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Diet And Intestinal Bacteria Linked With Healthier Immune Systems

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Insoluble dietary fibre, or roughage, not only keeps you regular, say Australian scientists, it also plays a vital role in the immune system, keeping certain diseases at bay.

The indigestible part of all plant-based foods pushes its way through most of the digestive tract unchanged, acting as a kind of internal broom. When it arrives in the colon, bacteria convert it to energy and compounds known as 'short chain fatty acids'. These are already known to alleviate the symptoms of colitis, an inflammatory gut condition.1

Similarly, probiotics and prebiotics, food supplements that affect the balance of gut bacteria, reduce the symptoms of asthma and rheumatoid arthritis, also inflammatory diseases. Until now no-one has understood why.

Published in *Nature*, breakthrough research by a Sydney-based team makes new sense of such known facts by describing a mechanism that links diet, gut bacteria and the immune system.

PhD student Kendle Maslowski and Professor Charles Mackay from the Garvan Institute of Medical Research, in collaboration with the Co-operative Research Centre for Asthma and Airways, have demonstrated that GPR43, a molecule expressed by immune cells and previously shown to bind short chain fatty acids, functions as an anti-inflammatory receptor,

"The notion that diet might have profound effects on immune responses or inflammatory diseases has never been taken that seriously" said Professor Mackay. "We believe that changes in diet, associated with western lifestyles, contribute to the increasing incidences of asthma, Type 1 diabetes and other autoimmune diseases. Now we have a new molecular mechanism that might explain how diet is affecting our immune systems."

"We're also now beginning to understand that from the moment you're born, it's incredibly important to be colonised by the right kinds of gut bacteria," added Kendle. "The kinds of foods you eat directly determine the levels of certain bacteria in your gut."

"Changing diets are changing the kinds of gut bacteria we have, as well as their by-products, particularly short chain fatty acids. If we have low amounts of dietary fibre, then we're going to have low levels of short chain fatty acids, which we have demonstrated are very important in the immune systems of mice."

Mice that lack the GPR43 gene have increased inflammation, and poor ability to resolve inflammation, because their immune cells can't bind to short chain fatty acids.

There is plenty of evidence to suggest that bacteria and their by-products play an important role in people. An American study published in *Nature* in 2006 2 compared the bacteria in the guts of obese and lean people. The obese people were put on a diet, and as they lost weight their bacteria profile gradually came to match that of the lean people.

Another study 3 looked at what diets might do to short chain fatty acid levels. Obese people were put on three different diets over time - high, medium and low fibre - and there was a direct correlation between the level of carbohydrate, or fibre, in the diet and the level of short chain fatty acids.

The conclusions drawn from the current research provide some of the most compelling reasons yet for eating considerably more unprocessed whole foods - fruits, vegetables, grains, nuts and seeds. 4

Dietary fibre, of course, has many known health benefits in addition to those discussed above, including reduced risk of cardiovascular disease and certain cancers 5, and various health

organizations around the world recommend daily minimum levels. 6 It is certain that the majority of people in countries like Australia, the United States and Britain eat much less fibre than they need to stay healthy.

"The role of nutrition and gut intestinal bacteria in immune responses is an exciting new topic in immunology, and recent findings including our own open up new possibilities to explore causes as well as new treatments for inflammatory diseases such as asthma", said Professor Mackay. Notes:

1. In several trials, people with colitis have been given dietary fibre, resulting in beneficial anti-inflammatory effects:
   Harig, J. M., Soergel, K. H., Komorowski, R. A. & Wood, C. M. Treatment of diversion colitis with short-chain-fatty acid irrigation. *N. Engl. J. Med.* 320, 23-28 (1989). http://www.ncbi.nlm.nih.gov/pubmed/2909876?dopt=Abstract
   Kanauchi, O. et al. Treatment of ulcerative colitis by feeding with germinated barley foodstuff: first report of a multicenter open control trial. *J. Gastroenterol.* 37 (suppl. 14), 67-72 (2002). http://www.ncbi.nlm.nih.gov/pubmed/12572869?dopt=Abstract
   Breuer, R. I. et al. Rectal irrigation with short-chain fatty acids for distal ulcerative colitis. Preliminary report. *Dig. Dis. Sci.* 36, 185-187 (1991). http://www.ncbi.nlm.nih.gov/pubmed/1988261?dopt=Abstract
   Scheppach, W. Treatment of distal ulcerative colitis with short-chain fatty acid enemas. A placebo-controlled trial. German-Austrian SCFA Study Group. *Dig. Dis. Sci.* 41, 2254-2259 (1996). http://www.ncbi.nlm.nih.gov/pubmed/8943981?dopt=Abstract
   Vernia, P. et al. Short-chain fatty acid topical treatment in distal ulcerative colitis. Aliment. Pharmacol. Ther. 9, 309-313 (1995). http://www.ncbi.nlm.nih.gov/pubmed/7654893?dopt=Abstract

2. Ley, R. Turnbaugh, P.J. Klein, S Gordon, J.I Human gut microbes associated with obesity. *Nature* 444, 1022-1023 (2006). http://www.nature.com/nature/journal/v444/n7122/abs/4441022a.html

3. Duncan, S.H Belenguer, A. Holtrop, G. Johnstone, A.M. Flint, H.J. Lobley, G.E. Reduced Dietary Intake of Carbohydrates by Obese Subjects Results in Decreased Concentrations of Butyrate and Butyrate-Producing Bacteria in Feces. *Applied and Environmental Microbiology*, 1073-1078 (2007) http://aem.asm.org/cgi/content/abstract/73/4/1073

4. There are many online sources where information can be found about foods and their levels of soluble and insoluble fibre - the effects of the latter investigated in this research. Some foods, such as wheat bran, chick peas, dried fruits (apricots, peaches, figs and dates) and berries (raspberries and blackberries) have particularly high levels of insoluble fibre. CSIRO produces a useful fact sheet. http://www.csiro.au/resources/DietaryFibre.html#1

5. O'Keefe, S Ou, J Aufreiter, S O'Connor, D Sharma, S Sepulveda, J Fukuwatari, T Shibata, K Mawhinney, T. Products of the Colonic Microbiota Mediate the Effects of Diet on Colon Cancer *Risk. J. Nutr*. 2009 139: 2044-2048. First published online November 1, 2009; doi:10.3945/jn.109.104380 http://jn.nutrition.org/cgi/content/abstract/139/11/2044

6. Australian Dietary Guidelines, produced by the National Health and Medical Research Council recommend a daily intake of 30-35 grams of fibre. http://www.health.gov.au/internet/healthyactive/publishing.nsf/content/eating
   The United States National Academy of Sciences, Institute of Medicine recommends a daily intake of 21-38 grams a day, depending on age and sex (the average American's daily intake is 12-18 grams). http://www.nap.edu/openbook.php?record_id=10490&page=339
   The British Nutrition Foundation recommends a daily intake of 18 grams (the average intake is 12 grams). http://www.nutrition.org.uk/home.asp?siteId=43§ionId=609&parentSection=324&which=1

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