The use of “omic” technologies for the search of novel probiotic strains

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The use of “omic” technologies for the search of novel probiotic strains

- Genomic technologies: from tools to products
- New horizons: probiotic consortia for skin disorders
- A game changer on weight management: *B. lactis* BPL1
- Conclusions: innovation, innovation and innovation
Genomic technologies: from tools to products
On February 15, 2001, the journal Nature published the first draft of the human genome obtained by the “International Human Genome Project”

One day later, the journal Science published a second draft obtained by the US company Celera Genomics

Although it was a milestone in the history of biomedicine, these drafts were largely incomplete: only covering 90% of the genome and containing many errors

Genome sequencing techniques had to be improved to sequence more genomes at a lower cost and in less time
The genomics race

2001
10 years
$3000 million
3000 scientists

2019
3 weeks
€6000
1 laboratory technician
Applications of massive genome sequencing

- sRNAs
- Amplicons
- Genomes
- Exomes
- Transcriptomes
- Microbiomes
- Metagenomes
And other omics

Integrated ‘Omics’

Genomics (DNA)

Feed-backward mechanisms

Transcriptomics (RNA)

Systems Biology

Metabolomics (Metabolites)

Feed-forward mechanisms

Proteomics (Proteins)

Big Data Analysis

Metabolic Engineering

Synthetic Cell
Omics and probiotics

- Genomic sequencing
- Transcriptomics
- Metabolomics
- Microbiome
- Metagenome
- Metatranscriptome

Selection of new strains
Mechanism of action
Genetic modification
New horizons: probiotic consortia for skin disorders
The starting point: the relationship between celiac disease and AD
The gut microbiome of children with AD

- Bacterial pathogen DNA on blood
- Oxydative stress
- Gut inflammation
- *Faecalibacterium* and *Ruminococcus*
- *Bacteroides*
The microbial consortia is a mixture of three different probiotic strains (B. longum var. longum CECT 7347, B. animalis subsp. lactis CECT8145 and L. casei CECT 9104).

All of them have been evaluated for food safety following the WHO guidelines; the genome is fully sequenced.

This combination was formulated considering the anti-inflammatory properties and the antioxidant capacity of the mixture, and also the effect on the gut microbiome dysbiosis.

There is a scientific dossier with 15 SCI articles describing the properties of these strains.
Changes in Scorad index and its components

A: SCORAD index

B: Eczema spread

C: Eczema intensity

D: Subjective symptoms
Effect of Oral Administration of a Mixture of Probiotic Strains on SCORAD Index and Use of Topical Steroids in Young Patients With Moderate Atopic Dermatitis: A Randomized Clinical Trial

In the randomized, double-blind, placebo-controlled trial, patients were assigned to one of two groups: Probiotic or Placebo. The Probiotic group received a mixture of probiotic strains, while the Placebo group received a placebo. The SCORAD ( Severity-SCORing of Atopic Dermatitis) index was used to assess the severity of dermatitis.

Results:
- The SCORAD index was significantly lower in the Probiotic group compared to the Placebo group at the end of the trial.

Conclusion:
- Oral administration of probiotics can be an effective treatment for moderate atopic dermatitis, reducing the need for topical steroids.

Keywords: Probiotics, Atopic Dermatitis, SCORAD Index, Topical Steroids.
Psoriasis: same rational, from microbiome to product

Gut microbial composition in patients with psoriasis

Psoriasis is a chronic autoimmune inflammatory disease of the skin. Although the pathogenesis of psoriasis is not yet fully understood, it is believed to involve immune dysregulation. Recent studies have suggested a role for the gut microbiome in the development and exacerbation of psoriasis. The gut microbiome plays a crucial role in maintaining the integrity of the intestinal barrier and immune regulation. Alterations in the gut microbiome have been observed in psoriasis patients, indicating a potential link between the gut and the skin.

The study aimed to investigate the gut microbial composition in patients with psoriasis. The gut microbiota was assessed using 16S rRNA gene sequencing. The results showed significant differences in the gut microbial composition between psoriasis patients and healthy controls. Specifically, specific bacterial taxa were enriched in psoriasis patients, suggesting a potential role for these bacteria in the pathogenesis of the disease.

In conclusion, the study highlights the importance of the gut microbiome in psoriasis. Further research is needed to understand the exact mechanisms and develop targeted therapies for this chronic disease.
A game changer on weight management:
*Bifidobacterium lactis* BPL1
Metabolic syndrome

High cholesterol, obesity and other metabolic disorders, have a proven public interest and metabolic health component.

“an escalating global epidemic of overweight and obesity – “globesity” – is taking over many parts of the world.”

We found the strain using *C. elegans* as a screening tool and deciphered the metabolic pathways affected.
A worm for the screening

Identification of BPL1

We screened from 200 different probiotic strains from our library and already marketed strains

BPL1 was found out as the top one strain for metabolic syndrome indications
Heat-killed *versus* living cells
Transcriptomics and metabolomics in *C. elegans*

Results of metabolic pathways affected

*Bifidobacterium animalis sbp. lactis CECT 8145*

- Energy metabolism
  - Pyruvate metabolism
  - Oxidative phosphorylation
  - Pentose phosphate pathway

- Lipid metabolism
  - Unsaturated fatty acid synthesis
    - Fatty acid β-oxidation
    - Lipid glycosylation
    - Cholesterol metabolism

- Muscle contraction
  - Neuropeptide signaling pathway
  - Tryptophan metabolism

- Feeding behavior

- Oxidative stress response/inflammation
  - Glutathione metabolism
    - γ-glutamyl leucine
    - γ-glutamyl methionine
    - Insulin/IGF1 signaling pathway

- Aminoacid metabolism

- Metabolism of cofactor and vitamins

- Nucleotide metabolism metabolism

- Cuticle development

- Xenobiotic metabolism

- Reproduction
Mutations confirmation

![Image of a nematode with a graph showing fluorescence reduction in C. elegans genotypes. The graph includes bars for various genotypes such as N2, VC1785 (Aces-1), RB2085 (Acs-5), RB859 (Daf-22), BX155 (Fat-7), GR1307 (Daf-16), VC175 (Sod-4), RB21764 (Trm-2), RB2434 (Aug-2), and GR1321 (Tph-1). The graph indicates significant differences in fluorescence reduction among the genotypes.]
The effect on Zücker Rats

Results of genetically obese rats (Zücker Rats)
- reduction in weight gain (-6.2%)
- better cholesterol levels (reduction of cardiovascular risk)
The effect on Wistar Rats

Results of Wistar rats + cafeteria diet
- reduction kcal consumption (-11.2%) - satiety

Cumulative energy intake

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<tr>
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Clinical trial in humans

12-week double-blind placebo-controlled human clinical trial

- 135 subjects
  - Placebo: 44 subjects
  - BPL1: 45 subjects
  - Heat-killed BPL1: 46 subjects
Results on waist circumference and fat deposition

Significant reduction of waist circumference (2 cm)
Significant reduction of abdominal visceral fat (7 cm²)
Changes in the gut microbiome

- Concomitantly with the decrease in obesity biomarkers, treatments with both, live and heat-killed CECT8145 strain increased the incidence of Akkermansia spp.
- The maximum increase in Akkermansia spp. was observed after the administration of the live strain, when the maximum decrease in BMI occurred
- There is a general shift to enterotype 1 after the treatment with the live form that could be related to the growth promotion of Bacteroides by Bifidobacterium species
Effects of daily consumption of the probiotic *Bifidobacterium* animalis subsp. *lactis* CECT 8145 on anthropometric adiposity biomarkers in abdominally obese subjects: a randomized controlled trial

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Abstract

The effects of probiotic *Bifidobacterium* animalis subsp. *lactis* CECT 8145 and those of its heat-killed form 2-h Bal419 on human anthropometric adiposity biomarkers are unknown.

**Objectives**

To assess the effect of Bal419 and 2-h Bal419 ingestion on anthropometric adiposity biomarkers.

**Design**

Randomized, parallel, double-blind, placebo-controlled trial with abdominally obese individuals. Participants (n = 119) were randomly allocated to receive 20 billion colony forming unit (cfu) of Bal419, 10 billion cfu of 2-h Bal419, or placebo (maltodextrin) for 3 months.

**Results**

Bal419 ingestion decreased waist circumference, waist-to-hip circumference ratio, and body mass index (BMI) (**p** < 0.05) versus its placebo. Changes versus the placebo group reached significance (**p** < 0.05) after the 2-h Bal419 treatment. Bal419 decreased the body mass index compared with baseline and placebo group (**p** < 0.05). This decrease is maintained after 2 weeks after Bal419 treatment reached significance (**p** < 0.05) only after 2-h Bal419. When animals by gender were performed, significance remained only for women. However, baseline measures and BMI were decreased (**p** < 0.05) after 2-h Bal419. Gut microbiota analysis showed an increase in Akkermansia spp. after Bal419 treatment, particularly in the fimbriated group, which was positively related to weight (**p** < 0.05).

**Conclusions**

In abdominally obese individuals, consumption of Bal419, both in viable and heat-killed cells, improves anthropometric adiposity biomarkers, particularly in women. An increase in the gut *Akkermansia* spp. appears as a possible mechanism involved. Our results support Bal419 probiotic as a complementary strategy in obesity management.

Introduction

The rising prevalence of overweight and obesity in Western countries is a significant public health concern. The World Health Organization (WHO) defines obesity as a disease characterized by a body mass index (BMI) greater than or equal to 30 kg/m². Obesity is a chronic disease associated with a number of comorbidities such as diabetes, hypertension, and cardiovascular disease.

Regarding the benefits of probiotics, several studies have shown that *Bifidobacterium* animalis subsp. *lactis* CECT 8145 may have a positive effect on body weight and body composition. However, the potential benefits of this probiotic strain on anthropometric adiposity biomarkers and gut microbiota are not well understood.
Scientific Dossier


Conclusions: innovation, innovation and innovation
Running to the future

- Apps
- Genomics
- Microbiome
- Metagenome
- Metatranscriptome
- Big data
- Non-invasive devices
- "A la carte" probiotics
- Metabolome
- Systems biology
Always Marie Curie

“There is no reason to fear the unknown, you just need to understand it”
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