Antibiotic Resistance: Is there a (blue) light at the end of the tunnel?

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LECTURE ABSTRACT

Although microbiologists have been ringing the alarm bell for years, the threat of antibiotic resistance has reached new prominence in the popular press that the issue should be added to the list of global emergencies. It is now indisputable that antibiotic resistance is life-threatening in the same sense as cancer, both in the number of cases and the likely outcome. New therapeutic approaches are urgently needed to combat antibiotic-resistant pathogens. In response, the United States Government has recently accelerated efforts to advance innovative research on antibiotic resistance, with special attention to treatment of multidrug-resistant Gram-negative bacteria, which are of particular concern because of their diverse and rapidly evolving mechanisms of resistance (***White House. National Action Plan for Combating Antibiotic-Resistant Bacteria. 2015***).

Antimicrobial blue light (aBL) in the spectrum of 400-470 nm, as an innovative non-antibiotic approach, has demonstrated its intrinsic antimicrobial activity resulting from the presence of endogenous photosensitizing chromophores in pathogenic microbes and subsequently, its promise as a counteractor of antibiotic resistance. In this tutorial, I will present an overview of our laboratory's recent efforts in exploring the utility of aBL for the management of antibiotic-resistant infections. Topics will include the susceptibilities to aBL inactivation of Gram-negative bacteria and other pathogenic microbes, mechanism of action of aBL, synergism of aBL with other non-antibiotic agents (e.g., plant-based antimicrobial, antibiotics) for enhanced antimicrobial activity, potential side effects of aBL on the host cells and tissues, potential development of aBL-resistance by microbial cells, novel techniques for interstitial aBL delivery in human tissues, preclinical studies of aBL therapy for localized infections (e.g., skin wound infections, implant-related infections in orthopeadics, keratitis, urinary tract infections) in murine models, and future study directions in the area of aBL therapy.

This presentation will overview the major challenges in evaluating biological cell products, illustrate the current variability of microscopy image-based measurements and their impact on scientific reproducibility, and introduce a measurement system called web image processing pipeline (WIPP) to address some of the challenges. WIPP is a client-server framework using Deep Zoom for viewing very large images. It consists of algorithms to extract object measurements from 2D microscopy images needed for inspecting the quality of cell products. In addition to WIPP software, several experimental cell and other image sets are accessible from http://isg.nist.gov/deepzoomweb to encourage the reuse of acquired data and a new development of algorithms applicable to big scientific data. The presentation will also include mechanisms for collaborating with NIST and engaging with the larger microscopy community.

SPEAKER BIOSKETCH

Tianhong Dai, PhD, is an assistant professor of Harvard Medical School working in Wellman Center of Photomedicine. His research interest is focused on light-based antimicrobial therapy for infections. In particular, Dr. Dai's laboratory has been interested for some time in using antimicrobial blue light (aBL) to treat localized infections. Dr. Dai and his team successfully carried out a preliminary study of aBL therapy for lethal *Pseudomonas aeruginosa* infections in third degree burns of mice and published a ground-breaking paper in *Antimicrobial Agents and Chemotherapy* (2013; 57:1238-45). The paper was selected to be featured in *Current Topics Section of Microbe*, April, 2013. Dr. Dai and his team then published further papers of aBL therapy for multidrug-resistant *Acinetobacter baumannii* infections, gonococcal infections, *Candida albicans* infections, and biofilm-associated infections in mouse burns in *Journal of Infectious Diseases* (2014; 209: 1963-71, 2016; 213:1380-7 and 2019; 219: in press) and *Virulence* (2016; 7:536-45).

Dr. Dai is the author or co-authors of over 90 peer-reviewed publications, and has been the Principle Investigator of NIH (R01, R21 and R13), DoD, CIMIT as well as grants from other funding sources. He is the founding Chair of the conference "*Photonic Diagnosis, Monitoring, Prevention, and Treatment of Infections and Inflammatory Diseases*" at the SPIE Photonics West, BiOS.

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