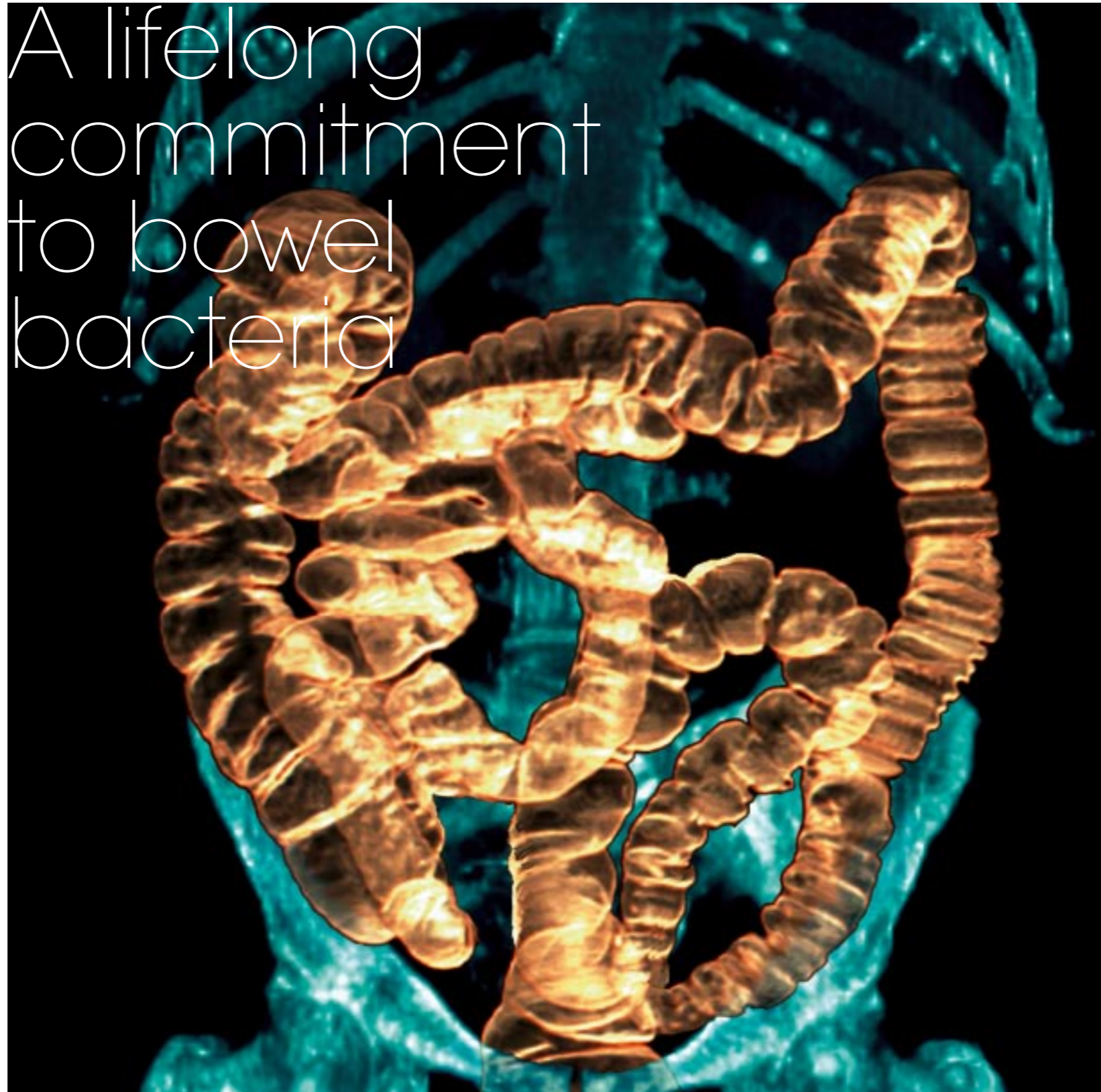


There are about as many bacterial cells in our bowel as there are human cells in our body. **Gerald Tannock** takes a look at the amazing community of bacteria that helps to set the very young on a fit and healthy life.

A lifelong commitment to bowel bacteria



► A false-coloured 3D CT scan of the abdomen of a 53-year-old patient, showing healthy intestines. Zephyr / Science Photo Library

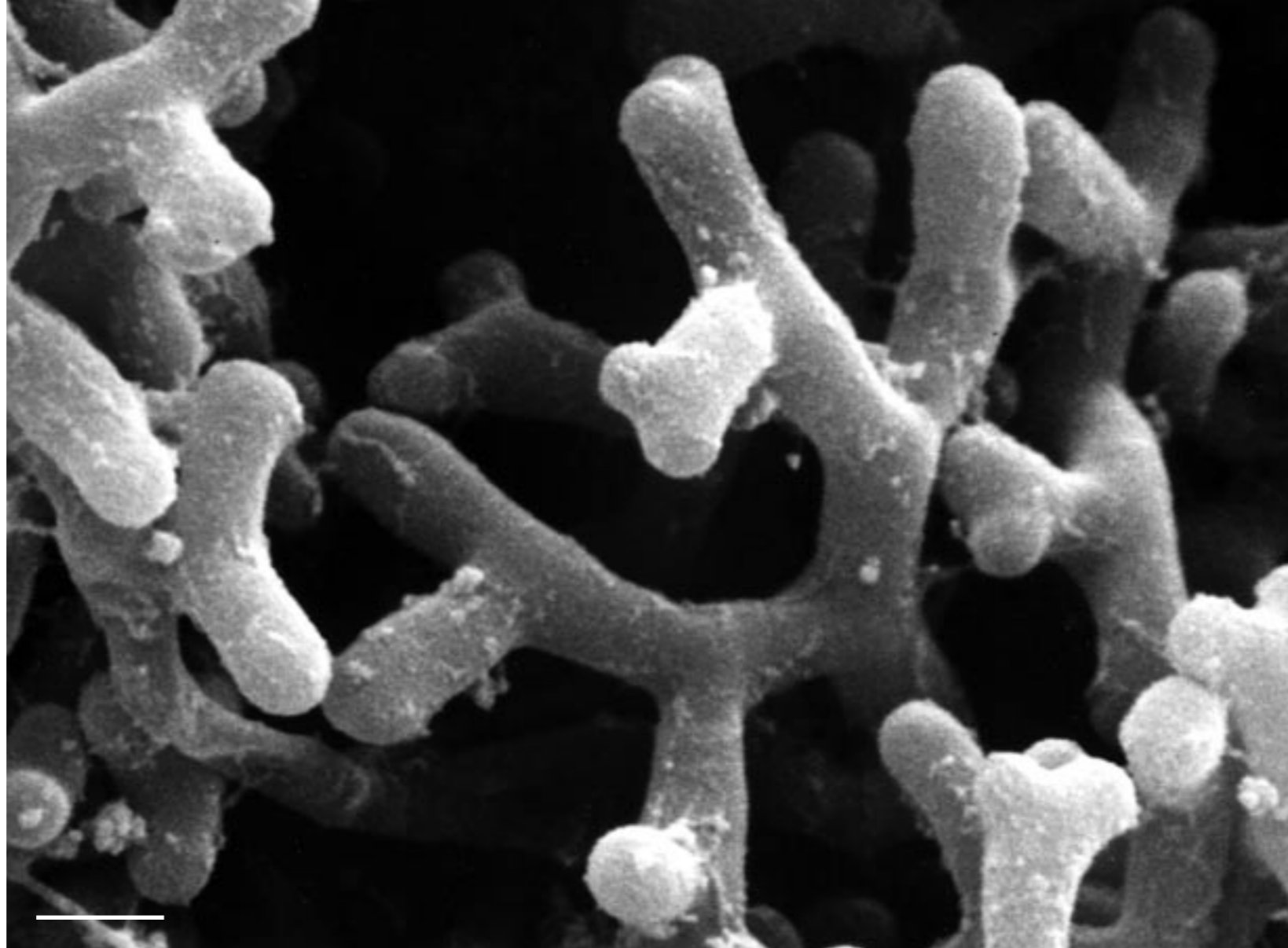
I have finally cum to the konklusion that a good reliable set ov bowels iz worth more to a man than enny quantity of brains.

Josh Billings (Henry Wheeler Shaw, American humorist, 1818–1885)

One can empathize, if not completely concur, with the sentiment expressed in the quotation attributed to the fictional, poorly educated, but commonsensical character Josh Billings. Constipation and diarrhoea are both unpleasant conditions reflecting bowel dysfunction, the latter often due to the activities of pathogenic microbes. Little appreciated, however, are the legions of bacteria that normally reside in the large bowel of humans and which constantly toil to digest complex molecules derived from the diet (such as fibre) and alimentary secretions (such as mucins in mucus). In doing so, the bacteria produce short-chain fatty acids, gases, indoles, phenols and amines as fermentation products. The bowel bacteria, sometimes referred to as commensals because they share the banqueting table that we lay in the large bowel, form a complex community about which relatively little is yet known. Hundreds of bacterial species are probably able to inhabit the human bowel, but not more than 50 % of the bacterial cells, based on comparisons of microscopic and plate counts, have been cultivated so far in the laboratory. Much of our knowledge of the taxonomy of these bacteria has been gained by the use of nucleic acid-based analytical methods, most of which target 16S rRNA gene sequences that form a cornerstone of bacterial phylogeny. From the application of these methods, which are culture-independent, we know that four bacterial phyla dominate the bowel community (*Firmicutes*, *Bacteroidetes*, *Actinobacteria*, *Proteobacteria*) and that there are about 10,000-fold more bacterial cells in the average large bowel than there are human beings on Earth.

Early days

Our lifelong commitment to feeding this large bacterial mass starts soon after birth when the bowel is apparently adventitiously inoculated with bacteria of environmental and maternal origins. Soon, a regulated and predictable succession of bacterial groups occurs in the bowel. Alone among mammalian species, the bowel community of human infants is dominated by *Actinobacteria* belonging to the genus *Bifidobacterium* which, by the time the baby is aged 3–6 months, comprise, on average, at least 40 % of the total bacterial community of stool, regardless of alimentation. These bacteria are especially endowed with the ability to detect and hydrolyse oligosaccharides, such as those found in human milk, using tightly regulated catabolic pathways.



◀ Bifidobacterial cells viewed by scanning electron microscopy. Bar 1 μm . G. Tannock

Thus, during the first few months of life, while immunological germinal foci develop in the bowel mucosa, the bowel of infants is colonized by large numbers of bifidobacteria.

Benefits for the bowel mucosa

Commensals interact with the bowel mucosa, at least in experimental animals, and in so doing influence the expression of mammalian genes. The up- or down-regulation of gene transcription as a result of bacterial exposure may be transient, but the succession of bacterial types to which the infant bowel mucosa is exposed could, in some instances, have long-lasting physiological, including immunological, ramifications as a result of molecular communications between bacterial and human cells. This conditioning of the bowel mucosa during infancy, which may have lifelong consequences, is integral to the concept of 'biological Freudianism': the biological (bacteriological) past is alive in the physiological present.

Impact on allergies

Allergies (eczema, hayfever, asthma) are more common today among the inhabitants of affluent countries than they were 60 years ago, yet remain uncommon in poorer nations. What has changed in affluent countries that could be responsible for this phenomenon? Doubtless there are thousands of possible correlations, including red herrings such as an increase in the number of telephones per head of population, but there may be bacteriological possibilities worthy of investigation. The kinds of bifidobacteria that babies are exposed to now may differ compared to 60 years ago. This might be because of better hygiene, different obstetrical practices and the relatively common use of antibiotics in modern paediatrics. We cannot investigate this possibility because we do not have bowel samples collected from infants born long in the past. Even if we did, the accuracy of the assay results might be compromised by the storage of the samples over decades. Comparisons of the bifidobacterial species present

in stool collected from infants born in countries with low or high prevalence of allergies, however, have revealed differences. The exposure of infants to different kinds of bacteria in different geographical regions of the World could be influenced by ethnicity and maternal diet, as well as the factors mentioned above. The bifidobacterial species detected in the stool of allergic babies compared to healthy infants has also been reported to differ. The varying compositions of bowel communities in human populations are meaningless, however, unless functional links to disease or health can be made. Fortunately, preliminary observations point to a differential response of immune cells to bifidobacterial species residing in the bowel of infants, opening extensive opportunities for the investigation of bifidobacterial–eukaryotic cell cross-talk in relation to health and disease.

Bowel commensals and health

Medical science continues to be more concerned with defining the abnormal

in relation to the normal in order to discover the means to heal. Thus medical knowledge focuses on the pathogenesis of diseases and the derivation of intervention strategies. These are noble causes, but while we know much about diseases, one wonders whether we really understand 'health'. Defining the functional roles of bifidobacterial species in early life might be illuminating in the contexts of both disease and health.

Francis Xavier believed that a Jesuit education until the age of 7 prepared a child to live a useful Christian life in no matter what circumstances they later ended up in. Modern educationists also understand that there are optimal periods during childhood in which the ability to process certain information (visual, sound, numbers, language) can be acquired. While the commitment to maintaining a bowel community is lifelong, critical beneficial interactions with commensals may occur during early childhood. Later, the presence of bowel bacteria may be incidental or, with increasing age and the development of chronic diseases, even malign.

Whatever your quantity of brains, you may find that the bowel community, together with its activities, an exciting and important field of research. The study of bowel commensals should concentrate on community function and interactive mechanisms, avoiding subversion by the wiles of high throughput sequencers and the creation of phylogenetic catalogues. Note could be taken of the advice given by the naturalist and putative 'father of ecology', whose comments concerning botany are equally relevant to modern microbial

ecology in general, and the bacteriology of the bowel in particular.

The standing objection to botany (microbial ecology) has always been, that it is a pursuit that amuses the fancy and exercises the memory, without inspiring the mind, or advancing any real knowledge; and, where the science is carried no further than a mere systematic classification, the charge is but too true ... Not that system is by any means to be thrown aside – without system the field of Nature would be a pathless wilderness – but system should be subservient to, not the object of, pursuit.

Gilbert White, curate of Selborne, 1778

Gerald W. Tannock

Department of Microbiology & Immunology, University of Otago, 720 Cumberland Street, PO Box 56, Dunedin, New Zealand (t +64 3 479 7713; f +64 3 479 8540; e gerald.tannock@stonebow.otago.ac.nz)

Further reading

Gore, C., Munro, K., Lay, C., Bibiloni, R., Morris, J., Woodcock, A., Custovic, A. & Tannock, G.W. (2007). *Bifidobacterium pseudocatenulatum* is associated with atopic eczema: a nested case-control study investigating the fecal microbiota of infants. *J Allergy Clin Immunol* (published ahead of print).

Tannock, G.W. (2005). Commentary: remembrance of microbes past. *Int J Epidemiol* 34, 13–15.