Friend or Foe? Scientists Determine How the Intestine Keeps Us Safe From Microbial Invaders

February 21 2007

How the immune system is switched on and off, or how it detects friend or foe, has baffled scientists for years. New research from the University of Pennsylvania School of Veterinary Medicine shows that tiny cells called intestinal epithelial cells play a central role in both turning on anti-microbial immune responses and turning off harmful responses that can cause chronic inflammation in the intestine.

The researchers report their findings in *Nature*.

"Our findings suggest that manipulating intestinal epithelial cell function could provide a method to improve the efficacy of oral vaccines or help treat inflammatory diseases of the intestine like inflammatory bowel disease or food allergies," said David Artis, an assistant professor in Penn Vet's Department of Pathobiology and senior author of the study.

One of the amazing things about the human body is that in places like the intestine the body's immune system can protect against all sorts of dangerous microbes, including parasites, bacteria and viruses such as HIV. At the same time, the immune system must be carefully controlled to prevent harmful responses to the food and the trillions of harmless bacteria that live in the human intestine.

"Understanding how our body's immune system decides whether to switch on or switch off a response in the gut is one of the critical

questions in intestinal biology," Artis said.

The body's intestinal immune system is continually exposed to the food we eat and harmless intestinal bacteria that help us digest that food. It is essential that immune cells do not react to food or harmless bacteria, or diseases like inflammatory bowel disease or food allergies can develop; however, following exposure to dangerous viral, bacterial or parasitic microbes, immune cells must respond and turn on the appropriate immune response to kill the microbes.

"Our recent studies identify intestinal epithelial cells as critical cells in making friend-or-foe decisions in the gut," Artis said.

"Intestinal epithelial cells are the first line of defense in the intestine and for many years have been thought of as a simple physical wall between our tissues and the outside world," said Colby Zaph, a co-author and Irvington Institute Research Fellow who works in the Artis laboratory. "By examining mice infected with Trichuris, a species of intestinal parasites known as whipworms, we have identified a critical role for intestinal epithelial cells in promoting immune responses to fight infection."

Mice that had a defect in intestinal epithelial cell function exhibited a complete failure in the ability to mount the type of immune response that eradicates infection. Further, in the absence of functional intestinal epithelial cells, mice developed a destructive inflammatory response similar to that observed in models of inflammatory bowel disease.

"Our finding that intestinal epithelial cells appear to regulate innate and adaptive immune responses in the gut offers the exciting prospect of harnessing the function of these cells in the design and use of future vaccines and anti-inflammatory drugs that are delivered orally," Zaph said.

Source: University of Pennsylvania