60 second interview with Dr Carl Hulston

Lecturer and researcher in exercise physiology, nutrition and metabolism at Brunel University

The obesity epidemic is still on the rise, with an increase in health problems associated with the metabolic syndrome, such as cardiovascular disease (CVD) and type II diabetes. We decided to have a minute's catch up with Dr Hulston [CH] to learn about his research in this area.

Who is your favourite scientist? And why/ what did they contribute to science?
CH: I would have to say Professor Bengt Saltin from the Copenhagen Muscle Research Centre – he is one of the world's most eminent exercise physiologists. Bengt has published over 400 papers since the 1960s, with seminal work on muscle metabolism and fuel utilisation during exercise.

What areas of research interest you?
CH: I'm particularly interested in exercise-nutrition interactions. For example, from an athletic point of view, eating the right food is essential to facilitate training adaptation. At the other end of the spectrum, poor diet and/or insufficient physical activity are undoubtedly causing the worldwide obesity/ diabetes epidemic.

Could altering the intestinal microbiota and/ or probiotics have any benefit?
CH: Eating too many calories and/or foods that are too high in saturated fats has been shown to alter the gut microbiota and we believe this may lead to the development of insulin resistance and type II diabetes. Improving gut health (with probiotic supplementation) may help to prevent diet-induced insulin resistance.

If you were able to determine that probiotics could help to prevent diet-induced insulin resistance, how would you like to see this work progress and how do you think it might be used in the 'real world'?
CH: If it was found that probiotics helped reduce insulin resistance the next step would be to identify the mechanisms involved, i.e. how does it work? It would also be particularly interesting to see if probiotics can reverse insulin resistance in type II diabetic patients. This would of course have major implications in the real world!

So when you are not doing science, what are your hobbies?
CH: Mainly cycling but I also enjoy running and hiking whenever possible.

Gut Week is coming!

Full details about this year's Gut Week – the annual digestive health awareness campaign, which highlights the vital role of the digestive system and emphasises the importance of maintaining good gut health – will be announced in Probiotic Bulletin in the summer.

In the meantime, did you know that as healthcare professionals you have a range of resources available to you via the campaign, to help you educate your patients about the importance of gut health?

We can provide you with information packs and leaflets for your surgeries, our science team can come and talk to your staff about probiotics and digestive health and we have an online information resource that can be accessed at www.gutweek.ie

Gut Week is into its 7th year

For further information contact the science team on 01 8047695 or science@yakult.ie

Science team notice board

Diary Dates

25th–26th May Health Events, Crowne Plaza, Northwood

16th–19th July Nutrition Society Summer Meeting, Queens, Belfast

International Yakult Symposium 2013

Stop Press!

22nd and 23rd April International Yakult Symposium 2013, Queen Elizabeth II Conference Centre, London

http://www.yakultsymposium.com/

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- A dedicated website for healthcare professionals; provides easy to read summaries of the major *L. casei* Shirota studies, nutritional information and FAQs: www.yakult.ie/hcp

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Pass it on

If you enjoy reading the Probiotic Bulletin, please forward it on and encourage your colleagues to email science@yakult.ie to sign up.

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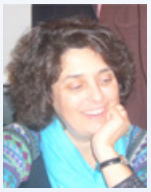
Probiotic Bulletin

AN UPDATE FOR HEALTHCARE PROFESSIONALS

Cigarettes and NK cell activity

A new human study on *Lactobacillus casei* Shirota gives further indications of a positive immune effect for smokers.


(Left to right) Prof Paolo Boscolo, Prof Marcella Reale, Prof. Raffaella Muraro

Did you know?

- €13,650* – The amount you would save in ten years if you gave up smoking ten cigarettes a day
- After ten years of giving up smoking, lung cancer risk drops to half that of a smoker
- If you stop smoking before the age of about 35, your life expectancy is only slightly less than people who have never smoked
- If you stop smoking before the age of 50, you decrease the risk of dying from smoking-related diseases by 50%

www.nhs.uk/Livewell/smoking/Pages/Betterlives.aspx

**based on UK statistics*

Dr Anna Castioni spoke to the research team, who are based at Università degli Studi "G. D'Annunzio" di Chieti e Pescara, in Italy:

Professor Muraro (RM), Professor Reale (MR) and Professor Boscolo (PB) – thank you for agreeing to discuss this research. Your study focussed on one component of the immune system: natural killer (NK) cells. What is their role in humans?

RM: NK cells are extremely important components of the immune system. They are involved in protecting against infection, and play a part in immune-surveillance against tumours. For example, they can prevent, at least in experimental models, metastatic dissemination. They can modulate inflammatory responses and the function of macrophages and granulocytes via the release of various chemical mediators. They also influence responses, mediated by T lymphocytes, to induce a TH1-type response that is particularly effective against various pathogens. Therefore, any reduction in NK cell activity will have a negative consequence for health. Which is why it is important to identify ways to help maintain NK activity, and to find ways to restore this in people who have low NK cell activity due to their lifestyle choices. Smokers are a good example of the latter.

How can lifestyle affect the innate immune system?

PB: It is hard to say which particular lifestyle has the most negative effect on the innate immune response. Studies have shown significantly reduced NK cell activity in individuals with poor lifestyle, those that are emotionally unstable or anxious, and those who are subject to stress from repetitive work or shift work. Previous studies have shown there is an inverse correlation between NK activity and the number of cigarettes smoked per day.

So, can you briefly describe the study?

RM: The aim of the study was to evaluate the effects of regular intake of *L. casei* Shirota in a population of healthy male adult smokers. We were interested in analysing changes in their NK cells' cytotoxic activity before and after probiotic intake. We also measured changes in their perception of particular psychological states and/or physical malaise, such as anxiety, as well as nausea/abdominal pain.

What kind of people did you enrol in the trial, and why?

PB: We recruited 72 healthy male smokers, with a median age of 50 years, who had similar working, lifestyle and socioeconomic status. This population was chosen because we know that cigarette smoking negatively influences the normal cytotoxic activity of NK cells and this reduced immune response results in an increased risk of disease.

What intervention was given to the subjects?

MR: Every day for three weeks, the subjects were randomly assigned to consume either a powder preparation of *L. casei* Shirota or a placebo preparation containing corn starch. Blood samples were taken from them, in order to evaluate hematochemical parameters and NK cells' cytotoxic activity. Results were compared to baseline values, i.e. before starting the intake.

What can be inferred from this study, from an immunological point of view?

MR: A significant increase in NK activity was observed in those subjects given *L. casei* Shirota compared to those given placebo. In fact, probiotic intake was associated with restoring their levels of NK activity, which had been reduced due to smoking. *L. casei* Shirota intake appeared to have a positive effect, without modifying any hematochemical parameters.

Continued on page 2...

Cigarettes and NK cell activity

Did you observe any differences in terms of the subjects' quality of life and symptoms that were assessed?

PB: Interestingly there was an increase in the percentage of subjects reporting no symptoms of physical malaise, after the period of taking the probiotic. Furthermore, there was also a reduction in their perception of symptoms of nausea and abdominal pain. This is not surprising, since beneficial effects of probiotics in the gastrointestinal tract are known, however the molecular mechanisms of interaction have not yet been fully established.

How should we interpret these results?

RM: The observations of increased NK activity and fewer symptoms of physical malaise suggest that smokers may benefit from regular intake of *L. casei* Shirota.

What conclusions have you drawn from this study?

MR: Certainly that regular intake of *L. casei* Shirota enhanced NK activity in our subjects, correcting the reduction induced by cigarette smoking and restoring NK activity compared to baseline levels. These observations suggest that there was a restoration of the innate immune response.

Do you think these results can be extended to the wider population?

RM: Our study examined one specific population group whose particular lifestyle impacts negatively on NK cell activity.

These positive results certainly suggest that further research is warranted to investigate other groups whose habits and/or lifestyles affect the immune system. It also suggests that there is a need to research further not only the effects of *L. casei* Shirota intake on NK activity but also its effects on other components of the immune system and the mechanisms of activity at a molecular level.

Reale M *et al* (2011) Daily intake of *Lactobacillus casei* Shirota increases natural killer cell activity in smokers. *B J of Nutr* **Dec 6:** 1–7 [epub ahead of print]

Università degli Studi "G. D'Annunzio" di Chieti e Pescara, Italy

New free resources

For healthcare professionals:

Keep information on hand with our ***NEW*** pocket sized Bristol Stool Scale information card, which includes the current advice from NICE on the use of probiotics in IBS and a summary of key findings from *L. casei* Shirota studies in constipation and diarrhoea.

Our new pocket sized 'Bristol Stool Scale' information card

For your patients:

Request our ***NEW*** 'Maintaining a Healthy Gut' leaflet for your patients.

Contact the science team at science@yakult.ie to request these new leaflets. You may also like to request a free educational talk on probiotic research for you and your colleagues.

Our new 'Maintaining a Healthy Gut' patients leaflet

The Little Book of Fitness

Request your free booklet now by emailing science@yakult.ie

The immune system and the intestinal microbiota: a 'special relationship'

Our front page featured an immune trial, so we thought a brief look at the inter-relationship between the gut, its microbiota and the immune system might help put this into context

What is the immune system?

A network of specialised cells, proteins, chemical messengers, tissues and organs that help protect the body from illness and infection. There are two main parts:

- the innate immune system, giving a rapid, but unfocused response
- the acquired or adaptive immune system, which gives a slower but specifically targeted response, based on previous exposure

The immune system comprises soluble factors (e.g. cytokines, acute phase proteins and immunoglobulins) and cellular factors (e.g. natural killer cells, macrophages, dendritic cells, lymphocytes such as T and B cells).

The gut is a very vulnerable part of the body – it is the main entry point for foreign substances into the body, yet has a huge surface area to cope with absorbing water and nutrients. This is why such a large proportion of the immune system is located in the gut. For example, 85% of all the body's lymph nodes are in the gut (MacDonald & Bateman, 2007), forming the gut-associated lymphoid tissue (GALT). This immune system faces the challenge of distinguishing between dietary antigens, pathogenic microbes and the commensal microbiota, so that it will mount an appropriate response when needed.

The intestinal microbiota is vital for the proper development and education of the immune system in infants, but remains an important influence throughout life.

Microbial tweets? Throughout life, the bacteria (and other antigens in the gut lumen) are in constant communication with the immune system – but how?

The main communication routes between bacteria and the immune system in the gut (see Figure 1)

Route 1: TLRs (toll-like receptors) on the brush border of epithelial cells distinguish pathogenic and commensal bacteria in the gut lumen by recognising pathogen-associated molecular patterns in bacterial cell walls. This triggers the epithelial cell to release cytokines into the lymphoid tissue. Cytokines can then interact in numerous ways with immune cells.

Route 2: M cells transport bacteria and antigens intact from the gut lumen to lymphoid tissue via a process called transcytosis. The material is then captured by antigen-presenting cells such as macrophages or dendritic cells, and presented to naive T and B cells.

Route 3: Immature dendritic cells can express proteins that can open tight junctions between epithelial cells. This allows the dendritic cell to extend dendrites to directly sample luminal antigens, without compromising the epithelial barrier function, to stimulate the appropriate immune response.

The immune response stimulated is determined by the type of bacteria interacting with the GALT. Visit www.yakult.ie/hcp for glossary of terms and more information.

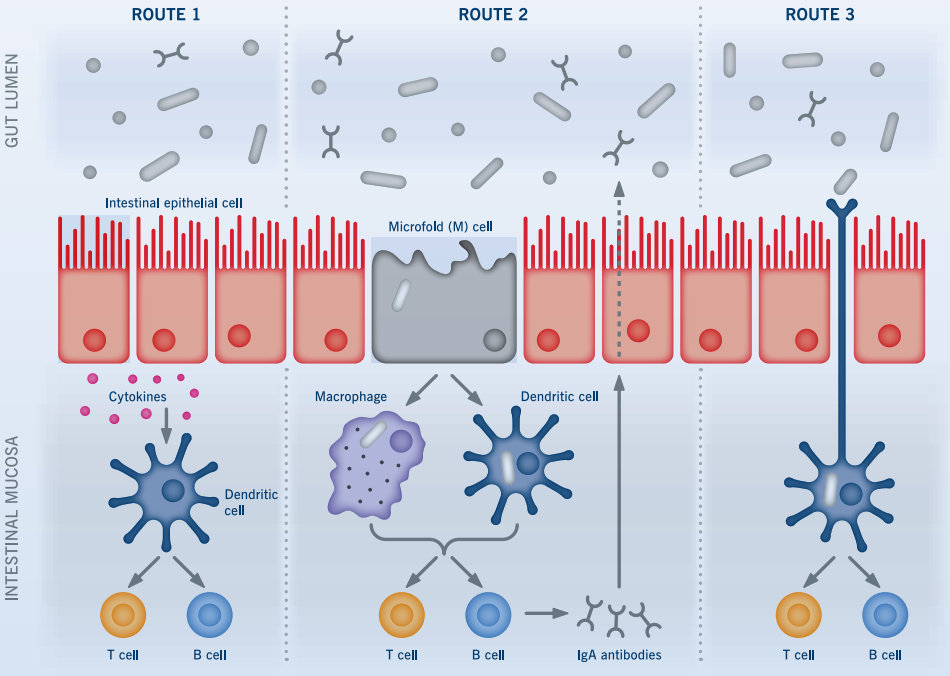


Figure 1: Adapted from: Janeway, C.A, Travers, P, Walport, M and Shlomchik, M.J (2005) Immuno Biology; the immune system in health and disease: 6th Edition, Garland Science Publishing, P433

Did you know?

A prospective study following 3625 people over a period of 11 years, found that medium and high cytotoxic activity of peripheral blood was linked to reduced risk of cancer, whereas low activity was linked to increased risk (Imai K *et al*. 2000. *Lancet* **356(9244)**: 1795–9).

Research round-up

Review: Probiotics and the host intestinal mucosa

In this detailed review the authors discuss the current knowledge of the molecular modes of action through which probiotics interact with the host, particularly the immune system. They emphasise that further structural characterisation of the cell wall components and surface layer proteins will shed light on strain-specific effects and they highlight the difficulty and the necessity of being able to translate *in vitro* findings to the human model. Genomic, high throughput technologies have provided new and powerful ways to study the intestinal microbiota and the influence that probiotics play within that environment. Interindividual differences in human genotype, enterotype and diet are likely to be key determinants of an individual's physiological responsiveness to probiotics.

Bron P *et al* (2011) Emerging molecular insights into the interaction of probiotics and the host intestinal mucosa. *Nature Rev Microbiol* **10(1):** 66–78

A pre- and probiotic combination may be better than prebiotics alone in reducing atopic dermatitis in children

Atopic dermatitis (AD; a form of eczema) is one of the most common allergic diseases in children. Sixty children aged between 2 and 14 who had moderate to severe AD were randomly assigned to receive prebiotic alone (950 mg/day of fructo-oligosaccharide; FOS) or a prebiotic-probiotic combination (950mg FOS plus $4x10^9$ *Lactobacillus salivarius* PM-A0006/day) for 8 weeks. At 8 weeks both groups showed modest improvement in AD clinical scores but the prebiotic-probiotic combination was significantly better than prebiotics alone. Studies with longer-term follow up are necessary to determine the benefits of prebiotic-probiotic combinations on AD in children.

Wu K *et al* (2012) *Lactobacillus salivarius* plus fructo-oligosaccharide is superior to fructo-oligosaccharide alone for treating children with moderate to severe atopic dermatitis: a double-blind, randomized, clinical trial of efficacy and safety. *Br J Dermatol* **166(1):** 129–136

Vegetarian and vegan diets alter faecal microbiota

Faecal samples of vegetarians (n=144), vegans (n=104) and omnivores (n=246) were collected and analysed using conventional microbiological methods. The faecal microbiota of vegetarian and vegan test subjects exhibited lower microbial counts of *Bifidobacterium* and *Bacteroides* species while total counts remained unchanged. Vegetarian and vegan diets also led to a significantly reduced faecal pH. The culturing techniques used in this study reflect only a limited number of species within the intestinal microbiota, however the authors conclude that strict vegetarian or vegan diets alter the microbiota significantly.

Zimmer J *et al* (2012) A vegan or vegetarian diet substantially alters the human colonic faecal microbiota. *Eur J Clin Nutr* **66(1):** 53–60

Probiotics may improve inflammatory complications in diabetes mellitus

Inflammation has been implicated in diabetes severity therefore this study examined the potential of *Lactobacillus casei* Shirota in reducing inflammation in diabetic rats. Diabetes was induced by streptozotocin in male rats and *L. casei* Shirota was administered for 3 weeks daily via oral gavage. *L. casei* Shirota supplementation lowered markers of pro-inflammatory cytokines (CRP and IL-6) and neutrophils but did not affect glucose levels or IL-4. In conclusion, this study indicated the potential of this probiotic for improving inflammation-associated complications in diabetes. Further work is warranted.

Zarfeshani A *et al* (2011) Effect of *Lactobacillus casei* on the production of pro-Inflammatory markers in streptozotocin-induced diabetic rats. *Probiotics & Antimicro Prot* (2011) **3:** 168–174