



SPONSORED BY:  
THE LAMB CENTER FOR PEDIATRIC RESEARCH

---

**LORA HOOPER, PH.D.**  
**IMMUNE ADAPTATIONS TO THE INTESTINAL MICROBIOTA**

---

OCTOBER 27, 2011  
4:00 P.M.  
208 LIGHT HALL



VANDERBILT  UNIVERSITY  
MEDICAL CENTER

## IMMUNE ADAPTATIONS TO THE INTESTINAL MICROBIOTA

---

Humans harbor 100 trillion intestinal bacteria that aid in the extraction of dietary nutrients. We are unraveling the immune mechanisms that promote symbiotic host-bacterial relationships by limiting the ability of resident bacteria to cross intestinal barriers. Using a germ-free mouse model, we have discovered that resident intestinal bacteria trigger epithelial cell expression of RegIII $\gamma$ , a member of the C-type lectin family of carbohydrate binding proteins. RegIII $\gamma$  directly kills Gram-positive bacteria and thus represents a novel class of antibacterial proteins. We have uncovered the molecular mechanism of RegIII $\gamma$  bactericidal activity, showing that it binds peptidoglycan on the surfaces of Gram-positive bacteria and carries out bacterial killing by forming a hexameric pore in the bacterial inner membrane. We have found that RegIII $\gamma$  expression is governed by epithelial Toll-like receptors and that expression is triggered when bacteria colonize intestinal surface tissues. Mice engineered to lack RegIII $\gamma$  show severe defects in the ability to limit bacterial colonization of the intestinal mucosal surface, and exhibit increased activation of intestinal adaptive immune responses. Thus, RegIII $\gamma$  represents a novel mechanism of lectin-mediated mucosal defense that is critical for maintaining homeostasis with the intestinal microbiota.



### **LORA HOOPER, PH.D.**

**ASSOCIATE PROFESSOR OF IMMUNOLOGY  
AND MICROBIOLOGY**

**UNIVERSITY OF TEXAS SOUTHWESTERN  
MEDICAL CENTER**

**INVESTIGATOR, HOWARD HUGHES  
MEDICAL INSTITUTE**

---

Lora Hooper is an Associate Professor in the Department of Immunology at the University of Texas Southwestern Medical Center at Dallas and an Investigator of the Howard Hughes Medical Institute. She is also Chair of the Immunology Graduate Program at UT Southwestern. She joined the UT Southwestern faculty in 2003 after completing a postdoctoral fellowship at Washington University. During her fellowship training, she became interested in interactions between intestinal bacteria and host cells in the mammalian gut. Her research team at UT Southwestern studies bacterial-epithelial interactions in the mammalian gut and the biochemistry of epithelial antimicrobial proteins. The approaches used in her lab range from biochemical and structural approaches for understanding epithelial antimicrobial proteins to mouse genetic approaches for determining how epithelial cells sense and respond to intestinal bacteria. These studies are aimed at gaining a basic mechanistic understanding of how the immune system deals with symbiotic intestinal bacteria. Her work is funded by the Howard Hughes Medical Institute, the National Institutes of Health, the Burroughs Wellcome Fund, the Crohn's and Colitis Foundation of America, and the Welch Foundation.

---