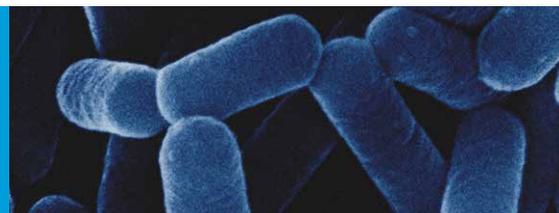


Probiotic Bulletin

A Newsletter for Healthcare Professionals



The role of probiotics in healthy people

A summary of new research

The role of probiotics in the maintenance of health is a subject of continuous interest amongst healthcare professionals, with a steady stream of positive research outcomes underpinning the growing confidence in recommending probiotic consumption. This article summarises recent evidence showing the effect of *Lactobacillus casei* Shirota on immune markers and metabolic risk factors in healthy people, and on healthy people in stressful situations.

In this issue:

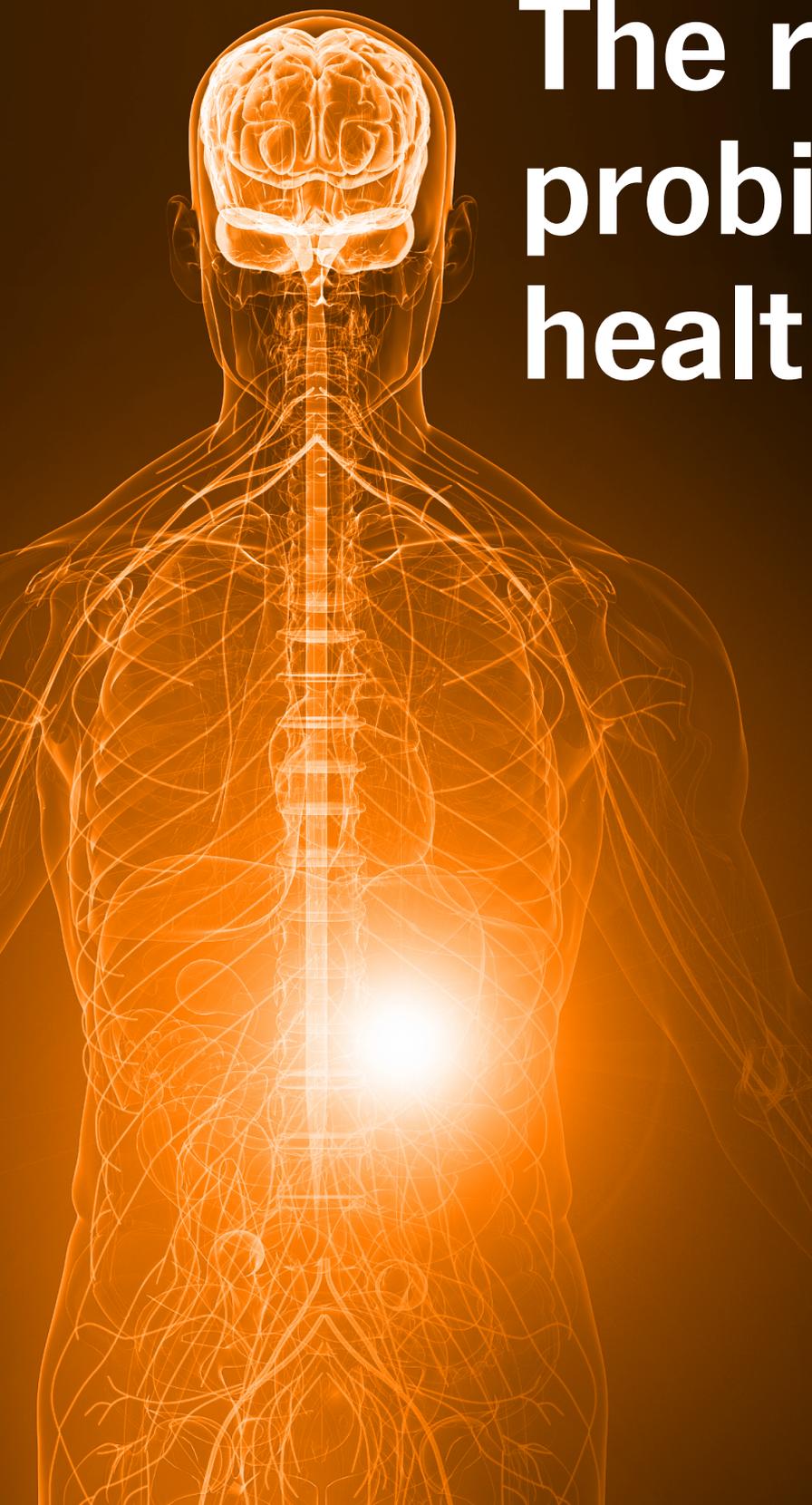
- Probiotics and healthy people 1-3

- More than just a feeling in your bones
- No Waste Food Waste
- Resource for HCPs – Nutrition in later life
- Love Your Gut 2017 4-5

- HCP Awards
- Student Awards 6

- New research papers
- Free *Nature Insight* 7

- International Yakult Symposium 2018 8



Response to stress

A recent study explored the impact of *Lactobacillus casei* Shirota (LcS) on physical, psychological and physiological stress responses of healthy medical students ahead of an exam¹.

The researchers conducted a double-blind randomised-controlled trial in 47 healthy students aged <30 years. The participants consumed either a fermented milk drink containing LcS (n=23) or a placebo milk (n=24) daily for 8 weeks, up until the day before their exam. Saliva samples, blood samples and questionnaire responses were collected 8 weeks, 2 weeks and 1 day before the exam, and then immediately after and 2 weeks after the exam. The primary focus was on the effects of LcS on stress-induced abdominal dysfunction and stress markers (both psychological and physiological), but they also examined whether LcS administration affected stress-induced changes in the composition of the gut microbiota, and gene expression profiles in peripheral leukocytes.

Abdominal dysfunction was measured by a questionnaire based on common abdominal symptoms, such as 'abdominal discomfort and pain' or 'distention'. The researchers found that the LcS group had a significantly lower total abdominal dysfunction score than the placebo group throughout the intervention period (P<0.05); the LcS group showed a gradual reduction in abdominal dysfunction score during the intervention, whereas there was no significant change in scores in the placebo group. In further analyses, the researchers stratified the

participants based on whether they had symptoms of 'abdominal pain and discomfort' during the pre-intervention phase or not. They showed that daily consumption of LcS not only improved symptoms in those who complained of 'abdominal discomfort and pain' pre-intervention, but also resulted in none of the pre-intervention symptom-free participants developing symptoms throughout the study period, unlike the placebo group.

In a similar manner to total abdominal dysfunction, feelings of stress (measured by visual analogue scales) were significantly lower throughout the intervention in the group receiving LcS than in the placebo group (P<0.05).

Salivary cortisol was measured as a physiological marker and indicator of stress. On the day before examination, salivary cortisol levels increased significantly in the placebo group, compared with baseline levels (P<0.05), but interestingly no significant rise in salivary cortisol levels were shown in the LcS group.

Changes in gene expression in response to stress, and the effects of LcS on this, were also explored by the researchers. In summary, they reported that the LcS administration significantly reduced the number of stress-responsive genes with changed expression at one day before, and immediately after the examination (Table 1).

Table 1: The number of stress-responsive genes with changed expression

Outcome	Probiotic group	Control group	P
One day before examination	86	179	<0.001
Immediately after examination	1	8	<0.05

The researchers also examined the effects of LcS on the gut microbiota of the participants and found that the daily consumption of LcS significantly reduced the percentage of *Bacteroidaceae* at the family level. Interestingly, it has been reported that higher percentages of *Bacteroidaceae* at the family level have been shown in the gut microbiota of people suffering with depression compared with healthy controls².

Overall, these findings suggest that LcS administration may suppress or relieve the biological response to stress when confronted with a brief naturalistic stressor such as an examination, which may be associated with a reduction in feelings of stress and abdominal dysfunction.

Immunity & Infections

Research into immunity and infections has also been conducted with LcS in healthy populations such as office workers or athletes³⁻⁵.

Most recently, a positive role of LcS on immune response in healthy adults has been reported by Harbige and colleagues⁶. In this study, an intermittent probiotic consumption regime was used to mimic likely intake in a societal setting. Fourteen healthy adults consumed a fermented milk drink with LcS for 4 weeks, followed by a 6-week break, and then resumed consumption for a further 4 weeks. A further four subjects who did not consume the fermented milk drink were used as controls. Blood and saliva samples were collected at regular intervals throughout the study to measure markers of immunity.

In the LcS group, concentrations of antibodies (salivary IgA1 and IgA2) and cytokines (IFN- γ) that play a key role in immunity were significantly higher after the 14-week intervention than at baseline ($P<0.05$). The LcS intervention also resulted in a significantly higher expression of T-cell and natural killer (NK) cell activation markers at weeks 10 and 14 respectively ($P<0.05$), compared with baseline. The findings from this study not only suggest a positive role for LcS in supporting immunity in healthy populations, but they also showed a secondary boosting effect of LcS on immunity following the intermittent consumption regime.

Metabolic risk factors

Risk factors for developing metabolic syndrome, and the subsequent increased risk of coronary heart disease and stroke, include obesity and insulin resistance. Dr Hulston and colleagues at Loughborough University studied high-fat, overfeeding-induced insulin resistance in a pilot study of 17 healthy, normal weight (BMI 18-25 kg/m²) subjects randomised to receive either a

probiotic (fermented milk drink containing LcS) or no probiotic. All subjects consumed their habitual diet for three weeks, after which they all consumed a high fat (65% of energy), high energy (50% increase in energy intake) diet for seven days⁷.

In the control group, the period of high-fat overfeeding led to a 0.3 mmol/L increase in fasting plasma glucose ($P<0.05$) and a 27% decrease in insulin sensitivity ($P<0.05$), whereas in the probiotic group fasting plasma glucose and insulin sensitivity was maintained. These pilot study results warrant further research to examine whether LcS has a role to play in reducing the risk of diet-induced metabolic diseases, such as type 2 diabetes, and this study is currently being followed up in a larger cohort by Dr Huston and his team to confirm these findings and explore potential mechanisms.

Summary

This summary focused on research that has been conducted in healthy subjects to highlight the effects of a specific strain of bacteria, *Lactobacillus casei* Shirota, on the average healthy person and has only focused on research published within the last few years. A recent review on whether probiotics in general are useful for the average consumer was published earlier this year⁸. The author concluded that there is some evidence that certain strains may be effective in improving very mild gastrointestinal symptoms or reducing the duration of a cold, and that emerging evidence has suggested that probiotics may have the potential to modulate physiological parameters beyond the gut and intestine.

More than just a feeling in your bones

Lei M *et al.* (2016) The effect of probiotic treatment on elderly patients with distal radius fracture: a prospective double-blind, placebo-controlled randomised clinical trial. *Beneficial Microbes* 7(5):631-637

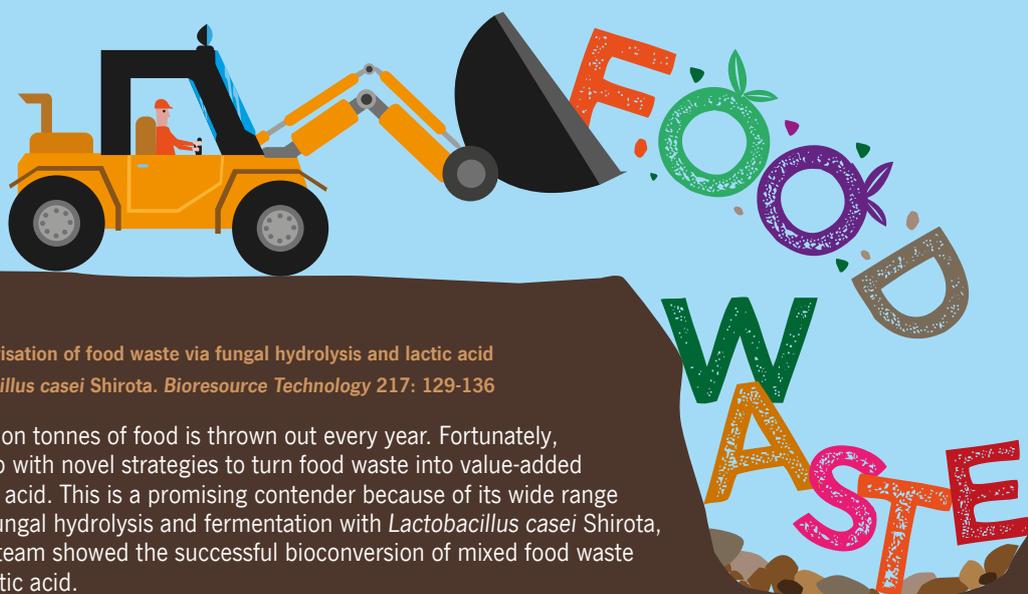
A group of researchers in China have been investigating the potential application of probiotics in elderly patients recovering from a distal radius fracture. A total of 396 patients (≥ 60 years of age) were randomly assigned a twice daily probiotic (skimmed milk with *Lactobacillus casei* Shirota (LcS)) or placebo (skimmed milk) for a 6-month period from the day of their fracture.

Monthly assessments in the 6-month period following their injury showed improvements in both group of patients as they recovered. However, those who were randomised to receive LcS showed significantly greater improvements in; disability of the arm, shoulder and hand (DASH) scores (1-5months); pain visual analogue scale (VAS) scores (1-4months); complex regional pain syndrome (CRPS) scores (1-3months); wrist flexion (1-4 months); and grip strength (2-5months).

Distal radius fractures have been reported as the most common upper extremity injury, which is of particular concern in the elderly population where healing is delayed. The positive findings from this study give hope for another potential application for probiotics in accelerating the recovery from a bone fracture.



NO WASTE



Kwan TH *et al.* (2016) Valorisation of food waste via fungal hydrolysis and lactic acid fermentation with *Lactobacillus casei* Shirota. *Bioresource Technology* 217: 129-136

Globally around 1.3 billion tonnes of food is thrown out every year. Fortunately, scientists are coming up with novel strategies to turn food waste into value-added products, such as lactic acid. This is a promising contender because of its wide range of applications. Using fungal hydrolysis and fermentation with *Lactobacillus casei* Shirota, Kwan and his research team showed the successful bioconversion of mixed food waste and bakery waste to lactic acid.

This research team have even explored strategies to make use of all by-products, such as producing plasticisers from extracted lipids¹, to create a zero-waste approach to the recycling of our food.

¹ Pleissner D, Lau KY, Zhang C *et al.* (2015) Plasticizer and surfactant formation from food-waste- and algal biomass-derived lipids. *ChemSusChem* 8(10): 1686-1691

Resource for HCPs

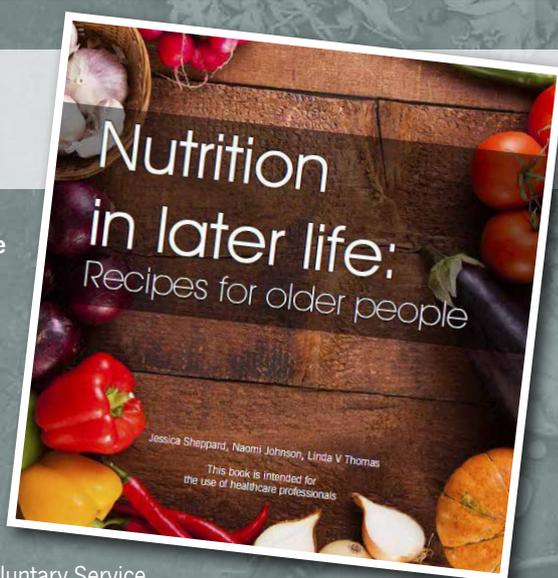
Introducing your free recipe book - **Nutrition in Later Life: Recipes for older people**

The science team at Yakult UK have written this free recipe book as a nutritional resource for healthcare professionals, particularly those caring for older people.

A range of delicious recipes for breakfast, lunch, dinner and dessert have been created and analysed by nutrition experts at Yakult, and approved by Rachel Barratt - a Registered Dietitian with specific expertise in the care of older persons. The recipes can be enjoyed by anyone, but specific focus has been given to the calorie and protein content of each recipe to make them suitable for individuals with increased energy and protein requirements.

For every printed copy of this book, Yakult UK Limited will donate 50p to the Royal Voluntary Service.

To order your free printed copy please contact us at science@yakult.co.uk or 0208 842 7600 or you can download your free copy at www.yakult.co.uk/hcp/resources/brochures.



Love Your Gut – Gut Health Awareness

This national digestive health campaign highlights the vital role of the digestive system and emphasises the importance of good gut health through educating the public. Whether it is through expert tips, recipes or first-hand experiences, the campaign aims to educate and drive awareness of digestive health issues and chronic conditions, as well as the importance of acting on symptoms fast.

The Digestive Health Assessment

For many people abdominal symptoms may just be warning signs that they are doing too much, or eating the wrong food and not giving themselves enough time to relax and digest it. However, there are symptoms that could be caused by gastrointestinal disease, for which they need to see a doctor. The Digestive Health Assessment has been created by leading gut health experts to help identify digestive complaints. By answering a series of simple questions they can check their digestive health and see whether it would be wise to seek help. Download a copy at: www.loveyourgut.com/hcp/

2017 Road Show

The Love Your Gut team of Dietitians and Nutritionists are on the lookout for health events and activities in hospitals and care homes, or within your local community, to attend as part of their 2017 Love Your Gut Road Show. This road show aims to raise awareness of gut health amongst patients and healthcare professionals. Please get in touch with the team at info@loveyourgut.com if you have an event that you would like them to attend.

Love Your Gut is an initiative of Yakult UK Limited in association with Core, Bowel & Cancer Research, St Mark's Hospital Foundation, The IBS Network, Bowel Disease Research Foundation, Primary Care Society for Gastroenterology and the Irish Society for Colitis and Crohn's Disease.





Healthcare Professional Awards

In 2016, we were delighted to sponsor a number of national awards, including the *Complete Nutrition (CN) Community Nutrition Professional of the Year* and the *RCNi Patient's Choice Award*.

CN Community Nutrition Professional of the Year

The CN Award provides the chance to recognise the achievements of a community nutrition professional whose great work has made a significant difference within the nutrition industry.

Yakult would like to congratulate the 2016 winner, Joanne Ridgeway (Lead Home Enteral Nutrition Dietitian for Adults, Lewisham & Greenwich NHS Trust), who was nominated by her colleague for inspiring the team to do their best for their patients.

Yakult would also like to pass on best wishes to all other nominees and Award winners. More information about these awards can be found at www.nutrition2me.com/cn-awards

RCNi Patient's Choice Award

Yakult were also pleased to sponsor the *RCNi Patient's Choice Award* for another year. This award gives members of the public the opportunity to thank a healthcare professional who has made a real difference to their or a loved one's care.

Yakult would like to congratulate the 2016 winner, Kelly Stackhouse (Lead Bowel Function Clinical Nurse Specialist, Sandwell and West Birmingham Hospitals NHS Trust), whose dedicated work is helping to 'break down the taboo around poo'.

Yakult would also like to congratulate Anna Bedrich, Rosie Mulholland, and Sarah Duffy on their nominations. More information about these awards can be found at: www.rcni.com/nurse-awards



Academic Achievement Awards

In 2016, Yakult sponsored 14 academic awards recognising the achievements of students at University. Yakult would like to congratulate all students whose hard work won them the Yakult Award last year, and wish them good luck for all future endeavours.



Dr Eirini Dimidi undertook her PhD at King's College London, focusing on the physiological, clinical and microbiological effects of probiotics in patients with functional constipation. Eirini was awarded Best Final Year Doctoral Student within the Diabetes and Nutritional Sciences Division.



Victoria Thomas studied Microbiology BSc (Hons) at Cardiff University and was awarded the Yakult Award for Best Final Year Project on the Microbiology BSc. Victoria has gone on to study a Medical Microbiology MSc at London School of Hygiene and Tropical Medicine.



Amy Wright studied at Ulster University where she gained a First Class Degree in Human Nutrition (Hons). Amy was awarded the Yakult Award for achieving the Highest Overall Mark on the Human Nutrition BSc. Amy has gone on to do a PGCE in Home Economics.



Emma Hooker and **Natalie Salvesen** both studied Human Nutrition MSc at the University of Glasgow with a specialisation in Public Health Nutrition, and graduated with distinctions. They have both been awarded the Yakult Award for Best Overall Student in MSc (Med Sci) Human Nutrition for 2015-2016.

Recent studies with *Lactobacillus casei* Shirota

LcS survival through the gut

This study, published from a research group in Vietnam, involved 26 healthy adult volunteers who consumed a fermented milk drink containing LcS for 14 days. After 7 and 14 days, LcS was recovered from faeces at an average of 5.0×10^7 and 5.4×10^7 CFU/g faeces, respectively.

The ability of LcS to survive the gut has been tested in numerous human studies - contact science@yakult.co.uk for a list.

Mai et al. (2017) *Asia Pacific Journal of Clinical Nutrition* 26(1):72-77

LcS and a reduced risk of hypertension

A five-year epidemiological study has looked at the relationship between the frequency LcS fermented milk products are consumed and the incidence of hypertension. In a group of 352 normotensive individuals (aged 65 to 93 years), onset of hypertension was significantly lower in those whose intake of LcS fermented milk products was ≥ 3 times a week.

Aoyagi et al. (2016) *Beneficial Microbes* 8 (1), 23-29

LcS fermented soy drink and isoflavone bioavailability

This placebo-controlled, cross-over trial investigated the effects a fermented soy drink has on bioavailability of serum isoflavones. The study involving seven healthy Japanese women, found bioavailability of isoflavones was enhanced after women consumed a single dose of the fermented soy drink (with LcS and isoflavone aglycones) compared to the placebo soy drink.

Nagino et al. (2016) *Biosci Microbiota Food Health* 35(1):9-17

LcS and immune status in endurance athletes

The ability of LcS to reduce incidence and duration of upper respiratory tract infection symptoms (URS) in endurance athletes was investigated in this double-blind, placebo-controlled trial, where 268 endurance athletes were randomised to receive either a probiotic drink or placebo twice daily for 20 weeks. They found no significant differences in URS between the probiotic and placebo groups, however the incidence of URS episodes was unexpectedly low (0.6 vs 2.1 previously reported) which may have prevented detection of any significant effect in this study. However, in cytomegalovirus (CMV) and Epstein Barr virus (EBV) seropositive participants respectively, CMV and EBV antibody titres fell within the probiotic group compared to the placebo group, signifying support to overall immune status.

Gleeson et al. (2016) *Eur J Appl Physiol* 116:1555-1563



A limited number
of hard copies can
be ordered
for free from
science@yakult.co.uk

Free Review

Intestinal Microbiota in Health and Disease
Nature Insight (2016) 535(7610): 47-103

This Yakult-sponsored supplement, which can be downloaded for free from Nature's website, provides clear and comprehensive summaries of the basic biological processes and important advances in the development of clinical applications in the field of microbiota-host interaction, accompanied by some excellent diagrams.

In the accompanying sponsor feature, scientists from Yakult's Central Institute in Japan (Kawai et al) introduce their research that is helping to address our understanding of the significance of the gut microbiota in maintaining human health and describe results of probiotic studies.

In this supplement:

- Intestinal microbiota in health and disease. Editorial. Kahrstrom CT, Pariente N & Weiss U
- A microbial perspective of human developmental biology. Charbonneau MR, Blanton LV, DiGiulio DB, Relman DA, Lebrilla CB et al.
- The microbiome and innate immunity. Thaiss CA, Zmora N, Levy M & Elinav E
- Interactions between the microbiota and pathogenic bacteria in the gut. Baumler AJ & Sperandio V
- Diet-microbiota interactions as moderators of human metabolism. Sonnenburg JL & Backhed F
- The microbiota in adaptive immune homeostasis and disease. Honda K & Littman DG
- Microbiome-wide association studies link dynamic microbial consortia to disease. Gilbert JA, Quinn RA, Debelius J, Xu ZZ, Morton J et al.

SAVE THE DATE!

International **Yakult**
Symposium 2018

19th – 20th April 2018

The next International Yakult Symposium will be held in Ghent, Belgium. At this symposium, several international scientists and experts will present their latest research on the microbiota, probiotics and *Lactobacillus casei* Shirota.

Further details will follow in the next newsletter and at www.yakultsymposium.com in the upcoming months.



STOP PRESS!

Yakult Study Day 2016 - educational videos now available!

Our popular study day, 'Latest Insights into Nutrition and Probiotic Research: A Study Day for Healthcare Professionals', was held in October 2016 at the British Medical Association in London.

All the presentations given on the day are now available at:
www.yakult.co.uk/hcp/symposia/uk-yakult-symposia



FUTURE WORKSHOPS

In 2017, we will be running small-scale workshops to support dietitians and student dietitians with interpreting the science behind probiotics, and understanding the application for probiotics in practice. Further information will follow in the next newsletter and at www.yakult.co.uk/hcp in the upcoming months, or get in touch with us if you wish to find out more!

Receive a **FREE** educational gut microbiota and probiotics talk for you and your colleagues in your place of work!
Contact a member of the Yakult science team today: +44 (0)20 8842 7600, science@yakult.co.uk or science@yakult.ie.

We also offer:

- Advice on probiotics
- Copies of our newsletter, reprints and other material
- Free trial period of product (subject to discussion)

To receive future copies of this bulletin contact science@yakult.co.uk or science@yakult.ie
We can also send paper copies (in bulk if required).

www.yakult.co.uk/hcp

www.yakult.ie/hcp

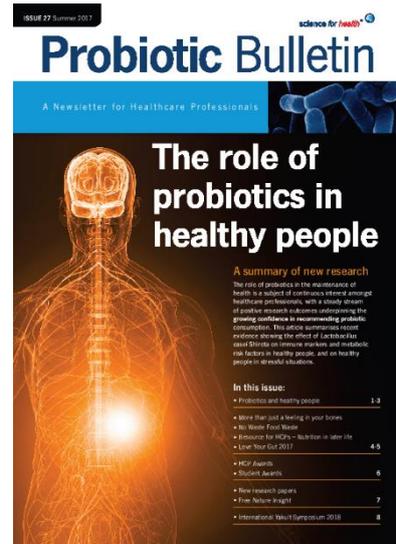
This booklet is intended for healthcare professionals. Not to be distributed to patients.

© Yakult UK Limited, Science Department, Anteros, Odyssey Business Park, West End Road, South Ruislip, Mdx HA4 6QQ
Tel: +44 (0)20 8842 7600; Email: science@yakult.co.uk or science@yakult.ie

References for Probiotic Bulletin, Issue 27

Pages 1-3: The role of probiotics in healthy people

1. Kato-Kataoka A, Nishida K, Takada M *et al.* (2016) *Applied and Environmental Microbiology* 82(12):3649-58.
2. Naseribafrouei A, Hestad K, Avershina E *et al.* (2014) *Neurogastroenterology & Motility* 26(8):1155-62.
3. Gleeson M, Bishop NC & Struszczyk L (2016) *European Journal of Applied Physiology* 116: 1555–1563.
4. Shida K, Sato T, Iizuka R *et al.* (2017) *European Journal of Nutrition* 56(1):45-53.
5. Gleeson M, Bishop NC, Oliveira M *et al.* (2011) *International Journal of Sport Nutrition & Exercise Metabolism* 21:55-64.
6. Harbige LS, Pinto E, Allgrove J *et al.* (2016) *Scandinavian Journal of Immunology* 84(6):353-64.
7. Hulston CJ, Churnside AA & Venables MC (2015) *British Journal of Nutrition* 113:596-602.
8. Lockyer S (2017) *Nutrition Bulletin* 42(1): 42-48.



For further information visit our website: www.yakult.co.uk/hcp
Contact the science team on science@yakult.co.uk or 0208 8427 600.