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Gut feeling: New study proposes probiotic mechanism for IBD benefits

By Stephen Daniells, 05-Jul-2011

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A protein on the surface of specific probiotic bacteria may promote anti-inflammatory responses in the gut and explain the potential role of select probiotics to ease symptoms of inflammatory bowel disease (IBD), says a new study.

Led by researchers from the Institut Pasteur de Lille in northern France, the new study indicates that the strain specific effects of probiotics against IBD may be related to the presence of certain proteins on the surface, which can interact with a receptor on the wall of the intestine to produce an inflammatory response.

However, certain strains that do not have this active protein – called peptidoglycan or PGN – on their surface were unable to react with the receptors (called NOD2) and were not associated with any protective properties, according to findings published in the BMJ Group's journal *Gut*.

"Although emerging evidence suggests that regulatory responses are crucial in circumventing inflammatory processes, our observations support an important role for probiotic and probiotic-derived components in regulating immune homeostasis," wrote the researchers.

"Insights gained through these findings will thus improve strain selection procedures and hopefully provide highly positive results in future clinical trials with probiotics in IBD."

Chronic inflammatory bowel disease (IBD) is a multi-factorial disease with an unknown cause. The prevalence of IBD rapidly increased in Europe and North America in the second half of the 20th century, and is reportedly becoming more common in the rest of the world as countries adopt a Western lifestyle.

Immediate and future implications

While regulatory bodies like the European Food Safety Authority (EFSA) remain unconvinced of the benefits of probiotics, despite a towering mountain of evidence, the new study not only supports the role of probiotics in people with IBD, it also indicates a potential mechanism.

In an accompanying editorial in the same journal, Professor Fergus Shanahan from University College Cork said the work has immediate and important implications for *"devising selection criteria for probiotics and illustrates the value of bioprospecting within the gut microbiota for bioactives suitable as functional foods or a new generation of drugs"*.

Going forward, the work also contributes to the potential promise of a 'bugs-to-drugs' strategy, he said.

Study details

The researchers tested the anti-inflammatory potential of two *Lactobacillus* strains *L. salivarius* Ls33 and *L. acidophilus* NCFM (both from Danisco) in a mouse model of colitis. The former is reported to be protective against IBD, while the latter strain is not protective.

Mice that were genetically engineered to be deficient in NOD2 and their response on exposure to the bacterial strains were compared with mice that possessed NOD2.

The results showed that the *"protective capacity of selected probiotic lactobacilli is NOD2-dependent"*, said the researchers. In animals that possessed NOD2, exposure to PGN from *L. salivarius* Ls33 was associated with local production of the anti-inflammatory compound, interleukin 10 (IL-10).

However, PGN from *L. acidophilus* NCFM did not elicit the same effect, showing the effects of strain specificity.

"We demonstrated both in vitro and in vivo that PGN purified from the protective L. salivarius Ls33 strain exhibited anti-inflammatory potential, while PGN derived from a non-protective strain did not," wrote the researchers.

Response

In his editorial, Professor Shanahan said the new study "*leaves several lingering questions*". The first of which is how mutations in NOD2 may explain previous disappointing results of lactobacillus probiotics in Crohn's disease patients. Prof Shanahan also asked how strong the anti-inflammatory property of these specific strains was, and whether other similar elements on other bacteria would produce a similar effect as PGN.

"*The field is rich,*" he concluded.

Source: *Gut*

2011, Volume 60, Pages 1050-1059, doi:10.1136/gut.2010.232918

"*Anti-inflammatory capacity of selected lactobacilli in experimental colitis is driven by NOD2-mediated recognition of a specific peptidoglycan-derived muropeptide*"

Authors: E. Macho Fernandez, V. Valenti, et al.

Editorial: *Gut*

2011, Volume 60, Pages 1026-1027, doi:10.1136/gut.2011.241026

"*Molecular mechanisms of probiotic action: it's all in the strains!*"

Author: F. Shanahan

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