

Press Release 2 October 2015

A genomic encyclopedia for lactobacilli

- ***comparative genomics of 213 strains expands biotechnology potential***
- The genome sequences of 213 strains of Lactobacilli and associated genera along with their encoded genetic catalogue for carbohydrate and protein metabolism are reported this week in Nature Communications.
- Novel CRISPR-Cas immune systems are described which may be exploited for genomic editing opening new biotechnological avenues of exploitation.
- A robust phylogenomic framework of existing species provides enormous potential for strain genotyping and new species classification.

A genomic encyclopedia for lactobacilli is published this week by a large international consortium led by Prof Paul O'Toole at the SFI-funded APC Microbiome Institute in University College Cork, Ireland.

Researchers from the APC and their collaborators at Inner Mongolia Agriculture University, Beijing Institute of Microbiology and Epidemiology, New York University, University of Limerick, University of Verona, University of Helsinki, Wellcome Trust Sanger Centre, Teagasc Food Research Centre Cork, North Carolina State University and Wageningen University, have reported the genome sequences of 175 *Lactobacillus* species and 26 genomes from 8 other genera historically associated with or grouped within the lactobacilli. These sequences are complimented by 12 genomes already publically available.

"This *Lactobacillus* genome sequencing initiative provides genomic clarity for a genus bedevilled by phenotypic confusion and inconsistent phylogeny. We have generated a resource data set whose analysis explained the phenotypic diversity of lactobacilli and associated genera, and suggested new units for classification" said Prof Paul O'Toole, lead author on the publication. "The data underline the extraordinary level of genomic difference across species currently assigned to a single genus, and they provide the definitive resource for mining lactobacilli. We predict this dataset will accelerate usage of lactobacilli for biotechnology."

Lactobacilli are a diverse group of over 200 species of bacteria which are used widely in food as starter cultures in a variety of fermented foods, probiotics and preservatives. Lactobacilli are part of the normal microbiota of humans and other animals. Many are considered probiotic and the global probiotics market is dominated by lactobacilli. Lactobacilli are very important commercially - the world cheese market alone is worth in excess of €50bn annually and the global demand for probiotics is expected to reach USD 44.9 billion by 2018 (<http://www.transparencymarketresearch.com/probioticsmarket.html>2013).

Lactobacilli have a long history of human usage including Generally Recognised as Safe or a Qualified Presumption of Safety by the Food and Drug Administration and European Food Safety Authority, respectively. Lactobacilli are being developed as delivery systems for vaccines and therapeutics and are also of use to the chemical industry where they are among the microbes most commonly used for producing lactic acid.

However, commercial exploitation of lactobacilli has been complicated by their metabolic diversity, unclear species identity and uncertain relationships between them and other commercially important lactic acid bacteria.

This genomic analysis provides an extensive resource for comparing, grouping and exploiting *Lactobacillus* species. The genomes of the lactobacilli range in size from 1.23Mb (*Lactobacillus sanfranciscensis*) to 4.91Mb (*L. parakefiri*) and the GC content varies from 31.93 to 57.02%. The core genome of the 213 strains comprises only 73 genes, the majority of which encode essential proteins for cell growth and replication. The genomic analysis highlights the remarkable diversity of pili and also carbohydrate active enzymes in lactic acid bacteria many of which represent unrecognised and unexploited enzymes for biotechnology. The phylogenetic tree shows that the genus *Lactobacillus* is paraphyletic i.e. that all the species descend from a common ancestor; however five other genera are grouped within the lactobacilli as sub-clades (sub-branches).

The genome resource also extends the knowledge base for exploiting mobile replicons including bacteriophage and plasmids. A widespread occurrence of diverse CRISPR-Cas immune systems is also revealed. A variety of Cas9 proteins are identified, which open avenues for next-generation Cas9-mediated genome editing as well as providing enormous potential for strain genotyping and enhancing phage resistance in industrial strains.

The research "Expanding the biotechnology potential of lactobacilli through comparative genomics of 213 strains and associated genera" DOI: 10.1038/ncomms9322 is published in Nature Communications

<http://www.nature.com/ncomms/2015/150929/ncomms9322/abs/ncomms9322.html>

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About the APC Microbiome Institute

The APC Microbiome Institute <http://apc.ucc.ie/> in Cork, the national centre for excellence in food and medicine research, is one of Science Foundation Ireland's national centres for research and it represents a partnership between UCC, Teagasc and CIT. Since its foundation in 2003 it has made several seminal contributions to the field and was ranked second in the world by Thomson Reuters for its area of science. In recognition of the significantly increased scale of APC activities and the importance of microbes in health, UCC has recently recognised the Cork scientists with the designation of institute.

APC scientists carry out research on gastrointestinal bacterial community (the microbiome). The microbiome is not only a target for treatment and prevention of disease, it is a repository for functional food ingredients, new drugs and biomarkers of disease. Over the

past decade APC scientists have related food and microbial diversity with health, have discovered new anti-microbials and anti-inflammatories and developed templates for future foods.