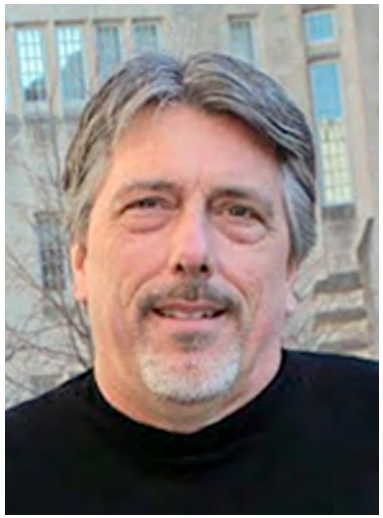

2016-2017 POCC Lecture Series

September 22, 2016, 8:00 PM

Prof. Michael S. VanNieuwenhze

Indiana University Bloomington

Design, Synthesis, and Utilization of Fluorescent Probes for Identifying Novel Approaches to Address Antibiotic Resistance

Carolyn Hoff Lynch Lecture Hall
Chemistry Building, University of Pennsylvania

The Philadelphia Organic Chemist's Club

POCClub.org

To join us for dinner before the lecture please contact POCC's secretary Thomas Razler (thomas.razler@bms.com) at least one week ahead of time.

Michael VanNieuwenhze received his B.A. degree from Kalamazoo College in 1984 and his M.S. from Yale University in 1988. He received his Ph.D. from Indiana University in 1992 where he developed methods for the de novo synthesis of carbohydrates, designed reagents for asymmetric allyl- and crotylmetal addition reactions, and studied fragment assembly aldol reactions for use in the synthesis of complex natural products. Dr. VanNieuwenhze conducted his postdoctoral research at The Scripps Research Institute in La Jolla, California where he studied transition-metal catalyzed asymmetric oxidation reactions while working in the laboratories of Professor K. Barry Sharpless (Nobel Laureate, 2001). In 1994, Professor VanNieuwenhze accepted a position in Discovery Chemistry Research at Eli Lilly and Company in Indianapolis. While at Lilly, Dr. VanNieuwenhze worked on programs in infectious diseases and neurosciences. In 2002, he accepted a faculty position at the University of California, San Diego and in 2007, he returned to the Department of Chemistry at Indiana University. His research is characterized by the use of chemistry to study problems of significant biological interest. Toward this goal, he has made multiple significant contributions that have advanced the understanding of the peptidoglycan biosynthetic pathway. A major component of his current research program is focused on the study and development of novel antibacterial agents and the development and utilization of methods for imaging the spatial and temporal dynamics of peptidoglycan biosynthesis.

Abstract: Bacterial resistance to commonly used antibacterial agents has become a significant public health concern. In order to address this concern, antibiotic agents with novel modes of action or new targets for chemotherapeutic intervention are urgently needed. Our approach toward this problem has involved the study of the peptidoglycan biosynthesis as well as the synthesis and study of chemical agents that inhibit steps within the peptidoglycan biosynthetic pathway. With respect to the former, we have recently developed a class of molecular probes, fluorescent D- amino acids (FDAAs), which have provided a long-sought tool to enable tracking the dynamics of peptidoglycan biosynthesis in live cells and in real time.[1] These probes have found several important applications, including: studying the peptidoglycan division and elongation machinery in *Streptococcus pneumoniae*[2] and in providing a solution to the long-standing riddle posed by the "Chlamydial anomaly",[3] among others.

This presentation will discuss the design and development of fluorescent D-amino acids and their applications for the study of peptidoglycan synthesis dynamics in broad range of bacterial species with diverse modes of growth and provide insight as to how these tools can be used to identify potential new targets for antibiotic intervention.

1. (a) Kuru, E.; Hughes, H. V.; Brown, P. J. B.; Hall, E.; Tekkam, S.; Cava, F.; de Pedro, M. A.; Brun, Y. V.; VanNieuwenhze, M. S., *Angew. Chem. Int. Ed.* **2012**, *51*, 12519-12523. (b) Kuru, E.; Tekkam, S.; Hall, E.; Brun, Y. V.; VanNieuwenhze, M. S., *Nat. Protoc.* **2015**, *10*, 33-52.

2. (a) Fleurie, A.; Manuse, S; Zhao, et al., *PLOS Genetics* **2014,** DOI: 10.1371/journal.pgen.1004275. (b) Tsui, H.-C. T.; Boersma, M.; Vella, S.; Kocaoglu, O.; Kuru, E.; Perceny, J.; Carlson, E. E.; VanNieuwenhze, M. S.; Brun, Y. V.; Shaw, S. L.; Winkler, M. E., *Mol. Microbiol.* **2014**, *94* (1), 21-40. (c) Fleurie, A.; Lesterlin, C.; Zhao, C.; Manuse, S.; Cluzel, C.; Campo, N.; Lavergne, J.-P.; Franz, M.; Macek, B.; Kuru, E.; VanNieuwenhze, M. S.; Brun, Y.; Sherratt, D.; Grangeasse, C., *Nature* **2014***, 516*, 259-262.

3. (a) Pilhofer, M.; Aistleitner, K.; Biboy, J.; Gray, J.; Kuru, E.; Hall, E.; Brun, Y. V.; VanNieuwenhze, M. S.; Vollmer, W.; Horn, M.; Jensen, G., *Nat. Commun.* **2013**, *4*, 2856. (b) Liechti, G.; Kuru, E.; Hall, E.; Kalinda, A.; Brun, Y. V.; VanNieuwenhze, M. S.; Maurelli, A. T., *Nature* **2013***, 506,* 507-510.