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440 832 0000

David R. Hill Research Assistant Professor

Academic Appointments

- 07/18 Now Research Assistant Professor Dept. of Internal Medicine, University of Michigan 🔽 E-mail Application of human pluripotent stem cell derived intestinal organoids to the hilldr study neonatal microbial colonization and the pathogenesis of necrotizing en-@med.umich.edu terocolitis. d2.david.hill 12/17 - Now Part-time Lecturer School of Health Sciences, Eastern Michigan University @gmail.com Course Director for Clinical Immunology, an upper level undergraduate course for students in the board certified Medical Technology program. Website 09/14 - 06/18 Research Fellow Dept. of Internal Medicine, University of Michigan hilldr.github.io Host-microbe interactions at the intestinal epithelial interface in human development using human pluripotent stem cell derived intestinal organoids. **Y** Twitter 06/13 - 08/14 Research Fellow Program in Glycobiology, Boston College @DRHill PhD Anti-inflammatory and prebiotic activity of human milk oligosaccharides and glycosaminoglycans in infant health and development. C GitHub 05/06 - 05/08 Research Assistant Dept. of Biology, Kent State University github.com/hilldr Worked with Dr. Helen Piontkivska on adaptive evolution in host-pathogen interactions using molecular phylogenetic analysis.
 - 05/05 07/08 **Research Assistant** Dept. of Pathobiology, Cleveland Clinic Researched the role of extracellular matrix in inflammatory cell recruitment and activation in inflammatory bowel disease in the laboratory of Dr. Carol A. de la Motte.

Education

- 2008 2013 Doctor of Philosophy Case Western Reserve University, Cleveland OH Molecular Medicine Characterized size-dependent induction of innate antimicrobial defense of the intestinal epithelium by hyaluronan and demonstrated that hyaluronan is a natural component of the human milk glycome that enhances protection from enteric disease. Dissertation: "The Role of Hyaluronan in Innate Intestinal Defense". Committee: Carol de la Motte, PhD, Vince Hascall, PhD, Jean-Paul Achkar, MD, Edward Maytin, MD, and Edward Greenfield, PhD. Training: Epithelial cell biology, innate immunity, and glycobiology **Bachelor of Science** 2004 - 2008 Kent State University, Kent OH **Biological Sciences** University Honors with Distinction in Biological Science. Thesis: "Evolution of Quorum-Sensing in the genus Burkholderia" Thesis completed under the direction of Dr. Helen Piontkivska.
 - Training: Bioinformatics, molecular phylogenetics.

David R. Hill, Curriculum Vitae

PubMed

Hill, DR [AU]

0000-0002-1626-6079

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Author profile: david-hill13



Publication Metrics





Publications

Generation of lung organoids from human pluripotent stem cells in vitro.

A J Miller, B R Dye, D Ferrer-Torres, **Hill, D R**, A W Overeem, L D Shea, J R Spence Nat Protoc (*Jan. 2019*). *2019*

Identification, isolation and characterization of human LGR5-positive colon adenoma cells. M K Dame, D Attili, S D McClintock, P H Dedhia, P Ouillette, O Hardt, A M Chin, X Xue, J Laliberte, E L Katz, G M Newsome, **Hill, D R**, A J Miller, Y H Tsai, D Agorku, C H Altheim, A Bosio, B Simon, L C Samuelson, J A Stoerker, H D Appelman, J Varani, M S Wicha, D E Brenner, Y M Shah, J R Spence, J A Colacino

Development 145.6 (Mar. 2018). 2018

In Vitro Induction and In Vivo Engraftment of Lung Bud Tip Progenitor Cells Derived from Human Pluripotent Stem Cells.

A J Miller, **Hill, D R**, M S Nagy, Y Aoki, B R Dye, A M Chin, S Huang, F Zhu, E S White, V Lama, J R Spence

Stem Cell Reports 10.1 (Jan. 2018) pp. 101-119. 2018

Morphogenesis and maturation of the embryonic and postnatal intestine.

A M Chin, **Hill, D R**, M Aurora, J R Spence Semin Cell Dev Biol *66 (June 2017) pp. 81–93. 2017*

Bacterial colonization stimulates a complex physiological response in the immature human intestinal epithelium.

Hill, D R, S Huang, M S Nagy, V K Yadagiri, C Fields, D Mukherjee, B Bons, P H Dedhia, A M Chin, Y H Tsai, S Thodla, T M Schmidt, S Walk, V B Young, J R Spence Elife *6 (Nov. 2017). 2017*

Real-time Measurement of Epithelial Barrier Permeability in Human Intestinal Organoids.

Hill, D R, S Huang, Y H Tsai, J R Spence, V B Young J Vis Exp 130 (Dec. 2017). 2017

Gastrointestinal Organoids: Understanding the Molecular Basis of the Host-Microbe Interface.

Hill, D R, J R Spence Cell Mol Gastroenterol Hepatol 3.2 (Mar. 2017) pp. 138–149. 2017

Differentiation of Human Pluripotent Stem Cells into Colonic Organoids via Transient Activation of BMP Signaling.

J O Múnera, N Sundaram, S A Rankin, **Hill, D**, C Watson, M Mahe, J E Vallance, N F Shroyer, K L Sinagoga, A Zarzoso-Lacoste, J R Hudson, J C Howell, P Chatuvedi, J R Spence, J M Shannon, A M Zorn, M A Helmrath, J M Wells

Cell Stem Cell 21.1 (July 2017) 51-64.e6. 2017

The human milk oligosaccharide 2'-fucosyllactose modulates CD14 expression in human enterocytes, thereby attenuating LPS-induced inflammation.

Y He, S Liu, D E Kling, S Leone, N T Lawlor, Y Huang, S B Feinberg, **Hill, D R**, D S Newburg Gut *65.1 (Jan. 2016) pp. 33–46. 2016*

LGR4 and LGR5 Function Redundantly During Human Endoderm Differentiation

Yu-Hwai Tsai, **David R. Hill**, Namit Kumar, Sha Huang, Alana M. Chin, Briana R. Dye, Melinda S. Nagy, Michael P. Verzi, Jason R. Spence

Cellular and Molecular Gastroenterology and Hepatology 2.5 (2016) 648-662.e8. 2016

Platelet hyaluronidase-2: an enzyme that translocates to the surface upon activation to function in extracellular matrix degradation.

S Albeiroti, K Ayasoufi, **Hill, D R**, B Shen, C A Motte Blood *125.9 (Feb. 2015) pp. 1460–9. 2015*

In vitro generation of human pluripotent stem cell derived lung organoids.

B R Dye, **Hill, D R**, M A Ferguson, Y H Tsai, M S Nagy, R Dyal, J M Wells, C N Mayhew, R Nattiv, O D Klein, E S White, G H Deutsch, J R Spence

David R. Hill, Curriculum Vitae

Elife 4 (2015). 2015

Transcriptome-wide Analysis Reveals Hallmarks of Human Intestine Development and Maturation In Vitro and In Vivo.

S R Finkbeiner, **Hill, D R**, C H Altheim, P H Dedhia, M J Taylor, Y H Tsai, A M Chin, M M Mahe, C L Watson, J J Freeman, R Nattiv, M Thomson, O D Klein, N F Shroyer, M A Helmrath, D H Teitelbaum, P J Dempsey, J R Spence

Stem Cell Reports (June 2015). 2015

Clinical applications of bioactive milk components.

Hill, D R, D S Newburg

Nutr Rev 73.7 (July 2015) pp. 463-76. 2015

Pasteurized Donor Human Milk Maintains Microbiological Purity for 4 Days at 4°C. A M Vickers, S Starks-Solis, **Hill, D R**, D S Newburg J Hum Lact *31.3 (Aug. 2015) pp. 401–5. 2015*

- Human milk hyaluronan enhances innate defense of the intestinal epithelium.
 Hill, D R, H K Rho, S P Kessler, R Amin, C R Homer, C McDonald, M K Cowman, C A Motte J Biol Chem 288.40 (Oct. 2013) pp. 29090–104. 2013
- Specific-sized hyaluronan fragments promote expression of human β-defensin 2 in intestinal epithelium.

Hill, D R, S P Kessler, H K Rho, M K Cowman, C A Motte J Biol Chem *287.36 (Aug. 2012) pp. 30610–24. 2012*

Hyaluronan-mediated leukocyte adhesion and dextran sulfate sodium-induced colitis are attenuated in the absence of signal transducer and activator of transcription 1.
S K Bandyopadhyay, C A Motte, S P Kessler, V C Hascall, Hill, D R, S A Strong Am J Pathol *173.5 (Nov. 2008) pp. 1361–8. 2008*

Non Peer-Reviewed Publications

- 2015 **D R Hill. Mutual understanding: uncovering the mechanistic basis of the host-symbiont relationship in human health.** Albert and Mary Lasker Foundation Newsletter.
- 2016 **D R Hill. Q&A with David Hill, winner of 2015 Essay Contest.** Albert and Mary Lasker Foundation Newsletter.

Other Media

2017 **Young, V B, Spence, J R, and D R Hill. Science AMA Series** r/science This is Dr. Jason Spence, Dr. David Hill and Dr. Vincent Young. We've done research on how helpful bacteria activate the processes that lead to a mature, healthy gastrointestinal tract and we're here today to talk about it. Ask Us Anything!

Patents

03/2014 **Composition to improve intestinal health** US 20140072621 A1 Compositions and methods are provided for treating patients suffering from compromised intestinal function, including inflammatory bowel disease. The method comprises orally administering a composition comprising hyaluronan, where said hyaluronan has a molecular weight within the range of about 35 kDa.

Grant Funding

11/2015Microbial Pathogenesis Training ProgramT32-Al007528-18This project characterized the host response to organisms associated with
necrotizing enterocolitis (NEC) using an *in vitro* model of the immature human
gastrointestinal tract.

06/2016 Michigan Institute for Clinical and Health Research Postdoctoral Translational Scholars Program UL1-TR000433-10 The rate of mortality in NEC cases has remained unchanged for decades due to the lack of tools to study the disease. This proposal will use newly developed cell culture techniques to study patient intestinal tissue in the laboratory and use this tissue to examine how microbes in the infant intestine may contribute to inflammation in NEC.

07/2016 **Training in Basic and Translational Digestive Sciences** T32-DK094775-03 Awarded for the study of NEC using intestinal organoid model systems. Declined due to conflict with PTSP grant acceptance.

07/2018 **Michigan Center for Gastrointestinal Research Pilot Feasibility Project** P30-DK034933 Identification of host-microbial interaction networks that mediate epithelial barrier function in human intestinal organoids colonized with clinical *E. coli*

Honors and Awards

isolates.

- 09/2008 **Portz Scholar in Undergraduate Research** National Collegiate Honors Council In recognition of a senior honors thesis entitled *Evolution of Quorum Sensing in the genus Burkholderia*
- 04/2010 **Best Poster Presentation** Lerner Research Institute, Cleveland Clinic Awarded for poster presented at the annual Molecular Medicine Retreat entitled *Low molecular weight hyaluronan promotes intestinal epithelial defense*
- 09/2012 **Best Oral Presentation** Lerner Research Institute, Cleveland Clinic Awarded for presentation of a talk entitled *Specific-sized hyaluronan fragments promote innate defense of the intestinal epithelium* at the annual Molecular Medicine Retreat.
- 07/2012 **Best Trainee Presentation** Gordon Research Seminar on Proteoglycans, Andover NH Awarded for presentation entitled *Specific-sized hyaluronan fragments promote innate defense of the intestinal epithelium.*
- 09/2012 **Basic Science Graduate Student Award** Cleveland Clinic Awarded for submission of original manuscript entitled *Specific-sized Hyaluronan Fragments Promote Expression of Human -Defensin 2 in Intestinal Epithelium*

10/2012 F. Merlin Bumpus Junior Investigator Award for Excellence in Basic Science Research Cleveland Clinic Awarded in recognition of contributions to the understanding of the role of extracellular matrix in innate defense of the intestinal epithelium

09/2015 **Lasker Foundation Essay Winner** Albert and Mary Lasker Foundation The Lasker Essay Contest engages young scientists and clinicians in a discussion about the big questions in biology and medicine today. Essay entitled *Mutual understanding: uncovering the mechanistic basis of the host-symbiont relationship in human health.*

Extramural Invited Presentations

- 10/2008 **National Collegiate Honors Council, Annual Conference** San Antonio TX Presented a Seminar entitled: *Evolution of Quorum-Sensing in the Genus Burkholderia*.
- 02/2014 **Boston Glycobiology Discussion Group** Boston MA Proteoglycans in intestinal disease: opportunities for therapeutic intervention.
- 06/2017Wright Patterson Air Force BaseDayton OHPresented a Seminar entitled: Gastrointestinal Organoids: Understanding the
Molecular Basis of the Host-Microbe Interface.Dayton OH
- 06/2018 Frontiers in Translational Tissue Modeling Workshop, Society of In Vitro Biology St. Louis MO Presented a Seminar entitled: Gastrointestinal Organoids: Understanding the Molecular Basis of the Host-Microbe Interface.

Peer Review Service

- British Journal of Nutrition 2016 Present
- Infection and Immunity 2017 Present
- · Cancer Investigation 2017 Present
- Experimental and Molecular Pathology 2017 Present
- Journal of International Medical Research 2017 Present
- Scientific Reports 2018 Present
- EBioMedicine 2018 Present
- Nutrition Reviews 2018 Present
- Cellular and Molecular Gastroenterology and Hepatology 2018 Present
- Integrative Cancer Therapies 2019

Consulting

04/12 - 07/17 **Proofreader** Makale Tercüme Editing Services, Ankara, Turkey Scientific review, editing, proofreading, and revision of papers, book chapters, case reports, and textbooks in medicine, biology, chemistry, psychology, and sociology written by non-native English writers for publication in English.

Didactic Courses

- 05/07 05/08 **Supplemental Instructor** Led daily supplemental instruction sessions in Biological Diversity and Evolutionary Biology for undergraduate science majors
- 06/11 08/11 Supplemental Instructor Cleveland Clinic Dept. of Molecular Medicine Organized weekly supplemental instruction session in graduate Biomedical Statistics
- 12/18 Now **Part-time Lecturer** School of Health Sciences, Eastern Michigan University Course Director for Clinical Immunology, an upper level undergraduate course for students in the board-certified Medical Technology program

Publons Profile ID: 1224345

Students and Trainees

- 2009 2013 Cleveland Clinic Artin Soroosh (MS); Kristin Krymowski (RN); Peter Han (MD/PhD); Ryan Verbic (MD); Ripal Amin (MS); Yeojung Kim (PhD)
- 2013 2014 **Boston College** David Han (DDS); Paul McCabe (MD); Carlos Cuenza (MD)
- 2014 2019 **University of Michigan** Shrikar Thodla (BS); Michael Dieterle (MD/PhD); Anna-Lisa Lawrence (PhD); Lisa Tran (PhD); Madeline Barron (PhD); Michelle Smith (PhD); Amanda Photenhauer (PhD); Courtney Lynn (MS); Veda Yadagiri (MS); Brooke Bons (BS); Brieann Koves (BS)

Volunteer Service

- 2010 **Peer Mentoring Program** Cleveland Clinic Appointed to committee formed to establish a peer mentoring program for incoming Molecular Medicine PhD students to aid in the transition to the increased demands and expectations of graduate education during the first year of study.
- 2010 2012 **Molecular Medicine Admissions Committee** Cleveland Clinic Appointed to represent current students in the selection of candidates for admission to the Molecular Medicine PhD program through the evaluation and discussion of written applications, letters of recommendation, and interviews.
- 2016 **Portal to the Public** Detroit Zoological Society Training Fellowship in public science communication centered around the design and implementation of an interactive exhibit on the physiology of the gastrointestinal tract for children ages 5-7.

Research Interests

- · Molecular mechanisms of host-microbe symbioses in the gastrointestinal tract
- Application of transcriptomics to infer gene regulation in in vitro model systems
- · Development and cellular differentiation of human epithelium
- Prebiotic and immunomodulatory activity of human milk components

Biography

My research explores the interplay between microbial colonization and expansion in the gut and the development of the gut itself. This process has been difficult to study in the past: there are no germ-free human research subjects. I apply innovative cell culture model systems to generate germ-free human intestinal tissue in the lab. My work has shown that these tissues can sustain symbiosis with mutualistic bacteria and that this relationship kickstarts maturation of the lining of the human intestine.

I am currently using lab-derived human intestinal tissue to explore the factors that contribute to the failure of the intestinal maturation in some premature infants. Identification of specific conditions that determine the success or failure of intestinal maturation following bacterial colonization may lead to treatments for devastating conditions such as necrotizing entero-colitis.