Nature Reviews Microbiology | Published online 29 Feb 2016; doi:10.1038/nrmicro.2016.31

MICROBIOME

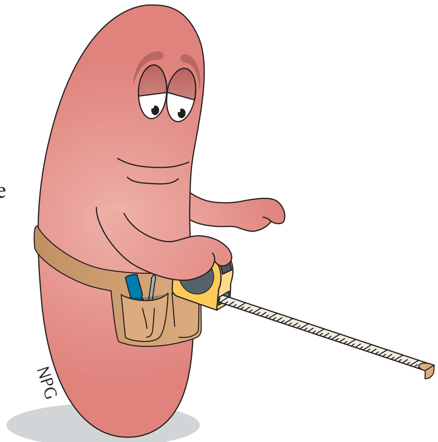
Restoring healthy growth in infants

Childhood undernutrition can lead to stunted growth and causes the death of millions of children each year, and despite extensive efforts, promoting healthy growth in affected infants remains a challenge. Three recent studies investigated the links between postnatal growth and the gut microbiota and identified microbial factors that could improve growth.

In the first of the three studies, Blanton *et al.* transplanted faecal samples from 6-month-old and 18-month-old healthy or undernourished Malawian children into 5-week-old germ-free mice that were fed a nutrient-poor formulation resembling the Malawian diet. Mice that were colonized with microbiota from healthy children gained more weight and lean body mass than mice that were colonized with microbiota from undernourished donors. Importantly, undernourished children harbour gut microbial communities that are typically found in younger, healthy individuals. These findings suggest a causal relationship between the immature gut microbiota from undernourished infants and impaired growth phenotypes. Moreover, the transfer and invasion of healthy microbiota into the guts of the undernourished mice by co-housing restored normal growth in the latter and, importantly, the same effect was observed if cultured strains of two invading species, *Ruminococcus gnavus* and *Clostridium symbiosum*, were transferred.

The second study investigated the effect of the gut microbiota on the somatotropic axis of the host, which controls postnatal growth and comprises growth hormones and insulin-like growth factors (IGFs). First, Schwarzer *et al.* showed that germ-free infant mice gained less weight and were shorter than wild-type litter mates that were fed on a standard laboratory diet, and that a nutrient-poor diet hindered the growth of juvenile germ-free mice more than the growth of wild-type mice, establishing that the microbiota maintains growth. Furthermore, germ-free mice had decreased levels of circulating IGF1, and treatment with recombinant IGF1 increased weight gain, lean body mass and femur length in these animals, whereas blocking IGF signalling in wild-type mice impaired growth. This suggests that the gut microbiota promotes growth by facilitating the production of IGF1 and/or its activity. Finally, mice monocolonized with two different strains of *Lactobacillus plantarum*, which were previously tested for growth promotion in *Drosophila melanogaster*, exhibited strain-specific increased growth, weight gain and activity of the somatic axis under conditions of chronic undernutrition, thereby recapitulating the positive effect of the wild-type microbiota on the growth of juvenile mice.

In the third study, Charbonneau *et al.* analysed human milk oligosaccharides (HMOs) from postpartum Malawian mothers and found that sialylated HMOs are more abundant in mothers with healthy infants compared with mothers with severely stunted infants, suggesting that HMOs have a crucial role in infant growth. Further investigating this, the authors colonized gnotobiotic mice and new-born piglets with a consortium of cultured bacterial strains isolated from the faecal microbiota of a 6-month-old undernourished Malawian infant. They found that supplementation with purified sialylated bovine milk oligosaccharide (S-BMO, which resembles HMOs that are abundant in the breast milk of mothers with healthy infants) had



a microbiota-dependent beneficial effect on growth and promoted a metabolic phenotype that improved the utilization of dietary components. *Bacteroides fragilis* and *Escherichia coli* in the microbiota showed the strongest transcriptional response to treatment with S-BMO. *B. fragilis* metabolizes S-BMO-derived sialyllactose into its constituent monosaccharides, which can be consumed by both the host as well as members of the microbiota, including *E. coli*; however, how this food web influences growth is still unclear.

In summary, the results of these studies suggest that certain microbial species can counteract the negative effects of undernutrition, and raise the possibility that the microbiota could be used as a therapeutic intervention to restore healthy growth.

Andrea Du Toit

ORIGINAL ARTICLES Blanton, L. V. *et al.* Gut bacteria that prevent growth impairments transmitted by microbiota from malnourished children. *Science* http://dx.doi.org/10.1126/science.aad3311 (2016) | Schwarzer, M. *et al.* *Lactobacillus plantarum* strain maintains growth of infant mice during chronic undernutrition. *Science* **351**, 854–857 (2016) | Charbonneau, M. R. *et al.* Sialylated milk oligosaccharides promote microbiota-dependent growth in models of infant undernutrition. *Cell* http://dx.doi.org/10.1016/j.cell.2016.01.024 (2016)