

ULCERATIVE COLITIS

Bacteria penetrate the inner mucus layer of the colon

“The inner mucus layer of the colon becomes permeable to bacteria after exposure to dextran sulfate,” says Gunnar C. Hansson, corresponding author of a new study published in *PLoS ONE*. This finding could help explain the pathogenesis of ulcerative colitis, which is currently unknown.

The colon has two mucus layers that contain mucin 2 (MUC2). Bacteria usually cannot penetrate the inner layer; however, “in mice that lack mucin 2 the bacteria come in direct contact with the epithelial cells,” explains Hansson. These mice develop colitis and then cancer, similar to the disease progression of ulcerative colitis in humans.

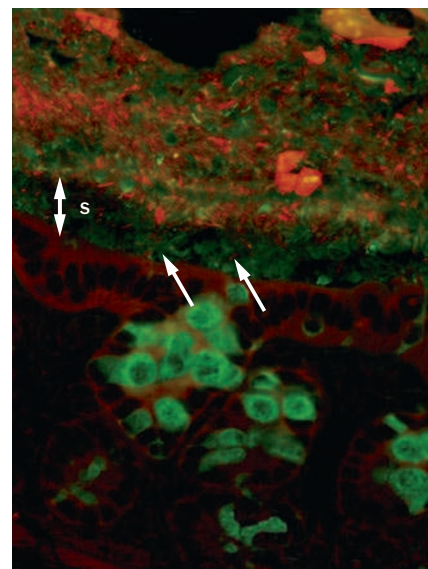
Dextran-sulfate-induced colitis in rodents is the most commonly used model of human ulcerative colitis. Colitis develops 3–5 days after dextran sulfate has been given, but there is no explanation for how this happens. Hansson and colleagues, therefore, decided to investigate whether “dextran sulfate affected the barrier of the inner mucus layer and allowed bacteria to reach the epithelia, as in the *Muc2*^{-/-} mice”. The researchers gave mice drinking water that

contained 3% dextran sulfate for 12–120 h and then analyzed tissue sections. By using fluorescent *in situ* hybridization they could show that the inner mucus layer did indeed become permeable to bacteria.

Confocal microscopy was then used to assess whether the inner mucus layer that forms on mouse colon biopsy samples became permeable to beads the size of bacteria (2 µm). “The inner mucus layer is normally impermeable to these beads, but dextran sulfate quickly altered the properties of the mucus layer to become permeable,” notes lead author Malin Johansson.

In the mouse model, the researchers found that bacteria can penetrate the inner mucus layer within 12 h of receiving dextran sulfate, long before any inflammation is observed. This suggests “colon bacteria are normally well separated from the epithelial cells and when the barrier is broken bacteria reach the epithelial surface and that the bacteria then initiate inflammation,” says Johansson.

The researchers are now studying patients who have ulcerative colitis that is at different stages of the disease. They



Green, mucin 2; red, bacteria; S, inner mucus layer (IML) normally devoid of bacteria; arrows, bacteria penetrating IML and reaching epithelial surface. Courtesy of G. C. Hansson.

hypothesize that these patients will have a dysfunctional inner mucus layer that allows bacteria to penetrate and reach the epithelial cells. “If this hypothesis holds, this is a new pathophysiological model for ulcerative colitis,” concludes Hansson.

Claire Greenhill

Original article Johansson, M. E. V. *et al.* Bacteria penetrate the inner mucus layer before inflammation in the dextran sulphate colitis model. *PLoS ONE* 5, e12238 (2010)