Complete genome sequence of the *Bifidobacterium animalis* subspecies *lactis* BL3, preventive probiotics for acute colitis and colon cancer

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Abstract

We report the genome sequence of *Bifidobacterium animalis* subspecies *lactis* BL3, which has preventive properties on acute colitis and colon cancer. The genome of BL3, which was isolated from Korean faeces, consisted of a 1 944 323 bp size single chromosome, and its G+C content was 60.5%. Genome comparison against the closest *Bifidobacterium animalis* strain revealed that BL3 had particularly different regions of four areas encoding flavin-nucleotide-binding protein, transposase, multidrug ABC transporter and ATP binding protein.

Keywords: *Bifidobacterium*, genome sequence, IBD, PacBio, probiotics
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Introduction

Inflammatory bowel disease (IBD) is a group of chronic inflammatory disorders occurring in the digestive tract [1]. Ulcerative colitis and Crohn disease, as principal types of IBD, can affect the entire gastrointestinal tract [2]. While ulcerative colitis affects the large intestine and rectum with continues inflammation, Crohn disease causes inflammation of the lining of overall digestive tract and can even spread deep into tissue [3–5].

IBD symptoms include abdominal pain, vomiting, diarrhoea, rectal bleeding and weight loss [6,7]. Currently there are no drugs for the treatment of IBD and only few therapeutic options for modulating intestinal inflammation; sustained IBD can be an increased risk factor for colorectal cancer [2]. IBD a complex disease caused by various factors such as environment, genetics, immunologic responses and inflammation [8]. However, recent studies have paid attention to gut microbiota and have suggested that alterations of the intestinal microbiome may contribute to inflammation and the progression of IBD [9,10]. Therefore, modulation of intestinal flora could be a therapy for IBD treatment.

Previously we isolated *Bifidobacterium animalis* subspecies *lactis* BL3 strain from Korean faeces, which showed a preventive effect on acute colitis and colitis-associated colon cancer by inhibiting NF-κB activity [11]. In order to gain better insight into the preventive effects of probiotic *Bifidobacterium* on IBD, we analysed the genome sequence of *B. animalis* subspecies *lactis* BL3. Currently only seven genomes of *B. animalis* subspecies *lactis* strains are available, so the genetic information of this species is still insufficient. Therefore, in this study we analysed the whole genome sequence of *B. animalis* subspecies *lactis* BL3 to elucidate and understand preventive effect of probiotics on IBD and related disorders. Further characterization of genomic contents in probiotic *Bifidobacterium* such as *B. animalis* subspecies *lactis* BL3 will be needed to develop health-promoting probiotics.

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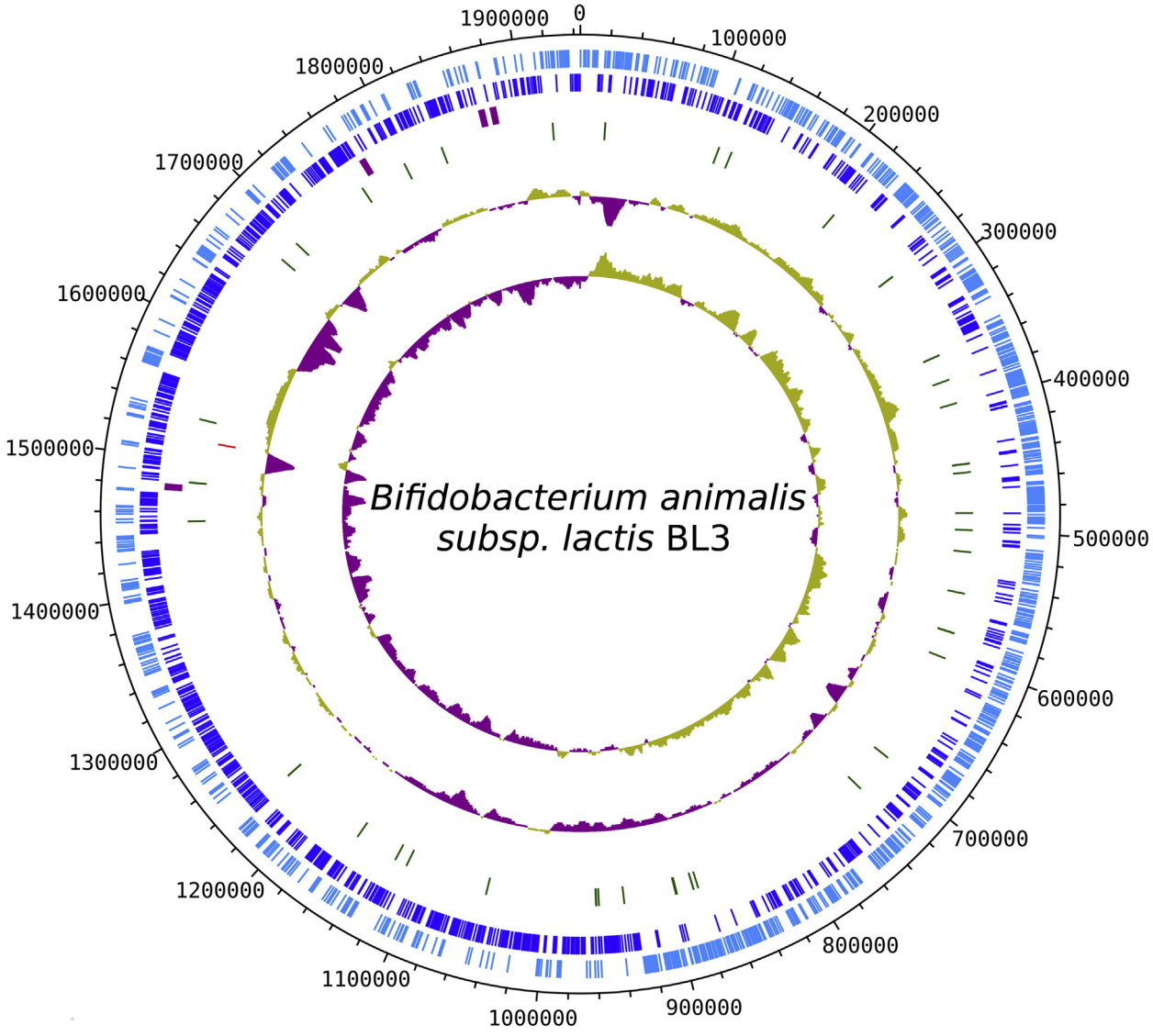

FIG. 1. Circular map of genomic features of *Bifidobacterium animalis* subspecies *lactis* BL3 plotting seven tracks. Track 1 (light blue; outset): forward-stranded coding CDS. Track 2 (blue): reverse-strand coding CDS. Track 3 (light purple): rRNA including 5S, 16S and 23S. Track 4 (green): tRNA. Track 5 (red): CRISPR array. Track 6 (light green and purple): GC content. Track 7 (light green and purple): GC skew.

Materials and methods

Bacteria strains and DNA preparation

Previously isolated *B. animalis* subspecies *lactis* BL3 from Korean faeces was cultivated on BL medium at 37°C for 18 hours in an anaerobic condition. Genomic DNA was extracted from the cultured bacterium with a QIAamp DNA Mini Kit (Qiagen, Germantown, MD, USA). The purity, quality and quantity of extracted DNA was examined by a NanoDrop 2000 UV-Vis spectrophotometer (Thermo Fisher, Waltham, MA, USA) and Qubit 2.0 fluorometer (Life Technologies, Carlsbad, CA, USA) respectively.

Genome sequencing, assembly and annotation

The whole genome of *B. animalis* subspecies *lactis* was sequenced by the PacBio RS II platform. A 20 kb DNA library, constructed according to the manufacturer's instructions, was sequenced by single-molecule real-time sequencing technology with P6 DNA polymerase and C4 chemistry. A total of 1038 high-quality sequences (182 595 subreads) were obtained from the sequencing. The sequences were assembled using HGAP 3.0, and annotation was carried out with National Center for Biotechnology Information (NCBI) Prokaryotic Genome Annotation Pipeline [12] through the NCBI Genome submission portal (GenomeSubmit, http://ncbi.nlm.nih.gov). DNAPlotter [13] was used to draw the chromosome topology of this genome. Functional classification