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Title	Harnessing the bacteriocin-producing capacity of the gut with a view to controlling microorganisms that have been associated with obesity and related metabolic disorders
Authors	Hegarty, James William
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UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Abstract

Obesity is a complex syndrome associated with a number of serious implications for human health. The gut microbiota in obesity and related metabolic conditions has received considerable attention. The aim of this project was to (1) harness the bacteriocin-producing capacity of the gut and (2) develop a bacteriocin-producing probiotic that can contribute to the prevention/treatment of obesity and related metabolic disorders.

Firstly, bacteriocin production among a selection of commercial probiotic products was examined. This investigation suggests that the commercial bacteriocin-producing probiotics are not very heterogeneous and that bacteriocin production is not being optimally harnessed as a probiotic trait.

To identify strains with activity against obesity-associated targets, a culture-based screen was undertaken. Four lead bacteriocin-producing isolates were identified which successfully inhibited species enriched in type 2 diabetic patients. DPC6988 was selected for further investigation.

We next investigated the impact of the bacteriocin-producing DPC6988, and another non-producing control strain, on gut microbial populations using an *ex vivo* model of the distal colon. Although both strains altered microbial populations over the 24 hr fermentation period, a number of beneficial changes were attributed to DPC6988 only.

Finally, the ability of DPC6988 to alter the gut microbiota and mitigate the metabolic abnormalities with respect to obesity in a DIO mouse model was examined. Despite alterations to the gut microbiota, treatment with this strain did not result in improvements to weight gain or metabolic health.

Overall this thesis resulted in the identification of a number of baceriocin-producing gut microbes. Further work with DPC6988 will be necessary to understand the extent to which this strain can contribute to the prevention/treatment of obesity and related disorders and, more generally, to optimally harness the ability of bacteriocin-producing strains to beneficially change the composition of the gut microbiota.