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MOLECULES

The major gut symbiont reduces its genome when it lives *in vitro*

Our bodies are colonized by a large mass of symbiont microorganisms, the majority of which resides in the gut. The fact is that the number of these microbes is close to, or, according to some estimates, may even exceed the number of our own cells [1,2]. The gut bacteria are known to participate in the digestive process by breaking down foodstuffs. They also produce a range of specific products that are vital for us, such as vitamins, and so our health directly depends on these 'insiders'.

The emerging field of probiotics suggests the use of beneficial gut bacteria as living drugs, for example to treat post-burn diarrhoea, or as dietary supplements to aid digestion [3–5]. To this end, strains of the genera *Bifidobacterium* are one of the most widely used probiotic microorganisms.

However, a controversy surrounds these kinds of probiotics applications: some studies do not support the usefulness of consumption of exogenous bifidobacteria to improve health, the others show that exogenous *Bifidobacterium* strains cannot stably colonize the gut [6,7]. All this points out that during cultivation of gut bifidobacteria *in vitro* these microorganisms probably lose the genes that are essential for the survival of probiotics *in vivo* and also important for their therapeutic efficacy.

A recent genomic study based on the original proprietary sequencing technologies developed at the Fidelity Systems, Inc. (Gaithersburg, MD, USA; www.fidelitysystems.com) provided solid evidence supporting this hypothesis [8]. By analyzing the genomes of successive microbial generations of a specific intestinal strain of bifidobacterium, *Bifidobacterium longum* DJO10A (Figure 1) long maintained as a laboratory culture, it was found that the bifidobacterium genome eventually experienced two large deletions when bacterial life is switched from a variable and complex environment, such as the gut, to the stable and simplified conditions of a fermentation broth.

Similar deletions were found when the genome of *B. longum* DJO10A that was minimally cultured in the laboratory was compared with

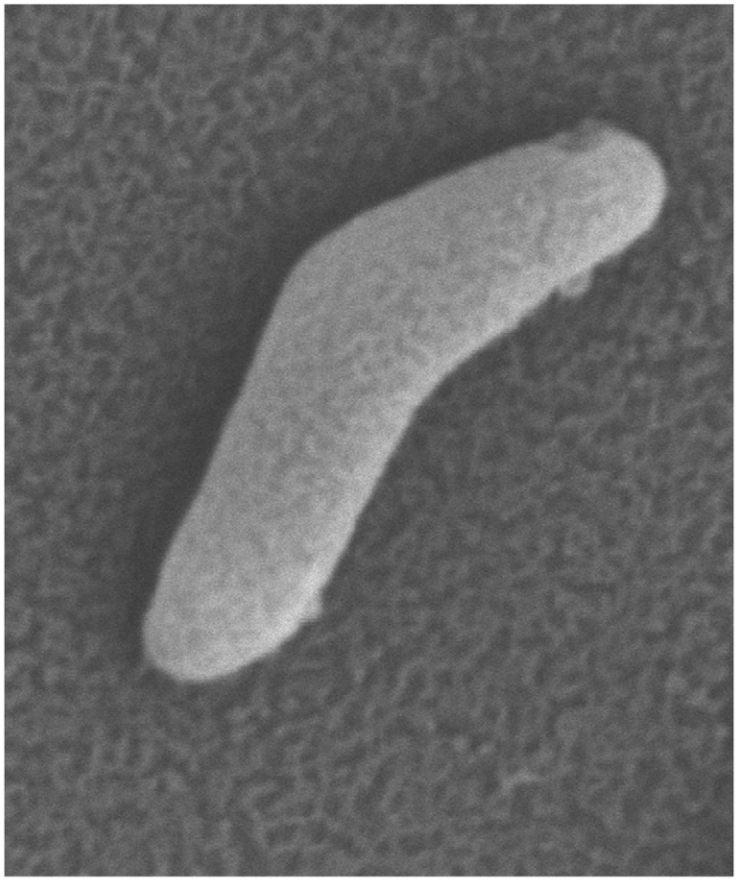

FIGURE 1

The micrograph of a boomerang-shaped, ~2 μm-long single cell of bifidobacterium *B. longum* DJO10A obtained with the scanning electron microscope (courtesy of Daniel J. O'Sullivan, University of Minnesota).

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that of a culture collection strain, *B. longum* NCC2705. These deletions eliminate the gene clusters assumed to be necessary to secure bacterial life in the human intestinal environment, specifically oligosaccharide and polyol utilization, arsenic resistance and lantibiotic production. Loss of these genes may, therefore, compromise the ability of exogenous bifidobacteria to re-colonize the gut. Further, as the new research has shown [8], the lab-cultured bifidobacterium had lost its competitive abilities in the simulated competition with typical intestinal microbiota.

What the scientists found might have implications for all probiotic pharmaceuticals and nutraceuticals, suggesting that they become ineffective as a result of cultivation of probiotic bacteria in artificial media. It is also possible that *in vitro* cultured probiotics could be modified in such a way that makes them do more harm than good [9]. Thus, this new research strongly supports the viewpoint that more scientific studies are warranted to evaluate the safety and efficacy of probiotics [10,11].

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