Neuroactive probiotics

Gregor Reid[1)2)]

Until relatively recent research by Bienenstock and Collins [1], the idea that probiotic bacteria administered to the intestine could influence the brain seemed almost surreal. In Mark Lyte's hypothesis paper [2] in this issue, such a concept is supported by studies showing that microbes can produce, and respond to, neurochemicals. These compounds can induce neurological and immunological effects in the host. The immunomodulatory effects of probiotics have been well documented, but so far not linked specifically with neurological outcomes.

The proposed step by step system to select bacteria for their neurological effects is interesting, but to be probiotic the ultimate test will have to be made in humans. Such studies will likely require drug registration given that the end result is influencing disease processes. Plus, the use of mutant strains in humans may necessitate inclusion of suicide containment systems in the organisms [3]. Such containment may also be necessary for the parent strain in order to control neurological effects depending upon the retention time of the probiotic in the intestine.

If lactobacilli, bifidobacteria and others mentioned in Lyte's paper, and used frequently as probiotics, produce neurochemicals, to what extent are the levels of physiological importance? This is particularly relevant in the case of serotonin production, given the wide use of serotonin-uptake inhibitors as anti-depressants. Thus, should this lead to restricting use of probiotics in patients who already have neurological pathology, or who are receiving therapy that affects mental well-being? Studies in animals have shown that *Lactobacillus acidophilus* NCFM induce opioid effects [4], yet there is little evidence that pain relief is associated with ingestion of this organism in any probiotic formulation. This may be because nobody has investigated this formally, or the levels of the molecules necessary are too low. Likewise, given that gamma-aminobutyric acid (GABA) is already potentially present in some fermented foods, should there not be some clinical evidence available already to suggest that eating these foods improves mental health?

To date, there is evidence showing anti-inflammatory effects of lactobacilli in the gut, but less strong evidence that they or bifidobacteria confer immunomodulatory effects in inflammatory bowel disease (IBD) patients that induce clinically significant amelioration of the disease. This does not rule out strains being identified with this benefit in the future, or being used to induce neurological effects (against pain, depression) in conjunction with immuno-modulatory drugs that target the site of inflammation.

In summary, the Lyte paper presents an idea for selecting probiotic strains with neurological applications, and linking this with immuno-modulatory effects. The novelty lies in highlighting the fact that microbial strains already being widely ingested through fermented foods and dietary supplements, some of which are termed probiotic, can produce neurochemicals. The degree to which these chemicals are secreted by the organisms in humans, are adsorbed and influence how people feel or behave is certainly worthy of future investigation. Likely, organisms already inside us carry out some degree of influence on our mental well-being. In that case, could the 'happy genes' really be influenced by organisms we inherited at birth, and for people suffering from certain forms of mental health problems could an adjunct treatment be a fecal or specific multi-species probiotic transplant? Food for thought.

References

1. **Bienenstock J**, **Collins S.** 2010. 99th Dahlem conference on infection, inflammation and chronic inflammatory disorders: psycho-neuroimmunology and the intestinal microbiota: clinical observations and basic mechanisms. *Clin Exp Immunol* **160**: 85–91.
2. **Lyte M.** 2011. Probiotics function mechanistically as delivery vehicles for neuroactive compounds: microbial endocrinology in the design and use of probiotics. *BioEssays* in press.
3. **Steidler L**, **Neirynck S**, **Huyghebaert N**, **Snoeck V**, et al. 2003. Biological containment of genetically modified *Lactococcus lactis* for intestinal delivery of human interleukin 10. *Nat Biotechnol* **21**: 785–9.
4. **Steidler L**, **Neirynck S**, **Huyghebaert N**, **Snoeck V**, et al. 2003. Biological containment of genetically modified *Lactococcus lactis* for intestinal delivery of human interleukin 10. *Nat Biotechnol* **21**: 785–9.
5. **Rousseaux C**, **Thuru X**, **Gelot A**, **Barnich N**, et al. 2007. *Lactobacillus acidophilus* modulates intestinal pain and induces opioid and cannabinoid receptors. *Nat Med* **13**: 35–7.

DOI 10.1002/bies.201100074

[1)] Department of Microbiology and Immunology, University of Western Ontario, London, Ontario, Canada
[2)] Canadian Research and Development Centre for Probiotics, The Lawson Health Research Institute, London, Ontario, Canada

Corresponding author:
Gregor Reid
E-mail: gregor@uwo.ca