The Faculty of Medicine of Harvard University

CURRICULUM VITAE

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Place of Birth: Bsharri, Lebanon

Education

1985	B.Sc.	Biological Sciences	University of Naples, Italy
1985	M.Sc.	Molecular Genetics	University of Naples and Institute of Genetics and Biophysics C.N.R., Italy
1987-1991	Ph.D.	Microbiology, Molecular Plant-Pathogen Interactions (Ph.D. Advisor: Nicholas Panopoulos)	University of California at Berkeley, USA

Postdoctoral Training

01/91-12/91	Post-Doctoral Fellow	Molecular Host Microbial Pathogenesis (Postdoctoral Advisor: Nicholas Panopoulos)	University of California at Berkeley
01/92-06/97	Post-Doctoral Fellow	Molecular Host-Pathogen Interactions (Postdoctoral Advisor: Frederick M. Ausubel)	Department of Molecular Biology, Massachusetts General Hospital, and Department of Genetics, Harvard Medical School

Faculty Academic Appointments

07/97-06/00	Instructor	Surgery, Microbiology, and Molecular Genetics	Harvard Medical School
07/00-12/07	Assistant Professor	Surgery, Microbiology, and Molecular Genetics	Harvard Medical School
01/08-12/17	Associate Professor	Surgery, Microbiology, and Immunobiology	Harvard Medical School
01/2018-	Professor	Surgery, Microbiology	Harvard Medical School

Appointments at Hospitals/Affiliated Institutions

Past

07/97-05/13	Assistant Microbiologist	Surgery	Massachusetts General Hospital
07/97-05/13	Assistant Molecular Biologist	Molecular Biology	Massachusetts General Hospital
01/98-05/13	Assistant Microbiologist	Division of Infectious Disease	Massachusetts General Hospital
01/09-12/16	Investigator	Chemical Biology	Massachusetts General Hospital
05/13-05/17	Associate Molecular Biologist	Molecular Biology	Massachusetts General Hospital

Current

07/1997-	Senior Scientific Staff	Research	Shriners Burns Hospital
04/2006-	Associate Faculty	Microbial Science Initiative	Harvard University
01/2008-	Investigator	The Center for the Study of Inflammatory Bowel Disease	Massachusetts General Hospital
06/2017-	Microbiologist	Surgery	Massachusetts General Hospital

Other Professional Positions

1985-1986	Research Associate	Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology-Hellas
1986-1987	Junior Specialist	Department of Plant Pathology, University of California at Berkeley
2002	Founding Fellow	Arab Academy of Sciences
2013	Scientific Founder	Spero Therapeutics
2013-18	Scientific Advisory Board	Spero Therapeutics, Effort 5 days per year
2021-	Scientific Advisory Board Member	Asclepius One Health An international independent Non-Profit Organization with global action & activity
2024-	Scientific Advisory Board Member	Center for Drug Discovery, Bouve College, Northeastern University

Major Administrative Leadership Positions

1997-	Director of Molecular Surgical Laboratory	Department of Surgery, Massachusetts General Hospital,
2018-2020	Co-Chair of Research Faculty Development	Department of Surgery, Massachusetts General Hospital
2018-2023	Senior Mentor	Department of Surgery, Massachusetts General Hospital
2022-2023	Vice Chair of the Dean's Faculty Leadership Council	Joint Committee on the Status of Women, Harvard Medical School
2023-2024	Co-Chair of the Dean's Faculty Leadership Council	Joint Committee on the Status of Women, Harvard Medical School
2024-2025	Active past Co-Chair of the Dean's Faculty Leadership Council	Joint Committee on the Status of Women, Harvard Medical School
2025	Chair of the Faculty Dean's Awards	Harvard Medical School
2026	Chair of Basic Science, Surgical Research Council	Department of Surgery, Massachusetts General Brigham (MGB)

Committee Service

2006-2009	Research Operations Committee Dept. Surgery, Massachusetts General Hospital	Member
2006-	Surgical Research Council Dept. Surgery, Massachusetts General Hospital	Member
2015	American Society for Microbiology	Member, Scientific Program Committee, Conference on Pseudomonas 2015
2015	Abstract Selection Committee, American Society for Microbiology, Annual Meeting	
2018-2020	Surgical Research Council, Dept. Surgery, Massachusetts General Hospital	Co-Chair of Research Faculty and Postdoctoral Fellow Career Development Committee

2018-	Joint Committee on the Status of Women, Harvard Medical School	Member
2018-2019	Joint Committee on the Status of Women, Harvard Medical School	Subcommittee Member, Work/Life Balance
2019-2020	Joint Committee on the Status of Women, Harvard Medical School	Subcommittee Member, Best practices related to the Massachusetts Equal Pay Act (MEPA)
2019-2022	Standing Committee on Promotions, Reappointments, and Appointments, Harvard Medical School	Member
2019-	Dean's Award Committee, Harvard Medical School	Member, Reviewer
2021-	Senior Peer-Mentoring Women Group Faculty	Massachusetts General Hospital Center for Faculty Development
2022-2023	Subcommittee of Professors on Promotions, Reappointments, and Appointments, Harvard Medical School	Member, Standing Committee of the Dean
2022-2023	Ad-hoc Chair, Subcommittee of Professors on Promotions, Reappointments, and Appointments	Standing Committee of the Dean, Harvard Medical School
2024-2025	Strategic Planning Committee, Joint Committee on the Status of Women, Harvard Medical School	Member

Professional Societies

1989-2000	The American Phytopathological Society	Member
1990-2000	International Society for Plant Molecular Biology	Member
1996-	American Society for Microbiology	Member
1997-	American Society for the Advancement of Science	Member
2000-2008	British Society for Plant Pathology	Member
2000-2012	Genetics Society of America	Member
2011-	American Chemical Society	Member

2016-	Hellenic Bioscientific Association of The USA www.hbusa.org	Member and Mentor
2015	Session Chair, American Society for Microbiology Annual Meeting	
2017-	Elected American Academy of Microbiology Fellow	

Grant Review Activities

2003-2009	National Science Foundation 2006, 2007, 2009	Ad Hoc Member Ad Hoc Member
2003	UNESCO	Ad Hoc Member
2007, 2009	National Institute of Health BASP (Bacterial Pathogenesis)	Ad Hoc Member
2014	National Institute of Health F-13 Fellowship Panel-Infectious Diseases and Microbiology	Ad Hoc Member
2015	U.S. Army Medical Research and Material Command Defense Medical Research & Development Program	Ad Hoc Member
2018	U.S. Army Medical Research and Material Command Programmatic Panel Congressionally Directed Medical Research Programs (CDMRP)	Ad Hoc Member
2018	National Institutes of Health, Catalyst Award in Diabetes, Endocrinology, and Metabolic Disease National Institute of Diabetes and Digestive and Kidney Diseases	Ad Hoc Member
2018	National Institutes of Health, Infectious Diseases, and Microbiology ZRG1-IDM- Y (82), SRG Exploration of Antimicrobial Therapeutics and Resistance	Ad Hoc Member
2018	National Institutes of Health Center For Scientific Review Special Emphasis Panel ZRG1 F13-Z (20) Infectious Diseases and Microbiology 11/05-11/06	Ad Hoc Member
2022	National Institutes of Health Center For Scientific Review Special Emphasis Panel ZRG1 IDIA-N (80) Infectious Diseases and Immunology	Ad Hoc Member

	03/17-03/18	
2025	National Institutes of Health Center For Scientific Review Special Bacteriology Fellowship applications- ZRG1 F07A (W)20 Infectious Diseases and Immunology 03/13-03/14	Ad Hoc Member
2026	National Institutes of Health Center For Scientific Review Special Panel Topics in Drug Development, Resistance, and Therapeutics 2026 Council ZRG1 DCAI-U 80 S, 02/23-02/24	Ad Hoc Member
2026	The Gillian Reny Stepping Strong Center for Trauma for Innovation	Member
2026	Armenise Foundation Armenise Harvard-INFACT Mid-Career Award in Emerging Infectious Diseases	Chair

Ad-hoc Reviewer (Foundations):

2004-2013	Swiss Science Foundation, Switzerland (2004, 2010, 2012, 2013)	Ad Hoc Reviewer
2004-2012	Welcome Trust 2004, 2005, 2012	Ad Hoc Reviewer
2006	Thraser Foundation, USA 2006	Ad Hoc Reviewer
2012	FWO Vlaanderen Research Foundation, Belgium 2012	Ad Hoc Reviewer Ad Hoc Reviewer
2012-2013	Canterbury Medical Research Foundation 2012 2013	Ad Hoc Reviewer Ad Hoc Reviewer
2014	Israel Science Foundation, Israel 2014	Ad Hoc Reviewer
2015	The Biotechnology and Biological Sciences Research Council, UK	Ad Hoc Reviewer
2016	Cure Kids Shares in Life Foundation Auckland, New Zealand	Ad Hoc Reviewer

2017	Israeli Ministry of Science and Technology	Ad Hoc Reviewer

Editorial Activities

Ad hoc Reviewer:

1. *ACS Chemical Biology*
2. *Annals of Surgery*
3. *Applied and Environmental Microbiology*
4. *BioMed Central-Microbiology*
5. *Blood*
6. *Cell*
7. *Cell Host & Microbe*
8. *Current Biology*
9. *Developmental Cell*
10. *ELife*
11. *EMBO Reports*
12. *Frontiers*
13. *Immunity*
14. *Infection and Immunity*
15. *Journal of Bacteriology*
16. *mBio*
17. *Molecular Microbiology*
18. *Microbiology*
19. *Nature*
20. *Nature Biotechnology*
21. *Nature Immunology*
22. *Nature Methods*
23. *Nature Microbiology*
24. *Nature Chemical Biology*
25. *Nature Communications*
26. *PNAS*
27. *PLoS Biology*
28. *PLoS One*
29. *PLoS Pathogens*
30. *Science*
31. *Stem Cell Reports*
32. *Science Advances*

Other Editorial Roles

Editorial Board:

1999-2002	Editorial Board	Molecular Plant Pathology
2001-2004	Faculty Member	Cellular Biology and Pathogenesis
2010-2015	Editorial Board	Journal of Pathogens
2010-	Review Editor & Editorial Board	Frontiers in Cellular and Infection Microbiology
2010-	Editorial Board	Pathogens
2011-	Review Editorial Board	Frontiers in Antimicrobials, Resistance, and Chemotherapy
2012-2013	Editorial Board	*PLoS* Biology
2013-2014	Advisory Editorial Board	*PLoS Biology*

2014-	Editorial Board	Athens Journal of Health
2014-	Editorial Board	Athens Journal of Sciences
2015-2017	Editorial Board	Enliven: Microbes and Microbial Techniques
2022-	Editor	mBio Antimicrobial Agents and Resistance

Associate Editor:

2008	Associate Academic Editor	*PLoS* Biology
2008	Associate Academic Editor	*PLoS* Pathogens
2014	Associate Academic Editor	British Microbiology Research Journal
2014-	Associate Editor for Infectious Diseases	Frontiers in Microbiology
2015-	Associate Editor for Infectious Diseases	Frontiers in Medicine
2016-	Associate Editor for Infectious Diseases	Frontiers in Public Health

Review Editor:

2015	Review Editor	Antimicrobial Resistance and Chemotherapy
2016-	Review Editor	Frontiers in Cellular and Infection Microbiology

Special Issue Editor:

2010-	Special Issue Editor	"Biosurfactants", International Journal of Molecular Sciences
2013	Special Issue Guest Editor	Pathogen Infection Models-A special issue of Pathogens
2015-	Guest Editor	Systems Microbiology: Frontiers in Microbiology
2015-	Guest Editor	Systems Microbiology: Frontiers in Bioengineering and Biotechnology
2017	Topic Editor-Special Research Topic	Frontiers in Microbiology; Microbial talk: Chemical signaling and signal destruction
2018-2019	Topic Editor-Special Research Topic	Frontiers in Microbiology: Beyond Antimicrobials: Non-Traditional Approaches to Combating Multidrug-Resistant Bacteria
2023-2025	Topic Editor-Special Research Topic	Frontiers in Immunology: Modulation of Pulmonary Immunity and Function by Bacterial and Host Metabolites
2025-	Topic Editor-Special Issue	Pathogens: New Insights into Virulence Strategies of Pathogenic Bacteria

Honors and Prizes

1985	Honors for Master's of Science Dissertation	University of Naples Master's of Science Dissertation
1987-1991	Carol William Smith Memorial, Graduate Student Scholarship	UC Berkeley
1992	Fogarty International - (declined)	NIH, Fogarty Post-Doctoral Fellowship (Declined)
1998-1999	Shriners Burns Hospital Scholar	SBH
2004-2005	Claflin Distinguished Scholar Award	Massachusetts General Hospital
2004	Department of Surgery Faculty Research Award	Massachusetts General Hospital
2014, 2016-2020, 2022	Excellence in Mentoring Award Nominations	Massachusetts General Hospital
2013,2014, 2017-2021	Excellence in Mentoring Award Nominations	Harvard Medical School
2015	Poster of Distinction Award Executive Committee on Research	Massachusetts General Hospital
2017	Elected Fellow	American Academy of Microbiology
2018	Faculty Mentoring Award Mentor with Distinction Recognition, John T. Potts Jr., MD	Massachusetts General Hospital
2018	Artium Magistrum, Master of Arts, Harvard University, Cambridge, USA	
2019	Poster of Distinction Award American Burn Association Annual Meeting	
2020	John Lawrence Massachusetts General Hospital Research Scholar	

Report of Funded and Unfunded Projects

Funding Information

Past

1998-2002 Multi-Host Pathogenesis Project
Aventis Research and Technologies GMBH, 201247
Principal Investigator, Total Direct Costs: $1,120,028.00
This project's major goal is to exploit inventions and technology relating to pathogenicity factors, genes involved in pathogenicity, and targets for drug and other product screening.

1998-2000 Use of a plant model to identify *Pseudomonas aeruginosa* virulence factors important in burn wound infections.
Shriners Burns Institute, 8670
Co-Investigator, Total Direct Costs: $ 121,952.00
This project aims to identify novel *P. aeruginosa* virulence factors by screening a *P. aeruginosa* mutant library in plants.

1998-2001	Role of Pyocyanin and Biofilm in Infection of Burn Wounds by *Pseudomonas aeruginosa* Shriners Burns Institute, 8800 Principal Investigator, Total Direct Costs: $ 567,989.00 This project focuses on characterizing the virulence factors identified from the screen of a *P. aeruginosa* mutant library in plants.
1999-2001	Study of Virulence Genes in *Pseudomonas aeruginosa* Cystic Fibrosis Foundation, #99G0 Principal Investigator, Total Direct Costs: $120,000.00 Assessment of *P. aeruginosa* virulence genes whose products could be used as new targets for the development of anti-virulence therapeutics against lung infections
2001-2006	Physiologic Regulation of Hematopoiesis by Notch National Institutes of Health, R01 5 RO1 HL068256-04 Co-Investigator, Total Direct Costs: $1,125,000.00 Physiologic Regulation of Hematopoiesis by Notch PI: Nadia Carlesso This proposal's overall objective is to define the physiologic role of Notch signaling in bone marrow homeostasis following *P. aeruginosa* infection using specific *P. aeruginosa* mutants.
2001-2012	Inflammation and the Host Response to Injury National Institutes of Health, 5 U54 GM62119-05, Investigator, Total Direct Costs: $33,845,040 Large Collaborative Project Award on Inflammation and the Host Response to Injury PI: Ronald Tompkins The overall scientific goal is to promote analysis of the design principles and dynamic behaviors that regulate this complex biological system, expecting that this understanding will ultimately impact patients' treatment.
2002-2005	Pyocyanin and Biofilm Genes of *Pseudomonas aeruginosa* Cystic Fibrosis Foundation, 210182 Principal Investigator, Total Direct Costs: $120, 000 This application aimed to elucidate the role that novel pyocyanin and biofilm-related genes, identified in our studies, play in lung infections caused by *P. aeruginosa.*
2002-2007	Study of *Pseudomonas aeruginosa* virulence factors in a burn mouse model, Microbia Inc. Principal Investigator, Total Direct Costs: $10,000 Virulence assessment of *P. aeruginosa* mutants using a burn and infection mouse model.
2002-2004	Cellular and Molecular Analysis of Inflammatory Responses Following Burn and Infection Shriners Burns Institute, 8509 Principal Investigator, Total Direct Costs: $517,131.00

This research aims to determine how certain *P. aeruginosa* virulence factors burden the immune system during inflammatory response following burn trauma. These factors are hoped to be targets for a new generation of anti-virulence therapies.

2003-2005 Identification of Anti-infective Compounds that Prevent Bacterial Infections in Patients with Burns
Shriners Burns Institute, 8800
Principal Investigator, Total Direct Costs: $ 532.840
The major goal of this proposal is to elucidate the regulatory network of the novel *P. aeruginosa* virulence-related quorum-sensing transcriptional regulator MvfR that controls the synthesis of antibacterial molecules to identify a new generation of antibiotic therapies

2003-2007 Photodynamic Therapy of Localized Infections
National Institute of Health, R01 5 R01 A1050875-03
Investigator, Total Direct Costs: $800,000.00
PI: John Hamlin- Wellman Laboratories, Photomedicine
The overall goal of this project is to explore a novel photochemical method for killing antibiotic-resistant pathogenic bacteria in localized models of infection

2004-2006 Study of The Virulence-Associated *Pseudomonas aeruginosa* Transcriptional Regulator MvfR Claflin Award
Principal Investigator, Total Direct Costs: $ 60,000

2004-2009 Burn Trauma Center-, 5 P50 GM021700-28
National Institute of Health
Investigator, Total Direct Costs: $ 6,509,675.00
The host response to burns and trauma is a collection of biological and pathological processes that critically depend on human metabolic response regulation. Over the past 28 years of P50 funding, our Center has had a tremendous and unique research opportunity to study metabolism physiology after injury. Since its inception, the Center has focused on the metabolic aspects of the patient's immuno-inflammatory reaction to injury.

2004 Identification of Anti-infective Compounds Produced by *Pseudomonas aeruginosa*
Faculty Surgery Award
Principal Investigator, Total Direct Costs: $25,000.00
New ways to control bacterial infections and prevent antimicrobial resistance are by identifying intrinsic anti-infective compound(s) produced by *Pseudomonas aeruginosa* that interfere with the pathogenic potential of this bacterium.

2005-2007 Determine and prevent the mechanism of activation of the *Pseudomonas aeruginosa* virulence transcription factor MvfR relevant in burn wound infections
Shriners Burns Institute, 8850
Principal Investigator, Total Direct Costs: $612,708.00

Determine and prevent the activation mechanism of the *Pseudomonas aeruginosa* virulence transcription factor MvfR relevant in burn wound infections.

2005-2007 Anti-infective Compounds of *Pseudomonas aeruginosa*
Cystic Fibrosis Foundation
Cystic Fibrosis Foundation, 05G0
Principal Investigator, Total Direct Costs: $180,000.00
This proposal aims to assess the efficacy of anthranilic acid analogs in interrupting the MvfR regulon as anti-virulence therapy against *Pseudomonas aeruginosa* lung infections.

2006-2011 Function of MvfR in *Pseudomonas aeruginosa* Virulence
National Institute of Health, R01 AI63433-01A1
Principal Investigator, Total Direct Costs: $1,250,000.00
This project aims to determine how MvfR modulates the expression of quorum sensing (QS)-controlled genes and how this regulation relates to the QS cascade and bacterial virulence with the ultimate goal of preventing its activation.

2007-2009 Modulation of muscle gene regulation in the host defense response to *Pseudomonas aeruginosa* infection
Shriners Burns Institute, 8892
Principal Investigator, Total Direct Costs: $426,940.00
The central goal of this study is to determine the role of skeletal muscle genes in host defense against *P. aeruginosa* infection, with the ultimate goal of promoting effective natural host defense responses to improve the treatment of *P. aeruginosa* infected individuals

2007-2009 Mitochondrial Uncoupling in Burns
Shriners Burns Institute, 8893
Investigator, Total Direct Costs: 800,000.00
PI: A. Aria Tzika
Elucidation of the role of mitochondrial functions in metabolic and tissue-specific responses to burn injury.

2009-2013 Control of Burn Wound Infections by Natural and Synthetic Molecules
Shriners Burns Institute, 87700
Principal Investigator, Total Direct Costs: $1,022,890.00
The major goal of this project is to identify the first anti-MvfR regulon inhibitors by performing a whole-cell high throughput screen of 300,000 chemical compounds

2009-2013 Study of Host Biochemical, Physiological, and Metabolic Changes that Occur in Response to a Specific Compound with Therapeutic and Protective Immunomodulatory Activity Against *Pseudomonas aeruginosa* Infections
Shriners Burns Institute, 87100
Principal Investigator, Total Direct Costs: $1,026,881.00
The major goal of this proposal is to assess the effects of *P. aeruginosa,* small excreted quorum sensing molecules on host functions and key mammalian innate immunity regulators

2009–2014	Identifying novel anti-infectives by high throughput screening in whole animals National Institute of Health, Transformative R01 AI085581-05, Co-Investigator, Total Direct Cost: $2,458,780.00 PI: Frederick Ausubel The major goal of this project is to identify new generation antibiotics that work by interfering with a pathogen's adaptation to host physiology.
2011-2013	Inhibitors against acute and antibiotic tolerant *Pseudomonas aeruginosa* lung infections Cystic Fibrosis Foundation, CFF11P0 Principal Investigator, Total Direct Costs $230,000.00 The proposed work's immediate goal is to assess the anti-virulence efficacy of the first-generation anti-quorum sensing and anti-MvfR regulon compounds for their impact on bacterial virulence and host pathogenesis.
2011-2015	Lipid Peroxidation as a Biomarker of Increased Susceptibility to Burn Wound Infection Department of Defense, DMRDP DM103014 Principal Investigator, Total Direct Cost: $1,591.247.95 This project's overall goal is to use lipid peroxidation and oxidative stress in skeletal muscle as innovative biomarkers to predict susceptibility to infection and combat multi-drug resistant infections.
2012-2015	Bridging Sustainable Distribution of TRDB Bioinformatics Resources National Institute of Health/NIGMS, R24 GM102656-03 Investigator, Total Direct Costs: $260,471.25 (PI: Xiao) This is a grant to maintain data accumulated during the large-scale collaborative project award "Inflammation and the Host Response to Injury" (Glue Grant).
2013-2014	Function of MvfR in *Pseudomonas aeruginosa* Virulence National Institute of Health/ National Institute of Allergy and Infectious Diseases, 2R56AI063433-06A1 Principal Investigator, Total Direct Cost: $282,909.00 This project aims to study the mode of action of novel classes of antimicrobial agents against the activation of the *P. aeruginosa* virulence transcription factor MvfR and its regulon.
2012-2015	Interruption of Signaling-Mediated Bacterial Persistent Infections National Institute of Health/ National Institute of Allergy and Infectious Diseases, R21AI105902 Principal Investigator, Total Direct Costs $274,974.00. This project aims to identify a new class of antimicrobial agents targeting the few bacterial cells that survive antibiotic treatment (and host defense killing mechanisms) and are ultimately responsible for persistent and relapsing infections. Phase I
2013-2015	Bacterial Antibiotic Tolerance in Burn Infections Shriners Burns Institute, Grant Number 85300 Principal Investigator, Total Direct Costs: $746,705.00

The goal of this project is to develop anti-virulence inhibitors that target the *P. aeruginosa* MvfR regulon and the synthesis of the MvfR-regulated molecule 2-aminoacetophenone that our lab discovered to promote antibiotic tolerant/persistent cells

2015–2017 Small molecule inhibitors of *P. aeruginosa* (Pqs) Quorum Sensing
National Institute of Health/ National Institute of Allergy and Infectious Diseases R33 AI098802-03
PI, Total Direct Costs of subcontract: $237,525.00
This project aims to identify inhibitors of the *pqs* operon of *Pseudomonas aeruginosa.*

2016-2018 Administrative Supplement of Interruption of Signaling-Mediated Bacterial Persistent Infections
National Institute of Health/ National Institute of Allergy and Infectious Diseases, 5R33 AI105902 – 04
Principal Investigator, Total Direct Costs: $155,468.00

2016-2018 A Quorum Sensing Signal Promotes Host Tolerance Training through Epigenetic Reprogramming
Principal Investigator, Harvard Medical School, Epigenetic Initiative-Seed Collaborative Grant, Total Direct Costs: $23,000.00

2015–2018 Interruption of Signaling-Mediated Bacterial Persistent Infections
National Institute of Health/ National Institute of Allergy and Infectious Diseases, R33 AI 105902 – 03
Principal Investigator, Total Direct Costs: $1,031,325.00

This project's major goal is to refine and test *in vivo* the inhibitors identified in Phase I (R21) that block the conversion of bacterial cells into the persister state that enables them to survive traditional antibiotic treatments and thereby cause persistent and relapsing infections.

2016-2020 Action of a novel quorum sensing immunomodulatory signal in persistent infections
Shriners Burns Institute #85200
Principal Investigator, Total Direct Costs: $1,235,135.00
This proposal aims to elucidate the mode of action of the QS molecule 2-aminoacetophenone in host tolerance/resilience to *Pseudomonas aeruginosa* infection in burn wounds.

2019-2020 Development of preventive tools to prevent and combat infections following burn trauma in children."
Shriners Burns Hospital 87100
Principal Investigator, Total Direct Costs: $850,000.00
The proposed research that will use the pipeline we developed is part of our translational strategy toward clinical utility that utilizes infection prediction host biomarkers to stratify pediatric patients at high risk for infection following trauma and before infection occurrence.

2021-2023 Regenerative Therapies for Mitochondrial Dysfunction Triggered by Burn and Infection

Shriners Burns Hospital #85132
Co-Principal Investigator, Rahme & Tzika
Total Direct Costs: $750,000.00
The overall goals of this application are: 1. to gain paradigmatic insights into hitherto unresolved mechanisms underlying the development of skeletal muscle mitochondrial dysfunction in response to burn and superimposed *Pseudomonas aeruginosa* infection, and 2. to test the therapeutic potential of a novel anti-bacterial (anti-Quorum Sensing) compound in combination with a selective mitochondrial agent in preventing Pseudomonas-associated mitochondrial dysfunction of skeletal muscle in a clinically relevant murine burn and infection model.

2021-2024 Predictive Approaches and Technology Development for Identification of Susceptibility to Multiple Independent Infections in Trauma Patients
National Institute of Health, 1R56AI155505 - 01A1
Principal Investigator, Total Award Amount (including Indirect Costs): $844,817.00

Current

07/2023-06/2028 A comprehensive investigation of Pseudomonas quorum sensing regulatory relationships and the consequences on quorum sensing inhibitors in complex communities
National Institute of Health, R01
Principal Investigator, Total Award Amount (including Indirect Costs): $3,741,840.00
The immediate goal of this application will fill existing gaps by addressing three fundamental questions *in a dynamic and human-relevant host environment*: 1) What are the regulatory relationships and functions of the three major *Pseudomonas aeruginosa (PA)* quorum sensing (QS) systems? 2) How do anti-QS therapies impact infection severity and QS regulatory interactions in *PA* mono- and polymicrobial settings? and 3) Whether QS and our novel QS inhibitors impact the development of resistance and limit perturbation of host-associated microbial communities.

2024-2026 Proof of concept experiments for T3SS inhibitors against burn wound infections
National Institute of Health, STTR 1R41AI183900-01
Name of PD/PI: Tim Opperman, Microbiotix, Inc.
Principal Investigator subcontract
Total Award Amount (including Indirect Costs): $360,000.00

2024-2025 Impending Epigenetic Modifications to Combat Chronic Infections in Burns
Shriners Burns Hospital
Principal Investigator
Total Award Amount (including Indirect Costs): $250,000

This application aims to elucidate the molecular and mechanistic aspects of lactylation, a recently identified metabolic stress-related histone modification, in macrophages' dysfunction in clearing infection in burns.

2018–2024 Molecular and Metabolic inter-kingdom actions of a bacterial quorum-sensing signal in promotion of host tolerance/resilience
National Institute of Health/ National Institute of Allergy and Infectious Diseases, R01AI134857
Principal Investigator, Total Award Amount (including Indirect Costs): $3,399,488
This application's specific goal is to decipher the mode of action of a bacterial product on the host metabolome and epigenome paradigmatically to gain insights into the first mechanistic example of a Quorum Sensing molecule that reprograms the host metabolome and epigenome to promote host tolerance/resilience.

2020-2025 Massachusetts General Hospital Scholar Award
The Massachusetts General Hospital Research Scholar Award provides unrestricted funding for forward-thinking researchers to take their work into new and uncharted territories.
The "Bait" That Will Open New Avenues Against Recalcitrant Bacterial Pathogens
Principal Investigator, Total Direct Costs: $500,000.00
The proposed study focuses on using synthesized derivatives of our anti-*Pseudomonas* agents as a "bait" to uncover our agents' potential broad utility against other recalcitrant pathogens, maximizing their applications and accelerating drug discovery in pathogens with highly growing incidences of antibiotic resistance.

2025-2030 Research Training in Alimentary Tract Surgery
National Institute of Health, T32 Fellowship Program
PI Hodin Richard, MD
Role: investigator/sponsor
T32 training grant for surgical residents of the Dept. of Surgery, MGH.

Current Pending Funding:

2026-2031 Unravelling the immunopathogenic properties of *Pseudomonas aeruginosa* volatile organic compounds
National Institute of Health, R01
PI: Rahme, Laurence
PI Gee Lau (ex-trainee). Total subcontract amount (including Indirect Costs): $1,169,000.00
The main objectives of this proposal are to (i) determine the importance of major volatile organic compounds (VOCs) produced by *P. aeruginosa* that cause goblet cell metaplasia and mucus hypersecretion in Cystic Fibrosis

airways; (ii) decipher the mechanism of induction; and (iii) examine the therapeutic potential of selective VOCs biosynthesis inhibitors.

2026–2031 R01AI134857
Molecular and Metabolic inter-kingdom actions of a bacterial quorum-sensing signal in promotion of host tolerance/resilience
National Institute of Health/ National Institute of Allergy and Infectious Diseases,
PI: Rahme, Laurence
Total Award Amount (including Indirect Costs): $3,399,488.00
This application's specific goal is to decipher the mode of action of a bacterial product on the host metabolome and epigenome paradigmatically to gain insights into the first mechanistic example of a Quorum Sensing molecule that reprograms the host metabolome and epigenome to promote host tolerance/resilience.

2026-2028 Tracing devise infections with dual bacterial-targeting CT nanoprobes
National Institute of Health, R21
PI Gkikas Emmanouil
PI subcontract Rahme L. Total Award Amount of the subcontract (including Indirect Costs): $255,119.00
The goal of this application is to address the gap in imaging bacterial biofilms on implantable devices by developing biofilm-specific contrast agents. These agents will leverage molecular recognition of bacterial components to enhance imaging using cost-effective and widely available X-ray and computed tomography (CT) technologies.

2026-2031 Advancing Pediatric Tumor Diagnosis: Combining MRS, Spatial and Single Nuclei Transcriptomics, Clinical Data, and Deep Learning for Enhanced Diagnostic Precision
National Institute of Health, R01
Co-Investigator; PI A Tzika
Total Award Amount (including Indirect Costs): $4,160,984
This study aims to develop a novel technology that combines state-of-the-art high-resolution spectroscopy with gene expression analyses of tiny biopsies and associated clinical data to improve diagnostic accuracy, sensitivity, and specificity. The work will serve patients with diseases for which biopsies are taken.

2026-2028 Pseudomonas aeruginosa MvfR/pqs quorum sensing system driven competition with Klebsiella pneumoniae and the impact of anti-virulence in treating polymicrobial infections
PI: Rahme, Laurence
Total Award Amount (including Indirect Costs): $452,229

2026-2028 Quorum-sensing–mediated reprogramming of epithelial cholesterol metabolism in Pseudomonas aeruginosa infection
PI: Rahme, Laurence
Total Award Amount (including Indirect Costs): $453,750

Report of Local Teaching and Training

Teaching of Students in Courses

1989-1990	Introduction to Microbiology of Natural Resources Class of 50 undergraduate students	University of California at Berkeley Two months, four hours per week (Teaching Assistant)
1991	Laboratory Course of Applied Microbiology and Genetic Engineering Class of 25 undergraduate students	University of California at Berkeley Two months, 7 hours per week University of California at Berkeley
2006	Microbiology and Immunology Medical students	Harvard Medical School Classes 2 hours twice per week for 4 weeks
2007	Microbiology and Immunology Medical students	Harvard Medical School Classes 2 hours twice per week for 4 weeks
2006	Microbial Science Friday Seminar presentation	Harvard University Invited teaching presentation
2008	Life Sciences LS190hf Diverse Microbial Strategies for Metabolism, Pathogenesis, and Chemical Signaling Graduate and advanced undergraduate students	Harvard University Two lectures 2 and a half hours
2016	Microbial Science Friday Seminars	Harvard University Invited teaching presentation
2019	Microbiology and Infectious Disease Advance Integrated Sciences Course Medical students	Harvard Medical School Invited teaching presentation
2020	Microbiology and Infectious Disease Advanced Integrated Sciences Course Medical students	Harvard Medical School Classes 3 hours once per week for 4 weeks
2023	Introduction to Health Science Research (PHSC 2650) Bouvé College of Health Sciences, Department of Pharmaceutical Sciences	Northeastern University Invited teaching presentation 90 m material preparation and grading 5 h

International

2012	Invited teaching presentations, Microbiology Department Graduate students	School of Biological Sciences, Naples Italy Four hours of lectures for 30 graduate and 10 undergraduate students

2012	Invited teaching presentation, Department of Fundamental Microbiology	University of Lausanne, Switzerland Two hours lecture for 10 graduate students

Formal Teaching of Residents, Clinical Fellows and Research Fellows (post-docs)

1997-	Organizer MGH and HMS community monthly interactive seminar series "Host-pathogen Interactions"	Massachusetts General Hospital Boston 10 seminars/year
2013	Faculty Mentoring Program Junior Faculty	Massachusetts General Hospital Met with faculty every 2-3 months for a year for about an hour-two hours

Formally Supervised Trainees

Laboratory and Other Research Supervisory and Training Responsibilities

1992-	Advising, supervising, and training, undergraduates, graduates, and medical students, in addition to residents and postdoctoral fellows	2 hours lab meeting per week and 1:1 supervision two hours per week

Formally Mentored Harvard Medical, Dental, and Graduate Students

Mentored Trainees and Faculty

2018- 2020 I have served as Co-Chair of The Research Faculty and Postdoctoral Fellow Career Development, Department of Surgery, MGH

Current Molecular Surgical Lab Trainees:

2019-	Arijit Chakraborty, Ph.D. Post-Doctoral Research Fellow for Massachusetts General Hospital. He published 2 manuscripts as a leading author and 3 as a co-author. Two additional manuscripts as a leading co-author are in preparation.
2023-	Shifu Aggarwal, PhD., Post-Doctoral Research Fellow for Massachusetts General Hospital. She published 2 manuscripts as a leading author. Two additional manuscripts are in preparation one as a leading co-author and one as a co-author.
2024-	Whan Oh, MSc., PhD., Post-Doctoral Research Fellow for Massachusetts General Hospital. He published 1 manuscript as a co-author and a second is in preparation as a co-author.

Past Molecular Surgical Lab Faculty:

2016- 2022	Arunava Bandyopadhaya, Ph.D. Instructor, Harvard Medical School and Massachusetts General Hospital. Assistant Immunologist, Department of Surgery, MGH. Current position, Senior Scientist Team Lead R&D Astellas Institute of Regenerative Medicine.
2019-2022	Amy Tsurumi, Ph.D., MPH. Instructor, Harvard Medical School, Assistant Molecular Biologist, Department of Surgery, MGH. She was promoted to Assistant Professor in 2022. Current position, Assistant Professor of

Surgery, Harvard Medical School, Assistant Molecular Biologist, Department of Surgery, MGH

2023 Vijay Kumar Sing, Ph.D Instructor, Harvard Medical School, Department of Surgery, Massachusetts General Hospital. Current position, Assistant Professor, Academy of Scientific and Innovative Research, India.

2019-2020 Ulienton Pinto, Visiting Assistant Professor, University of Sao Paolo.

Past Post-doctoral trainees

1997-2001 Hui Cao, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Lead Scientist at Pharma

Published three manuscripts, including one in *PNAS;* Received a Damon Runyon Post-doctoral Fellowship.

1998-2001 Gee Lau, Ph.D. Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Associate Professor, Department of Pathobiology, the University of Illinois at Urbana-Champaign. Published four manuscripts, including one in *PNAS.* Received a Research Award from the American Lung Association for his work in my laboratory.

1998-2002 Boyan Goumnerov, MD. Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Vice President, Clinical Operations, Fluro Pharma, Boston, MA. He published six manuscripts, including two in *PNAS*.

2000-2003 Regina Baldini, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Associate Professor of Biochemistry, Instituto de Quimica, Sao Paolo, Brazil. Published four manuscripts, including one in *PNAS.* Received a FASP Post-doctoral Fellowship and a FASP Young Award.

2000-2002 Gomathi Krishnan, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Clinical and Translational Research Informatics Specialist for the Stanford Center for Clinical Informatics. She published two manuscripts, including one in *PNAS* as a co-author.

2000-2012 Jianxin He, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Director of Molecular Biology, Assay, Biotechology, Inc. In 2007 was promoted to Senior Research Associate and published twelve manuscripts, including one in *PNAS* as a lead author.

2001-2002 Anastasia Tampakaki, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Associate Professor, Agricultural, University of Athens, Greece. She published two manuscripts as a co-author.

2001-2003 You-Hee Cho, Ph.D., Professor of Molecular Microbiology, Department of Life Sciences, College of Natural Sciences, Sogang University Seoul.

2002-2005 Eric Déziel, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Professor-Investigator, INRS-Institut Armand-Frappier, Laval, Quebec. He published twelve manuscripts, including two in *PNAS,* received the Canadian NRC Post-doctoral Fellowship, and as a faculty, he received in 2012 The Canadian Research Chair in Sociomicrobiology.

2002-2005 Qunhao Zhang, MD, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Associate Professor New England School of Acupuncture. Post-doctoral trainee. He published six manuscripts as a coauthor and two as a lead author.

2002- 2012 Georgios Apidianakis, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Associate Professor of Biology, the University of Cyprus, Promoted to Instructor at Harvard Medical School in 2007, is the recipient of the Shriners Post-doctoral Fellowship in 2003, published twelve manuscripts, including two in *PNAS*, one in *Nature Protocols,* and one in *EMBO Reports*; in 2010, received a Young Investigator Award from Department of Defense and a Pilot Investigator Award from Shriners Hospital for Children, Boston.

2003-2004 Kathleen Padfield, MD, Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Anesthesiologist, Stepping Hill Hospital, Manchester, UK. She published eight manuscripts, including one in *PNAS* as a lead author.

2003-2005 Suresh Gopalan, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, CEO & Founder, ReSurfX, Published four manuscripts as a coauthor, including one in *PNAS*.

2003-2007 Gaoping Xiao, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Vice President, Business Development, Syd Labs, Inc, Boston, MA. He published six manuscripts, two as a lead author.

2005-2008 Biliana Lesic, Ph.D. Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Lead Research Scientist host-microbe interactions, Danone, France. She has published a total of eight manuscripts. She is the lead author on three of them. One of her publications provides the first definitive demonstration of the utility of selective anti-virulence compounds that increase host survival to *P. aeruginosa* infection. Several journals extensively highlighted this work, including a lengthy commentary published in *Nature Microbiology Reviews*. She received the Marie Curie Award in 2008 as a junior faculty at Institute Pasteur, France, but subsequently, she moved to industry.

2005- 2009 Meenu Kesarwani, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Senior Research Associate, University of Cincinnati. She published five manuscripts. She is the lead author on one of them, which describes the first bacterial molecule that switches cells from acute to bacterial persistence stage.

2007-2013 Ronen Hazan, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Associate Professor, Faculty of Dental Medicine of the Hebrew University, Jerusalem, Israel. Recipient of Shriners Post-doctoral Fellowship in 2007. Published eleven manuscripts in total, including four as a lead author. One of his manuscripts was published in *Current Biology,* and an editorial accompanied it. Several journals, including Science Signaling, highlighted his work.

2006- 2010 Melissa Starkey, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Clinical Guidelines Senior Administrator, American College of Physicians in the Clinical Policy Department. Recipient of The Shriners Post-doctoral Fellowship. Published

five manuscripts. Lead author of the first highly efficacious *in vivo* anti-virulence compounds against acute and relapsing/antibiotic-tolerant infections.

2008-2010 Aikaterini Constantinou, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Assistant Professor, University of Patras, Greece. She published eight manuscripts, including two as a lead author.

2009-2010 Panayiotis Panopoulos, Ph.D., European Community Examiner, Hospital Policy Compliance, Brussels, Belgium. He published one manuscript as a co-author.

2009-2011 Yok-Ai Que, M.D., Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Associate Professor, Department of Intensive Care, Senior Physician, Bern University Hospital, Bern, Switzerland. He has published twelve manuscripts, two as a lead author. He received a career development award in 2012 from The Swiss National Foundation.

2014-2015 Mohammed Hadi Gharedaghi, MD, Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Anesthesiologist, Children's Hospital Boston. He is the co-author of two manuscripts.

2012-2016 Jeremy Yan, Ph.D. Post-Doctoral Research Fellow for Massachusetts General Hospital. He published two manuscripts. MBA candidate, Harvard Business School.

2013-2017 Tomoe Kitao-Ando, Ph.D. Current position, Assistant Professor, Department of Biochemistry, Gifu University, Japan. She published five manuscripts, and two are in preparation. She was the recipient of the Federal Japanese Fellowship in 2014.

2013-2017 Damien Maura, Ph.D., Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Senior Scientist, Enbiotix, Cambridge,

MA. He published 12 manuscripts and has two in preparation—recipient of the Shriners Post-doctoral Fellowship in 2013.

2013- 2018 Alicia Ballok, Ph.D., Scientist, Evelo, Biosciences Cambridge, MA. She has published two manuscripts and was—recipient of the Cystic Fibrosis Post-doctoral Fellowship in 2015.

2015-2016 Fatemah Adiliaghdam, M.D., Ph.D. Surgery resident Beth Israel Hospital, Boston, MA. She published three manuscripts.

2017-2018 Asako Ogura, MD, MPH, Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Physician, Department of Plastic Surgery, Japan. She has published three manuscripts.

2019-2020 Sajjad Ahmad, Ph.D. Visiting graduate student National Center for Bioinformatics, Quaid-Azam University, Islamabad, Pakistan. Recipient of the Higher Education Commission Scholarship- International Research Support Initiative Program of Pakistan.

2019-2020 Ulienton Pinto, Visiting Assistant Professor, University of Sao Paolo.

2018-2021 Marianna Almpani, MD, Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Internal Medicine Resident, Massachusetts General Hospital. Recipient of the Shriners Post-Doctoral Fellowship in 2018 and the ABA Poster award in 2019.

	She has published 9 manuscripts, 1 as a leading author, 2 as co-leading author and 6 as a co-author.
2010-2016	Arunava Bandyopadhaya, Ph.D. Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Senior Scientist Team Lead R&D Astellas Institute of Regenerative Medicine. He published ten manuscripts. He was promoted to Instructor in October 2016. He was the recipient of the Eleanor Shore Award in 2017.
2012-2019	Amy Tsurumi, Ph.D., MPH. Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Assistant Professor, Harvard Medical School. Instructor (2019-2022), Harvard Medical School, Assistant Molecular Biologist, Department of Surgery, MGH. She published 12 manuscripts. She was the recipient of the Shriners Post-Doctoral Fellowship in 2015. She was promoted to Instructor in April 2019 and Assistant Professor in 2022. PI of R03, Pending funding as a PI: R21 and Co-investigator on my ongoing grants.
2021-2022	Claire De Cresenzo, MD. Surgical Resident in her research year. Recipient of the NIH R25 Fellowship- Next Generation Physician-Scientist Training Pathway (MGH Next-Gen PSTP) (R25). Two manuscripts in preparation.
2021-2022	Jefferson Proano Zamudio, MD. Post-Doctoral Research Fellow for Massachusetts General Hospital, trauma division. He participated in the R56 funded studies.
2021-2022	Dias Argandykov, MD. Post-Doctoral Research Fellow for Massachusetts General Hospital, Trauma division. He participated in the R56-funded studies.
2022	Aulina Chowdhury, DO. Post-Doctoral Research Fellow for Massachusetts General Hospital. She participated in the R56-funded studies. Current position, Clinical Research Specialist, Boston Children's Specialist
2022	Shruti Patil, MD. Post-Doctoral Research Fellow for Massachusetts General Hospital. She participated in the R56-funded studies.
2021-2023	Kelsey Wheeler, Ph.D. Post-Doctoral Research Fellow. Graduate of MIT December 2020. She published 1 manuscript as a co-author, 1 as leading author under review and 1 in preparation. Current position, Research Assistant Professor, MIT.
2022-2023	Asel Kabashi, MD. Post-Doctoral Research Fellow for Massachusetts General Hospital. Current position, Pathology Resident
2018-2023	Vijay Kumar Sing, Ph.D. Post-Doctoral Research Fellow for Massachusetts General Hospital. Recipient of the SERB Indo-U.S. Postdoctoral Fellowship. He published 3 manuscripts as a leading author and two additional manuscripts in preparation as a leading author. Current position, Assistant Professor, India
2024-2025	Filip Kovacic, Ph.D. Post-Doctoral Research Fellow for Massachusetts General Hospital. He published 1 manuscript as a co-author and one additional manuscript in preparation as a leading author and another as a co-author.

Undergraduate Students Who Wrote Senior Honors Theses:

2006 Christos Astrakas, MD, Resident in Dermatology at Deutsche Rentenversicherung. Senior Honors Thesis Student, Biology Department, University of Alexandroupolis, Greece. Title of thesis: The role of PqsE in *Pseudomonas aeruginosa* virulence. Co-author in one manuscript published in *PLoS Pathogens*.

2002 Hasan Baydoun, MD, Orthopedic Surgeon, Center for Orthopedics Shoulder & Sports Medicine, PA, USA. Title of thesis: The Effect of *Pseudomonas aeruginosa* infection on immune responses: The role of the Quorum sensing Regulator MvfR. Presented at the American University of Beirut, Department of Biology.

Graduate Students- Who Wrote Master Theses

2009-2010 Maya Khezam, B.Sc., M.Sc. Regulatory Affairs Associate, Biosimilars at Baxalta. MSc. Candidate, American University of Beirut, Department of Biology, Lebanon. Title of thesis: Putative Effectors of the Type VI Secretion System in *Pseudomonas aeruginosa*: Promising Targets for Anti-Virulence Agents. Daily supervision (6/2009- 2/2010).

2011-2012 Benjamin Strobel, M.Sc. Ph.D. Team Leader translational medicine & Genomics Biomarker Team, Boehringer Ingelheim, Germany. M.Sc. Candidate from Institut für Mikrobiologie und Biotechnologie, Ulm University, 89069 Ulm, Germany. Title of thesis: Quorum sensing determines cell fate in *Pseudomonas aeruginosa*: the roles of HQNO and 2-AA in auto-lysis and antibiotic tolerance. Published one manuscript. Daily supervision (3/1/2011-12/31/2011).

2013-2014 Viktor Schneidt, M.Sc., Ph.D. Senior Biotechnologist, Operations, Lonza, Switzerland. M.Sc. Candidate from Institut für Mikrobiologie und Biotechnologie, Krebsforschungszentrum German Cancer Research Center Ulm University, Ulm, Germany. Title of thesis: *MvfR-regulated biofilm formation in Pseudomonas aeruginosa.* Daily supervision (3/1/2013-2/18/2014).

2014-2015 George Massey, M.Sc. candidate, Boston University, Department of Medical Sciences. Title of thesis: Identification of a small molecule inhibitor of virulence factors in multidrug-resistant *Acinetobacter baumannii.* Daily supervision (9/1/2014-4/2/2015).

2016 Frederick Walte, B.Sc. M.Sc. Scientist, Ruhrpharm AG, Germany. M.Sc. Candidate in Pharmaceutical Sciences, Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), Saarbrücken, Germany. Title of Thesis: Quest for protease X cleaving the transcriptional regulator MvfR of Pseudomonas aeruginosa. Daily supervision (03/2016-09/2016).

2020-2021 Thomas Schumacher, Master's student candidate in pharmaceutical biotechnology at Ulm University and University of Applied Sciences in Biberach, Germany. He performs the experimental part of his master's under my supervision in my laboratory for 12 months.

Faculty Mentoring

2018- 2020 I have served as Co-Chair of The Research Faculty and Postdoctoral Fellow Career Development, Department of Surgery, MGH

2011-2018 A. Aria Tzika, Ph.D. Promoted to Associate Professor of Surgery in 2018, Harvard Medical School. Director of NMR Surgical Laboratory.

2014 -2016 Oral Ebru, PhD., Promoted to Associate Professor, Harvard Medical School, Associate Director, Harris Orthopedic Lab, Orthopedic Surgery. Meet four times per year.

2017-2021 Arunava Bandyopadhaya, Ph.D. Instructor, Harvard Medical School, Assistant Immunologist Department of Surgery, MGH. Meet twice per week.

2018- Marianna Bei, D.M.D., Ph.D., Assistant Professor, Center for Engineering in Medicine, Department of Surgery, MGH.

2019- Nima Saeidi, Ph.D., Associate Professor, Department of Surgery, MGH. Assistant Professor 2017-2022. Promoted to Associate Professor 09/2022.

2019 -2020 Lael Yonker, MD Co-Director, Assistant Professor, MGH Cystic Fibrosis Center, K08 co-mentor. Meet once per month.

2019-2023 Amy Tsurumi, Ph.D., MPH. Assistant Professor. Instructor (2019-2022), Harvard Medical School, Assistant Molecular Biologist, Department of Surgery, MGH. Meet twice per week. Promoted to Assistant Professor of Surgery in 2022.

2020- Paris Jafari, PharmD., Ph.D., Assistant Professor, Dept. of Pharmaceutics and Pharmaceutical Chemistry, University of Utah.

2020- Senior Mentor to Faculty and Residents, Department of Surgery, MGH

2019-2020 Ulienton Pinto, Visiting Assistant Professor, University of Sao Paolo.

2022- He Shijie, Ph.D., Instructor, Harvard Medical School, Department of Surgery MGH.

Graduate Students- Who Wrote Ph.D. Theses

2010-2011 Diogo Abreu, Ph.D., Postdoctoral Fellow at Institute of Biosciences, University of São Paulo, Brazil. Ph.D. Candidate. Recipient of the Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP 8 months Fellowship to complete his Ph.D. thesis in my laboratory. Graduate student of Regina Baldini, Ph.D. - ex-post-doctoral fellow of the Rahme Lab trainee. Published one manuscript. Daily supervision (3/1/2010-12/12/2010).

2013 Aikaterini Kefala, Ph.D. candidate, University of Crete, University of Crete, Department of Biochemistry, Crete, Greece. Published one manuscript. Daily supervision (2/1/2013-6/2/2013).

2016 Giuseppe Allegretta, B.Sc. Ph.D. candidate in Pharmaceutical Sciences, Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), Saarbrücken, Germany. Daily supervision (2/1/2016-8/31/2016)

2016-2017 Antonio G. Gomes de Mello Martins B.Sc., Ph.D. candidate in Pharmaceutical Sciences, Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), Saarbrücken, Germany. Daily supervision (11/1/2016-8/31/2017)

2017 Gilberto Kaihami, BSc., University of São Paulo, Brazil. Ph.D. candidate. Recipient of the Fundação de Amparo à Pesquisa do Estado de São

Paulo - FAPESP 9 months Fellowship to complete his Ph.D. thesis in my laboratory. Daily supervision (3/1/2017-12/31/2017)

2020 Alexandra Dimitriou, Ph.D. candidate, National Kapodistrian University of Athens, Division of Pharmacy, Athens, Greece. She will complete three years of her Ph.D.—program in my laboratory.

Graduate Students- Thesis Committee Member

2007 Geoff Dilly, a Ph.D. candidate in the Department of Organismic and Evolutionary Biology, Harvard University. Preliminary Qualifying Examination (PQE) Committee.

2009 Wisuwat Songnuan, Ph.D. Candidate in the Program in Biological and Biomedical Sciences, Harvard University. The dissertation examining committee: Studies of Pathogen Defense in *Arabidopsis thaliana* Roots.

2009 Xavier Rios, Ph.D., Ph.D. Candidate in the Program in Biophysics, Harvard University. Preliminary Qualifying Examination (PQE) Committee: One bug to bug them all: Developing an *E. coli* Type-Four Secretion System as a universal macromolecule donor.

2020 Alexandra Dimitriou, Ph.D. candidate, National Kapodistrian University of Athens, Division of Pharmacy, Athens, Greece.

Exceptional Premedical Students (20 total)

1999-2000 John Tsongalis, MD, Ph.D. Current position, Northampton Family Practice Associates, Pre-medical student, daily supervision. Co-author in two *PNAS* publications. Accepted to UMass Medical School MD/Ph.D. program.

1998, 2003 Hasan Baydoun, MD, Orthopedic Surgeon at Main Street Center for Orthopedics Shoulder & Sports Medicine, USA. Pre-medical student.

2014 Seda Babroudi, B.S., MD candidate, Tufts Medical School, early admission.

2014-2015 George Massey, MD. Current position, Psychiatrist, Carle Foundation Hospital. Boston University MSc., student performed his experimental MSc Thesis in my laboratory. Daily supervision. Accepted to Boston University Medical School, Boston, MA.

2023-2024 Sujin Cha, BSc, Technician for Massachusetts General Hospital.

Exceptional Summer Interns. (40 total)

2008-2011 Rui Wang, Commonwealth High School Summer Research Trainee BS. Biological Engineering, MIT.
She published a first-author manuscript for the work performed during the internship. She received the Siemens Award for her research project conducted in the lab, resulting in a first-author publication.

2022, 2023 Maryam Abdel, Marriotts Ridge High School, Ellicott City, MD
Recipient of the 2024 Regeneron Science Talent (STS) Scholar and in 2023 Regeneron International Science and Engineering Fair 2nd place award in microbiology. Current: 2024 Undergraduate Havard University.

2021, 2022 Erin Kim, Phillips Academy, Andover, MA Recipient of the 2021 MGH

Image Award and the 2023 Regeneron Science Talent Scholar. Current: 2024 Undergraduate Brown University, RI

Formal Teaching of Peers (e.g., CME and other continuing education courses)

2000- Shriners Hospital Educational Presentation Series Boston Twice/year

Local Invited Presentations

1996	Pathogenesis Seminars, Harvard Medical School
2001	Pathogenesis Series Seminars, Harvard Medical School
2003	Department of Microbiology, Harvard Medical School Annual Retreat, Cape Cod, MA
2006	Microbial Science Initiative Seminar, MSI Chalk talk. Harvard University
2014	Immunology and Infectious diseases seminar series, TH Chan Harvard School of Public Health, Boston, MA
2016	Microbial Science Initiative Seminar, MSI Chalk talk. Harvard University
2016	3rd Annual HMS Epigenetics Symposium, Harvard Medical School, Boston, MA
2016	Invited research seminar of the Center for the Study of Inflammatory Bowel Diseases (CSIBD), Mass. General Hospital, Boston, MA
2017	Surgery Grand Rounds, Department of Surgery, Mass. General Hospital, Boston, MA
2018	Beacon Hill Women Forum, Boston, MA
2018	Department of Surgery, MGH, Boston, MA
2018	Mucosal Immunology and Biology Research Center, Mass. General Hospital, Boston, MA
2019	Department of Microbiology, Harvard Medical School, Annual Retreat, Cape Cod, MA
2022	Forsyth Institute, Cambridge, MA
2022	2024 Shriners Hospital for Children
2023	Northeastern University, Boston, MA
2023	UMass Chan Medical School
2024	Shriners Hospital for Children, Boston MA
2025	Shriners Hospital for Children, Boston MA
2026	Shriners Hospital for Children, Boston MA

Report of Regional, National, and International Invited Teaching and Presentations

Invited Presentations and Courses (No presentations were sponsored by outside entities)
Please note that several invitations between 2001-2016 were declined due to family reasons.

Regional

1995	Invited Lecture, Cubist Biotechnology, Boston, MA
1998	Invited presentation for Gordon Conference on Biological Mechanisms of Bacterial Regulation New Hampshire
1999	Seminar, Department of Microbiology, University of Massachusetts Amherst, Amherst, Massachusetts

2000	Seminar, Dartmouth University, Department of Microbiology and Immunology, Dartmouth, New Hampshire
2006	Seminar, Dartmouth University, Department of Microbiology and Immunology, Dartmouth, New Hampshire
2007	Seminar, Department of Medicine, Division of Infectious Diseases, University of Massachusetts Medical School, Worchester, Massachusetts
2011	Invited presentation, Cystic Fibrosis Retreat, Lebanon, New Hampshire
2015	Seminar, Department of Immunology and Infectious Diseases, Harvard T.H. Chan, School of Public Health, Boston, Massachusetts
2018	Seminar, Department of Chemistry, the University of Massachusetts at Lowell, Lowell, Massachusetts
2021	Invited presentation, Forsyth Institute, Cambridge, Massachusetts
2023	Invited presentation, Center for Drug Discovery, Scholl of Health Sciences, Northeastern University, Boston, MA
2023	Invited presentation, Department of Microbiology, UMass Medical School, Worchester, MA
2025	Invited presentation, Scholl of Health Sciences, Northeastern University, Boston, MA

National

1996	Seminar, Department of Microbiology, University of Pennsylvania, School of Medicine, Philadelphia, Pennsylvania
1997	Invited presentation Microbial Pathogenesis and Host Responses Cold Spring Harbor Laboratory, New York
1998	Seminar, University of Pennsylvania, Department of Microbiology, Philadelphia, Pennsylvania
1999	Seminar, Department of Microbiology, University of Washington, Seattle, Washington
1999	Invited lecture, American Society for Microbiology, Chicago, Illinois
1999	Invited lecture, National Academy of Science (USA) Colloquium on Virulence and Defense in Host-Pathogen Interactions: Common Features Between Plants and Animals, Stanford, California
2000	Invited presentation, 11th International Conference on *Arabidopsis* Research, Madison, Wisconsin
2000	Seminar, Cornell University, Department of Plant Pathology, Ithaca, New York
2001	Invited presentation, Keystone Symposia on "Genetic Manipulation of Insects," Taos, New Mexico
2003	Invited presentation, Annual Meeting of the American Phytopathological Society, Madison, Wisconsin
2005	Invited presentation, Cystic Fibrosis Foundation Williamsburg Conference Williamsburg, Virginia
2007	Invited presentation, ASM Conference on *Pseudomonas*, American Society for Microbiology, Seattle, Washington
2007	Invited presentation, 3rd ASM Conference on Cell-Cell Communication in Bacteria, American Society for Microbiology, Austin, Texas

2014	Invited presentation, 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Washington, DC
2014	Invited presentation, 47th Annual Meeting of SLB IEIIS (Society for Leukocyte and Biology and The International Endotoxin and Innate Immunity Society) Salt Lake City, Utah
2014	Invited presentation, Department of Defense. The 2014 Joint Program Committee – 2 (JPC-2), Fort Detrick, Maryland
2015	Invited presentation, Keystone Symposia, Gram-Negative Resistance, Lake Tahoe, California
2015	Invited presentation, American Society for Microbiology, Pseudomonas Symposium, Washington DC
2015	Invited Round Table Chair of World Anti-Microbial Resistance Congress, Washington, DC
2016	Invited lecture, 7th Annual Perlman Symposium on Antibiotic Discovery and Development at the University of Wisconsin-Madison, Madison, Wisconsin
2016	Invited presentation, American Society for Microbiology-ASM microbe 2016, Boston, Massachusetts2016 Co-Chair, American Society for Microbiology- ASM microbe 2016: Session 134 - Fresh Approaches to Antibiotic Drug Discovery: Breaking from Convention. Boston, Massachusetts
2017	Invited presentation, American Society for Microbiology- ASM, 6th ASM Conference on Cell-Cell Communication in Bacteria, October 16-19, 2017, Athens, GA
2021	Invited presentation, Department of Biological Sciences, Rensselaer Polytechnic Institute, Troy, New York
2022	Visiting Professor, Invited presentation CHARM (Collaborative to Halt Antibiotic-Resistant Microbes) inaugural presentation, University of California San Diego (UCSD), Division of Host-Microbe Systems and Therapeutics

International

1991	Invited presentation, University of Vancouver, Canada
1994	Invited presentation, ARAPENET III, Conference on *Arabidopsis thaliana*, France
1998	Invited presentation, International Meeting of Plant Pathology, Edinburgh, Scotland
1999	Invited presentation, Giovanni Armenise-Harvard Foundation, Italy
1999	Plenary presentation, International Conference on Technology Transfer in Biotechnologies as a Catalyst for National Development, Beirut, Lebanon
2000	Invited presentation, 41st Annual *Drosophila* Research Conference, Pittsburg, Pennsylvania
2000	Invited lecture, International Conference on Scientific and Technological Entrepreneurship in Universities and Research Institutes, Beirut, Lebanon
2001	Seminar, American University, Department of Biochemistry, Beirut, Lebanon

2001	Invited presentation, Federation of European Microbiological Society "*Pseudomonas*," Brussels Belgium
2002	Invited Keynote Speaker, Annual Meeting of the American Phytopathological Society, Edinburgh, Scotland
2003	Seminar, Institute for Molecular Biology and Biotechnology, Heraklion, Crete, Greece
2005	Invited presentation, Federation of European Microbiological Society "*Pseudomonas*," Marseille, France
2007	Invited presentation, Department of Biology, University of Crete, Heraklion, Crete, Greece
2008	Invited presentation, 33rd FEBS Congress on Biochemistry of cell Regulation, Athens, Greece
2012	Invited presentation, Department of Microbiology, University of Naples, Naples, Italy
2012	Invited Lecture, Department of Fundamental Microbiology, University of Lausanne, Switzerland
2015	Invited presentation, 5th HIPS-Symposium of the Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS), Saarbrücken, Germany
2016	Keynote speaker, National Symposium Swiss Burn & Wound Research Network at Universite de Lausanne, Lavey Medical, Lausanne, Switzerland
2016	Experts' Panel, 2nd International Symposium on Alternative to Antibiotics (ATA), 12-15 December, OIE Headquarters, Paris, France.
2018	Invited presentation, 1st One Health Forum, December 15, 2018, Athens, Greece, War Museum.
2022	Invited lecture, SAFE-ID Swiss Academy Foundation for Education in Infectious Diseases- 31st Challenge in Infectious Diseases, 16-18 June Engelberg, Switzerland
2024	Invited lecture, Molecular Biology/Developmental Neurobiology University of Crete Medical School, Crete, Greece
2025	Invited presentation, International Center for Genetic Engineering, Arturo Falaschi- Cell-Cell Communications, Insights and Future Trends, October 28-30, Triest, Italy

INNOVATION

Patents and Patent Applications (15 total)

Laurence Rahme, Jianxin He, Regina Baldini, Jens Solsbacher, Peter Wagner

VIRULENCE-ASSOCIATED NUCLEIC ACIDS AND PROTEINS AND USES THEREOF
Patent Publication # US20030022349A1; Application # 09/975,719. Filed: 10/10/2001
As Principal Investigator, my colleagues and I disclosed bacterial virulence polypeptides and nucleic acid sequences (e.g., DNA) encoding such polypeptides and methods for producing such polypeptides by recombinant techniques. Based on the present invention, a pathogenic infection may be treated, prevented, or reduced by administering to an infected mammal or plant a therapeutically effective amount of a composition that inhibits the expression or activity of a polypeptide encoded by the virulence factors. Also provided are methods for utilizing such polypeptides to screen for antibacterial or bacteriostatic compounds. The role of the genes

identified as relevant in bacterial pathogenesis has since been validated by multiple labs in the US and abroad.

Laurence G. Rahme, Hui Cao, Francois Lepine, Eric Deziel, Ronald G. Tompkins
METHODS FOR THE PREVENTION OR TREATMENT OF BACTERIAL AND FUNGAL INFECTIONS
Patent Publication# US20100184804 A1; Filed: 10/30/2002
Also published as: EP1450802A2, US20050119302, WO2003037259A2, WO2003037259A3

As a Principal Investigator, my colleagues and I improved methods for treating, stabilizing, or preventing a bacterial or a fungal infection in a plant or an animal, such as a mammal. In particular, these methods involve the use of a compound that MvfR controls, and that affects the expression of an MvfR protein or that promotes its modification or inactivation, or a compound produced by *P. aeruginosa* strain PA14, but not by *P. aeruginosa* containing an mvfR mutation, in late stationary phase culture. The efficacy of the compounds identified has since been used and validated by multiple US and abroad labs.

Stephen Calderwood, Ji Choi, Costi Sifri, Boyan Goummerv, **Laurence Rahme**, Frederic Ausubel
PSEUDOMONAS VIRULENCE FACTORS AND USES THEREOF
Patent Publication# US 20050089988A1; 10/497,846. Filed: 1/2003
Also published as: WO2003057900A2, WO2003057900A3

My colleagues and I identified and characterized a number of nucleic acid molecules, polypeptides, and small molecules (e.g., phenazines) involved in conferring pathogenicity and virulence to a pathogen. This discovery, therefore, provides a basis for drug-screening assays aimed at evaluating and identifying “anti-virulence” agents which are capable of blocking pathogenicity and virulence of a pathogen, e.g., by selectively switching pathogen gene expression on or off, or which inactivate or inhibit the activity of a polypeptide which is involved in the pathogenicity of a microbe. Drugs that target these molecules are useful as such anti-virulence agents. The role of the genes identified as relevant in bacterial pathogenesis has since been validated by multiple labs in the US and abroad.

Laurence Rahme, Jianxin He, Regina Baldini, Jens Solsbacher, Peter Wagner
VIRULENCE-ASSOCIATED NUCLEIC ACIDS AND PROTEINS AND USES THEREOF
Patent Publication# US20050059018A1; WO2004024937A2 Filed 9/12/2003

As a Principal Investigator, my colleagues and I disclosed methods and compositions relating to bacterial virulence polypeptides and nucleic acid sequences (e.g., DNA) encoding such polypeptides. Based on the present invention, a pathogenic infection may be treated, prevented, or reduced by administering to an infected mammal or plant a therapeutically effective amount of a composition that inhibits the expression or activity of a polypeptide encoded by the virulence factors. Also disclosed are methods for producing such polypeptides by recombinant techniques and strategies for utilizing such polypeptides to screen for antibacterial or bacteriostatic compounds. The genes identified as relevant in bacterial pathogenesis and the methods developed have since been validated by multiple labs in the US and abroad.

Laurence Rahme, Eric Deziel, Francois Lepine, Ronald G. Tompkins, Gaoping Xiao
METHODS FOR IDENTIFYING CANDIDATE COMPOUNDS FOR TREATING, REDUCING, OR PREVENTING PATHOGENIC INFECTIONS
Patent Publication # WO2005069989A3; Application # US 10/586,403. Filed: 01/21/2005
Also published as: US20070292851, US8906602 B2, WO2005069989A2

As a Principal Investigator, my colleagues and I developed methods for identifying candidate compounds for treating, reducing, or preventing a pathogenic infection, the methods including (a) contacting a pathogenic cell with a candidate compound; and (b) measuring the production of a molecule selected from the group consisting of a 4-hydroxy-2-alkylquinoline (HAQ) molecule, 4-hydroxy-2-heptylquinoline (HHQ) molecule, or a derivative or precursor thereof in the cell, a candidate compound that reduces the production relative to production of the molecule by a cell not contacted with the candidate compound, identifying a candidate compound useful for treating, reducing, or preventing a pathogenic infection. The methods developed have since been validated by multiple labs in the US and abroad.

Frederick Ausubel, **Laurence Rahme**
VIRULENCE ASSOCIATED NUCLEIC ACID SEQUENCES AND USES THEREOF
Patent Publication # US20070105167A1; Filed 02/03/2006. Also published as: CA2310561A1, CN1309720A, EP1040200A1, EP1040200A4, US6355411, US20070105167, WO1999027129A1
As a member of Fred Ausubel Lab and later as a PI, my colleagues and I disclosed bacterial virulence polypeptides and nucleic acid sequences (e.g., DNA) encoding such polypeptides methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing such polypeptides to screen for antibacterial or bacteriostatic compounds. The genes identified as relevant in bacterial pathogenesis and the methods developed have since been validated by multiple labs in the US and abroad.

Laurence Rahme, Francois Lepine, Eric Deziel
ANTI-INFECTIVE AND IMMUNOMODULATORY COMPOUNDS
Publication #: WO2006130832 A3. Filed: 06/02/2006
Publication #: US20130209515 A1; Application # US 13/596,680. Filed 08/28/2012
Also published as: US20090215819, WO2006130832A2, WO2006130832A3
As Principal Investigator, my colleagues and I developed pharmaceutical compositions and methods that include the use of anti-virulence compounds that potentiate the host-immune response or limit or prevent the expression or activity of individual virulence factors. In addition, the compositions have immunomodulatory activity, and therefore can be used to prime host defenses to prevent or limit bacterial, fungal, and viral viability. In the inventions' compositions and methods, specific steps of the bacterial-, fungal-, or viral-host interaction are targeted to prevent pathogenesis (e.g., infection). Such an anti-virulence approach should decrease pathogenic organisms' ability to acquire resistance to the protective anti-infective compounds, as they act at disarming the pathogen from its ability to cause infection without affecting its viability. The compounds identified have since been validated by other labs in the US and abroad.

Laurence G. Rahme, Hui Cao, Francois Lepine, Eric Deziel, Ronald G. Tompkins
METHODS FOR THE PREVENTION OR TREATMENT OF BACTERIAL AND FUNGAL INFECTIONS
Patent Publication# US20100184804 A1. Filed: 11/20/2009
As a Principal Investigator, my colleagues and I improved methods for treating, stabilizing, or preventing a bacterial or a fungal infection in a plant or an animal, such as a mammal. In particular, these methods involve the use of a compound that MvfR controls, and that affects the expression of an MvfR protein or that promotes its modification or inactivation, or a compound produced by *P. aeruginosa* strain PA14, but not by *P. aeruginosa* containing an mvfR mutation, in late stationary phase cultures.

Ronald G. Tompkins, A. Aria Tzika, Yong-Ming Yu, **Laurence Rahme**, Jeevendra A. Martyn
METHODS FOR THE PREVENTION AND TREATMENT OF BURN INJURIES AND SECONDARY COMPLICATIONS

Patent Publication # US20100331265A1; 12/727,647. Filed 03/19/2010. Publication # US20140288012A1; Application # 14/061,370. Filed 10/23/2013
Also published as: CN102573881A, CN103933542A, EP2408463A2, EP2408463A4, US20140288012, WO2010120431A2, WO2010120431A3
My colleagues and I developed methods for treating a subject suffering from a burn injury or associated complications by administering an effective amount of an aromatic-cationic peptide to the subject. For example, a burn injury may be associated with distant pathophysiological effects, such as hypermetabolism, skeletal muscle dysfunction, and organ damage. The disclosure also relates to methods for protecting a subject from a burn injury by administering an effective amount of an aromatic-cationic peptide to a subject at risk of a burn injury.

METHODS FOR THE PREVENTION AND TREATMENT OF BURN INJURIES AND SECONDARY COMPLICATIONS

Publication number: 20200323945
Type: Application
Filed: April 6, 2020
Publication date: October 15, 2020
Applicant: The General Hospital Corporation d/b/a Massachusetts General Hospital

Laurence Rahme, Francois Lepine, Melissa Starkey, Biliana Lesic-Arsic
ANTIBIOTIC TOLERANCE INHIBITORS
Patent Publication # WO2012/116010A3. Application # PCT/US2012/026028.
Filed: 2/22/ 2011
Also published as: EP2678319A2, EP2678319A4, US8877940, US20140066454, US20150266827, WO2012116010A2
As a Principal Investigator, my colleagues and I developed the first compounds efficacious against the formation of the antibiotic tolerant/persister cells. In addition, these compounds are the first to target both acute and relapsing/persistent *P. aeruginosa* infections in mice. The present disclosure relates to benzimidazole-benzamide derivatives and the use thereof, e.g., to treat acute and relapsing infections. The compounds identified have since been validated by other labs in the US and abroad.
Assignee: THE GENERAL HOSPITAL CORPORATION

Laurence Rahme, Shuangchun Yan, Yok-Ai Que, Amy Tsurumi
Methods and assays relating to the treatment of infection
Patent Publication #:10550431. Filled: 11/03/2014; Date of Patent: February 4, 2020
As Principal Investigator, my colleagues and I developed technology directed to the prognosis, diagnosis, and treatment of infection following trauma, e.g., after burn injury.
Assignee: THE GENERAL HOSPITAL CORPORATION

Laurence Rahme, Shuangchun Yan, Yok-Ai Que, Amy Tsurumi
METHODS AND ASSAYS RELATING TO THE TREATMENT OF INFECTION
Patent Publication #: 20160237497. Filled: 11/03/2014; Issued Aug 18, 2016
As Principal Investigator, my colleagues and I developed predictive technology directed to the prognosis, diagnosis, and treatment of infection following trauma, e.g., after burn injury. We have developed a pipeline that can be used following trauma to stratify patients and identify individuals at high risk for infection days/ weeks before infection occurrence. The technology is based on transcriptome signatures and clinical characteristics and the use of bioinformatics tools. The biomarker “prognostic” panel developed can be used alone to provide personalized therapy and tailor proper therapy courses to increase patient outcomes, minimize antibiotic use, and decrease costs.

Assignee: THE GENERAL HOSPITAL CORPORATION

Derek Shieh Tan, Cheng Ji, Indrajeet Sharma, Debarshi Pratihar, James, P. Coleman, Everett, C. Pesci**, Laurence Rahme**
Patent Publication #: WO/2017/059446. Filled: 03.10.2016; Publication date: 06.04.2017
My colleagues and I developed methods for inhibiting anthranilate-CoA synthetase (PqsA). The compounds may interact with Pqstoto disrupt the activity of PqsA in converting anthranilic acid to anthranilyl-CoA. The compounds developed may inhibit anthranilate-CoA synthetase (PqsA) or inhibit PQS and HHQ biosynthesis in an infectious microorganism by contacting the microorganism with a compound or composition developed. Additionally, provided are methods for inhibiting anthranilate-CoA synthetase (PqsA) or inhibiting PQS and/or HHQ biosynthesis in an infectious microorganism in a subject by administering to the subject a compound or composition developed.
Assignee: THE GENERAL HOSPITAL CORPORATION

Laurence Rahme; Francois Lepine, Damien Maura; Carmela Napolitano, Antonio Felici; Michele Negri; Stefano Fontana; Daniele Andreotti
BROAD SPECTRUM ANTIVIRULENCE, ANTI-PERSISTENCE COMPOUNDS
Patent Publication #: WO/2019/079759
International Filing Date: 19.10.2018. Publication date: May 2021
Priority Date: 62/574,500: 19.10.2017; 62/663,105: 26.04.2018 US
In the present application, my colleagues and I provide malonamide compounds and derivatives thereof (e.g., N-aryl malonamides (NAM), acetamides, oxalamides, and the like) that are useful, for example, for the treatment of acute, chronic/persistent, and/or relapsing infections. Pharmaceutical compositions, methods of treating diseases (e.g., bacterial infections), and methods of reducing bacterial virulence are also provided.
Assignee: THE GENERAL HOSPITAL CORPORATION

Laurence Rahme, Amy Tsurumi, Pat Flaherty, Colleen Ryan
Multi-Biomarker Prediction Models for Multiple Infection Episodes Following Blunt Trauma.
Publication number: 20220412993. **Publication date:** December 29, 2022
Type: Application **Filed:** December 7, 2020
MGH 25737 USPTO # Filling Date: Dec 7, 2020; Appln No.: 17/781,646 Filing Date: 6/1/2022
Described herein are methods that use blood biomarkers to identify an increased risk of multiple independent infection episodes (MIIE) before clinical signs of infection appear. Thus, provided herein are methods for detecting or predicting risk of developing multiple independent infection episodes (MIIE) in a subject who has experienced blunt trauma.
Assignee: THE GENERAL HOSPITAL CORPORATION

2022-2024
Four additional Provisional Invention Disclosures are filled and are pending conversion.

Report of Scholarship

Publications
Peer-reviewed publications in print or other media
(* Rahme first author; ** Rahme lab trainees)

The listed publications collectively define a multidisciplinary research program that integrates molecular microbiology, chemical biology, genomics, immunology, and translational science to elucidate how quorum-sensing-regulated metabolites control bacterial virulence and reprogram

host responses to drive persistence. This body of work establishes a unified framework linking microbial communication, host immunometabolism and epigenetic regulation, and therapeutic innovation to address antibiotic-refractory infections.

Research investigations

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Thesis

1. **Rahme L.G**. Tn*5* Mutagenesis of *Rhizobium leguminosarum*: Isolation of Nod$^-$ and Fix$^-$ Mutants. M.Sc. [Dissertation]. Naples, Italy: University of Naples and Institute of Genetics and Biophysics C.N.R.;1985.

2. **Rahme L.G**. The *hrp* ("Harp") Genes of *Pseudomonas syringae* pv. *phaseolicola*: Organization, Transcription, Signaling and Role in the Plant-Bacterium Interactions. Ph.D. [Dissertation]. Berkeley (CA): University of California at Berkeley, Berkeley, CA;1991.

Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings (since 2012-2017 partial list Peer Reviewed)

1. ** Bandyopadhaya A, Kesawarni M, Que YA, and **Rahme LG**, "A bacterial excreted molecule modulates host response to promote tolerance to infection" Harvard surgery day symposium, Harvard Medical School, Boston 2012.

2. **Bandyopadhaya A, Kesawarni M, Que YA, and **Rahme LG**, "A bacterial excreted molecule modulates host response to promote tolerance to infection" 114th American Society of Microbiology meeting, Boston 2014.

3. ** Bandyopadhaya A, Diogo de A. Meireles and **Rahme LG**. "KerV, a novel virulence factor of *Pseudomonas aeruginosa* dampens host defense response by modulating the expression of the type VI secretion effector protein HcpC" 114th American Society of Microbiology meeting, Boston 2014.

4. **Starkey M, Lepine F, Maura D, Bandyopadhaya A, Lesic B, He J, Kitao-Ando T, Righi V, Milot S, Tzika A, Rahme LG. *Identification of Anti-Virulence Compounds that Disrupt Quorum-Sensing Regulated Acute and Persistent Pathogenicity.* 2014 Boston Bacterial Meeting, Boston, USA.

5. ** Bandyopadhaya A, Diogo de A. Meireles and **Rahme LG**. "KerV, a novel virulence factor of *Pseudomonas aeruginosa* dampens host defense response by modulating the expression of the type VI secretion effector protein HcpC" 67th Annual meeting of the MGH Scientific Advisory Committee, MGH, Boston 2014.

6. **Maura D, Starkey M, Lepine F, Bandyopadhaya A, Lesic B, He J, Kitao-Ando T, Righi V, Milot S, Tzika A, **Rahme LG**. *Identification of Anti-Virulence Compounds that Disrupt Quorum-Sensing Regulated Acute and Persistent Pathogenicity.* ICAAC 2014, Washington DC, USA, Sept. 2014.

7. **Bandyopadhaya A, Diogo de A. Meireles, **Rahme LG**. KerV A novel virulence factor of *Pseudomonas aeruginosa*, dampens host defense response by modulating the expression of the Type VI secretion effector protein HcpC. 2014 Boston Bacterial Meeting, Boston, USA.

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9. **Yan S, Tsurumi A, Que YA, Ryan CM, Bandyopadhaya A, Morgan AM, Flaherty PJ, Tompkins RG, **Rahme LG** Prediction of Multiple Infections After Severe Burn Trauma. Military Healthcare System Research Symposium 2014. Fort Lauderdale, FL, USA.

10. **Yan S, Tsurumi A, Que YA, Ryan CM, Bandyopadhaya A, Morgan AM, Flaherty PJ, Tompkins RG, **Rahme LG**. Identification of Patients at Increased Risk of Developing Severe Infections. MGH Clinical Research Day 2014. Boston, MA, USA.

11. **Bandyopadhaya A, Tsurumi A, Maura D, Jeffery K, **Rahme LG**. "Bacterial Quorum Sensing excreted molecules promote host tolerance through chromatin modifications" 14TH International Conference on the Chemistry of Antibiotics and other Bioactive Compounds, 2015

12. **Bandyopadhaya A, Tsurumi A, Maura D, Jeffery K, **Rahme LG**. "Bacterial Quorum Sensing excreted molecules Promote Host Tolerance Through chromatin modifications" Keystone Symposia on "Innate Immunity and Determinants of Microbial Pathogenesis" Olympic valley, USA, 2015.

13. **Bandyopadhaya A, Tsurumi A, Maura D, Jeffery K, **Rahme LG**. "Bacterial Quorum Sensing excreted molecules Promotes Host Tolerance Through chromatin modifications" 68th Annual meeting of the MGH Scientific Advisory Committee, MGH, Boston, 2015.

14. **Bandyopadhaya A, Tsurumi A, Maura D, Jeffery K, **Rahme LG**. "A Quorum Sensing Signal Promotes Host Tolerance Training Through Epigenetic

Reprogramming" Epigenetics Symposium, Harvard Medical School, Boston, USA Oct, 2015.

15. **Tsurumi A, Que YA, Yan S, Tompkins RG, **Rahme LG**, Ryan CM, "Do Standard Burn Mortality Formulae Work on a Population of Severely Burned Children and Adults?" 47 Annual American Burn Association Meeting, April 21-24, 2015, Chicago, IL.

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20. **Adiliaghdam F, Gharedaghi M, Yan S, Hamarneh SR, Morrison SA, **Rahme LG**, Hodin RA. Intestinal Alkaline Phosphatase Prevents Burn Induced Intestinal Permeability and Bacterial Translocation. Academic Surgical Congress 2015. Feb 3-5. Las Vegas, Nevada, USA

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22. ****Ballok, AE, **Rahme LG**. *Pseudomonas aeruginosa* Virulence Phenotypes are impacted by 2,4-Dihydroxyquinoline (DHQ), an Abundant Product of the PQS Operon. October 10, 2015. NACFC Phoenix, Arizona, USA.

23. ** Maura D., Starkey M, Lepine F, Bandyopadhaya A, Gharedaghi MH, Lesic B., He J, Kitao-Ando T, Massey G, Righi V, Milot S, Tzika A, **Rahme LG**. Identification of Anti-virulence Compounds that Disrupt Quorum-Sensing Acute and Persistent Pathogenicity in Multiple Bacterial Pathogens. 14th International Conference on the Chemistry of Antibiotics and other Bioactive Compounds (ICCA), Galveston, TX, USA, Oct. 2015

24. **Yan S, Tsurumi A, Que YA, Ryan CM, Bandyopadhaya A, Morgan AM, Flaherty PJ, Tompkins RG, **Rahme LG**. Early Prediction of Severe Infections in Patients. Boston-area Antimicrobial Research Network Symposium, 2015. Broad Institute, Boston, MA, USA.

25. **Bandyopadhaya A, Tsurumi A, Maura D, Jeffery K, **Rahme LG**. "Bacterial Quorum Sensing excreted molecules promote host tolerance through chromatin modifications" 14TH International Conference on the Chemistry of Antibiotics and other Bioactive Compounds, October 13-16 2015. Galveston Island, Texas, USA.

26. **Kitao-Ando T, **Rahme LG**. Synthetic Inhibition of *Pseudomonas aeruginosa* cell-cell communication toward the development of next-generation antimicrobial drug. BMB2015 Biochemistry and Molecular Biology, Kobe Port Island, Japan, Dec 2015.

27. **Bandyopadhaya A, Tsurumi A, Maura D, Jeffery K, **Rahme LG**. "Bacterial quorum sensing excreted molecule promotes host tolerance training via chromatin modification" 8th Young Investigator Meeting, Manesor, India, Feb, 2016. (Poster & Oral presentation, Invited).

28. **Bandyopadhaya A, Tsurumi A, Maura D, Jeffery K, **Rahme LG**. "A Quorum Sensing Signal Promotes Host Tolerance Training Through Chromatin Modifications" 2016 Research Fellows Poster Celebration, Massachusetts General Hospital, May, 2016.

29. Rahme LG. Anti-Virulence Strategies & The Politics of Quorum Sensing Molecules. Perlman Symposium. Wisconsin, USA. May 2016.

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33. Rubio A, Antolini M, Benetta E, Costantini C, Felici A, Fontana S, **Rahme LG**, Teague J, P Thommes P, P Turnpenny P, Warn P, Parr T, Pucci M, Zahler B. Assessing Target Engagement *In Vitro* and *In Vivo* of MvfR inhibitors in *Pseudomonas aeruginosa.* Froniers in Antibacterial Drug Discovery, Sept 14-15, 2016, Stockholm, Sweden.

34. ****Ballok, AE, **Rahme LG**. In Vitro Assessment of a Novel Antivirulence Compound for Treatment of *Pseudomonas aeruginosa* in Cystic Fibrosis". Poster Presentation. NACFC Orlando, Florida, USA. October 2016

35. Diogo de A. Meireles [1], Apidianakis Y, do Nascimento AP, He J, **Rahme LG**, Baldini RL. Altered levels of the housekeeping protein DnaQ affect multiple traits in *Pseudomonas aeruginosa*. ICAAC/ASM Annual Meeting, June, 2016 Boston, MA. USA.

36. **Bandyopadhaya A, Tsurumi A, Maura D, Jeffery K, **Rahme LG**. "A Quorum Sensing Signal Promotes Host Tolerance Training Through Chromatin Modifications" Epigenetics Symposium, Harvard Medical School, Boston, USA Oct, 2016.

37. **Maura D, Starkey M, Lepine F, Bandyopadhaya A, Lesic B, He J, Kitao-Ando T, Righi V, Tzika A. **Rahme LG** Bacterial Anti-Virulence Strategy as an alternative to antibiotics. Alternatives to Antibiotics, Dec 12, 2016. Paris, France.

38. **Adiliaghdam F., Kuehn F, Najibi M, Tsurumi A, Ramirez J, Munoz A, Lie E, Hosa R, Vasan R, Hamarmeh S, Rahme LG, Hodin R. An oral enzyme supplement to prevent the aging process., Harvard Surgery Research Day Symposium, Harvard Medical School, May 2017, Boston, MA.

39. Felici A, Antonili M, Estevez VG**,** Fontana S, Pucci M, **Rahme LG,** Feriani D, Andreaotti D. Rational design, synthesis and in vitro characterization of novel potent inhibitors of Pseudomonas aeruginosa multivirulence factor regulator (MvfR). American Society for Microbiology- ASM-Microbe 2017. June 2017, New Orleans.

40. **Maura D, Drees S, Bandyopadhaya A, Kitao T, Negri M, Milot S, Deziel E, Zahler R, Pucci M, Felici A, Fetzner S, Lépine F, **Rahme LG.** Small Molecules targeting the Pseudomonas aeruginosa MvfR Quorum Sensing System: Discovery of Dual Target Inhibitors and Potentiation of Antibiotic-Mediated Biofilm Disruption. Re-Entering Antibacterial Discovery and Development Summit. Oct 2017, Boston, MA

41. **Ballok A, Lanter BB, Hurley BP, and **Rahme LG.** Small Molecule Inhibitors of the MvfR Quorum Sensing Pathway Reduce Neutrophil Recruitment and Cytotoxicity of *Pseudomonas aeruginosa* in Mono and Polymicrobial Lung Infection Models. Antinicrobials and Resistance: Opportunities and Challenges. Keystone Symposia Oct 2017, Santa Fe, New Mexico.

42. Adiliaghdam F*, Almpani M*, Gharedaghi MH, Najibi M, Hodin RA, **Rahme LG.** Targeting bacterial quorum sensing to improve intestinal barrier function following burn - site infection. Abstract for poster presentation at the "Thinking Global 2018" forum of the Broad Institute.

43. Adiliaghdam F*, Almpani M*, Gharedaghi MH, Najibi M, Hodin RA, **Rahme LG.** Targeting bacterial quorum sensing to improve intestinal barrier function following burn - site infection. Peer-reviewed for poster presentation at the "Abstract for poster presentation at the 2018 Military Health System Research Symposium.

44. **Tsurumi A, Que YA, Ryan CM, Flaherty PJ, Tompkins RG, Almpani M, Dhole YV, Goodfield LF, and **Rahme LG.** Developing a Blood Biomarker Model for Predicting Multiple Infection Episodes Following Blunt Trauma. Abstract for poster presentation at the New England Surgical Society 2018 Annual Meeting.

45. **Almpani M, Tsurumi A, Peponis T, Dhole YV, Goodfield LF, Tompkins RG, **Rahme LG.** Do Trauma Severity Scores Successfully Predict Hypersusceptibility To Infections In Trauma Patients? Abstract for poster presentation at the New England Surgical Society 2018 Annual Meeting.

46. ** Almpani M, Adiliaghdam F, Hodin RA, Rahme LG. Novel anti-infectives against intestinal barrier derangement following burn-site infection. Abstract for poster presentation at the American Burn Association 2019 Annual Meeting. Best Poster Presentation Award.

Narrative Report

My work is driven by a translational ethos: to apply fundamental scientific discoveries to develop tangible therapeutic solutions. I draw on a broad interdisciplinary background spanning molecular biology, biochemistry, molecular genetics, immunology, chemistry, bioinformatics, statistics, microbiology, plant pathology, and clinical research. This diverse expertise enables me to tackle a wide array of high-impact research challenges and guide collaborative projects at the intersections of biology, engineering, medicine, and technology.

I am committed to a One Health approach, which recognizes the interconnectedness of human, animal, and environmental health. My lab investigates molecular mechanisms underpinning host-pathogen interactions in vertebrate and non-vertebrate models to develop host-protective interventions against human, animal, and plant infections.

We have developed innovative strategies to combat bacterial virulence in stubborn microbes and, through drug discovery, limit antibiotic resistance and tolerance development. Major lab projects focus on regulatory systems that govern bacterial virulence and host responses to infection and trauma. Emphasis is given to developing novel antibacterial therapeutics, dissecting complex bacterial molecular mechanisms that govern virulence, and deciphering the mode of action of bacterial-secreted small molecules in mono- and polymicrobial settings in the inter-kingdom modulation of host metabolic and immune responses. Moreover, on the clinical site, a significant amount of effort is put into developing novel preventive and therapeutic personalized interventions by developing novel tools and prediction models for identifying novel host targets of resilience or susceptibility to infection, trauma, and neurodegeneration.

Several seminal publications underscore our discoveries of novel bacterial mechanisms and pathways that govern virulence and chronic infections; processes of gene regulatory networks involved in the host response to infection, injury, and host susceptibility or resilience to infection; and infection-cancer relationships.

Key research directions in my lab include:

- Regulatory systems governing bacterial virulence
- Novel anti-infective and anti-virulence therapeutics
- Host responses to infection and trauma
- Inter-kingdom signaling and modulation of immune/metabolic responses
- Predictive biomarkers of infection susceptibility
- Neurodegeneration and neural immunity

Our work is detailed below across six major thematic areas:

I. Host-Pathogen Interactions in Model Systems

We developed non-vertebrate and vertebrate infection models to study host-pathogen interactions of the nosocomial and recalcitrant bacterial pathogen *Pseudomonas aeruginosa*. These models allow real-time investigation of bacterial pathogenesis and host responses.

Our discovery that *P. aeruginosa* can cause disease in both plants and animals using a shared subset of virulence factors (3) allowed us to develop a series of non-vertebrate models of infection (3, 4, 6, 7, 8, 10, 15-17, 51, 62, 87). These models permit *in vivo* and a high-throughput manner identification and interrogation of virulence functions and the study of immunomodulatory and metabolic effects promoted by virulence factors. Moreover, they permit high-throughput assessment of therapeutic compounds' efficacy and additional aspects of host-pathogen interactions in a dynamic and antagonistic setting. Our studies employing the fruit fly *Drosophila melanogaster* as a model host provided insights into bacterial pathogenesis significant host defense players. They revealed previously unknown genes responsive to bacterial infection (20, 24*,* 36, 51*,* 72*,* to mention a few). Our work significantly contributes to signatures of early host responses characterizing susceptible or non-susceptible interactions. In addition, we developed clinically relevant murine models of infection to elucidate the antagonistic interplay between host and pathogen. These models permit the identification of specific bacterial virulence and host functions, the interrogation of immuno-inflammatory and metabolic effects elicited *in vivo,* and the testing of the efficacy of novel anti-infectives in acute, relapsing, and chronic infections, a significant aspect of our program.

Our pioneer strategy using non-vertebrate hosts to identify novel bacterial virulence factors relevant to human infections has been highlighted over the years in several journals. An impactful article on this initiative was published in the *Science* journal in 2000 DOI: 10.1126/science.290.5500.2245

II. Discovery of Novel Bacterial Virulence Mechanisms

Our model systems enabled the identification of new **virulence factors** in *P. aeruginosa,* including two **pathogenicity islands** and the **multiple virulence factor regulator (MvfR)**—a global transcriptional regulator of quorum sensing (QS) and biofilm formation (Refs #3, 4, 7, 8, 10,11, 12, 19, 20, 24, 124). We identify the Multiple virulence factor Regulator, MvfR, also known as PqsR. Our work uncovered several **MvfR-regulated low molecular weight**

molecules that impact biofilm, antibiotic tolerance, programmed cell death, and inter-kingdom immune modulation (18,21,33, 83, 93 to mention a few). The identification of MvfR (#4 *PNAS*, #11 *PNAS*) led us to discover a novel quorum sensing (QS) system (#18 *PNAS*; *#22 Mol. Microbiol*). Bacteria utilize QS to synchronize virulence functions and achieve cell-to-cell communication at inter- and intra-species levels. Our studies revealed novel critical insights into this factor's role and its regulon in acute and chronic/persistent infections. They opened the way for studying and inhibiting antibiotic tolerance, a currently untreatable phenomenon.

We elucidated the physiological role of several QS secreted molecules and revealed a novel **bacterial programmed cell death system** (93), drawing mechanistic parallels to eukaryotic apoptosis and offering new therapeutic targets. Moreover, through the dissection of complex bacterial molecular mechanisms that govern virulence, we are deciphering the mode of action of the MvfR/pqsABCDE system in mono- and polymicrobial settings and in the modulation of host metabolic and immune responses (64,67,75, 84,86,87,98, 125, 126, 132 to name a few).

III. Anti-Virulence Therapeutics

Building on our MvfR discoveries, we pioneered **non-ligand-based MvfR anti-virulence agents** that disarm pathogens without killing them, minimizing selective pressure and preserving the microbiome, an extremely promising concept in the context of many human pathologies in which patients already have a disturbed microbiome. Our agents mitigate acute and persistent P. aeruginosa infections, targeting biofilm and antibiotic-tolerant/persister cell formation, addressing key gaps in combating **multi-drug-resistant (MDR) bacteria** (35,43, 88, 104,122, 115, 122).

This approach laid the groundwork for forming **Spero Therapeutics**, which is focused on developing next-generation anti-infectives. Unlike conventional antibiotics, our strategy targets **pathogenicity rather than viability**, holding promise for broad-spectrum application and enhanced resistance management.

IV. Immune and Metabolic Host Responses

We investigate host responses to trauma and infection, with an emphasis on **immuno-inflammatory and metabolic reprogramming (**24-27, 32, 36, 38, 41, 51, 66, 72, 81, 94, 109, to name a few Notably, we identified a quorum-sensing molecule, **2'-aminoacetophenone** that modulates host inflammation and metabolism via **epigenetic mechanisms**, representing the first inter-kingdom quorum-sensing signaling molecule with such activity (75, 81, 98, 103, 123, 126).

In collaboration with clinical teams, we have studied trauma and burn cohorts to uncover molecular signatures of infection susceptibility and resilience, resulting in multiple **seminal publications** and translational insights (ref# 25, 37, 40, 42, 53, 54,55, 60,61,63, 68, 76, 78, 89, 90, 91, 95, 110,114, 116, 123 to name a few).

V. Tools & Predictive Biomarkers for Infection Susceptibility

The increasing prevalence of antimicrobial resistance necessitates new infection-prevention strategies. Moreover, different patients can experience varied infection outcomes despite similar injury severity, arguing the importance of considering each patient's underlying susceptibility and elucidating relevant molecular mechanisms. Thus, methods to identify specific patients with

increased risk of infection outcomes during recovery could be advantageous for ensuring the timely and appropriate delivery of preventative and therapeutic measures.

We led the development of the **Infection Susceptibility Risk Prognostic Biomarkers (ISRPB)**—a first-in-class RNA-based predictive panel for identifying patients at high risk for multiple infections **days before clinical signs emerge** (89, 91, 95, 114, 116, 123, 129). This first-in-class predictive multi-biomarker panel is based on retrospective analysis of RNA gene expression profiles from patients' blood.

This **precision medicine** approach enables early, targeted interventions and reduces unnecessary antibiotic use, helping to curb resistance. It differs from existing approaches and technologies focusing on rapid pathogen or sepsis detection *after* infections are established. The ISRPB panel marks a **paradigm shift** in infection prevention and personalized care, with applications extending beyond trauma patients.

VI. Neurodegeneration and Innate Neural Immunity

We are exploring the **role of innate immunity in neurodegeneration** in a novel **Drosophila model we developed**. The genetically tractable *Drosophila melanogaster* model of chronic neuroinflammation entailed a knocking down (KD) of *Cactus*, the fly orthologue of the mammalian *IκB, specifically in the* dopaminergic neurons. This work focuses on the impact of chronic NF-κB activation in dopaminergic neurons and aims to unravel whether neuroinflammation is a cause or consequence of degeneration. The goal is to identify early **biomarkers** and new therapeutic targets for neurodegenerative diseases.

In summary, our overall interdisciplinary approaches against bacterial infections remain fundamentally different from the existing approaches. In 2017, I was honored to be elected as a Fellow of the American Academy of Microbiology (ASM). In 2020, I received the prestigious Massachusetts General Hospital Scholar Award. The Massachusetts General Hospital Research Scholar Award provides unrestricted funding for forward-thinking researchers to take their work into new and uncharted territories.

Teaching/Mentoring

I am committed to forward-thinking interdisciplinary research and teaching programs on basic science and the translation of fundamental discoveries into novel therapeutic interventions.

I taught Microbiology and Immunology courses to medical students at Harvard Medical School (HMS) in 2006-2007, 2019, and 2020. Moreover, as a visiting Professor, I taught graduate and undergraduate students at the Department of Microbiology, School of Biological Sciences, Naples, Italy, in 2012, and the Department of Fundamental Microbiology, University of Lausanne, Switzerland, in 2015. Also, I gave seminars locally, nationally, and internationally.

I have trained and mentored over 100 post-doctoral fellows, graduate and undergraduate students, residents, and junior faculty in various capacities. The Surgical Research Laboratory team includes one Assistant Professor and four post-doctoral fellows. I have served as a senior MSc. thesis advisor for eight graduate students who conducted research in my laboratory. Advisor to seven visiting Ph.D. candidates who also performed part of the Ph.D. research project in my laboratory, and advisor to more than twenty summer high school interns and fifteen summer undergraduate interns. Many of my former trainees have become Assistant

Professors, while others have pursued careers in clinical practice or industry. I am deeply committed to guiding my trainees toward successful and independent careers in academic research.

In 2012 and 2013, I mentored junior faculty as part of the MGH Faculty Office Mentoring Program. Since 2018, I have been a member of the Surgical Research Council, Department of Surgery, MGH. Between 2018 and 2000, I served as Co-Chair of The Research Faculty and Postdoctoral Fellow Career Development Committee of the Department of Surgery, and also, in 2019-2020, as a mentor of a visiting Assistant Professor sponsored by the CAPES Harvard/Brazil Program. In addition, I served as a faculty mentor to Ph.D. or M.D. fellows of The Hellenic Bioscientific Association of the USA by providing guidance and career advice in biomedical sciences.

2018, I was recognized as *a distinguished mentor* with a John T. Potts Jr., MD, MGH Faculty Mentoring Award. I was nominated for the Excellence in Mentoring Award at MGH in 2014, 2016-2020, and 2022. In addition, I received HMS nominations in 2013, 2014, and 2015-2021.

Administration & Committees

Since 1997, as the Director of the Molecular Surgical Laboratory (MSL) in the Department of Surgery at MGH, I have overseen all MSL's administrative, academic, and research-related responsibilities and activities. The Research Excellence Motto of the MSL is Synergy, Education, Mentoring, Innovation, Value (SEMIV). As a director and senior faculty member of the Department of Surgery, MGH, I have directed more than 100 Ph.D. and MD trainees and faculty in this position. In this capacity, I also support and guide junior faculty and trainees in grant preparation and scientific writing. I also train doctoral, post-doctoral, medical students, medical residents, and junior faculty. Under my supervision, the MSL also manages animal, human, and biosafety protocols.

As a Principal Investigator (PI) and Director of MSL, I have obtained and administered ~ $23,000,000 of direct costs in research funding. In addition, as Co-PI, subcontract PI, or Co-Investigator, I have received an additional $4,800,000 of direct cost in research funding, and as a Research Fellowship sponsor, $1,500,000. Moreover, I have been instrumental in establishing the collaborative efforts between MGH and Stanford University that resulted in a ten-year NIH grant award U54 GM62119 Inflammation and the Host Response to Injury, which received $33,845,040 in direct costs.

During my tenure as a Co-Chair of The Research Faculty and Postdoctoral Fellow on the Career Development Committee of the Surgical Research Council of the Department of Surgery at MGH, I have mentored faculty and post-doctoral fellows in addition to coordinating, invigorating, and reinforcing research activities, cultivating and maintaining a healthy research environment, support women and promote diversity, equity, and inclusion. Furthermore, I advocated the sharing of resources within the division and department to inspire and motivate collaborations, promote progress and innovation, and establish new synergies between surgeon-scientists and basic research scientists.

I have served and continue to serve on several committees. At MGH, as a member of the Surgical Research Council at the Dept. of Surgery, I served on the promotion, scholarship, and award committee. These committees review and recommend to the Chair regarding promotions,

appointments, or awarding funding to junior faculty. In addition, at MGH, I served as a member of the senior peer-mentoring women's group faculty at the Center for Faculty Development.

At Harvard Medical School (HMS), since 2019, I have served as a member of the Dean's Award Committee, and in 2025, I served as the Chair of this committee. Between 09/2019-06/2022, I served as a member of the Standing Committee on Promotions, Reappointments, and Appointments of HMS Faculty, and 09/2022-06/2023, I served as a member of the Subcommittee of Professors (SOP) and ad-hoc Chair of SOP. SOP is a standing committee of the Dean, comprised of professors at HMS/HSDM. The SOP reviews and recommends to the Dean all appointments to the rank of Professor.

Since 2012, I have been a Joint Committee on the Status of Women (JCSW) member. JCSW is an administrative committee of the Dean of the Faculty of Medicine at HMS, representing faculty, staff, residents, and students. In 2018, I served as a Professional Equity Committee subcommittee member. On 09/2022, I was elected Faculty Vice Co-Chair to the Leadership Council of JCSW at HMS. During 2023-2024, I served as Faculty Co-Chair along with a Staff Co-Chair of this Leadership Council, and currently, I'm serving as an active past Faculty Co-Chair and a member of its strategic planning committee.