BIOGRAPHICAL SKETCH

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NAME: Julian G. Hurdle

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

POSITION TITLE: Professor & Director of CIID in Texas A&M Institute of Biosciences and Technology

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of the West Indies, Barbados	BSc_{Hons} First Class	07/2000	Chemistry & Biology
University of Leeds, U.K.	PhD	03/2005	Molecular Microbiology
University of Leeds, U.K.	Res. Associate	11/2006	Microbiology/Biochem
Univ. of Tennessee Health Science Cntr, TN	Postdoc	07/2009	Molecular Microbiology
St Jude Children's Res. Hospital, TN	Res. Specialist	07/2010	Molecular Microbiology
University of Texas at Arlington, TX	Assis. Professor	12/2014	Clostridial Research
Texas A&M Institute of Biosciences & Technology	Professor	1/2025 to Present	Clostridial Research

A. Personal Statement

I am the Director of the Center for Infectious & Inflammatory Diseases (CIID) at the Institute of Biosciences and Technology (IBT), where I lead an interdisciplinary and translational infectious disease research group. My laboratory focuses on three primary areas: the clinical impact and mechanisms of antibiotic resistance, host-pathogen interactions, and the discovery and evaluation of anti-infectives, particularly narrow-spectrum agents that preserve healthy gut microbes. With over 25 years of experience, I am recognized as an expert in antimicrobial resistance and bacterial pathogenesis. I have led numerous multi-disciplinary collaborations resulting in high-impact findings that influence current treatment approaches and future therapeutic strategies. I have also served as a consultant for antibacterial development in both pre-clinical and clinical stages, and as a past member of the NIH study section on Drug Discovery and Mechanisms of Antimicrobial Resistance.

B. Positions and Honors

See Table above for a summary of relevant employment history.

Other Relevant Experiences and Professional Memberships

2013 -2017 Member, NIH Drug Discovery and Mechanisms of Antimicrobial Resistance Study Section. Editorial board membership: *ACS Infectious Diseases*; *Antimicrobial Agents & Chemotherapy*; *Frontiers in Cellular and Infection Microbiology*; *Journal of Bacteriology*.

C. Contributions to Science

Overall Summary of Contributions to Science

Antibiotic resistance and pathogenesis. (***a1***) ***Antibiotic resistance.*** We described a novel epistatic mechanism of metronidazole resistance, between iron transport and oxidoreductases (*Antimicrobial Agents and Chemotherapy, PMID: 32457109*), solved how to reproducibility detect metronidazole resistance in clinical isolates (*J. Clin. Microbiol. PMID: 34132582*); and solved a long-standing enigma of how epidemic *C. difficile* evolved metronidazole resistance and spread worldwide. We discovered and characterized the mechanism in

global clinical isolates, showing *C. difficile* evolved a cryptic mutation in nitroimidazole reductase alongside fluoroquinolone resistance (*Nat. Comm. PMID: 37438331*) to spread around the world causing treatment failures (*Open Forum Infect. Dis. PMID: 34381844*). We pioneered understanding of *C. difficile* evolution of resistance to vancomycin via another cryptic mechanism (*J. Antimicrob. Chemotherapy, PMID: 31873741*) and clinical outcomes of vancomycin resistance (*Clinical Infect. Dis., PMID: 38382090*). (***a2***) ***Pathogenesis.*** We discovered that acquisition of ferrous iron via FeoB1 transporter is critical for *C. difficile* infectivity and toxin production in mice, which is supported by ongoing studies on the discovery of inhibitors that disrupt iron metabolism to specifically disarm *C. difficile* in the gut (*unpublished work*); in collaboration with Dong at Harvard University, we described host cell receptors that *C. difficile* toxin B uses to damage gut epithelia and submucosa to cause neurogenic inflammation (*Nature PMID: 27680706, 37699522*).

Drug discovery and bacterial physiology. (***b1***) ***Chemical and molecular genetics.*** Throughout Hurdle's career, he has applied chemical genetic concepts to understand bacterial physiology, while also discovering chemical starting points for next generation therapeutics; reflecting his status as an inter-disciplinary scientist. This is evident across several papers and bacterial pathogens (*C. difficile*, MRSA, *M. tuberculosis*). For example, ***b1.1.*** a small molecule pharmacophore known as tetramic acid was applied to metronidazole to retain this drug in the GI tract, which partly addressed a long-standing debate on the role of pharmacokinetics to metronidazole treatment failure (*J. Antimicrob. Chemotherapy, PMID: 26286574*). ***b1.2.*** We are actively pursuing the fatty biosynthesis enzyme FabK to discover narrow-spectrum anti-*C. difficile* antibiotics and periodontal treatments, taking advantage of structure-based drug discovery in collaboration with Dr. Kirk Hevener at Univ. Tenn. Health Science Center (*ACS Infectious Dis.* & *Antimicrobial Agents and Chemotherapy, PMID: 30501172, 38265216, 38597503*). The molecules are also being used to understand how targeted therapeutics reshape gut metabolome for colonization resistance to *C. difficile*. We developed the first high-throughput screening platform for non-antibiotics that inhibit *C. difficile* toxin production without inhibiting growth, and spare the gut microbiome, with resulting hits the subject of cellular mechanistic studies and current invention disclosures. We also apply some molecules as genetic probes to discover new drug targets (*J. Biological Chemistry, PMID: 39343002*). ***b1.3.*** In a well-cited review article in *Nature Reviews Microbiology* (*PMID: 21164535*), I laid out why the bacterial membrane is a valid target site for novel antibacterials. This was inspired by my work on eradication of MRSA biofilms by the membrane-active antibiotic reutericyclin (*Antimicrobial Agents and Chemotherapy PMID: 19581456*).

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/julian.hurdle.1/bibliography/public/

D. Ongoing Research Support (Main Current Funding)

R01AI139261 (Role: PI) Hurdle 08/2018 - 01/2028
NIH/NIAID: Decoding the Clinical Impact of the Recent Evolution of Metronidazole Resistance on *Clostridium difficile* Infection

1R01AI182231-01A1 (Role: co-I) Hevener (PI) 09/2024 - 08/2029
NIH/NIAID: (University of Tennessee Health Science Center): Development of Microbiome-Sparing Antibacterials for *Clostridioides difficile* Infection

R21DE032798-01A1 (Role: PI) 10/2023 - 09/2025
NIH/NIDCR: Evaluation of a microbiota-sparing therapeutic concept for periodontal disease, involving removal of pathogenic Porphyromonas and Fusobacterium