

## The Paneth Cell: A Guardian of Gut Health



The article by Podany et al<sup>1</sup> in the current issue of *Cellular and Molecular Gastroenterology and Hepatology* makes observations that significantly advance our understanding of Paneth cells and zinc transporters in maintenance of a healthy gut barrier and microbiota of the small intestine. Paneth cells secrete large quantities of antimicrobial enzymes, cytokines, and hormones, and are found in increasing numbers in the ileum, the section of the small intestine with the most microbes. Paneth cells contain relatively large amounts of zinc in secretory granules and it is speculated that this zinc allows for optimal stabilization and function of these secreted macromolecules.<sup>2</sup> Paneth cells sense populations of microbiota through Toll-like receptors, and respond with release of their bactericidal granules.<sup>3</sup>

In a carefully performed animal study, Podany et al<sup>1</sup> localized zinc transporter 2 to Paneth cell granules, probed its function, and studied the differences between wild-type and knock-out mice for zinc transporter 2. The histology of the epithelium was remarkably normal in the 2 types of mice. The consequences of zinc transporter 2 deficiency include increases in the numbers of *Bacteroidales* S24–7, suggesting these microbe populations are regulated by Paneth cells. Zinc transporter 2-deficient mice also were found to have luminal aspirates that were less efficient in killing these enteric pathogens, and the knock-out mice showed more systemic inflammation.

These observations again show that certain microbiota are cultivated, whereas others are culled, by host factors. The microbiota are determined by more than the diet and environmental exposures. This observation also suggests why efforts to alter the microbiota through diet and probiotics often are difficult to achieve.

Environmental enteropathy is implicated as a causative factor in stunting, which accounts for 21% of disability-adjusted life-years in the world. In this animal model, Paneth cell defects result in systemic inflammation and gut barrier disruption, hallmarks of environmental enteropathy. Perhaps the Paneth cell is playing an important role in this scourge of the world's children? How might these knock-out mice grow in a contaminated environment such as those in which environmental enteropathy is endemic?

This study also prompts speculation about the effect of zinc deficiency on small-intestinal integrity. Zinc deficiency is said to affect many millions of individuals in the developing world, many of whom also have compromised gut

integrity.<sup>4</sup> Further animal studies in which dietary zinc intake is restricted may provide a glimpse of the mechanism by which these conditions co-exist.

Of course, animal studies do not directly mirror human pathobiology, and it will be interesting to discover correlates about the role of zinc transporter 2 in the human intestine. For now I commend Podany et al<sup>1</sup> for moving the scientific community further along in our understanding of how the microbiota and their mammalian hosts co-exist and cooperate, and how the Paneth cell maintains gut health.

MARK MANARY, MD  
Department of Pediatrics  
Washington University  
St. Louis, Missouri

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### Correspondence

Address correspondence to: Mark Manary, MD, Department of Pediatrics, Washington University, 660 South Euclid Avenue, St. Louis, Missouri 63110. e-mail: [manary@kids.wustl.edu](mailto:manary@kids.wustl.edu); fax: (314) 454-4345.

### Conflicts of interest

The author discloses no conflicts.

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2352-345X

<http://dx.doi.org/10.1016/j.jcmgh.2016.02.001>