreiswirth) 12/16/2020 - 12/15/2021 Drug resistance profiles of bacterial and fungal isolates from superinfections in hospitalized COVID-19 patients

Astellas Pharma Perlin (PI), Role: **Project Coordinator** 12/31/2017 - 01/31/2020 Reference Center for Molecular Evaluation of Drug Resistance to Echinocandin and Triazole Antifungal Drugs

Pending funding decision:

NIH/NIAID U19Impact Score: 24Casadevall (PI), Role: Mycology Core DirectorCore Impact Score: 203/1/2025 - 2/28/2030Accelerator for the rapid development of countermeasures targeting drug resistant fungal pathogens

Citations:

- Kordalewska M[⊠], Zhao Y, Lockhart SR, Chowdhary A, Berrio I, Perlin DS. Rapid and Accurate Molecular Identification of the Emerging Multidrug-Resistant Pathogen *Candida auris*. J Clin Microbiol. 2017 Aug;55(8):2445-2452. doi: 10.1128/JCM.00630-17. Epub 2017 May 24. PMID: 28539346; PMCID: PMC5527423.
- Kordalewska M[∞], Lee A, Zhao Y, Perlin DS. Detection of *Candida auris* antifungal drug resistance markers directly from clinical skin swabs. Antimicrob Agents Chemother. **2019** Sep 9;63(12). doi: 10.1128/AAC.01754-19. Epub 2019 Oct 7. PubMed PMID: 31591112; PubMed Central PMCID: PMC6879264.
- 3. Kordalewska M[⊠], Perlin DS. Deciphering *Candida auris* Paradoxical Growth Effect (Eagle Effect) in Response to Echinocandins. Methods Mol Biol. **2022**;2517:73-85. doi: 10.1007/978-1-0716-2417-3_6. PMID: 35674946.
- 4. **Kordalewska M**[⊠], Perlin DS. 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. PMID: 36008670.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

- **2024 -** Ad-hoc reviewer, European Science Foundation (ESF)
- **2023 Assistant Professor**, Department of Medical Sciences, Hackensack Meridian School of Medicine, Nutley, NJ, USA
- **2021** Expert Participant, Medical Research Council and University of Exeter workshop "Drivers of Antifungal Resistance: Strategic Perspectives and Priorities", May 04, 2021
- **2020 Research Assistant Member (Faculty)**, Infectious Diseases; Center for Discovery and Innovation, Hackensack Meridian Health, Nutley, NJ, USA
- **2020 -** Topics Editor, *Journal of Fungi*
- 2020 Member, *Microbiology Society*
- **2019 2020** Senior Research Associate, Infectious Diseases; Center for Discovery and Innovation, Hackensack Meridian Health, Nutley, NJ, USA
- **2019** Participant, Wellcome Genome Campus Advanced Course: Fungal Pathogen Genomics, May 7-12, 2019; Wellcome Genome Campus, Hinxton, UK
- **2018 -** Member, International Society for Human and Animal Mycology
- 2018 Member, New York Academy of Sciences
- **2017** Peer reviewer, 80+ manuscripts in multiple journals including Antimicrobial Agents and Chemotherapy, Clinical Microbiology and Infection, Critical Reviews in Microbiology, Emerging Microbes and Infections, Frontiers in Cellular and Infection Microbiol, Frontiers in Microbiology, International Journal of Antimicrobial Agents, Journal of Fungi, Journal of Global Antimicrobial Resistance, Journal of Infection, Medical Mycology, Microbiology Spectrum, Mol. Diagnosis & Therapy, mSphere, Mycoses, Nature Communications, PLOS ONE, Scientific Reports

- 2017 Member, American Society for Microbiology
- 2017 External Expert Reviewer, The National Science Centre, Poland
- **2016 2019 Postdoctoral Fellow**; Public Health Research Institute, Rutgers Biomedical and Health Sciences, Newark, NJ, USA
- **2015 2016** Junior QC Specialist; Polpharma Biologics, Gdansk, Poland
- 2015 Scientific-Technical Worker; BLIRT S.A., Gdansk, Poland
- 2014 2015 Member, European Society of Clinical Microbiology and Infectious Diseases
- **2014** Research Scholar; Public Health Research Institute, Rutgers The State University of New Jersey, Newark, NJ, USA
- **2011 2016 PhD student**; Department of Molecular Biotechnology and Microbiology, Faculty of Chemistry, Gdansk University of Technology, Gdansk, Poland
- 2011 Member, Polish Society of Microbiologists
- 2009 2011 Research and Teaching Fellow; Medical University of Gdansk, Gdansk, Poland
- **2004 2009** Master of Science and Engineering student; Department of Pharmaceutical Technology and Biochemistry, Faculty of Chemistry, Gdansk University of Technology, Gdansk, Poland

Honors

- **2024** Invited Speaker, Microbiology and Immunology Seminar, Georgetown University, Washington, DC, USA
- 2023 Finalist, ILSE Translational Research Competition, Union, NJ
- 2018 International Society for Human and Animal Mycology 2018 Attendance Grant
- 2018 ASM Student and Postdoctoral Travel Award ASM Microbe
- **2017** European Confederation of Medical Mycology Young Investigators Travel Award Trends in Medical Mycology 2017
- 2015 25th European Congress of Clinical Microbiology and Infectious Diseases Travel Grant
- **2015** Industrial Internship award "The Center for Advanced Studies the development of interdisciplinary doctoral studies at the Gdansk University of Technology in the key areas of the Europe 2020 Strategy"
- **2014** International Fellowship award "The development of interdisciplinary doctoral studies at the Gdansk University of Technology in modern technologies"

C. Contributions to Science

Antifungal drug resistance mechanisms in Candida auris

In addition to rising incidence rates of *Candida* spp. infections, a trend of increasing cases of infection with non*albicans Candida* species has been observed. The recent simultaneous emergence of *Candida auris* on all inhabited continents has posed a serious global threat to healthcare due to its propensity for drug resistance and persistence (human skin and hospital environment) leading to nosocomial outbreaks. In contrast to most *Candida* species, where antifungal drug resistance is the exception, clinical isolates of *C. auris* are often characterized by elevated minimal inhibitory concentration (MIC) values to one or multiple antifungal drug classes. Results of my research work in the past few years have improved our understanding of the molecular mechanisms contributing to the antifungal drug resistance in *C. auris*.

- a. Chowdhary A, Prakash A, Sharma C, Kordalewska M, Kumar A, Sarma S, Tarai B, Singh A, Upadhyaya G, Upadhyay S, Yadav P, Singh PK, Khillan V, Sachdeva N, Perlin DS, Meis JF. A multicentre study of antifungal susceptibility patterns among 350 *Candida auris* isolates (2009-17) in India: role of the *ERG11* and *FKS1* genes in azole and echinocandin resistance. J Antimicrob Chemother. **2018** Apr 1;73(4):891-899. doi: 10.1093/jac/dkx480. PubMed PMID: 29325167.
- b. Kordalewska M[⊠], Lee A, Park S, Berrio I, Chowdhary A, Zhao Y, Perlin DS. Understanding Echinocandin Resistance in the Emerging Pathogen *Candida auris*. Antimicrob Agents Chemother. 2018 Jun;62(6). doi: 10.1128/AAC.00238-18. Print 2018 Jun. PubMed PMID: 29632013; PubMed Central PMCID: PMC5971591.
- c. Healey KR, Kordalewska M, Jiménez Ortigosa C, Singh A, Berrío I, Chowdhary A, Perlin DS. Limited ERG11 Mutations Identified in Isolates of Candida auris Directly Contribute to Reduced Azole Susceptibility. Antimicrob Agents Chemother. 2018 Oct;62(10). doi: 10.1128/AAC.01427-18. Print 2018 Oct. PubMed PMID: 30082281; PubMed Central PMCID: PMC6153782.

d. Kordalewska M[⊠], Cancino-Prado G, Nobrega de Almeida Júnior J, Brasil Brandão I, Tigulini de Souza Peral R, Colombo AL, Perlin DS. Novel Non-Hot Spot Modification in Fks1 of *Candida auris* Confers Echinocandin Resistance. Antimicrob Agents Chemother. **2023** Jun 15;67(6):e0042323. doi: 10.1128/aac.00423-23. Epub 2023 May 24. PubMed PMID: 37222585; PubMed Central PMCID: PMC10269051.

Drivers of echinocandin resistance in Candida glabrata

Candida glabrata is a member of the human microbiome and can cause systemic infection upon immune suppression. Both the incidence of *C. glabrata* invasive fungal infections and its rates of multidrug resistance have increased in recent years. For the past few years, I have been investigating factors contributing to the echinocandin resistance development in *C. glabrata* with special emphasis on 1) frequencies of mutations leading to echinocandin resistance *in vitro* and *in vivo*; 2) correlations between gene mutations, enzyme kinetic inhibition, minimal inhibitory concentration (MIC) values, pharmacodynamic resistance, and clinical outcomes.

- a. Healey KR, Nagasaki Y, Zimmerman M, Kordalewska M, Park S, Zhao Y, Perlin DS. The Gastrointestinal Tract Is a Major Source of Echinocandin Drug Resistance in a Murine Model of *Candida glabrata* Colonization and Systemic Dissemination. Antimicrob Agents Chemother. 2017 Dec;61(12). doi: 10.1128/AAC.01412-17. Print 2017 Dec. PubMed PMID: 28971865; PubMed Central PMCID: PMC5700336.
- b. Shields RK, Kline EG, Healey KR, Kordalewska M, Perlin DS, Nguyen MH, Clancy CJ. Spontaneous Mutational Frequency and FKS Mutation Rates Vary by Echinocandin Agent against *Candida glabrata*. Antimicrob Agents Chemother. **2019** Jan;63(1). doi: 10.1128/AAC.01692-18. Print 2019 Jan. PubMed PMID: 30373796; PubMed Central PMCID: PMC6325211.
- c. Hou X, Healey KR, Shor E, Kordalewska M, Ortigosa CJ, Paderu P, Xiao M, Wang H, Zhao Y, Lin LY, Zhang YH, Li YZ, Xu YC, Perlin DS, Zhao Y. Novel *FKS1* and *FKS2* modifications in a high-level echinocandin resistant clinical isolate of *Candida glabrata*. Emerg Microbes Infect. **2019**;8(1):1619-1625. doi: 10.1080/22221751.2019.1684209. PubMed PMID: 31711370; PubMed Central PMCID: PMC6853239.

Rapid detection and identification of Candida auris and other pathogenic fungi

Precise and timely identification of fungal isolates to the species level is extremely important, especially when they are recovered from high-risk patients, as fungal infections in these individuals can be serious, difficult to treat and rapidly fatal. However, traditional diagnostic procedures are often tedious and time consuming, delaying implementation of adequate therapy. Application of nucleic acid amplification-based methods enables shortening of the time required for analysis to be completed and makes it almost entirely independent from the diagnostician's experience. For the past few years, I have been working on developing novel molecular platforms for fast, robust, easy to perform and interpret detection/identification of fungal (yeast and mold) pathogens.

- a. **Kordalewska M**[⊠], Brillowska-Dąbrowska A, Jagielski T, Dworecka-Kaszak B. PCR and real-time PCR assays to detect fungi of *Alternaria alternata* species. Acta Biochim Pol. 2015;62(4):707-12. doi: 10.18388/abp.2015_1112. Epub **2015** Oct 27. PubMed PMID: 26610309.
- b. Kordalewska M[⊠], Jagielski T, Brillowska-Dąbrowska A. Rapid Assays for Specific Detection of Fungi of Scopulariopsis and Microascus Genera and Scopulariopsis brevicaulis Species. Mycopathologia. 2016 Aug;181(7-8):465-74. doi: 10.1007/s11046-016-0008-5. Epub 2016 Jun 2. PubMed PMID: 27255522; PubMed Central PMCID: PMC4937093.
- c. Kordalewska M[⊠], Zhao Y, Lockhart SR, Chowdhary A, Berrio I, Perlin DS. Rapid and Accurate Molecular Identification of the Emerging Multidrug-Resistant Pathogen *Candida auris*. J Clin Microbiol. 2017 Aug;55(8):2445-2452. doi: 10.1128/JCM.00630-17. Epub 2017 May 24. PubMed PMID: 28539346; PubMed Central PMCID: PMC5527423.
- d. Sexton DJ, Kordalewska M, Bentz ML, Welsh RM, Perlin DS, Litvintseva AP. Direct Detection of Emergent Fungal Pathogen *Candida auris* in Clinical Skin Swabs by SYBR Green-Based Quantitative PCR Assay. J Clin Microbiol. **2018** Dec;56(12). doi: 10.1128/JCM.01337-18. Print 2018 Dec. PubMed PMID: 30232130; PubMed Central PMCID: PMC6258843.

Molecular diagnostics platforms for the detection of antifungal drug resistance markers

Although antifungal susceptibility testing (broth microdilution) is standardized, it is important to recognize that performance of phenotypic tests is time-consuming, analysis of the results is not always straightforward, which may lead to difficulties in defining drug-susceptible and -resistant isolates. To overcome these issues, it is possible to apply molecular tools, since sequence data are highly informative and accurate. Molecular resistance determinants detection assays can be applied for high-throughput screening and provide information on isolates susceptibility much quicker than standard methods (especially when performed with DNA isolated directly from clinical specimens). For the past few years, I have been working on development and validation of real-time PCR assays, which exploit thermodynamic properties of molecular beacons and enable easy differentiation of wild-type (drug-susceptible) and mutant (drug-resistant) amplicons.

- a. Zhao Y, Nagasaki Y, Kordalewska M, Press EG, Shields RK, Nguyen MH, Clancy CJ, Perlin DS. Rapid Detection of *FKS*-Associated Echinocandin Resistance in *Candida glabrata*. Antimicrob Agents Chemother. 2016 Nov;60(11):6573-6577. doi: 10.1128/AAC.01574-16. Print 2016 Nov. PubMed PMID: 27550360; PubMed Central PMCID: PMC5075061.
- b. Hou X, Lee A, Jiménez-Ortigosa C, Kordalewska M, Perlin DS, Zhao Y. Rapid Detection of *ERG11*-Associated Azole Resistance and *FKS*-Associated Echinocandin Resistance in *Candida auris*. Antimicrob Agents Chemother. 2019 Jan;63(1). doi: 10.1128/AAC.01811-18. Print 2019 Jan. PubMed PMID: 30397051; PubMed Central PMCID: PMC6325222.
- c. Kordalewska M[⊠], Lee A, Zhao Y, Perlin DS. Detection of Candida auris antifungal drug resistance markers directly from clinical skin swabs. Antimicrob Agents Chemother. 2019 Sep 9;63(12). doi: 10.1128/AAC.01754-19. Epub 2019 Oct 7. PubMed PMID: 31591112; PubMed Central PMCID: PMC6879264.
- d. Kordalewska M[⊠], Perlin DS. 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. PMID: 36008670.

Complications of COVID-19 in severely ill patients

Since the beginning of the COVID-19 pandemic, I have been involved in research projects related to understanding of factors contributing to the disease severity with a special emphasis on development of secondary bacterial and fungal infections and microevolution of SARS-CoV-2 in severely ill patients.

- a. **Kordalewska M[⊠]**, Guerrero KD, Garcia-Rubio R, Jiménez-Ortigosa C, Mediavilla JR, Cunningham MH, Hollis F, Hong T, Chow KF, Kreiswirth BN, Perlin DS. Antifungal Drug Susceptibility and Genetic Characterization of Fungi Recovered from COVID-19 Patients. J Fungi (Basel). **2021** Jul 11;7(7). doi: 10.3390/jof7070552. PubMed PMID: 34356931; PubMed Central PMCID: PMC8306261.
- b. Chen L, Zody MC, Di Germanio C, Martinelli R, Mediavilla JR, Cunningham MH, Composto K, Chow KF, Kordalewska M, Corvelo A, Oschwald DM, Fennessey S, Zetkulic M, Dar S, Kramer Y, Mathema B, Germer S, Stone M, Simmons G, Busch MP, Maniatis T, Perlin DS, Kreiswirth BN. Emergence of Multiple SARS-CoV-2 Antibody Escape Variants in an Immunocompromised Host Undergoing Convalescent Plasma Treatment. mSphere. 2021 Aug 25;6(4):e0048021. doi: 10.1128/mSphere.00480-21. Epub 2021 Aug 25. PubMed PMID: 34431691; PubMed Central PMCID: PMC8386433.
- c. Dar S, Erickson D, Manca C, Lozy T, Shashkina E, Kordalewska M, Mediavilla JR, Chen L, Rojtman A, Kreiswirth BN. The impact of COVID on bacterial sepsis. Eur J Clin Microbiol Infect Dis. 2023 Aug 19. doi: 10.1007/s10096-023-04655-0. Epub ahead of print. PMID: 37597051.
- d. Kordalewska M[⊠], Perlin DS. *Candida* in COVID-19: Gut-Lung Axis, Dysbiosis, and Infections. Curr Fungal Infect Rep. **2023**. doi: 10.1007/s12281-023-00476-y.

 $^{\mbox{\tiny \square}}$ corresponding author

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1RqFzt9yn9agmj/bibliography/public/