

No link between probiotics and obesity

An ISAPP response to Raoult D. 2009. Probiotics and obesity: a link? *Nature Rev Microbiol.* 7:616

As specialists in the probiotic field, we would like to respond to the editorial by Raoult (2009) which we believe provides misleading information on probiotics and their impact on host metabolism. We believe the author doesn't distinguish between the value of probiotics in optimizing growth of the young animal [an observation supported by multiple studies in agricultural animals but sparsely in undernourished humans (Saran)] and increasing the risk of unhealthy fat accumulation in humans.

The impact of probiotics in farm animals has been shown to include (1) an increase in size and weight, but not in fat mass (Sabatkova et al 2008; Khaksefidi et al 2005); (2) reduction in fat mass in farm animals gaining weight (Stoyanov et al 2004; Haryanto 2000); or (3) no impact on growth (Willis and Reid 2008). These observations are consistent with weight gain resulting from improved gut function and resistance to infection rather a metabolic imbalance. Thus, in the context of the livestock industry, probiotics are used to promote growth and lean mass, but not adiposity.

When considering results in humans, it is important to clarify that none of the studies mentioned by Raoult showed a statistically significant increase of weight gain when compared with the placebo group (Chouraqui et al. 2008; Guandalini et al. 2000). The slight, but non-significant, increase of body weight observed by Chouraqui et al. in infants fed a probiotic formula was concomitant with a slight increase of height, indicating an effect on growth. Guandalini et al. showed a non-significant increase of weight gain 24 h after the administration of the *Lactobacillus rhamnosus* GG, which was associated with a highly significant reduction of acute diarrhoea. A reduction of dehydration, and not a gain of fat mass, was responsible for the slight increase of weight gain in infants fed probiotics. In short, in spite of the widespread use of probiotics in modern as well as traditional diets, there is no evidence that consumption of probiotics leads to any weight gain.

What is the evidence for the role of the microbiota in obesity? The association between obesity and reduction in Gram-negative bacteria and an increase in Gram-positive Firmicutes comes from work of Gordon's group. However, these data are mainly based on statistical correlations which cannot distinguish cause and consequences. Furthermore, the cited evidence has been partly contradicted by other studies (Collado et al., 2008; Santacruz et al., 2009; Schwartz et al., 2009; Turnbaugh et al., 2009; Duncan et al., 2008). For instance, in the study by Turnbaugh et al. (2009) including 154 lean and obese human subjects, a 16S rRNA gene sequencing approach revealed a higher proportion of Actinobacteria and a lower proportion of Bacteroidetes among obese subjects but no significant difference in Firmicutes. In another study (Schwartz et al., 2009), comparison of microbiota of 98 subjects including lean, overweight and obese subjects using real-time PCR and FISH revealed a higher or same Bacteroidetes/Firmicutes ratio among overweight and obese subjects. Finally, Duncan et al. (2008) compared major fecal bacterial groups in adult lean and obese human subjects using fluorescent in situ hybridization (FISH) and found no evidence supporting a role of the Bacteroidetes/Firmicutes ratio in human obesity. Interestingly, more specific changes in the gut microbiota are associated with obesity which support the interest of targeted modulation of the gut microbiota in the control of obesity. Kalliomaki et al. (2008) conducted a retrospective study comparing fecal microbiota of overweight and



normal weight children and at 6 and 12 mo and at 4 and 7 yrs of age and found 2-fold increase in *Bifidobacterium* levels in children who were normal weight.

Taken together, these results suggest that the evidence for probiotic-induced weight gain in animals is predicated on amelioration of GI disturbances, and not due to increased fat deposition. Observations have been reported, as Raoult indicates, that the microbiota of obese subjects is different from that of lean subjects, and can be altered with weight loss (Ley et al. 2006). The changes that have been identified are at the phylum level, and as indicated above, are not consistent among studies. It should be remembered that evidence that probiotic consumption leads to any sustained compositional change in the microbiota of the consumer is lacking, and transient changes are modest, compared to the total microbiota composition. This does not preclude the possibility of probiotic-induced physiological impacts, but there is no suggestion among the many human studies conducted on probiotics that weight gain is a side-effect of probiotic consumption.

Finally, readers should note that Raoult confuses probiotics (live microbes) and prebiotics (selectively fermented substrates for beneficial colonizing microbes), and is inaccurate with regard to the microbiological identity of different probiotics. Strains of the *Bifidobacterium* genus, commonly used as probiotics, and indicted by Raoult as contributors to increased levels of Firmicutes, are members of the phylum Actinobacter, not Firmicutes.

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