Functional screening of a human gut metagenomics library uncovers genetic elements that confer enhanced intestinal colonization by gut commensal microbes.

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Abstract

To persist in the gut, bacteria must colonize their host [1]. Gut bacteria express various molecules able to promote attachment to host cells. These adhesins rely on interactions with host cell surface receptors acting as a bridge between bacteria and their host [4]. Proteoglycans and sugars are amongst the types of structures that can act as host receptors. Adhesion is a critical first step prior to attachment, colonization and persistence; and therefore a key event to be studied [2].

Introduction

Metagenomics is a powerful tool that allows for the culture-independent analysis of complex microbial communities. One of the most complex and dense microbial ecosystems known is that of the human distal colon, with cell densities reaching up to 10^{12} per gram of faeces. With the majority of species as yet uncultured, there are an enormous number of novel genes awaiting discovery. In the current study, we describe the identification and subsequent analysis of putative glycan-binding adhesive clones from the human gut microbiome using combined functional metagenomics and bioinformatics based approaches.

Findings

A fosmid library of human gut microbiota in the surrogate host *Escherichia coli* EPI300 was screened for enhanced adherence capability. Two out of 42,000 fosmid clones, FC3 and FC21, exhibited enhanced capabilities to adhere to Caco-2 cells in functional screens. DNA segments inserted into the FC3 and FC21 clones were 28 and 8.6Kb, respectively. FC21 is a 5 gene operon belonging to the dominant commensal gut species *Bifidobacterium adolescentis*. Sequence analysis of FC3 revealed that the 28Kb insert is a fragment with no current known homologs in the database, suggesting that the insert DNA is derived from a microbe with an unknown genome sequence. Further Blastx analysis of FC3 strongly suggests that the DNA fragment is derived from species belonging to the genus Clostridium. Consistent with this finding, a large portion of the predicted gene products were highly homologous to those of Clostridium spp. It is hoped that the identification of novel glycan binding adhesins will help to further elucidate adherence mechanisms, and will assist our increased understanding of how resident bacteria persist within the human gastrointestinal tract.

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References

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