BIOGRAPHICAL SKETCH

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NAME: Young, Vincent B.

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

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology, Cambridge, MA	BS	06/1985	Life Sciences
Stanford University, Stanford, CA	MD	06/1992	
Stanford University, Stanford, CA	PhD	06/1992	Micro & Immunology
Massachusetts General Hospital, Boston, MA	Resident	06/1998	Medicine/ Infectious Diseases
Massachusetts Institute of Technology, Cambridge, MA	Postdoc	09/2000	

A. Personal Statement

For over 20 years my research and clinical interest has involved studying the pathogenesis of enteric bacteria. I have active research projects studying this pathogenesis of *C. difficile* in humans and in murine models of infection. I was an active participant in the Human Microbiome Project, and have been at the interface of classic microbial ecology and bacterial pathogenesis. For the past 15 years I have been conducting research that investigates the role of complex microbial communities in the health and disease of their mammalian hosts. I have extensive experience in managing and participating in team science collaborations.

Ongoing and completed projects I would like to highlight include:
U01 AI124255: Systems biology of *Clostridium difficile* infection
Young, Vincent Bensan (contact PI); Schloss, Patrick D, MPI
03/2016-02/2021

U19 AI116482: Engineered human intestinal organoids: a modular system to model enteric disease
Young, Vincent Bensan (contact PI) ; Spence, Jason; Takayama, Shuichi; Wobus, Christiane E, MPI
03/2015-02/2021

R21 AI120599: Host and Microbial Biomarkers Related to the Development of Complicated *Clostridium difficile* Infection
Young, Vincent Bensan, PI
07/2015-06/2018

U54 000481/U54 000607: Microbiome and Clinical Predictors of Enteric MDRO Acquisition (MAriMbA) CDC EpiCenters Program
Hayden, Mary (contact PI); **Young, Vincent Bensan**, site PI

08/2016-06/2020 and 06/2021-05/2026

R01 AI162787: The microbiome and aging in *Clostridioides difficile* infection
Young, Vincent Bensan (contact PI); Yung, Raymond L, MPI
04/2022-03/2027

1. Abernathy-Close L, Barron MR, George JM, Dieterle MG, Vendrov KC, Bergin IL, **Young VB**. Intestinal inflammation and altered gut microbiota associated with inflammatory bowel disease render mice susceptible to *Clostridioides difficile* colonization and infection. mBio. 2021 Jun 29;12(3):e0273320. PubMed Central PMCID: PMC8262858.
2. Barron MR, Sovacool KL, Abernathy-Close L, Vendrov KC, Standke AK, Bergin IL, Schloss PD, Young VB. Intestinal Inflammation Reversibly Alters the Microbiota to Drive Susceptibility to Clostridioides difficile Colonization in a Mouse Model of Colitis. mBio. 2022:e0190422. Epub 2022/07/29. doi: 10.1128/mbio.01904-22. PubMed PMID: 35900107.
3. Dieterle MG, Putler R, Perry DA, Menon A, Abernathy-Close L, Perlman NS, Penkevich A, Standke A, Keidan M, Vendrov KC, Bergin IL, **Young VB**, Rao K. Systemic inflammatory mediators are effective biomarkers for predicting adverse outcomes in *Clostridioides difficile* infection. mBio. 2020 May 5;11(3) PubMed Central PMCID: PMC7403776.
4. Nagao-Kitamoto H, Leslie JL, Kitamoto S, Jin C, Thomsson KA, Gillilland MG 3rd, Kuffa P, Goto Y, Jenq RR, Ishii C, Hirayama A, Seekatz AM, Martens EC, Eaton KA, Kao JY, Fukuda S, Higgins PDR, Karlsson NG, **Young VB**, Kamada N. Interleukin-22-mediated host glycosylation prevents *Clostridioides difficile* infection by modulating the metabolic activity of the gut microbiota. Nat Med. 2020 Apr;26(4):608-617. PubMed Central PMCID: PMC7160049.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2016 -	Professor, University of Michigan, Department of Internal Medicine, Infectious Diseases Division and Microbiology & Immunology, Ann Arbor, MI
2010 - 2016	Associate Professor, University of Michigan, Department of Internal Medicine, Infectious Diseases Division and Microbiology & Immunology, Ann Arbor, MI
2007 - 2010	Assistant Professor, University of Michigan, Department of Internal Medicine, Infectious Diseases Division and Microbiology & Immunology, Ann Arbor, MI
2000 - 2007	Assistant Professor, Michigan State University, College of Human Medicine, Department of Microbiology & Molecular Genetics, National Food Safety & Toxicology Center, East Lansing, MI
1999 - 2000	Instructor, Harvard University, Medical School, Boston, MA
1999 - 2000	Clinical Assistant, Harvard University, Harvard Medical School, Boston, MA
1998 - 2000	Research Fellow, Massachusetts General Hospital, Infectious Diseases, Boston, MA
1998 - 2000	Graduate Assistant, Massachusetts General Hospital, Infectious Diseases, Boston, MA
1996 - 2000	Postdoctoral Fellow, Massachusetts Institute of Technology, Department of Bioengineering & Environmental Health, Cambridge, MA
1995 - 1996	Clinical Fellow, Massachusetts General Hospital, Internal Medicine/Infectious Diseases, Boston, MA
1995 - 2001	Associate Staff Physician, Massachusetts Institute of Technology, Medical Department, Cambridge, MA

1992 - 1995 Resident physician, Massachusetts General Hospital, Department of Internal Medicine, Boston, MA

Honors

2016 William Henry Fitzbutler Collegiate Professorship, University of Michigan
2010 Jerome W. Conn Award for Excellence In Research, University of Michigan Department of Internal Medicine
2002 MSU IRGP New Investigator Grant, Michigan State University Foundation
1998 Award: Fellow Abstract Competition, Infectious Diseases Society
1992 Dean's Award for Clinical Excellence, Stanford University School of Medicine
1985 Scholarship/Grant, Medical Scientist Training Program
1984 Research Grant, Alpha Tau Omega Fraternity
1983 Scholarship, Alpha Tau Omega Fraternity Foundation

C. Contributions to Science

1. Dissecting the role of the gut microbiota in antibiotic-associated diarrhea and *C. difficile* infection. The disruption of the indigenous gut microbiota by antibiotic administration is thought to be the driving force in the development of antibiotic-associated diarrhea (AAD) and infection with the toxin-producing bacterium *C. difficile*. My work has begun to understand the mechanisms by which these changes can lead to a loss of intestinal homeostasis. In the setting of AAD, antibiotics appear to destroy the ability of the gut microbiota to ferment complex carbohydrates to short-chain fatty acids. This results in both the loss of an epithelial food source and signaling molecule and the imposition of an osmotic load. Our more recent work on *C. difficile* infection (CDI) indicates that the complex relationship between the indigenous gut microbiota and the host is disturbed during antibiotic administration and this opens up ecologic niches that can be exploited by *C. difficile*. This work has also shown the importance examining both the structure and the function of the gut microbiota in order to understand this intricate relationship in health and disease.
   a. Leslie JL, Jenior ML, Vendrov KC, Standke AK, Barron MR, O'Brien TJ, Unverdorben L, Thaprawat P, Bergin IL, Schloss PD, **Young VB**. Protection from lethal *Clostridioides difficile* infection via intraspecies competition for cogerminant. mBio. 2021 Mar 30;12(2) PubMed Central PMCID: PMC8092246.
   b. Dieterle MG, Putler R, Perry DA, Menon A, Abernathy-Close L, Perlman NS, Penkevich A, Standke A, Keidan M, Vendrov KC, Bergin IL, **Young VB**, Rao K. Systemic inflammatory mediators are effective biomarkers for predicting adverse outcomes in *Clostridioides difficile* infection. mBio. 2020 May 5;11(3) PubMed Central PMCID: PMC7403776.
   c. Nagao-Kitamoto H, Leslie JL, Kitamoto S, Jin C, Thomsson KA, Gillilland MG 3rd, Kuffa P, Goto Y, Jenq RR, Ishii C, Hirayama A, Seekatz AM, Martens EC, Eaton KA, Kao JY, Fukuda S, Higgins PDR, Karlsson NG, **Young VB**, Kamada N. Interleukin-22-mediated host glycosylation prevents *Clostridioides difficile* infection by modulating the metabolic activity of the gut microbiota. Nat Med. 2020 Apr;26(4):608-617. PubMed Central PMCID: PMC7160049.
   d. Seekatz AM, Wolfrum E, DeWald CM, Putler RKB, Vendrov KC, Rao K, **Young VB**. Presence of multiple *Clostridium difficile* strains at primary infection is associated with development of recurrent disease. Anaerobe. 2018 Oct;53:74-81. PubMed Central PMCID: PMC6274632.

2. Applications of microbial ecology to gastrointestinal disease. My early independent research career was characterized by exploring how the study of microbial communities could impact the study of disease within the GI tract including antibiotic-associated diarrhea, the inflammatory bowel diseases and infectious colitis. This research began well before the Human Microbiome Project and afforded me the

ability to carefully test how knowledge of the structure and function of the gut microbiota could impact host health and disease. Work in this area looked both a murine models of inflammatory bowel disease and human ulcerative colitis. Key publications have shown that changes in the microbiome as associated with the development of gut inflammation and serve to drive the abnormal inflammatory response in the gut.

a. Hill DR, Huang S, Nagy MS, Yadagiri VK, Fields C, Mukherjee D, Bons B, Dedhia PH, Chin AM, Tsai YH, Thodla S, Schmidt TM, Walk S, **Young VB**, Spence JR. Bacterial colonization stimulates a complex physiological response in the immature human intestinal epithelium. Elife. 2017 Nov 7;6 PubMed Central PMCID: PMC5711377.
b. **Young VB**, Raffals LH, Huse SM, Vital M, Dai D, Schloss PD, Brulc JM, Antonopoulos DA, Arrieta RL, Kwon JH, Reddy KG, Hubert NA, Grim SL, Vineis JH, Dalal S, Morrison HG, Eren AM, Meyer F, Schmidt TM, Tiedje JM, Chang EB, Sogin ML. Multiphasic analysis of the temporal development of the distal gut microbiota in patients following ileal pouch anal anastomosis. Microbiome. 2013 Mar 4;1(1):9. PubMed Central PMCID: PMC3971607.
c. Nagalingam NA, Kao JY, **Young VB**. Microbial ecology of the murine gut associated with the development of dextran sodium sulfate-induced colitis. Inflamm Bowel Dis. 2011 Apr;17(4):917-26. PubMed Central PMCID: PMC3058753.
d. **Young VB**, Schmidt TM. Antibiotic-associated diarrhea accompanied by large-scale alterations in the composition of the fecal microbiota. J Clin Microbiol. 2004 Mar;42(3):1203-6. PubMed Central PMCID: PMC356823.

3. Use of tissue-engineered model systems to study host-microbe interactions. Human intestinal organoids (HIOs) are stem cell-derived three-dimensional tissues that were initially developed to study the developmental biology of the gut. I have utilized HIOs to study the molecular responses of the HIO epithelium and microbes in vitro. HIOs can be used to model both beneficial and pathogenic interactions between a model gut epithelium and colonizing microbes. Our work suggests that HIOs represent a system that represents intermediate complexity between simple in vitro and cell culture systems and animal models to gain unique insight into host-microbe interactions.

a. Hill DR, Huang S, Tsai YH, Spence JR, **Young VB**. Real-time measurement of epithelial barrier permeability in human intestinal organoids. J Vis Exp. 2017 Dec 18; PubMed Central PMCID: PMC5755602.
b. Hill DR, Huang S, Nagy MS, Yadagiri VK, Fields C, Mukherjee D, Bons B, Dedhia PH, Chin AM, Tsai YH, Thodla S, Schmidt TM, Walk S, **Young VB,** Spence JR. Bacterial colonization stimulates a complex physiological response in the immature human intestinal epithelium. Elife. 2017 Nov 7;6 PubMed Central PMCID: PMC5711377.
c. Leslie JL, **Young VB**. A whole new ball game: Stem cell-derived epithelia in the study of host-microbe interactions. Anaerobe. 2016 Feb;37:25-8. PubMed Central PMCID: PMC4747824.
d. Leslie JL, Huang S, Opp JS, Nagy MS, Kobayashi M, **Young VB**, Spence JR. Persistence and toxin production by *Clostridium difficile* within human intestinal organoids result in disruption of epithelial paracellular barrier function. Infect Immun. 2015 Jan;83(1):138-45. PubMed Central PMCID: PMC4288864.

4. Leading and contributing to teams of scientists in collaborative, interdisciplinary approaches to complex biomedical questions. Historically, the "team science" approach to biomedical research was not common. However, the bulk of my career has involved working, both as a leader and a member in large teams of scientists to address complex questions including the study of cystic fibrosis, inflammatory bowel disease,

C. difficile infection, antibiotic resistance and foodborne illness. I have come to appreciate that although there can be difficulties in maintaining the team approach, I enjoy the opportunity to work together, combining various interests and expertise to push the scientific envelope.

a. Das NK, Schwartz AJ, Barthel G, Inohara N, Liu Q, Sankar A, Hill DR, Ma X, Lamberg O, Schnizlein MK, Arqués JL, Spence JR, Nunez G, Patterson AD, Sun D, **Young VB**, Shah YM. Microbial metabolite signaling is required for systemic iron homeostasis. Cell Metab. 2020 Jan 7;31(1):115-130.e6. PubMed Central PMCID: PMC6949377.
b. Shimasaki T, Seekatz A, Bassis C, Rhee Y, Yelin RD, Fogg L, Dangana T, Cisneros EC, Weinstein RA, Okamoto K, Lolans K, Schoeny M, Lin MY, Moore NM, **Young VB**, Hayden MK. Increased relative abundance of *Klebsiella pneumoniae* carbapenemase-producing *Klebsiella pneumoniae* within the gut microbiota is associated with risk of bloodstream infection in long-term acute care hospital patients. Clin Infect Dis. 2019 May 30;68(12):2053-2059. PubMed Central PMCID: PMC6541703.
c. Hill DR, Huang S, Nagy MS, Yadagiri VK, Fields C, Mukherjee D, Bons B, Dedhia PH, Chin AM, Tsai YH, Thodla S, Schmidt TM, Walk S, **Young VB**, Spence JR. Bacterial colonization stimulates a complex physiological response in the immature human intestinal epithelium. Elife. 2017 Nov 7;6 PubMed Central PMCID: PMC5711377.
d. **Young VB**, Raffals LH, Huse SM, Vital M, Dai D, Schloss PD, Brulc JM, Antonopoulos DA, Arrieta RL, Kwon JH, Reddy KG, Hubert NA, Grim SL, Vineis JH, Dalal S, Morrison HG, Eren AM, Meyer F, Schmidt TM, Tiedje JM, Chang EB, Sogin ML. Multiphasic analysis of the temporal development of the distal gut microbiota in patients following ileal pouch anal anastomosis. Microbiome. 2013 Mar 4;1(1):9. PubMed Central PMCID: PMC3971607.

A full listing of publications can be found at
https://www.ncbi.nlm.nih.gov/myncbi/vincent.young.3/bibliography/public/