

**BIOGRAPHICAL SKETCH**

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NAME: Noto, Jennifer McMillan

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

POSITION TITLE: Research Assistant Professor of Medicine

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 (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Mary Washington, Fredericksburg, VA	BS	05/2003	Biology
Virginia Commonwealth University Medical Center, Richmond, VA	PhD	08/2008	Microbiology and Immunology
Vanderbilt University Medical Center, Nashville, TN	Postdoctoral Fellowship	09/2014	Microbiology and Cancer Biology

**A. Personal Statement**

I am an experienced microbiologist with formal training in microbiology, molecular biology, cellular biology, immunology, and animal models of disease and cancer. I have a strong and vested interest in basic biomedical and translational research, teaching, and mentoring, and have the appropriate training and expertise to successfully contribute and execute the proposed research projects.

Our main research focus is to define specific mechanisms by which the obligate human pathogen, *Helicobacter pylori*, induces gastric inflammation and neoplastic transformation. *Helicobacter pylori* colonizes greater than half the world's population; however, only a fraction of infected individuals ever develop gastric cancer. It has become readily apparent that interaction among specific *H. pylori* virulence factors, host determinants, and environmental factors further augment the risk for gastric cancer. Thus, identifying specific biomarkers and risk factors that augment the risk for *H. pylori*-induced gastric carcinogenesis is our ultimate goal.

**B. Positions and Honors****Positions and Employment**

2003-2008	Doctoral Research, Department of Microbiology and Immunology, Virginia Commonwealth University School of Medicine, Richmond, VA
2008-2014	Postdoctoral Fellowship, Department of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Vanderbilt University Medical Center, Nashville, TN
2011-2016	Lecturer, Department of Pathology, Microbiology and Immunology, Vanderbilt University, Nashville, TN
2013-2016	Teaching Assistant, Vanderbilt Program for Talented Youth, Vanderbilt Summer Academy, Vanderbilt University, Nashville, TN
2015-2017	Lecturer, Division of Math and Natural Sciences, Nashville State Community College, Nashville, TN
2014-present	Research Instructor, Department of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Vanderbilt University Medical Center, Nashville, TN
2016-present	Lecturer, Department of Medicine, Division of Infectious Diseases, Vanderbilt University, Nashville, TN

- 2017-present Adjunct Professor, Division of Math and Natural Sciences, Nashville State Community College, Nashville, TN
- 2017-present Research Assistant Professor, Department of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Vanderbilt University Medical Center, Nashville, TN

### **Other Experience and Professional Memberships**

- 2005-2009 Member, Virginia Branch of the American Society for Microbiology
- 2005-2009 Member, American Society for Microbiology
- 2008-2014 Member, National Postdoctoral Association
- 2009-present *Ad hoc* reviewer for 32 discipline-specific journals
- 2010-present Member, American Association for the Achievement of Science
- 2014-present Member, American Gastroenterology Association
- 2017-present Review Editor, *Frontiers in Infectious Diseases*

### **Honors**

- 2007 Travel Grant, 4<sup>th</sup> Mid-Atlantic Microbial Pathogenesis Meeting, Wintergreen, VA
- 2007 Best Presentation, Virginia American Society for Microbiology, University of Richmond, Richmond, VA
- 2010 Travel Scholarship, AGA Gastrointestinal Response to Injury Conference, Scottsdale, AZ
- 2010 1<sup>st</sup> Place Poster Presentation, Vanderbilt-Ingram Cancer Center, Nashville, TN
- 2011 Gastroenterology FY11 Service Award, Division of Gastroenterology, Vanderbilt University Medical Center, Nashville, TN
- 2011 Young Investigator Award, 16<sup>th</sup> International Workshop on *Campylobacter*, *Helicobacter* & Related Organisms, Vancouver, British Columbia, Canada
- 2012 Award of Excellence in Research, Division of Gastroenterology, Vanderbilt University Medical Center, Nashville, TN
- 2013 Postdoc of the Year 2012-2013, Vanderbilt Medical Alumni Association and Office of Biomedical Research, Education and Training, Nashville, TN
- 2013 Poster of Distinction, Digestive Disease Week 2013, Orlando, FL
- 2014 Postdoctoral Scholar of the Year, Vanderbilt-Ingram Cancer Center, Nashville, TN
- 2015 FASEB Travel Award, FASEB Gastrointestinal Tract XVI, Steamboat Springs, CO
- 2017 Societe Francaise de Microbiologie Best Poster Presentation Award, Nantes, France
- 2018 Poster of Distinction, Digestive Disease Week 2018, Washington, DC

### **C. Contributions to Science**

1. During my Doctoral Research at Virginia Commonwealth University School of Medicine, my research emphasis was on the pathogenesis of the obligate human pathogen *Neisseria gonorrhoeae*, the causative agent of the sexually transmitted disease gonorrhea. My research focused on the pathogenic mechanisms by which *N. gonorrhoeae* acquires iron from its human host. My research goal was to determine the mechanism of transferrin-iron uptake and utilization by *N. gonorrhoeae*, with the ultimate goal of targeting these *Neisseria* transferrin binding proteins as potential vaccine candidates. This work resulted in the characterization of the transferrin binding protein, TbpA, which is a potential vaccine candidate against both *N. gonorrhoeae* and *N. meningitidis* infection.
  - a. **Noto JM**, Cornelissen CN. Identification of TbpA residues required for transferrin-iron utilization in *Neisseria gonorrhoeae*. *Infect Immun*. 2008; 76(5): 1960-1969. PMID: PMC2346694
  - b. Siburt CJ, Roulhac PL, Weaver KD, **Noto JM**, Mietzner TA, Cornelissen CN, Fitzgerald MC, Crumbliss AL. Hijacking transferrin bound iron: protein-receptor interactions essential for iron transport in *N. gonorrhoeae*. *Metallomics*. 2009; 1(3): 249-255. PMID: PMC2749328
  - c. Banerjee S, Siburt CJ, Mistry S, **Noto JM**, DeArmond P, Fitzgerald MC, Lambert LA, Cornelissen CN, Crumbliss AL. Evidence of Fe<sup>3+</sup> interaction with the plug domain of the outer membrane transferrin receptor protein of *Neisseria gonorrhoeae*: implications for Fe transport. *Metallomics*. 2012; 4(4): 361-372. PMID: PMC3391718
2. During my tenure at Vanderbilt University Medical Center, my research has focused primarily on pathogenic mechanisms by which the obligate human pathogen *Helicobacter pylori* induces chronic gastric inflammation

and cancer, with the ultimate goal of identifying risk factors and biomarkers that predispose patients to gastric cancer. Due to my training in iron and nutritional immunity, I sought to determine role of iron deficiency in *H. pylori*-induced gastric inflammation and cancer. Findings from this work demonstrated that iron deficiency augments and accelerates the development of *H. pylori*-induced gastric carcinogenesis in both rodent models and human populations. Further, mechanistic studies demonstrated that iron deficiency specifically regulates and heightens the virulence of *H. pylori* to increase gastric inflammation and the risk for development of cancer.

- a. Tan S, **Noto JM**, Romero-Gallo J, Peek RM, Amieva M. *Helicobacter pylori* perturbs iron trafficking in the epithelium to grow on the cell surface. *PLoS Pathog.* 2011; 7(5): e1002050. PMID: PMC3093365
  - b. **Noto JM**, Gaddy JA, Lee JY, Piazuelo MB, Friedman DB, Colvin DC, Romero-Gallo J, Suarez G, Loh J, Tan S, Morgan DR, Wilson KT, Correa P, Cover TL, Amieva MR, Peek RM. Iron deficiency accelerates *Helicobacter pylori*-induced carcinogenesis in rodents and humans. *J Clin Invest.* 2013; 123(1): 479-492. PMID: PMC3533289
  - c. **Noto JM**, Lee JY, Gaddy JA, Cover TL, Amieva MR, Peek RM. Regulation of *Helicobacter pylori* virulence within the context of iron deficiency. *J Infect Dis.* 2015; 211(11): 1790-1794. PMID: PMC4447831
  - d. **Noto JM**, Chopra A, Loh JT, Romero-Gallo J, Piazuelo MB, Watson M, Leary S, Beckett AC, Wilson KT, Cover TL, Mallal S, Israel DA, Peek RM. Pan-genomic analyses identify key *Helicobacter pylori* pathogenic loci modified by carcinogenic host microenvironments. *Gut.* 2017; Epub ahead of print. PMID: 28924022
3. During my tenure at Vanderbilt University Medical Center, my research has also focused the role of microRNAs in *H. pylori*-induced inflammation and cancer, with the ultimate goal of identifying key miRNAs and host factors targeted during acute and chronic *H. pylori* infection.
- a. **Noto JM**, Peek RM. The role of *microRNAs* in *Helicobacter pylori* pathogenesis and gastric carcinogenesis. *Front Cell Infect Microbiol.* 2011; 1(21) 1-19. PMID: PMC3417373
  - b. **Noto JM**, Peek RM. Gastric-to-intestinal transdifferentiation and cancer. *Proc Natl Acad Sci USA.* 2012; 109(50): 20173-20174. PMID: PMC3528517
  - c. **Noto JM**, Piazuelo MB, Chaturvedi R, Bartel CA, Thatcher EJ, Delgado A, Romero-Gallo J, Wilson KT, Correa P, Patton JC, Peek RM. Strain-specific suppression of *microRNA-320* by carcinogenic *Helicobacter pylori* promotes expression of the anti-apoptotic protein, Mcl-1. *Am J Physiol Gastrointest Liver Physiol.* 2013; 305(11): G786-796. PMID: PMC3882435
  - d. Zhang Y, **Noto JM**, Hammond CE, Barth JL, Argraves WS, Backert S, Peek RM, Smolka AJ. *Helicobacter pylori*-induced post-transcriptional regulation of H-K-ATPase  $\alpha$ -subunit gene expression by miRNA. *Am J Physiol Gastrointest Liver Physiol.* 2014; 306(7): G606-613. PMID: PMC4116396
4. During my tenure at Vanderbilt University Medical Center, my research has also focused on specific host factors, such as MMP-7, KLF5, as well as the microbial components of the host microbiota that augment the risk for *H. pylori*-induced inflammation and cancer, with the ultimate goal of identifying host biomarkers and other microbial risk factors that predispose patients to gastric carcinogenesis.
- a. Ogden SR, **Noto JM**, Allen SS, Patel DA, Romero-Gallo J, Washington MK, Fingelton B, Israel DA, Lewis ND, Wilson KT, Chaturvedi R, Zhao Z, Shyr Y, Peek RM. Matrix metalloproteinase-7 and premalignant host responses in *Helicobacter pylori*-infected mice. *Cancer Res.* 2010; 70(1): 30-35. PMID: PMC2804939
  - b. **Noto JM**, Khizanishvili T, Piazuelo MB, Chaturvedi R, Romero-Gallo J, Delgado AG, Khurana SS, Sierra JC, Krishna US, Suarez G, Powell AE, Goldenring JR, Coffey RJ, Yang VW, Correa P, Mills JC, Wilson KT, Peek RM. *Helicobacter pylori* promotes the expression of Krüppel-like factor 5, a mediator of carcinogenesis, *in vitro* and *in vivo*. *PLoS ONE.* 2013; 8(1): e54344. PMID: PMC3553174
  - c. **Noto JM**, Krakowiak MS, Piazuelo MB, Hardbower DM, Romero-Gallo J, Delgado A, Chaturvedi R, Correa P, Wilson KT, Peek RM. Matrix metalloproteinase 7 restrains *Helicobacter pylori*-induced gastric inflammation and premalignant lesions in the stomach by altering macrophage polarization. *Oncogene.* 2015; 34(14): 1865-1871. PMID: PMC4237684
  - d. **Noto JM**, Peek RM. The gastric microbiome, its interaction with *Helicobacter pylori* and its potential role in the progression to stomach cancer. *PLoS Pathog.* 2017; 13(10): e1006573. PMID: PMC5629027

5. During my tenure at Vanderbilt University Medical Center, my research has also been highly collaborative with the laboratory of Dr. Alex Zaika, where our research has focused on the mechanisms by which *H. pylori* regulate the tumor suppressor, p53, and the role p53 plays in *H. pylori*-induced gastric inflammation and cancer.
- Wei J, **Noto J**, Zaika E, Romero-Gallo J, Correa P, El-Rifai W, Peek RM, Zaika A. Pathogenic bacterium *Helicobacter pylori* alters the expression profile of p53 proteins isoforms and p53 response to cellular stresses. *Proc Natl Acad Sci USA*. 2012; 109(38): E2543-2550. PMID: PMC3458371
  - Wei J, **Noto JM**, Zaika E, Romero-Gallo J, Piazzuelo MB, Schneider B, El-Rifai W, Correa P, Peek RM, Zaika AI. Bacterial CagA protein induces degradation of p53 protein in a p14ARF-dependent manner. *Gut*. 2015; 64(7):1040-1048. PMID: PMC4312278
  - Bhardwaj V, **Noto JM**, Wei J, Andl C, El-Rifai W, Peek RM, Zaika A. *Helicobacter pylori* bacteria alter the p53 stress response via ERK-MDM2 pathway. *Oncotarget*. 2015; 6(3): 1531-1543. PMID: PMC4359312
  - Horvat A, **Noto JM**, Wei J, Zaika E, Palrasu M, Ramatchandirin B, Schnider BG, El-Rifai, W Peek RM, Zaika AI. Regulation of p14ARF tumor suppressor by *Helicobacter pylori* in gastric epithelial cells. *Oncogene*. 2018; Epub ahead of print. PMID: 29849123

**Complete List of Published Work in My Bibliography:**

<https://www.ncbi.nlm.nih.gov/sites/myncbi/1F9fekjktzd5T/bibliography/47364475/public/?sort=date&direction=ascending>

**D. Additional Information: Research Support and/or Scholastic Performance**

**Ongoing Research Support**

5R01 DK058587      Peek (PI)                      07/01/2016 - 06/30/2021  
NIH/NIDDK

*Helicobacter pylori* and gastrointestinal biology

The goal of this grant is to define the relationship between adherence of *H. pylori* to host cells and disease.

Role: Co-Investigator

5R01 CA077955      Peek (PI)                      04/01/2018 - 03/31/2023  
NIH/NCI

*H. pylori* relationship to digestive diseases and cancer

The goal of this grant is to investigate the role of p120 in gastric cancer that is induced by *H. pylori*.

Role: Co-Investigator

2P01 CA116087      Peek (PI)                      03/12/2014 - 12/31/2018  
NIH/NCI

*H. pylori*-induced inflammation and gastric cancer

The goal of this Program Project Grant is to define the role of aberrant epithelial signaling induced by pathogenic *H. pylori* strains in gastric carcinogenesis.

Role: Co-Investigator