BIOGRAPHICAL SKETCH

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NAME: Balkovec, James M.

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

POSITION TITLE: Scientific Advisor

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
University of Pittsburgh, Pittsburgh, PA	BS	05/1980	Chemistry
University of Wisconsin, Madison, WI	Ph.D.	05/1985	Organic Chemistry
Columbia University, New York, NY	Postdoctoral	05/1987	Organic Chemistry

A. Personal Statement

The ongoing infectious disease (ID) crisis has reached a critical stage where resistance continues to challenge the utility of existing drugs while novel pathogens appear with increasing frequency. The COVID-19 pandemic underscored the critical importance of preemptive development of novel drugs for difficult-to-treat infections. My goal as a medicinal chemist has been to discover life-saving medicines and advance them into the clinic. I have led internal and external chemistry teams in multiple therapeutic areas. As part of my responsibilities, I led multidisciplinary project teams encompassing chemistry, structural biology, biology, microbiology, pharmacology, DMPK, toxicology, and CMC. I have a proven track record with numerous publications and patents, and I am an inventor of a first-in-class antifungal agent, Cancidas®, and led the team that discovered BrexaFemme®, an oral drug for treating vulvovaginal candidiasis. I contributed to the development of the recently approved, once-weekly antifungal, Rezzayo® and am a co-inventor of a novel “universal” biologic drug for seasonal and pandemic influenza currently in clinical trials. My history of successful works demonstrate a passion for wanting to make meaningful contributions in the ID area. I have worked as a laboratory scientist and have directed programs focused on small molecules, natural products, proteins, large molecules, and biologics. I have a breadth of relevant experience in organic synthesis, structural analysis, QSAR, enzyme, receptor and cell-based assays, animal models of disease, pharmacology, DMPK, toxicology, and related disciplines important in identifying and optimizing quality leads for development. I am currently engaged in multiple programs seeking to develop novel drugs in the antibacterial, antifungal, antiviral, pain and cancer therapeutic areas. Several publications that highlight my breadth of accomplishments in problem solving and medicinal chemistry techniques are listed:

1. Gao, Y.-D., Olson, S. H., Balkovec, J. M., Zhu, Y., Royo, I., Tang, W., Tan, E., Evers, R. & Mosley, R. T. (2007). Attenuating PXR activation: a molecular modeling approach. Xenobiotica, 37(2), 124-138.
2. Parker Jr., D. L., Walsh, S., Li, B., Kim, E., Sharipour, A., Smith, C., Chen, Y.-H., Berger, R., Harper, B., Zhang, T., Park, M., Shu, M., Wu, J., Xu, J., Dewnani, S., Sherer, E. C., Hruza, A., Reichert, P., Geissler, W., Sonatore, L., Ellsworth, K., Balkovec, J., Greenlee, W. & Wood, H. B. (2015). Rapid development of two factor IXa inhibitors from hit to lead. Bioorganic and Medicinal Chemistry Letters, 25(11), 2321-2325.
3. Cernak, T., Gesmundo, N., Dykstra, K., Yu, Y., Wu, Z., Shi, Z.-c., Vachal, P., Sperbeck, D., He, S., Murphy, B., Sonatore, L., Williams, S., Madeira, M., Verras, A., Reiter, M., Lee, C.E, Cuff, J., Sherer, E., Kuethe, J., Goble, S., Perrotto, N., Pinto, S., Shen, D.-M., Nargund, R. Balkovec, J., DeVita, R. & Dreher, S. (2017). Microscale high-throughput experimentation as an enabling technology in drug discovery: application in the

discovery of (piperidinyl)pyridinyl-1H-benzimidazole DGAT1 inhibitors. Journal of Medicinal Chemistry, 60(9), 3594-3605.

4. Yu, Y., Wu, Z., Shi, Z.-C., He, S., Lai, Z., Cernak, T. A., Vachal, P., Liu, M., Liu, J., Hong, Q., Jian, T., Guiadeen, D., Krikorian, A., Sperbeck, D. M., Verras, A., Sonatore, L. M., Murphy, B. A., Wiltsie, J., Chung, C. C., Gorski, J. N., Liu, J., Xiao, J., Wolff, M., Tong, S. X., Madeira, M., Karanam, B. V., Shen, D.-M., Balkovec, J. M., DeVita, R. J., Pinto S. & Nargund, R. P. (2019). Accelerating the discovery of DGAT1 inhibitors through the application of parallel medicinal chemistry (PMC). Bioorganic and Medicinal Chemistry Letters, 29(11), 1380-1385.

B. Positions and Honors

Positions and Employment

2022-	Director, Medicinal Chemistry Core, CDI/HMH, Nutley, NJ
2020-	Vice President and Cofounder, Kathera Biosciences, Union, NJ
2014-18	Senior Vice President of Research, Cidara Therapeutics, San Diego, CA
2012-	Principal Consultant, ChemTract Consulting, Martinsville, NJ
1987-2011	Senior Chemist through Senior Scientific Director, Merck & Co, Rahway, NJ

Other Experience and Professional Memberships

2022-23	Guest Editor, Journal of Fungi
2018	Organizing Committee, Stork Memorial Symposium Columbia University
2012-17	Chemical Consultants Network
2012-15	Local Councilor, Theobald Smith Society (New Jersey Local ASM)
2006	Organizer, 231st American Chemical Society Meeting, MEDI Division
1994-	Member, American Association for Microbiology (ASM)
1993-98	Organizing Committee, Chemistry as a Life Science, Rutgers University
1992-	Referee for Journal of Medicinal Chemistry, Tetrahedron, European Journal of Medicinal Chemistry, Bioorganic and Medicinal Chemistry
1987-	Member, ACS Medicinal Chemistry Division
1980-2011	Member, ACS Organic Division
1979-	Member, American Chemical Society (ACS)

Honors

2006	Michael H. Fisher Award in Medicinal Chemistry, Merck & Co
2006	Heroes of Chemistry Award, American Chemical Society
2001	Industrial Innovation Award, American Chemical Society
2001	Guest Professorship, Tianjin University
2001	Thomas Alva Edison Award, R&D Council of NJ
1985	National Institutes of Health Research Service Award
1979	Silverman Award, University of Pittsburgh

C. Contribution to Science

1. Antibacterial. Contributions to both small molecule and biologic-based antibiotics. These include a) novel cationic betalactam derivatives with expanded activity against Gram-negative pathogens, b) Class B metallobetalactamase inhibitors that synergize with betalactam antibiotics against resistant infections and, c) novel LPS binding peptides covalently linked to a human Fc that are immunoprophylactic agents to treat and protect against resistant Gram-negative infections.

    a. Balkovec, J. M.; Szymonifka, M. J.; Heck & J. V.; Ratcliffe, R. W. (1991). Basic Carbapenem Analogs: Synthesis And In Vitro Activity of 1β-Methyl-2-(Pyridylmethylthio)-Carbapenems, Journal of Antibiotics, 44(10), 1172-1177.
    b. Toney, J. H.; Hammond, G. G.; Fitzgerald, P. M. D.; Sharma, N.; Balkovec, J. M. , Rouen, G. P.; Olson, S. H.; Hammond, M. L.; Greenlee M. L. & Gao, Y.-D. (2001). Succinic acids as potent inhibitors of plasmid-borne IMP-1 metallo-β-lactamase, Journal of Biological Chemistry, 276(34), 31913-31918.

c. Balkovec, J. M.; Blizzard, T.; Borchardt, A.; Brady, T. P.; Chen, Z.-Y.; Do, Q.-Q.; Doehrmann, S.; Jiang, W.; Lam, T.; Locke, J. B. & Noncovich, A. (2020) Compositions and Methods for the Treatment of Bacterial Infections, WO2020014469.
d. Lovey, A., Krel, M., Borchardt, A., Brady, T., Cole, J. N., Do, Q.-Q., Fortier, J., Hough, G., Jiang, W., Noncovich, A., Tari, L., Zhao, Q., Balkovec, J. M., Zhao, Y. & Perlin, D. S. (2021). Development of novel immunoprophylactic agents against multidrug resistant Gram-negative bacterial infections, Antimicrobial Agents and Chemotherapy, 65, AAC.00985-21.

2. Antifungal. Research detailing the discovery of the orally active GSi ibrexafungerp (BrexaFemme®), novel small molecule bispecific immunoprophylactics targeting Gram-negative pathogens, the long-acting echinocandin Rezzayo® (CD101), and the discovery and development of caspofungin (Cancidas®).
   a. Balkovec, J. M., Hughes, D. L., Masurekar, P. S., Sable, C. A., Schwartz, R. E. & Singh, S. B. (2014). Discovery and Development of First in Class Antifungal Caspofungin (CANCIDAS®) - A Case Study, Natural Products Reports, 31(1), 15-34.
   b. Ong, V., Hough, G., Schlosser, M., Bartizal, K., Balkovec, J., James, K. & Krishnan, R. (2016). Preclinical Evaluation of the Stability, Safety and Efficacy of CD101, a Novel Echinocandin, Antimicrobial Agents and Chemotherapy, 60(11), 6872-6879.
   c. Jones, C. N., Ellett, F., Robertson, A. L., Forrest, K. M., Judice, K., Balkovec, J. M., Springer, M., Markmann, J. F., Vyas, J. M., Warren, S. H. & Irimia, D. (2019). Bifunctional Small Molecules Enhance Neutrophil Activities Against Aspergillus fumigatus In Vivo and In Vitro, Frontiers in Immunology, 10:644.
   d. Apgar, J. M., Wilkening, Parker, Jr., D. L., R. R., Meng, D., Wildonger, K. J., Sperback, D., Greenlee, M. L., Balkovec, J. M., Flattery, A. M., Abruzzo, G. K., Galgoci, A. M., Giacobbe, R. A., Gill, C. J., Hsu, M.-J., Liberator, P., Misura, A. S., Motyl, M., Nielsen-Kahn, J., Powles, M., Racine, F., Dragovic, J., Fan, W., Kirwan, R., Lee, S., Liu, H., Mamai, A., Nelson, K. & Peel, M. (2021). Ibrexafungerp: an orally active β-1,3-glucan synthesis inhibitor, Bioorganic and Medicinal Chemistry Letters, 32:127661.

3. Antiviral. Published patent applications that encompass long-acting, broad spectrum immunoprophylactic agents for use in treating influenza infections where I am a co-inventor.
   a. Balkovec, J. M., Bensen, D. C., Borchardt, A., Brady, T. P., Chen, Z.-Y., Cole, J., Do, Q.-Q. T., Doehrmann, S., Jiang, W., Lam, T., Noncovich, A. & Tari, L. (2020). Compositions and Methods for the Treatment of Viral Infections, WO2020051498.
   b. Balkovec, J. M., Bensen, D. C., Borchardt, A., Brady, T. P., Chen, Z.-Y., Cole, J., Do, Q.-Q. T., Doehrmann, S., Jiang, W., Lam, T., Noncovich, A. & Tari, L. (2021). Compositions and Methods for the Treatment of Viral Infections, WO2021046549.

4. Inflammation and Metabolic Disease. Details of the discovery of selective glucocorticoid receptor modulators for inflammation, one of the development candidates targeting 11β-hydroxysteroid dehydrogenase Type 1 for the treatment of metabolic syndrome, and novel diacylglycerol acyltransferase inhibitors for treating obesity.
   a. Thompson, C. F., Quraishi, N., Ali, A., Mosley, R.T., Tata, J. R., Hammond, M. L., Balkovec, J. M., Einstein, M., Ge, L., Harris, G., Kelly, T. M., Mazur, P., Pandit, S., Santoro, J., Sitlani, A., Wang, C., Williamson, J., Miller, D. K., Yamin, T.-T. D., Thompson, O'Neill, E. A., C. M., Zaller, D.M., Forrest, M.J., Carballo-Jane, E. & Luell, S. (2007). Novel Glucocorticoids Containing a 6,5-Bicyclic Core Fused to a Pyrazole Ring: Synthesis, In Vitro Profile, molecular modeling studies, and in vivo experiments, Bioorganic and Medicinal Chemistry Letters, 17(12), 3354-3361.
   b. Ali, A., Balkovec, J. M., Greenlee, M., Hammond, M. L., Rouen, G., Taylor, G., Einstein, M., Ge, L., Harris, G., Williamson, J., Kelly, T. M., Mazur, P., Pandit, S., Santoro, J., Sitlani, A., Wang, C., Forrest, M. J., Carballo-Jane, E., Luell, S., Du, F., Lowitz, K. & Visco, D. (2008). Discovery of Betamethasone 17α-Carbamates As Fully Dissociated Glucocorticoid Receptor Modulators In The Rat, Bioorganic and Medicinal Chemistry, 16(16), 7535-7542.
   c. Maletic, M., Leeman, A., Szymonifka, M., Mundt, S. S., Zokian, H. J., Shah, K., Dragovic, J., Lyons, K., Thieringer, R., Vosatka, A. H., Balkovec, J. & Waddell, S. T (2011). Bicyclo[2.2.2]octyltriazole Inhibitors

of 11β-Hydroxysteroid Dehydrogenase Type I. Pharmacological Agents for the Treatment of Metabolic Syndrome, Bioorganic and Medicinal Chemistry Letters, 21(8), 2568–2572.

d. He, S., Lai, Z., Hong, Q., Shang, J., Reibarkh, M., Kuethe, J. T., Liu, J., Guiadeen, D., Krikorian, A. D., Cernak, T. A., Dykstra, K. D., Sperbeck, D. M., Wu, Z., Yu, Y., Yang, G. X., Jian, T., Verras, A., Sonatore, L. M., Wiltsie, J., Chung, C. C., Murphy, B. A., Gorski, J. N., Liu, J., Xiao, J., Wolff, M., Tong, S. X., Madeira, M., Karanam, B. V., Shen, D.-M., Balkovec, J. M., Pinto, S., Nargund, R. P. & DeVita, R. J. (2019). Benzimidazole-Based DGAT1 Inhibitors with a [3.1.0] Bicyclohexane Carboxylic Acid Moiety, Bioorganic and Medicinal Chemistry Letters, 29(10), 1182-1186.

5. Organic Synthesis. Contributions to the synthesis of complex organic molecules of biological significance. The research helped to advance the field of synthetic organic chemistry by introducing new synthetic methodologies and strategies for synthesis.

   a. Trost, B. M.; Balkovec, J. M. & Mao, M. K. T. (1983). A Biomimetic Approach to Plumericin, Journal of the American Chemical Society, 105(22), 6755-6757.

   b. Balkovec, J. M. & Black, R. M. (1992). Reduction Studies of Antifungal Echinocandin Lipopeptides. One Step Conversion of Echinocandin B to Echinocandin C, Tetrahedron Letters, 33(32), 4529-4532.

   c. Tse, B.; Blazey, C. M.; Tu, B. & Balkovec, J. (1997). Determination of the Absolute Stereochemistry of (-)-Galbonolide A, Journal of Organic Chemistry, 62(10), 3236-3241.

   d. Stork, G.; Niu, D.; Fujimoto, R.; Koft, E. R.; Balkovec, J. M.; Tata, J. & Dake, G. R. (2001). The first stereoselective total synthesis of quinine, Journal of the American Chemical Society, 123(14), 3239-3242.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1U19AI171401-01 Perlin, Rice (PIs) 05/16/22-04/30/25
The Metropolitan AntiViral Drug Accelerator (MAVDA) brings together world-class virologists, academic drug discovery researchers, and multidisciplinary Functional Cores to accelerate the discovery and development of novel antiviral agents to address current and future pandemic threats.
Role: Director, Medicinal Chemistry Core

R01 AI141183 Perlin (PI) 02/21/19-01/31/24
Novel bi-specific immunotherapeutic against high-threat Gram-negative pathogens. The major goal of this program is to identify an immunotherapeutic agent for the treatment of high threat Gram-negative infections.
Role: Consultant

R01AI138986 Perlin (PI) 03/22/18-04/30/23
Novel bi-specific immunoprophylactics against multi-drug resistant Gram-negative bacterial infections. The goal is to identify an immunoprophylactic agent for the prevention and control of resistant Gram-negative bacterial infections.
Role: Consultant

R43 AI162468 Parent (PI) 06/17/21-05/31/22 (with extension)
SBIR Grant focused on development of novel antifungal agents
Role: Investigator