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LETTER TO THE EDITOR

Use of genetically modified microbes for human health

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Sir,

The publication by Ott et al. (1) restates the important, and topical, use of microbes in treating disease, in this case lymphoid immunodeficiencies. However, not everyone agrees that recombinant bacteria should be used in humans, and one particular submission to this journal called for a ban of such uses, a viewpoint that we wish to now strongly challenge (2).

The primary concerns, quite rightly, are safety and avoidance of overt environmental release. However, we believe that there are very good reasons for continuing to develop novel recombinant probiotic technologies. In a precedent-setting case, the insertion upstream and downstream of *thyA* flanking a series of *hIL10* expression cassettes in *Lactococcus lactis* MG1363 (3) was sufficient for the Dutch regulatory agency to permit human trials with this organism. The results showed expression of human interleukin 10 (IL-10) and no detectable environmental release of the organism occurred. This was due to the requirement for thymidine or thymine for growth and survival (4).

Bacterial genetic alterations occur all the time in nature, often precipitated by the action of humans, as exemplified by overuse of antibiotics. Genomic sequencing has shown that *Lactobacillus* species hold no major virulence properties, and this is leading to

the creation of recombinant strains that may potentially prevent HIV, enhance host cell deficiencies, treat inflammatory disease, and provide oral vaccination routes for the prevention of viral and bacterial pathogens (5,6).

Collectively, scientists and regulators must explore ways to balance safety and environmental exposure with the benefits that recombinant organisms might provide. Whether the end target is immunodeficiencies or other diseases, particularly those causing enormous suffering and death around the world, the use of recombinant lactobacilli or avirulent 'pathogens' should be permitted if sufficiently stringent preclinical testing has been performed and adequate surveillance systems are in place. Such rational steps, and reasoned arguments, differ markedly from the approach taken by Cummins and Ho (2), whose use of words such as 'rogue', 'nasty', and 'warfare', and an unknown definition of probiotics – instead of a generally agreed upon definition (7,8) – appear to focus more on sensationalism than on common sense.

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