BIOGRAPHICAL SKETCH

NAME: Dantas, Gautam

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

POSITION TITLE: Conan Professor of Laboratory and Genomic Medicine, Departments of Pathology and Immunology, Biomedical Engineering, Molecular Microbiology, and Pediatrics

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YY	FIELD OF STUDY
Macalester College, St Paul, MN	B.A.	05/00	Biology and Chemistry
University of Washington, Seattle, WA	Ph.D.	08/05	Biochemistry
Harvard Medical School, Boston, MA	Postdoctoral	07/09	Genetics

A. Personal Statement

My research interests and training lie at the interface of microbial genomics, biochemistry, systems biology, and computational biology. I received my PhD in biochemistry from the University of Washington under the mentorship of David Baker, and post-doctoral training in microbial genomics from Harvard Medical School under the mentorship of George Church. Research in my laboratory is focused on (1) understanding and predicting how diverse microbiomes respond to chemical and biological perturbations, (2) harnessing these insights to rationally design strategies to curtail antibiotic resistant pathogens and remedy pathological host-microbiome states, and (3) engineering microbial platforms for novel industrial and therapeutic applications. I have co-authored over 140 research manuscripts, including 8 papers in *Science*, *Nature*, and *Cell*, and hold 5 patents in microbial biotechnology and therapeutics. I lead an interdisciplinary research and training group of basic scientists, engineers, and clinicians, spanning formal expertise in microbiology, biochemistry, genomics, pathology, infectious diseases, pediatrics, gastroenterology, ecology and evolution, systems biology, biomedical engineering, chemical engineering, cancer biology, and computational biology. I am a member of the Edison Family Center for Genome Sciences & Systems Biology and an Associate Member of the Siteman Cancer Center. In addition to my research efforts, I am deeply committed to education, mentoring, and training. I am the co-Chief of Research for the Division of Laboratory and Genomic Medicine. I am also the co-Director of the Computational & Systems Biology (CSB) graduate program, have served on the steering committee for both the CSB and Molecular Microbiology & Microbial Pathogenesis graduate programs, regularly teach in 3 graduate-level courses, and have served on over 100 qualifying exam and thesis committees. In November 2019, I participated in the “Maximizing Research Mentoring Relationships Workshop” led by an NRMN-trained facilitator, and I will continue to regularly participate in formal mentor training. Over the past 13 years, I have mentored 18 postdoctoral fellows (12 PhD, 5 MD/PhD, 1 MD), 34 graduate students (including 3 MSTP), 2 medical students, 10 research technicians, and over 100 undergraduate interns. I have graduated 18 PhD, 1 MD/PhD, and 1 MSc students; three are independent faculty, six are in post-doctoral training, one is a K-12 teacher, and ten work in biotech. Six of my postdoctoral mentees have earned faculty positions, and four work in the biotech industry. I am committed to providing a nurturing, well-supported, and actively mentored environment for my team to collaboratively tackle basic science and translational research problems.

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

1. R01AI155893 (PI: Dantas) 06/08/21 – 05/31/26 Role: PI
NIH (NIAID). *Impact of early-life perturbations on pediatric microbiome maturation*
2. P01AG026276 (PI: Morris) 06/01/21 – 05/31/26 Role: Co-Investigator
NIH (NIA). *Antecedent Biomarkers for AD: The Adult Children Study (ACS)*
3. U01-AI123394 (PI/MPI: Dantas, Wencewicz) 02/11/16 – 01/31/26 Role: PI/MPI
NIH (NIAID). *Structural, mechanistic, and evolutionary characterization of tetracycline destructases.*
4. R01-HS027621 (PI/MPI: Kwon, Burnham, Dantas) 09/01/20 – 06/30/25 Role: PI/MPI
AHRQ. *Environmental hygiene strategies to decrease the burden of antibiotic-resistant organisms in ICU sinks.*
5. R01-AT009741 (PI/MPI: Dantas, Moon, Stappenbeck) 08/10/18 – 07/31/23 Role: PI/MPI
NIH (NCCIH). *Tunable therapeutic modulation of the gut microbiome by engineered probiotics*.
6. 75D30121C11970 (Dantas) 07/01/21 – 06/30/23 Role: PI
CDC. *Interrogating the phylogenomics and mobilome of colonizing multidrug resistant organisms (MDROs) in hospitalized patients and community-dwellers in Pakistan*.

7. INV-038625 (PI: Tarr) 11/01/21 – 10/31/22 Role: Co-Investigator
Bill and Melinda Gates Foundation. *Stool transcriptomics technology development.*
8. DESC0018324 (Dantas) 09/15/17 – 09/14/22 NCE Role: PI
DOE. *Systems Engineering of Rhodococcus Opacus to Enable Production of Drop-in Fuels from Lignocellulose.*
9. W81XWH1810225 (PI: Dantas) 09/30/18 – 09/29/22 NCE Role: PI
DOD. *Dynamics of gut microbiota-pathogen interactions and acquisition of antibiotic resistance during travel to high infectious burden regions*.
10. R01-OH011578 (PI/MPI: Dantas, Shukla) 09/01/18 – 08/31/22 Role: PI/MPI
CDC/NIOSH. *Occupational Exposure and Risk from Dairy Microbiome and Resistome to Dairy Farm Workers*.
11. U01-CK000587 (Lanzas, PI) 08/01/20 – 07/31/22 Role: Co-Investigator
CDC (NCEZID). *Multi-scale modeling and phylodynamics for healthcare associated infections.*
12. R01-HD092414 (PI/MPI: Tarr, Dantas) 09/06/17 – 05/31/22 Role: PI/MPI
NIH (NICHD). *Phylogenomic, Transcriptomic, Viromic, and Immunoproteomic Determinants of Necrotizing Enterocolitis.*
13. Microbial Pathogenesis in AD Grant (PI: Dantas) 01/04/21 – 01/04/22 Role: PI
IDSA. *Investigating gut microbiome composition and functions during stages of Alzheimer's disease.*
14. FY2018-OADS-01 (Dantas) 09/30/18 – 09/29/19 Role: PI
CDC. *Impact of early life antibiotic treatment in preterm infants on MDRO colonization and infection.*
15. Pak-US S&T (Dantas) 09/15/15 – 09/14/18 Role: PI
USAID. *Multidrug-Resistant Pathogen Surveillance in Pakistani and U.S. Hospitals.*
16. Gates Grand Challenges (Dantas) 11/01/16 – 04/30/18 Role: PI
Bill and Melinda Gates Foundation. *Quantifying the Impacts of Antibiotic Prophylaxis on Antimicrobial Resistance (AMR) in Vulnerable Pediatric Populations in Africa*.

Citations:

a. Boolchandani M, D'Souza AW, **Dantas G**. Sequencing-based methods and resources to study antimicrobial resistance. **Nature Rev. Genetics**. 2019 Mar 18. doi: 10.1038/s41576-019-0108-4. PMCID: PMC6525649.
b. Ferreiro A, Crook N, Gasparrini AJ, **Dantas G**. Multiscale Evolutionary Dynamics of Host-Associated Microbiomes. **Cell**. 2018 Mar 8;172(6):1216-1227. doi: 10.1016/j.cell.2018.02.015. PMCID: PMC5846202.
c. Crofts TS, Gasparrini AJ, **Dantas G**. Next-generation approaches to understand and combat the antibiotic resistome. **Nature Rev. Microbiology**. 2017 Apr 10. doi: 10.1038/nrmicro.2017.28. PMCID: PMC5681478.
d. Langdon A, Crook N, **Dantas G**. The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation. **Genome Med.** 2016 Apr 13;8(1):39. doi: 10.1186/s13073-016-0294-z. PMID: 27074706; PMCID: PMC4831151.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023-present Conan Professor of Lab and Genomic Medicine, Washington U. School of Medicine (WUSM)
2022-present Co-Chief, Div. of Lab and Genomic Medicine, Dept of Pathology & Immunology, WUSM
2020-present Education Committee, Dept. of Pathology & Immunology, Washington University School of Medicine (WUSM), St. Louis, MO
2020-2022 Chair, Faculty Promotions Committee, Div. of Laboratory and Genomic Medicine, WUSM
2018-present Professor, Dept. of Pathology & Immunology, Dept. of Biomedical Engineering, Dept. of Molecular Microbiology, Dept., of Pediatrics, WUSM
2016-present Co-Director, Computational and Systems Biology PhD Program, WUSM
2016-2021 New Investigator Awards Committee, WUSM
2015-2018 Associate Professor, Dept. of Pathology & Immunology, Dept. of Biomedical Engineering, and Dept. of Molecular Microbiology, WUSM
2013-2016 Faculty Search Committee, CGSSB, WUSM
2012-present PhD Steering Committee, Computational and Systems Biology Prog., WUSM
2012-2016 PhD Steering Committee, Molecular Microbiology Program, WUSM
2012-present Member, American Society for Microbiology
2012-2014 Faculty Search Committee, Dept. of Molecular Microbiology, WUSM
2011-2015 Assistant Professor, Dept. of Biomedical Engineering, WUSM
2011-present Community Advisory Board, Young Scientist Program, WUSM

2011-2016 Monsanto Life Science Graduate Fellowship Committee, WUSM
2011-2012 Faculty Search Committee, Dept. of EECE, WUSM
2011-2012 Faculty Search Committee, Dept. of Biology, WUSM
2011-present Member, American Association for the Advancement of Science
2011-2012 Member, American Society of Transplantation
2010-present Member, Division of Biology and Biomedical Sciences, WUSM
2010-2011 Faculty Search Committee, Dept. of Biological Systems Engineering, WUSM
2010-2016 PhD Admissions Committee, Molecular Microbiology Program, WUSM
2010-2015 Member, American Gastroenterology Association
2010-present Faculty Mentor, Summer Undergraduate Research Fellows, WUSM
2009-2015 Assistant Professor, Dept. of Pathology and Immunology, WUSM
2006-2009 Research Fellow, Dept. of Genetics, Harvard Medical School, Boston, MA.
2007-2008 Teaching Fellow, Life Sciences Research, Harvard University, Cambridge, MA.
2001-2002 Teaching Assistant, Biochemistry, University of Washington, Seattle, WA.
2000-present Phi Lambda Upsilon, The National Honorary Chemistry Society
1998-2000 Teaching Assistant, Organic Chemistry, Macalester College, St. Paul, MN.

Honors

2019 Fellow, American Academy of Microbiology
2018 Washington University Distinguished Educator Award
2016 Young Scientist Program Most Active Principal Investigator
2015 Academy of Science – St Louis Innovator Award
2014-2018 Edward Mallinckrodt Jr. Foundation Scholar Award
2012-2017 NIH Director's New Innovator Award
2012-2014 Kenneth Rainin Foundation Innovator and Breakthrough Awards
2008 Harvard University Certificate of Distinction in Teaching
2004 Newcomb Cleveland Prize (AAAS) for Outstanding Publication in Science
2000 B.A. with Honors in Chemistry and Biology, Macalester College
1998-2000 Violet O. Beltmann Undergraduate Research Scholarship

C. Contributions to Science (* = equal contribution; _ = corresponding author)

1. **Computational design of new and improved proteins**. My graduate training (2000-2005) was focused on the development of a new computational protein design method, RosettaDesign, its application to design new and improved protein structures, and the rigorous experimental characterization and analyses of the designed proteins to evaluate and improve the design process (**J Mol Biol**, 2003; 2007). A highlight of my thesis work was the fully-automated design of a protein sequence and structure never before found in Nature, where I demonstrated that the experimental protein adopted the identical atomic-level structure of the designed computational model (**Science**, 2003). This was a basic-science triumph, validating our understanding of fundamental concepts governing protein molecular architecture, as well as an engineering feat, demonstrating that future design of protein therapeutics need not be limited to sequences and structures observed in nature; this breakthrough was recognized by the 2004 Newcomb Cleveland Prize.

a. **Dantas G***, Kuhlman B*, Callender D, Wong M, Baker D. A large scale test of computational protein design: folding and stability of nine completely redesigned globular proteins. **J Mol Biol.** 2003 Sep 12;332(2):449-60. PMID: 12948494.
b. Kuhlman B*, **Dantas G***, Ireton GC, Varani G, Stoddard BL, Baker D. Design of a novel globular protein fold with atomic-level accuracy. **Science**. 2003 Nov 21;302(5649):1364-8. PMID: 14631033.
c. **Dantas G**, Corrent C, Reichow SL, Havranek JJ, Eletr ZM, Isern NG, Kuhlman B, Varani G, Merritt EA, Baker D. High-resolution structural and thermodynamic analysis of extreme stabilization of human procarboxypeptidase by computational protein design. **J Mol Biol**. 2007 Mar 2;366(4):1209-21. Epub 2006 Dec 2. PMID: 17196978; PMCID: PMC3764424.

2. **Metagenomic analyses of environmental bacterial communities and their antibiotic resistomes.** Following my graduate training in molecular biochemistry, I sought out post-doctoral training (2006-2009) in microbial genomics, with a focus on high-throughput approaches for understanding and modeling the incredible biochemical potential encoded within microbial communities from diverse habitats. This quantitative ecological perspective for studying microbial functions has also framed the major research themes of my independent laboratory (2009-present). We provided the first genetic evidence for the dissemination of multiple antibiotic

resistance elements between cultured, non-pathogenic, multi-drug-resistant, soil Proteobacteria (**Science**, 2008) and common, globally-distributed, clinical pathogens (**Science**, 2012). In contrast, our subsequent culture-independent investigation of 18 soils revealed that while soil microbes harbor an extensive resistome, the majority of these resistance genes have a diminished capacity for horizontal gene transfer, compared with human pathogens (**Nature**, 2014). We have also used multi-omic approaches to define mechanisms of antibiotic catabolism by environmental bacteria, which may allow bioremediation of antibiotic-contaminated environments and discovery of novel antibiotic-remodeling enzymes (**Nature Chem Bio**, 2018). We complement our metagenomic resistome work with high-resolution biochemical, mechanistic, and structural analyses, as exemplified by the tetracycline destructases, a novel family of flavoenzymes we discovered in soils and pathogens, capable of degrading clinically relevant tetracyclines via a previously undescribed mechanism, against which we have now designed novel small molecule inhibitors (**Chem Bio**, 2015; **Nature Chem Bio**, 2017; **ACS ID**, 2019l; **Comm Bio**, 2020).

a. **Dantas G***, Sommer MO*, Oluwasegun RD, Church GM. Bacteria subsisting on antibiotics. **Science**. 2008 Apr 4;320(5872):100-3. doi: 10.1126/science.1155157. PMID: 18388292.
b. Forsberg KJ*, Reyes A*, Wang B, Selleck EM, Sommer MO, **Dantas G****. The shared antibiotic resistome of soil bacteria and human pathogens. **Science**. 2012 Aug 31;337(6098):1107-11. doi: 10.1126/science.1220761. PMCID: PMC4070369.
c. Forsberg KJ*, Patel S*, Gibson MK, Lauber CL, Knight R, Fierer N, **Dantas G****. Bacterial phylogeny structures soil resistomes across habitats. **Nature** 2014; 509: 612. doi: 10.1038/nature13377. PMCID: PMC4079543.
d. Park J*, Gasparrini AJ*, Reck MR, Symister CT, Elliott JL, Vogel JP, Wencewicz TA, **Dantas G****, Tolia NH. Plasticity, dynamics, and inhibition of emerging tetracycline resistance enzymes. **Nature Chemical Biology**. 2017 May 8. doi: 10.1038/nchembio.2376. PMCID: PMC5478473.

3. **Functional interrogation of the microbiomes and resistomes of human commensal and pathogenic bacteria**. Using a combination of shotgun metagenomic sequencing and functional metagenomics, we have shown that the resistomes of uncultured adult (**Science**, 2009; **Science Advances**, 2015) and pediatric human gut microbiota (**Microbiome**, 2015; **Nature Microbiology**, 2016) are largely novel and sequence-divergent compared to resistance genes captured from cultured samples, but contain key members which can exchange resistance genes with human pathogens. By extending these analyses to longitudinal sampling of co-localized human and environmental microbiota in intensive healthcare settings (**Nature Medicine**, 2018; **Nature Microbiology**, 2019) and resource-poor settings in the developing world (**Nature**, 2016; **Clin Infect Dis**, 2019), we have identified hotspots for transmission of resistant bacteria and horizontal gene transfer of resistance genes. In tandem, we have developed predictive, machine learning-based algorithms to quantify the impact of specific antibiotic treatments on taxonomic and functional microbiome architectures (**Nature Microbiology**, 2016 and 2019). We have also used our diverse functional resistome datasets to build Resfams, a profile HMM-based database of antibiotic resistance proteins, which significantly outperforms the accuracy and precision of traditional methods for annotating resistance from sequence (**ISME J**, 2015).

a. Gibson MK, Wang B, Ahmadi S, Burnham CAD, Tarr PI, Warner BB, **Dantas G****. Developmental dynamics of the preterm infant gut microbiota and antibiotic resistome. **Nature Microbiology**. 2016. doi: 10.1038/nmicrobiol.2016.24. PMCID: PMC5031140.
b. Pehrsson EC, Tsukayama P, Patel S, Mejía M, Sosa-Soto G, Navarrete KM, Calderon M, Cabrera L, Hoyos W, Bertoli MT, Berg DE, Gilman RH, **Dantas G****. Interconnected microbiomes and resistomes in low-income human habitats. **Nature**. 2016. doi: 10.1038/nature17672. PMCID: PMC4869995.
c. Baumann-Dudenhoeffer AM, D'Souza AW, Tarr PI, Warner BB, **Dantas G****. Infant diet and maternal gestational weight gain predict early metabolic maturation of gut microbiomes. **Nature Medicine**. 2018 doi: 10.1038/s41591-018-0216-2. PMCID: PMC6294307.
d. Gasparrini AJ, Wang B, Sun X, Kennedy EA, Hernandez-Leyva A, Ndao IM, Tarr PI, Warner BB, **Dantas G****. Persistent metagenomic signatures of early-life hospitalization and antibiotic treatment in the infant gut microbiota and resistome. **Nature Microbiology**. 2019 Dec;4(12):2285-2297. doi: 10.1038/s41564-019-0550-2. PMCID: PMC6879825.

4. **Understanding and predicting pathogen transmission dynamics and response to clinical interventions.** We are applying our powerful experimental and computational resistome interrogation tools to better understand and model resistance dissemination between diverse habitats over time, and for improving the speed and accuracy of diagnosing pathogens and their resistance properties in the clinic (**Clin Chem**, 2019; **mBio**, 2019; **JAC**, 2019; **PNAS**, 2019). In collaboration with several clinicians and physician-scientists, we have

investigated and predicted the efficacy of conventional antimicrobial or newer microbiota-directed therapeutics against urgent threat pathogens, such as *Clostridiodes difficile*, along with elucidating the collateral acute and persistent impacts of these treatments on the human gut microbiome and resistome (**OFID**, 2020; **Microbiome**, 2020; **mSphere**, 2021; **Genome Medicine**, 2021; **eLife**, 2022). Extending these studies to global scales, we have highlighted substantial MDR pathogen burdens in hospital built-environments, providing evidence for spatiotemporal-dependent transmission, and demonstrating potential mechanisms for multispecies surface persistence (**Nature Communications**, 2019; **JAC**, 2019).

a. Potter RF, Lainhart W, Twentyman J, Wallace MA, Wang B, Burnham CA**, Rosen DA**, **Dantas G****. Population Structure, Antibiotic Resistance, and Uropathogenicity of Klebsiella variicola. **mBio**. 2018. doi: 10.1128/mBio.02481-18. PMCID: PMC6299229.
b. D'Souza AW, Potter RF, Wallace M, Shupe A, Patel S, Sun X, Gul D, Kwon JH, Andleeb S, Burnham CD, **Dantas G****. Spatiotemporal dynamics of multidrug resistant bacteria on intensive care unit surfaces. **Nature Commun**. 2019 Oct 8;10(1):4569. doi: 10.1038/s41467-019-12563-1. PMCID: PMC6783542.
c. Langdon A*, Schwartz DJ*, Bulow C, Sun X, Hink T, Reske KA, Jones C, Burnham CD, Dubberke ER*, **Dantas G****. Microbiota restoration reduces antibiotic-resistant bacteria gut colonization in patients with recurrent Clostridioides difficile infection from the open-label PUNCH CD study. **Genome Medicine**. 2021. doi: 10.1186/s13073-021-00843-9. PMID: 33593430.
d. Fishbein SR, Robinson JI, Hink T, Reske KA, Newcomer EP, Burnham CD, Henderson JP, Dubberke ER**, **Dantas G****. Multi-omics investigation of Clostridioides difficile-colonized patients reveals pathogen and commensal correlates of C. difficile pathogenesis. **ELife**. 2022. doi: 10.7554/eLife.72801. PMID: 35083969.

5. **Systems-level engineering of novel microbial activities with chemotherapeutic and biotechnological activities.** As a complement to our ecological and translational work on understanding microbial community functions, we use synthetic biology to (i) improve bacteria-mediated biofuel production, and (ii) develop engineered microbes for diagnosis and treatment of gastrointestinal disorders. We are engineering bacteria to convert low-value plant biomass (i.e. lignocellulose) to value-added commodities (**AEM**, 2015; **NAR**, 2016; **Metab. Eng.**, 2018). In a complementary vein, engineered commensal microbes are exciting platforms for in situ drug synthesis and delivery, as well as diagnostics. Our work with engineered therapeutic microbes has two aims. First, we are engineering commensal yeast and bacterial strains that can detect and respond to infectious and metabolic disease with tunable therapeutic payloads, using in vitro assays, and gnotobiotic and conventional mouse models (**Cell Host Microbe**, 2019; **ACS Synth Biol**, 2020 & 2021). In parallel, we aim to understand the selective pressures that drive adaptation of these commensal microbes in the host, so as to better predict their behavior and safety profiles in the contexts of health and disease (**JMB**, 2014; **Cell**, 2018; **Nature Comm**, 2022).

a. Crook N*, Ferreiro A*, Gasparrini AJ, Pesesky MW, Gibson MK, Wang B, Sun X, Condiotte Z, Dobrowolski S, Peterson D, **Dantas G****. Adaptive Strategies of the Candidate Probiotic E. coli Nissle in the Mammalian Gut. **Cell Host Microbe**. 2019 Apr 10. doi: 10.1016/j.chom.2019.02.005. PMCID: PMC6487504.
b. Crook N*, Ferreiro A*, Condiotte Z, **Dantas G****. Transcript Barcoding Illuminates the Expression Level of Synthetic Constructs in *E. coli* Nissle Residing in the Mammalian Gut. **ACS Synth Biol**. 2020 May 15;9(5):1010-1021. doi: 10.1021/acssynbio.0c00040. PMCID: PMC7293544.
c. Kwak S, Mahmud B, **Dantas G****. A Tunable and Expandable Transactivation System in Probiotic Yeast Saccharomyces boulardii. **ACS Synth Biol**. 2021. doi: 10.1021/acssynbio.1c00384. PMID: 34939781.
d. Rottinghaus AG*, Ferreiro A*, Fishbein SRS, **Dantas G****, Moon TS**. Genetically stable CRISPR-based kill switches for engineered microbes. **Nature Communications**. 2022. doi: 10.1038/s41467-022-28163-5. PMID: 35115506.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/gautam.dantas.1/bibliography/public/