

Title: Role of *Bacteroides* spp. and *Escherichia coli* in inflammatory bowel disease

Principle investigator: Denis Krause

Lay version

One of the things that seems to happen in inflammatory bowel disease is that a thick layer of bacteria grows on the wall of the intestines. There is quite a lot of literature that shows that pathogenic bacteria like to attach to surfaces because when they do, it gives them protection from the environment and it also allows them to filter out nutrients from the gut contents. Also, if they are pathogenic bacteria and are causing inflammation then contact with the gut wall is important. In our previous work we have shown that *Escherichia coli* are probably important in forming this thick layer on the intestinal wall. We also think that *Bacteroides* are important because *E. coli* alone don't cause disease but they do when growing with other bacteria like *Bacteroides*. What we want to prove is that if we stop the bacteria from adhering to the gut wall and forming a thick layer then inflammation will become less serious. *E. coli* attach to the gut wall with attachments on their cell wall and we will make mutant *E. coli* that don't have these attachments. Without these attachments they should not be able to bind to the gut wall, and if our hypothesis is true, then inflammation should go away. If we can show that biofilm formation is important in IBD then we will be able to design very specific therapeutics to IBD. During the last year we have made been able to isolate a whole new set of *E. coli* from the biofilms attached to the biopsy tissue. We have also developed a technique based on fluorescent microscopy in which we are able to look at the bacteria attached to the gut wall without actually detaching the bacteria which usually happens in traditional microbiology. During the next year we will be characterizing these bacteria and completing the microscopy study.

Technical version

It is becoming clear that not all bacteria have the same effect on the immune system in IBD and certain sub-populations of *Escherichia coli* and *Bacteroides* spp may be implicated. In our current research we have been able to determine that certain genotypes of *E. coli* are more frequently associated with IBD than others. We have also found a number of genes (serine protease autotransporters [SPATE], Ag43) in these *E. coli* that are more frequently associated with disease. From our own studies, and others, we hypothesize that *E. coli* and *Bacteroides*, together, but not exclusively, form an aberrant biofilm on the mucosa of IBD patients. Several studies in other diseases have shown that *Bacteroides* is often involved in polymicrobial diseases, and some, like periodontal disease involve *Bacteroides*. We believe that *Bacteroides* and *E. coli* are major players in biofilm formation on the gut wall and promote the inflammatory response in IBD.

Earlier experiments in Balfour Sartor's laboratory has provided strong evidence of a synergistic role between *Bacteroides* and *E. coli*, and work in Alexander Swidsinski's laboratory have demonstrated that a modified biofilm is formed in IBD. During the last year *E. coli* and *Bacteroides* from biopsies obtained via the "Tissue bank" were isolated. At present we have a collection of approximately 150 coliforms and *Bacteroides*. These strain are currently having the caparonin 80 gene sequenced. These strains will then be characterized for virulence factors. We have also developed fluorescent *in situ* hybridization probes for *E. coli* and *Bacteroides* based on peptide nucleic acid probe backbones as apposed to the traditional sugar phosphate backbone. We have done this because it gives us a high level of discriminatory power. In the next year these tasks will be completed.

Publications

Peer reviewed

- Sepehri, S., R. Kotlowski, C.N. Bernstein, and D.O. Krause. 2007. Microbial diversity of inflamed and noninflamed gut biopsy tissues in inflammatory bowel disease. *Inflamm Bowel Dis*. Epub ahead of print.
- Kotlowski, R., C.N. Bernstein, Mark Silverberg, and D.O. Krause. 2007. Population-based case-control study of alpha 1-antitrypsin and SLC11A1 in Crohn's disease and ulcerative colitis. *Inflamm Bowel Dis*.

Conference abstracts

- Hernandez, Juan, and Denis O. Krause. 2007. "Relationships between B2 and D pathogenic genotypes and quorum sensing genes in a diverse set of human and rumen gut isolates of Escherichia coli." American Society for Microbiology, General 107th Meeting, Toronto, Canada, May 21-25.

Invited presentations

- Krause, Denis O. 2007. "Is there a IBD bug out there?" Saskatoon Chapter of Crohn's and Colitis Foundation, Saskatoon, SK, October 6.
- Krause, Denis O. 2007. "Is there a gut bug in IBD?" Regina Chapter of Crohn's and Colitis Foundation, Regina, SK, September 7.
- Krause, D.O. 2007. "Microbial etiologies in inflammatory bowel disease." Gut Forum, University of Manitoba, June 5.

Community events

- Krause, Denis O. 2007. "Is there a IBD bug out there?" Saskatoon Chapter of Crohn's and Colitis Foundation, Saskatoon, SK, October 6.
- Krause, Denis O. 2007. "Is there a gut bug in IBD?" Regina Chapter of Crohn's and Colitis Foundation, Regina, SK, September 7.