

## BIOGRAPHICAL SKETCH

<b>NAME</b> Paul Forsythe	<b>POSITION TITLE</b> Associate Professor		
<i>EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Queen's University Belfast, U.K.	BSc (Hons)	07/1993	Biochemistry
Queen's University Belfast, U.K.	MSc	09/1994	Laboratory Medicine
Queen's University Belfast, U.K.	PhD	01/1998	Immunopharmacology

### A. Positions and Honors.

<b><u>Positions held</u></b>	
1999-2003	Post-Doctoral Fellow, Pulmonary Research Group, Department of Medicine, University of Alberta, Edmonton, Alberta, Canada
2003-2005	Post-Doctoral Fellow, The Brain-Body Institute St Joseph's Healthcare and Department of Pathology and Molecular Medicine, McMaster University and Hamilton, Ontario, Canada
2005-2008	Research Associate, The Brain-Body Institute, McMaster University and St. Joseph's Healthcare, Hamilton, Ontario, Canada
2008-2014	Assistant Professor (CLA), Department of Medicine, McMaster University
2014-2019	Assistant Professor, Department of Medicine, Division of Respiriology, McMaster University
2019-	Associate Professor, Division of Respiriology, McMaster University
<b><u>Other Experience and Professional Memberships</u></b>	
2019-present	Associate Editor, Gut Microbiome
2016-Present	International Society of Microbiota: Scientific Advisory Board Member
2015-Present	International Probiotic Association (IPA): Scientific Advisory Board Member
2010-present	Member, Collegium Internationale Allergologicum
2020	NASA Space Biology Integrative Physiology Panel Chair
2019	NASA Space Biology Integrative Physiology Panel Member
2017-2019	Canadian Institutes for Health Research, Respiratory Systems Panel Member
2017	Crohn's & Colitis Foundation (US), Environmental Triggers Panel Member
2017	Irish Science Foundation (ISF), Career Development Award Panel Member
2016	National Institutes of Health (USA), Allergic Diseases Cooperative Research Centers (U19), Review Panel Member
<b><u>Honors and awards</u></b>	
2017 Most significant research contribution: 7 <sup>th</sup> World Congress on Targeting the Microbiota.	
2016 Biogaia-Ivan Casas Probiotics Award.	
2012 Department of Medicine Career Award, McMaster University.	

### B. Selected peer-reviewed publications (in chronological order).

Full publication list available <https://www.ncbi.nlm.nih.gov/myncbi/paul.forsythe.1/bibliography/public/>  
**Selected publications (of 32 in past 5 years, 78 total)**

1. Liu Y, Steinhausen K, Bharwani A, Mian MF, McVey Neufeld KA, **Forsythe P**. Increased persistence of avoidance behaviour and social deficits with *L.rhamnosus* JB-1 or selective serotonin reuptake inhibitor treatment following social defeat. *Sci Rep*. 2020;10(1):13485. PMID: 32778662
2. Kayyal M, Javkar T, Firoz Mian M, Binyamin D, Koren O, McVey Neufeld KA, **Forsythe P**. Sex dependent effects of post-natal penicillin on brain, behavior and immune regulation are prevented by concurrent probiotic treatment. *Sci Rep*. 2020;10(1):10318. PMID: 3258738
3. Liu Y, Firoz Mian M, McVey Neufeld KA, **Forsythe P**. CD4(+)CD25(+) T Cells are Essential for Behavioral Effects of *Lactobacillus rhamnosus* JB-1 in Male BALB/c mice. *Brain Behav Immun*. 2020; 88:451-460. PubMed PMID: 32276029
4. Bharwani A, West C, Champagne-Jorgensen K, McVey Neufeld KA, Ruberto J, Kunze WA, Bienenstock J, **Forsythe P**. The vagus nerve is necessary for the rapid and widespread neuronal activation in the brain following oral administration of psychoactive bacteria. *Neuropharmacology*. 2020 *Neuropharmacology*. 2020;170:108067. PubMed PMID: 32224131.
5. McVey Neufeld KA, Bienenstock J, Bharwani A, Champagne-Jorgensen K, Mao Y, West C, Liu Y, Surette MG, Kunze W, **Forsythe P**. Oral selective serotonin reuptake inhibitors activate vagus nerve dependent gut-brain signalling. *Sci Rep*. 2019;9(1):14290. PubMed Central PMCID: PMC6776512
6. Shimbori C, Upagupta C, Bellaye PS, Ayaub EA, Sato S, Yanagihara T, Zhou Q, Ognjanovic A, Ask K, Gaudie J, **Forsythe P**, Kolb MRJ. Mechanical stress-induced mast cell degranulation activates TGF- $\beta$ 1 signaling pathway in pulmonary fibrosis. *Thorax*. 2019 ;74(5):455-465. PMID: 30808717
7. **Forsythe P**. Mast Cells in Neuroimmune Interactions. *Trends Neurosci*. 2019 Jan;42(1):43-55. PubMed PMID: 30293752.
8. Zehra S, Khambati I, Vierhout M, Mian MF, Buck R, **Forsythe P**. Human Milk Oligosaccharides Attenuate Antigen-Antibody Complex Induced Chemokine Release from Human Intestinal Epithelial Cell Lines. *J Food Sci*. 2018 Feb;83(2):499-508. PubMed PMID: 29377120.
9. Kapadia M, Mian MF, Michalski B, Azam AB, Ma D, Salwierz P, Christopher A, Rosa E, Zovkic IB, **Forsythe P**, Fahnestock M, Sakic B. Sex-Dependent Differences in Spontaneous Autoimmunity in Adult 3xTg-AD Mice. *J Alzheimers Dis*. 2018;63(3):1191-1205.. PMID: 29710702
10. Bienenstock J, Kunze WA, **Forsythe P**. Disruptive physiology: olfaction and the microbiome-gut-brain axis. *Biol Rev Camb Philos Soc*. 2018 Feb;93(1):390-403. PubMed PMID: 28675687.
11. Leclercq S, Mian FM, Stanisz AM, Bindels LB, Cambier E, Ben-Amram H, Koren O, **Forsythe P**, Bienenstock J. Low-dose penicillin in early life induces long-term changes in murine gut microbiota, brain cytokines and behavior. *Nat Commun*. 2017 Apr 4;8:15062. PubMed PMID: 28375200.
12. Bharwani A, Mian MF, Surette MG, Bienenstock J, **Forsythe P**. Oral treatment with *Lactobacillus rhamnosus* attenuates behavioural deficits and immune changes in chronic social stress. *BMC Med*. 2017 Jan 11;15(1):7. PubMed PMID: 28073366.
13. Delungahawatta T, Amin JY, Stanisz AM, Bienenstock J, **Forsythe P**, Kunze WA. Antibiotic Driven Changes in Gut Motility Suggest Direct Modulation of Enteric Nervous System. *Front Neurosci*. 2017;11:588. PMID: 29104530
14. Khambati I, Han S, Pijnenburg D, Jang H, **Forsythe P**. The bacterial quorum-sensing molecule, N-3-oxo-dodecanoyl-L-homoserine lactone, inhibits mediator release and chemotaxis of murine mast cells. *Inflamm Res*. 2017 Mar;66(3):259-268. PubMed PMID:27896412.
15. Bharwani A, Mian MF, Foster JA, Surette MG, Bienenstock J, **Forsythe P**. Structural & functional consequences of chronic psychosocial stress on the microbiome & host. *Psychoneuroendocrinology*. 2016 Jan;63:217-27. PubMed PMID: 26479188.
16. Castillo-Courtade L, Han S, Lee S, Mian FM, Buck R, **Forsythe P**. Attenuation of food allergy symptoms following treatment with human milk oligosaccharides in a mouse model. *Allergy*. 2015 Sep;70(9):1091-102 PubMed PMID: 2596666

### C. Research Support.

## **Ongoing**

### **Weston Foundation Microbiome Initiative 2019-2021**

Title: Enhancing the effectiveness of probiotic treatment in allergy

Role: Co- Principal Investigator

Goal: Assess the effects of probiotic derived microvesicles in mouse models of food allergy and asthma

### **Ontario Ministry of Agriculture, Food and Rural Affairs (OMAFRA): 2016-2021**

Title: Understanding feather pecking in laying hens: The microbiome-gut-brain-axis

Role: Co-Principal Investigator

Goal: To understand the mechanisms underlying feather pecking behavior in laying hens.

### **Natural Sciences and Engineering Research Council of Canada (NSERC): 2016-2022**

Title: Inter-kingdom signalling: Modulation of mast cells by commensal bacteria.

Role: Principal Investigator

Goal: To determine the mechanisms underlying the ability of commensal bacteria to modulate mast cell activity.

### **Canadian Institutes of Health Research (CIHR): 2016-2021**

Title: Evaluation of Brain Metabolites Following Microbiotic Diet. Quantitative Assessment of glutamate, GABA and serotonin using Magnetic Resonance Spectroscopy and Chemical Exchange Saturation Transfer.

Role: Co-Investigator

Goal: To identify probiotic effects on brain chemistry.

## **Completed**

### **Weston Foundation Microbiome Initiative 2017-2019**

Title: "Towards a clinical trial of microbiome-based therapies for post-traumatic stress disorder"

Role: Principal Investigator

Goal: Assess the effects of probiotics and prebiotics on the immune and nervous system in a mouse model of PTSD.

### **International Development Research Centre (IDRC): 2015-2019**

Joint Israel-Canada Research Program

Title: The Effect of Antibiotics in Early-life on Brain Function and Behaviour

Role: Principal Investigator

Goal: To understand mechanisms underlying the effect of antibiotic treatment on brain function.

### **Office of Naval Research (ONR): 2015-2019**

Title: Gut Microbes: Positive Effects on Negative Responses to Environmental Stressors

Role: Co-Principal Investigator

Goal: To identify the role of the gut microbiota in modulating stress responses and the associated mechanisms of communication between gut microbes and the central nervous system.

My research falls within the field of psychoneuroimmunology, utilizing multi-disciplinary approaches to address cross-talk between components of the nervous and immune systems, and how such communication may influence the development of diverse pathophysiological responses such as inflammation, allergic disease and mood/behavioral disorders. To date I have >8400 citations and an H-factor of 41.

### 1. Gut Microbes, Allergy & Asthma

My early independent research was focused on obtaining an understanding of the mechanisms underlying the protective effects of gut microbes and their products in allergy and asthma. This work led to the first report that oral treatment with a probiotic organism can attenuate major characteristics of an asthmatic response, including airway eosinophilia, local cytokine responses, and hyper-responsiveness to methacholine. (Forsythe P, Inman MD, Bienenstock J. Oral treatment with live *Lactobacillus reuteri* inhibits the allergic airway response in mice. *Am J Respir Crit Care Med* 2007;175:561-569). I then went on to identify the important role of T regulatory cells in mediating the anti-inflammatory effects of the bacteria (Karimi K, Inman MD, Bienenstock J, Forsythe P. *Lactobacillus reuteri*-induced regulatory T cells protect against an allergic airway response in mice. *Am J Respir Crit Care Med* 2009;179:186-193). More detailed investigation determined the contribution of regulatory dendritic cells and mast cell stabilization to the beneficial effect of specific gut microbes in allergic disease (Karimi K, Kandiah N, Chau J, Bienenstock J, Forsythe P. A *Lactobacillus rhamnosus* Strain Induces a Heme Oxygenase Dependent Increase in Foxp3+ Regulatory T Cells. *PLoS One* 2012;7:e47556; Forsythe P, Wang B, Khambati I, Kunze WA. Systemic Effects of Ingested *Lactobacillus Rhamnosus*: Inhibition of Mast Cell Membrane Potassium (IKCa) Current and Degranulation. *PLoS One* 2012;7:e41234). My expertise in the area of gut microbes and allergic disease has been recognized by invitations to give "State of the Art" and plenary presentations at a number of international meetings as well as single author commentaries on this topic. I am also a member of the scientific advisory board of the International Probiotic Association and the International Society of Microbiota.

### 2. Microbe-Gut-Brain axis

A more recent focus of my research has been on neuroactive and immunomodulatory properties of gut bacteria with the aims of understanding the relationship between the gut microbiota and changes in brain and behaviour in response to stressors. Here I initially investigated the role of the vagus nerve, responding to microbial cues that lead to afferent signaling to the brain with neurochemical and behavioral consequences. Development of this work led to joint primary authorship of the first report demonstrating that specific non-pathogenic microbes could modulate brain chemistry and behavior in normal mice and did so through vagus mediated signaling between the gut and the brain. (Bravo JA\*, Forsythe P\*, Chew MV, Escaravage E, Savignac HM, Dinan TG, Bienenstock J, Cryan JF. Ingestion of *Lactobacillus* strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. *Proc Natl Acad Sci U S A* 2011;108:16050-16055). This study has been cited >1400 times to date (Google Scholar). I have further expanded on this work investigating the relationship between gut microbes, the immune system and stress (Bharwani A, Mian MF, Foster JA, Surette MG, Bienenstock J, Forsythe P. Structural & functional consequences of chronic psychosocial stress on the microbiome & host. *Psychoneuroendocrinology*. 2016;63:217-27) and investigating microbe based strategies to attenuate the detrimental effects of stress (Bharwani A, Mian MF, Surette MG, Bienenstock J, Forsythe P. Oral treatment with *Lactobacillus rhamnosus* attenuates behavioural deficits and immune changes in chronic social stress. *BMC Med*. 2017;15(1):7). This work has led to my development of a research program, funded by the Weston Foundation, to establish microbe based strategies for the treatment of post-traumatic stress disorder. My expertise in this area of gut-brain signaling has been recognized by invitations to give presentations, including plenary, "State of the Art" and keynote addresses, on the topic at international meetings (20 in the last 5 years) and the publication of invited commentaries. Two of my publications were selected for the Microbiota-gut-brain axis edition of *Nature Collections* (Gut microbiota: Microbiota and behaviour: visiting the sins of the mother. *Nat Rev Gastroenterol Hepatol*. 2016;13:502-4 and Low-dose penicillin in early life induces long-term changes in murine gut microbiota, brain cytokines and behavior *Nat Commun*. 2017;8:15062.).