

First Annual Report from Dr. Bruce Vallance for his CCFC Grant in Aid of Research on
“Goblet Cell Mediators and their Impact on Mucosal Protection and Susceptibility to Colitis”.

It has long been suspected that Inflammatory Bowel Diseases (IBD) develop in genetically susceptible people because of defects that allow bacteria to escape from their intestines, passing into the blood where they can activate the immune system causing inflammation. One of the features of the intestine that usually prevents the escape of bacteria is mucus, a gel like substance that coats the inner surface of the intestine, acting both as a protective barrier that traps bacteria, and as a lubricant to prevent damage from ingested food. The mucus barrier is produced by specialized cells in the intestine called goblet cells and interestingly, IBD is often accompanied by a decrease in the thickness of the mucus barrier, as well as a drastic reduction in goblet cell numbers. Currently it is unclear what factors cause these changes in goblet cells and mucus, and whether reduced mucus expression helps bacteria escape the intestines and cause or perpetuate IBD.

Since receiving our funding from CCFC, we have published a manuscript showing that goblet cell numbers and mucus production in the intestine both decrease during experimental colitis and that these changes require the actions of specialized immune cells called T lymphocytes. These results suggest that the inflammation that occurs during IBD may damage intestinal goblet cells and thereby cause the reduction in mucus seen in the intestines of IBD patients. Currently we are identifying specific proteins released by T lymphocytes that can bind to goblet cells and alter their function, with the goal of trying to prevent this from occurring during IBD. In additional studies performed in collaboration with Dr. Kris Chadee’s laboratory in Calgary, we are also examining whether impaired mucus production affects susceptibility to IBD. Using mice that are missing their intestinal mucus barrier, we have found that these mice are less able than normal to contain bacteria within their intestines, and actually develop a form of spontaneous IBD. Our current studies are now addressing what immune factors are involved in triggering IBD in these mice.

Published Papers:

1. Bergstrom K.S., Guttman J.A., Rumi M., Ma C., Bouzari S., Khan M.A., Gibson D.L., Vogl A.W., Vallance B.A. Modulation of intestinal goblet cell function during infection by an attaching and effacing bacterial pathogen. *Infect Immun.* 2008 Feb;76(2):796-811.

Published Abstracts:

1. Bergstrom, K.S.B., Rumi, M., Khan, W., Ma, C., Khan, M.A., and Vallance, B.A.. (2006) In Vivo Goblet Cell Responses to an Enteric Bacterial Pathogen in a Mouse Model of Infectious Colitis AGA Digestive Diseases Week 2006. May 21-25, 2006 Los Angeles, California, U.S.A. (Poster Presentation) Published in *Gastroenterology* 132(4), Annual Abstract Supplement , #S1655.

Abstracts:

1. Bergstrom, K.S.B., Guttman, J.A., Ma, C., Khan, M.A., Gibson, D.L., and Vallance, B.A.. (2007) In Vivo Modulation of Colonic Goblet Cell Function During *C. rodentium* Infection. Canadian Association of Gastroenterology: Topics in GI Diseases VII. Kingsbridge, Ontario, Canada October 12-14, 2007 (oral presentation). (Please see attached letter.)

2. Bergstrom, K.S.B., Guttman, J.A., Ma, C., Khan, M.A., Gibson, D.L., and Vallance, B.A.. (2007) In Vivo Modulation of Colonic Goblet Cell Function During *C. rodentium* Infection. American Association of Gastroenterology (AGA) Gastrointestinal Response to Injury Conference Montebello, Quebec, Canada. October 3-6, 2007. (Poster and Oral Presentation) (Please see attached letter.)

Was one of the 9 out of 40 abstracts selected to give an oral presentation to an audience of approximately 150 researchers, made up of both established investigators and trainees.

3. Bergstrom, K.S.B., Ma, C., Khan, W., Velcich, A., and Vallance, B.A.. Muc2 is a Critical Component of Host Innate Defense Against Attaching and Effacing Bacterial Pathogens *In Vivo*. Experimental Medicine Student Research Day, June 13 2008. (Poster Presentation).

4. Bergstrom, K.S.B., Ma, C., Khan, W., Velcich, A., and Vallance, B.A.. . Muc2 is a Critical Component of Host Innate Defense Against Attaching and Effacing Bacterial Pathogens *In Vivo*. Student Research Forum, Child & Family Research Institute. June 19, 2008. (Poster Presentation)

Oral Presentation:

1. Goblet Cells and Their Role in Mucosal Protection During Bacterial Induced Colitis. Pediatric Gastroenterology Research Rounds, B.C. Childrens Hospital. January 16, 2008.

2. Role of Resistin-Like Molecule-Beta/Found in Inflammatory Zone 2 (Relm β /Fizz2) during *C. rodentium* Infection. Inflammatory Bowel Disease Meeting. Jack Bell Research Centre. May 15, 2008