PRO GUT

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FROM THE SCIENTIST'S DESK

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The human gut is the home to trillions of microbes of several hundred species that form complex communities. The gut microbiota is recognized as the largest reservoir of microorganisms as compared to any other known ecosystem. The collective genomes of microorganisms residing in the gut sometimes described as 'the second genome' is 100 fold more than that of the human host genome. Among many others, the role of this large body of microorganisms range from energy harvest, exclusion of pathogens by forming a microbial shield and in the normal functioning of the immune system. It goes without saying that an imbalance in this finely tuned ecosystem caused by dietary changes or due to use of antibiotics or due to some such reason could lead to a variety of diseases and associated pathological conditions. The appreciation of the role of these microbes has also formed the basis of using microorganisms for therapy both in the treatment and prevention of diseases. Although microbial based therapies such as probiotics have been in practice for more than a century, it is in the past two decades or so that the science behind these therapies and the underlying mechanism of actions are better understood. Much of the understanding is also forthcoming because of the explosion of knowledge in the area of the human microbiome. As the understanding matures, it is predicted that microbial therapies will become increasingly used. The formation of the Yakult India Microbiota and Probiotic Science Foundation has come at an appropriate time to disseminate this large body of scientific information to the medical and scientific fraternity.

FROM A CLINICIAN'S PERSPECTIVE

Probiotics made an entry into clinical practice in a big way over a decade ago. They have been around for some time, and were in use by practitioners for several indications but without a deep understanding of the underlying science and, for that matter, without even knowing the difference between curd or yogurt from probiotic, or one probiotic from another. Things have changed; awareness about the science and its role in the prevention and treatment of clinical conditions has improved, and the right questions are being asked in many forums. So, today, many clinicians know, or at least want to know, the bacterial strain in probiotic formulations, difference between a drug and a food and the optimal dose and duration, which is, as it should be.

Much of this has come from initiatives such as the Yakult India Microbiota and Probiotic Science Foundation. We should be seeing a more widespread and informed clinical use for probiotics.

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CALENDAR WATCH

Probiotics in the Prevention of Lifestyle Disorders
Dates: 15th–16th December 2012
Venue: Sheraton Hotel, Bangalore
Web link: http://www.yimpsf.in

Nutraingredients Probiotech & Microbiota 2013
Dates: 5th–6th February, 2013
Venue: Hotel Metropole, Brussels
Further details at: http://www.amiando.com/probiota.html

Keystone Symposia Conference: The Gut Microbiome: The Effector/Regulatory Immune Network (B3)
Dates: 10th–15th February 2013
Venue: Sagebrush Inn and Conference Center, Taos, New Mexico, USA
Web link: http://www.keystonesymposia.org/index.cfm?e=web.Meeting.Program&meetingid=1231

Gut Microbiota for Health 2013
Dates: 24th–26th February 2013
Venue: Madrid (Spain)
Web link: http://registration.gutmicrobiotaforhealth.com/

1st International Probiotics Prebiotics and Functional Food Congress
Dates: 11th–13th April 2013
Venue: Sueno Hotel Side, Antalya – Turkey
Web link: http://www.ppd2013.org/tr/

7th International Yakult Symposium 2013: The Intestinal Microbiota and Probiotics: Exploiting their influence on health
Dates: 22nd and 23rd April 2013
Venue: The Queen Elizabeth II Conference Centre, London, UK
Web link: http://www.yakultsymposium.com/

ISAPP 2013: 11th Annual Meeting of the International Scientific Association for Probiotics and Prebiotics – Probiotics, Prebiotics, and the Host Microbiome: The Science of Translation
Dates: 12th to 14th June 2013
Venue: The New York Academy of Sciences, 7 World Trade Center, 250 Greenwich St, 40th Fl, New York
Web link: http://www.nyas.org/Events/Detail.aspx?cid=c60ea8d5-44f0-4aaa-a8ff-3e5f008186f6

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FROM THE PRESIDENT'S DESK

President
Prof. N.K. Ganguly

Now is an exciting time to study the hundred trillion microorganisms that densely populate the gut and influence the normal physiology of the host. The recent realisation that these microorganisms can influence susceptibility to disease will aid in the design of therapies that target it for improvement of health. The goal is formidable but is becoming easier due to the recent advances in sequencing technologies. The field of research on microbial interventions that target the gut microbiota for prevention and alleviation of clinical disease is undergoing acceleration at an unprecedented pace. It is paving the path for the next generation prevention and treatment therapies like probiotics.

The Yakult India Microbiota and Probiotic Science Foundation is born from the growing need and interest in the area that aims to provide an impetus to the emerging science of Gut Microbiota and Probiotics.

The Foundation's primary objective is to disseminate latest research in the field to the medical community by providing a common scientific platform to share and exchange knowledge and views and expand into newer areas of probiotic research by organising an annual probiotic symposium. This forum will prompt basic scientists, microbiologists and nutritionists to bring new perspectives to the science of probiotics and clarify some of the major issues such as efficacy and acceptable outcomes that surrounds implementation of probiotic usage in the country.

THE GRAND PLAN

- To organise an annual probiotic symposium which will blend fundamental and applied research related to the use of probiotics for the enhancement of human health.
- Webcast the Symposium to target a larger audience.
- Publish the proceedings of the symposium as a book for global distribution.
- Launch a periodical newsletter on the latest developments in the area of Gut Flora and Probiotics.

The first annual symposium

"Health Impact of Probiotics – Vision and Opportunities"

was convened in Mumbai in December 2011.

OUR VISION – OUR GOAL

- To engender and disseminate information on high quality, multidisciplinary, scientific investigation in the field of probiotics.
- Channelise International knowledge and expertise in the field of probiotics and foster and maintain research links with scientists of similar interest.
- Promote collaborative research to advance the development of scientifically substantiated, health-promoting probiotic products.

RESEARCH UPDATE

Antibiotic associated and *Clostridium difficile* Diarrhoea

The use of antibiotics most often disturbs the gut flora and is associated with clinical symptoms such as diarrhoea which occurs in as many as 30% patients. Symptoms range from mild and self-limiting to severe particularly in *Clostridium difficile* infections which becomes an important reason for non-adherence to antibiotic treatment.

A systematic review and meta-analysis of 82 Randomized Controlled Trials (63 meta-analysis) that met inclusion criteria and included 11,811 participants indicated a statistically significant association of probiotic administration with reduction of Antibiotic Associated diarrhoea with an RR of 0.58. The result was consistent across a number of subgroup and sensitivity analyses. The treatment effect equates to an NNT of 13. The relative efficacy of probiotic interventions may be strain specific, however this analysis found no evidence that the effectiveness varies systematically even by probiotic genus.

Hempel S et al. Probiotics for the prevention and treatment of Antibiotic Associated Diarrhoea: A Systematic Review and Meta-analysis. Journal of American Medical Association 2012. 307(18): 1959–1969.

A Cochrane review of twenty trails that met eligibility criteria and included 3818 adults and children, revealed that probiotics reduced the incidence of CDAD by 66% (pooled relative risk, 0.34 {95%CI, 0.24 to 0.49}. Using probiotics as a prophylactic intervention, a population that had a 5% incidence of antibiotic associated CDAD (median control group risk) probiotics would prevent 33 episodes (Ci, 25 to 38 episodes) per 1000 persons.

Johnston BC et al. Probiotics for the prevention of Clostridium difficile-Associated diarrhea: A Systematic Review and Meta-analysis. Ann Intern Med 2012. [Epub ahead of print].

WHAT'S NEW

- *Lactobacillus casei* strain Shirota acquires self-affirmed (GRAS)* status in the US
- Research study and toxicology data conclude it to be safe for use as a food ingredient

Adapted from: http://www.globenewswire.com/newsroom/news.html?d=252387

*Generally Recognized As Safe

Lactobacillus rhamnosus MTCC 5462 – whole genome shotgun sequencing

Lactobacillus rhamnosus MTCC 5462, a gastrointestinal isolate from an infant fecal sample collected at Anand Agricultural University in India exhibited an ability to reduce cholesterol and stimulate immunity. The whole genome of the strain was sequenced and compared with the published genome sequence of *Lactobacillus rhamnosus* GG (ATCC 53103).

Prajapati JB et al. Whole-genome shotgun sequencing of Lactobacillus rhamnosus MTCC 5462, a strain with probiotics potential. J Bacteriol 2012. 194(5): 1264.

Probiotics may enhance the clearance of Human Papilloma Virus related cervical lesions

A prospective controlled pilot study evaluated the role of a probiotic intervention in the clearance of Human Papilloma Virus in 54 women with an HPV + low grade squamous intraepithelial lesion diagnosed in their pap smear.

To evaluate the possible role of a probiotic, *Lactobacillus casei* strain Shirota was given to the intervention group (n=27) for a period of six months whereas the control group was devoid of any kind of treatment. Probiotic users had a twice as high chance of clearance of cytological abnormalities (60 vs. 31%, p=0.05). HPV was cleared in 19%of the control patients versus 29%of probiotic users (p=0,41) suggesting that the probiotic studied promoted the clearance of HPV related cytological abnormalities. If confirmed, this would represent an entirely new option for the management of cervical cancer precursors.

Verhoven et al. Probiotics enhance the clearance of human Papilloma virus – related cervical lesions: a prospectivecontrolled pilot study. Eur J Cancer Prev 2012. [Epub ahead of print].

Intestinal microbiota in functional bowel disorders: a Rome Foundation Report

The Rome Foundation, an independent organization, aims at improving the understanding of the host gut – microbial interactions in the pathogenesis of functional gastrointestinal disorders (FGID).

In this report the authors provide a critical review of the current hypothesis regarding the pathogenic involvement of microbiota in FGID and quantitative and qualitative changes in the of the fecal gut microbiota particularly in Irritable Bowel Syndrome. They also deliberate on the promising role of dietary manipulation with probiotics, prebiotics, synbiotics and non absorbable antibiotics and the clinical guidance of gut microbiota in IBS.

Simren M et al. Intestinal microbiota in functional bowel disorders: a Rome Foundation report. Gut 2012. [Epub ahead of print].

Probiotics may be beneficial in prevention of acute diarrhoea

The largest community based study that was conducted at NICED, Kolkata, India showed that *Lactobacillus casei* strain Shirota plays an important role in the prevention of acute diarrhoea in children (1-5 years of age) with a protective efficacy of 14% in the probiotics group (95% Confidence Interval 4-23, P<0.01 in adjusted model).

Sur D et al. Role of probiotic in preventing acute diarrhoea in children: a community-based, randomized, double-blind placebo-controlled field trial in an urban slum. Epidemiol Infect 2011. 139: 919–926.

Probiotics may be useful in lowering cholesterol

The cholesterol-lowering efficacy of a yoghurt formulation containing microencapsulated bile salt hydrolase (BSH)-active *Lactobacillus reuteri* NCIMB 30242, taken twice per day over 6 weeks, in hypercholesterolaemic adults was evaluated. 114 subjects were randomised to consume either yoghurts containing microencapsulated *L. reuteri* NCIMB 30242 or placebo yoghurts during the interventional study which included a 2-week washout, 2-week run-in and 6-week treatment period. The result shows that consumption of the probiotic was efficacious and safe for lowering LDL-C, TC, apoB-100 and non-HDL-C in hypercholesterolaemic subjects.

Jones ML et al. Cholesterol-lowering efficacy of a microencapsulated bile salt hydrolase-active Lactobacillus reuteri NCIMB 30242 yoghurt formulation in hypercholesterolaemic adults. Brit J Nutr 2012. 107(10): 1505–13.

Probiotics may play an important role in preventing the onset of non-alcoholic fatty liver disease (NAFLD) in mice

Endotoxemia, Small Intestinal Bacteria Overgrowth (SIBO) and increased intestinal permeability have been associated with the development of Non Alcoholic fatty liver Disease. In a mouse model of Fructose induced steatosis, regular intake of *Lactobacillus casei* strain Shirota attenuated the increase of hepatic steatosis as well as plasma alanine amino transferase (ALT) levels. LcS treatment markedly attenuated the activation of the Toll – like receptor (TLR) 4 signalling cascade found in the livers of mice treated with fructose.

Wagnerberger S et al. Lactobacillus casei Shirota protects from fructose-induced liver steatosis: A mouse model. J Nutritional Biochem 2012. [Epub ahead of print].

MUST READ

Latest compilation of Nature reviews that captures some of the most exciting insights into microbiota research and the advances in sequencing technologies for the analysis of the MiCROBIOME.

Gut Microbes and Health Intestinal Networks in Health and Disease
(www.nature.com/nature/supplements/insights)

Probiotics and the Host Intestinal Mucosa

A detailed review on the current understanding of the host microbe interaction for the augmentation of the immune system. Special emphasis on the structural characterization of the cell wall components and surface layer proteins to throw light on strain specific effects. Interindividual differences in human genotype, enterotype and diet are likely to be the key determinants of an individual's physiological response to probiotics.

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

A Science Special issue: The Gut Microbiota

A collaborative production of the world's leading scientific journal, Science and its sister journal Science Translational Medicine, The Gut Microbiota is a unique and remarkable collection of articles from the some of the leading experts in the field. A must read for those interested in the in the wonderfully complex relationship between humans and their microbial symbionts.

http://www.sciencemag.org/site/special/gut_micro/
Science 8 June 2012: 336(6086). Sc Transl Med 6 June 2012:4 (137)

A combination of probiotic fermented milk and chlorophyllin may have an anticarcinogenic effect on aflatoxin B1Induced liver carcinogenesis in rats

Evaluation of the hepatoprotective effect of probiotic fermented milk containing *Lactobacilus casei* strain Shirota and *Lactobacillus rhamnosus* GG alone as well as in combination with chlorophyllin (CHL) acts as an anti oxidant in male wistar rats administered aflatoxin B1 by enhancing the activities of anti oxidant enzymes such as glutathione peroxidase, superoxide dismutase, catalase and glutathione S-transferase.

Kumar M et al Anticarcinogenic effect of probiotic fermented milk and chlorophyllin on aflatoxin-B_1-induced liver carcinogenesis in rats. Brit J Nutr 2012. 107(7):1006–16.

Intestinal parasites interact with the microbial community modifying the balance between the host and commensal microbiota

There is a growing interest in explaining the rationale on the possible interactions between the microbiota, immune response, inflammatory process and intestinal parasites. This review discussed the various mechanisms by which the intestinal parasites such as protozoa, nematodes, helminthes interact with the bacterial community in the gut modifying the balance between the host and gut microbiota. G. duodenalis represents a good model for highlighting some mechanisms of the existing interaction with the intestinal microbiota.

Berrilli F et al. Interactions between parasites and microbial communities in the human gut. Frontiers in Cellular and Infection Biology 2012. [Epub ahead of print].

The Gut Microbiota – a potential nutritional and pharmacological target for the management of obesity related disorders

Animal and human data demonstrates that phylogenic changes occur in the microbiota composition of obese individuals. Further more evidence from animal models suggest that alterations of the gut microbiota with obesity results in increased energy extraction and lipid deposition, altered release of entero hormones, increased intestinal permeability and metabolic endotoxemia. Treatment with Pro and Prebiotics may reverse many of the metabolic effects linked with the altered microbiota in obese patients.

Marik P Colonic flora, probiotics, obesity and diabetes. Frontiers in Endocrinology, 2012. [Epub ahead of print].

Around 1.4 million of the 9 million child deaths in 2008 were due to diarrhoea with 49% of the deaths occurring in five countries namely India, Nigeria, Democratic Republic of the Congo, Pakistan and China

(Black et al. 2010; Wardlaw et al. 2010)

NEW RELEASE

Health Impact of Probiotics – Vision and Opportunities" is the vision and product of the Yakult India Microbiota and Probiotic Science Foundation to develop a repository of information in the field of probiotics.

Edited by Internationally renowned scientists, Prof. Yoshifumi Takeda and Dr. G. Balakrish Nair, the book captures the proceedings of the first probiotic symposium conducted by the foundation at Mumbai in December 2011.