Antibiotics Can Interfere with Priming of Neutrophils by Gut Microbiota

Administering broad-spectrum antibiotics to infected patients can also knock out benign intestinal bacteria, which play a key role in overall immunity by priming neutrophils in bone marrow, say researchers at the University of Pennsylvania (Penn) School of Medicine in Philadelphia. Because such losses of gut flora can disrupt host-immune responses, heavy-duty antibiotic treatments thus raise the risk for such patients of developing severe secondary infections, particularly while in hospital settings. On the plus side, replacing the bacterial signals that routinely prime neutrophils may someday provide a valuable means for offsetting these disruptive effects of broad-spectrum antibiotics, suggests Jeffrey Weiser, a professor of microbiology and pediatrics at Penn, and his collaborators.

Neutrophils, a crucial component of the innate immune system, are a first line of defense against microbial pathogens. These host cells respond through Nod1 receptors, which recognize peptidoglycan fragments from bacterial cell walls. Indeed, fragments being shed from gut microbiota travel via the bloodstream to neutrophils in bone marrow, keeping those cells of the innate immune system primed and ready to defend the host, according to Penn postdoctoral fellow Thomas Clarke, who works with Weiser.

The Penn researchers determined that this impact of antibiotics is mediated through neutrophils by comparing neutrophils from the bone marrow of mice treated with broad-spectrum antibiotics to those that remained untreated. The neutrophils from untreated mice proved far more effective in killing cells of Streptococcus pneumoniae and Staphylococcus aureus in vitro, according to Clarke and Weiser. Moreover, neutrophils from germ-free mice also do badly at killing those bacterial pathogens. However, the killing efficiency of extracted neutrophils improves soon after those mice are moved from germ-free cages into ordinary cages containing bacteria.

Next the Penn researchers probed the role of Nod1 in neutrophils by studying mutant mice that lack that receptor. Sure enough, marrow-derived neutrophils from mice that are missing Nod1 are ineffective in killing S. pneumoniae and S. aureus. Other data show that peptidoglycan fragments are translocated from the gut and act systemically to prime neutrophils in the bone marrow. Details appear in the February 16, 2010 Nature Medicine (16:228–231).

“This paper is a real game changer,” says Daniel Douek, section chief of Human Immunology at the National Institute of Allergy and Infectious Diseases in Bethesda, Md. “Broad-spectrum antibiotics may, in fact, contribute to secondary infections by altering innate signaling from gut bacteria to the immune system.” This interpretation challenges the traditional view of innate immunity as a dormant system that is mainly activated when faced with invading pathogens.

The human intestinal tract contains as many as 10^14 bacteria, but their role in host immunity is poorly understood. “The [Penn] work stresses that we have a symbiotic relationship with the enormous number of bacteria that live in our bodies,” Douek says.

Carol Potera
Carol Potera is a freelance writer in Great Falls, Mont.

Nanoparticles Render Visible Light Lethal to Microorganisms

Palladium oxide (PdO) nanoparticles are a key component for rendering visible light lethal for bacteria and viruses, according to materials scientist Jian Ku Shang at the University of...