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Author(s)	Lynch, Alli
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University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Abstract

In this study, a functional metagenomic screen was first carried out to identify genes encoding novel bacterial effectors that could solubilise cholesterol, and thus potentially have a role in cholesterol turnover in the gut. Through this screen a gene was identified, called *choA*, which is responsible for the production of a novel N-acylated amino acid called N-acyl-3-hydroxy-palmitoyl glycine or commendamide, and work presented here determined that commendamide was responsible for the solubilisation of cholesterol micelles. In addition to this cholesterol solubilising activity, commendamide was also shown to possess potent haemolytic activity. Furthermore, phylogenetic and phenotypic analysis determined that ChoA, and its related activities, is present throughout the order Bacteroidales, implying a role for commendamide in the adaptation of these important gut genera to their environments. In all sequenced members of the order Bacteroidales (including the genus *Bacteroides*) the *choA* gene is immediately downstream from another acyltransferase, called *choB*. Together *choB* and *choA* were shown to be responsible for the production of a novel group of mono- and di-acylated glycine lipids (GL). *Bacteroides* are important beneficial members of the human gut microbiota and this study presents data to show that GLs are an important fitness determinant for *Bacteroides thetaiotaomicron* both *in vitro* and *in vivo*. Finally this study presents data to show that there is a link between the stringent response (and (p)ppGpp production) in *B. thetaiotaomicron* and the ability to survive exposure to air, an important element in the transmission of *Bacteroides* from host to host.