

BioGaia competitive science

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Chief Scientific Officer

BioGaia®

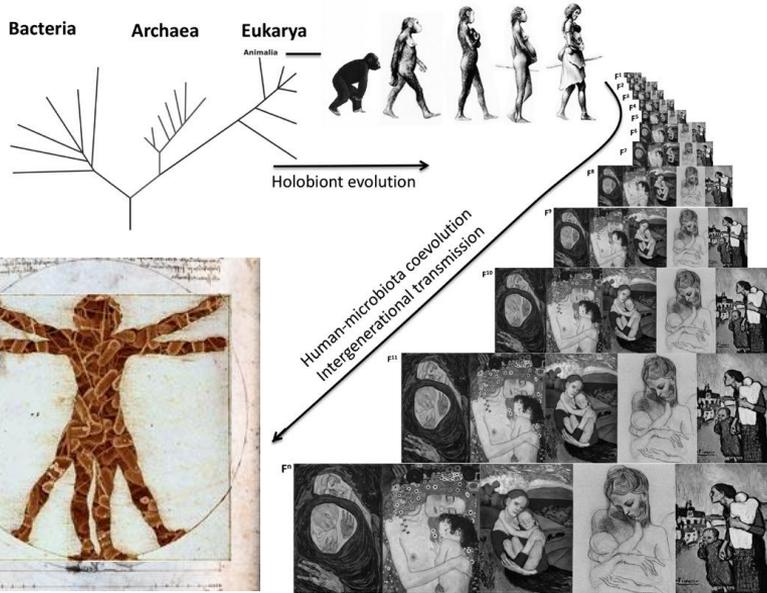


Outline

- Probiotics in the microbiome era
- BioGaia at a glance
- Why science is a competitive advantage in probiotics?
- BioGaia: 30 years of innovation
- Perspectives



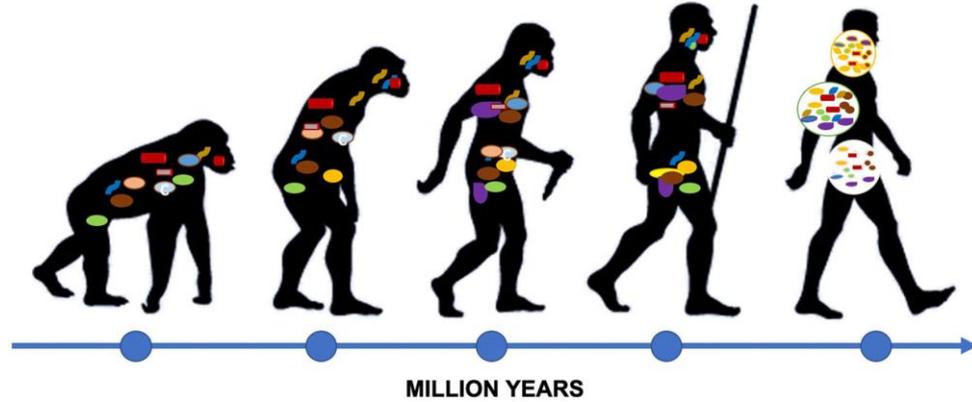
The host-microbiome holobiont & its co-evolution



Leonardo da Vinci, 1490

Bello et al., Gut, 2019

HOST/MICROBIOTA COEVOLUTION
Selective pressures: climate changes, switch from herbivour to carnivour habits, exposures to famine, infections, industrialization

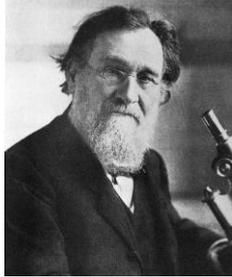


Santoro et al., Seminars in Immunopathology, 2020

Probiotics: definition



Food and Agriculture Organization
of the United Nations

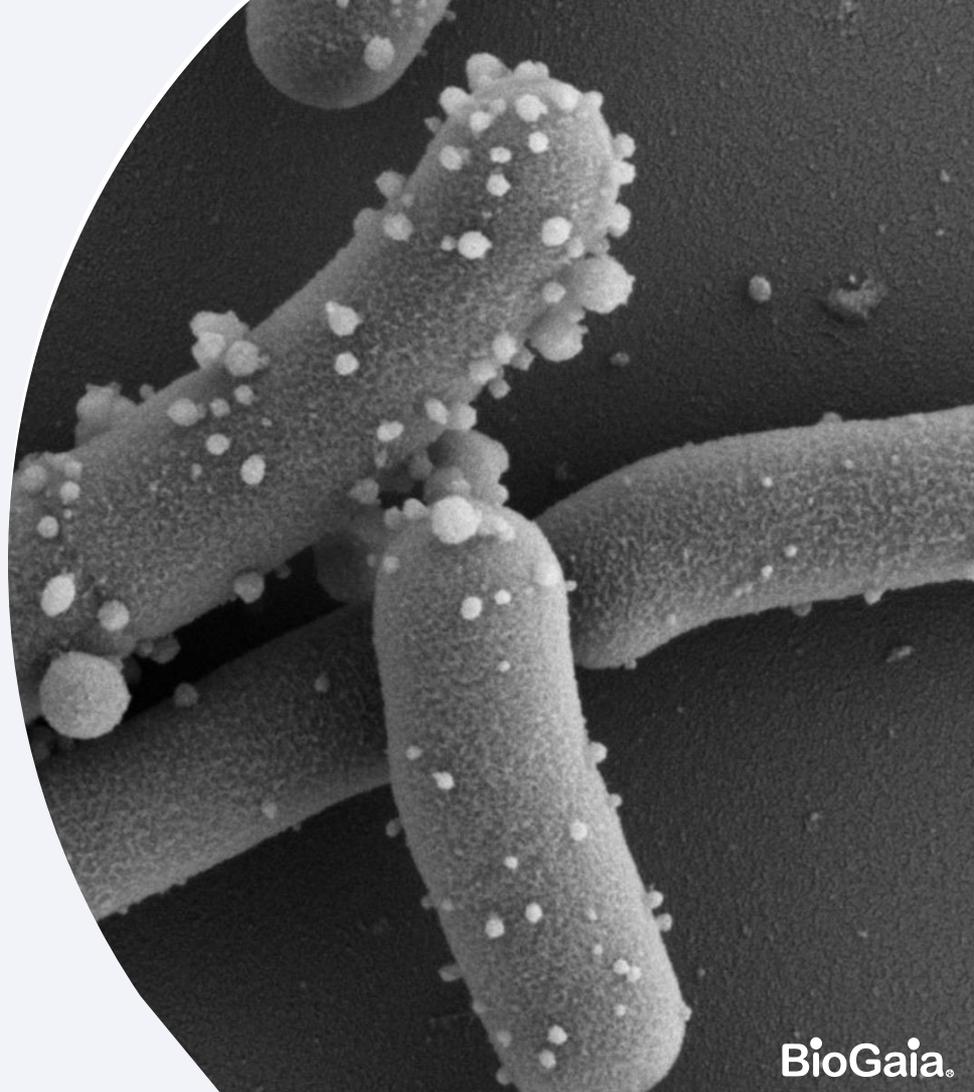


World Health Organization

Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria

Report of a Joint FAO/WHO Expert Consultation on
Evaluation of Health and Nutritional Properties of Probiotics in Food Including
Powder Milk with Live Lactic Acid Bacteria

**‘Live micro-organisms which
when administered in adequate amounts
confer a health benefit on the host’**



BioGaia at a glance

BioGaia is a Swedish probiotic company that has been at the forefront of microbiome research for more than 30 years. BioGaia develops, markets and sells probiotic products within the areas of gut, oral, and immune health.



Founded in 1990

Over SEK 1 billion in net sales

Over 600 granted patents

Products in more than 100 markets

Three market areas (EMEA, APAC and Americas)

Listed on Mid Cap list of Nasdaq OMX
Nordic Exchange Stockholm



Our vision:

**To be the most trusted
probiotic brand in the world.**

Our mission:

**To provide the world with probiotics
that have clinically proven positive
effects on health and well-being.**

Probiotics for the Whole Family

GUT HEALTH

IMMUNE HEALTH

ORAL HEALTH

CHILDREN



Protectis ORS / Protectis MINIPACK /
Protectis KIDS / Protectis BABY



Pharax KIDS / Protectis BABY vitamin D /
Protectis KIDS vitamin D



Prodentis KIDS

ADULTS



Gastrus / Protectis



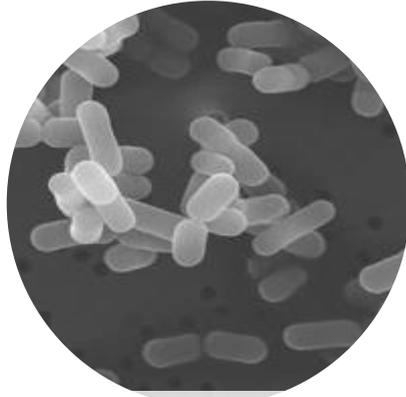
Protectis vitamin D



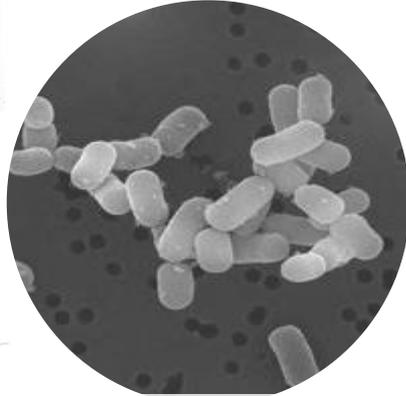
Prodentis

It all started in the Andes...

For millennia, mothers and babies have shared a special biological bond—the microbiota.



L. reuteri DSM 17938



L. reuteri ATCC PTA 6475



Casas found Reuteri in the Andes

By Nino Sisti

The source of the Reuteri strain forming the basis of BioGaia's products is the breast milk of a Peruvian nursing mother, Ivan Casas. BioGaia's former head of research, wanted samples from a population, which lived at natural, a life as possible. He chose the Andes and was assisted with his samples at a hospital at an altitude of 3,200 m.

By then – 1991 – research into Reuteri bacteria was somewhat advanced. Some years earlier, Prof. Walter Dobrogosz of North Carolina State University and Prof. Sven Lidgren of Uppsala University, Sweden, discovered that *Lactobacillus reuteri* (Reuteri) produces an active antimicrobial substance. The substance was called reuterin.

"It was a new phenomenon – unknown in other lactobacilli – that Reuteri produced a substance, which was active against other microorganisms and conceivably also against viruses," says Ivan Casas, who at the time was a visiting professor at North Carolina State University. "Reuteri is found naturally in the intestinal tract of both animals and humans, and it

was here a natural substance with a positive effect was found – that was very interesting."

With the support of Venture Capital, the research group worked on the bacteria for three years focusing on the use of reuterin. Its members knew that Reuteri had a probiotic effect. Then came the bad news: Venture Capital wanted to move out of the probiotics industry. Suddenly the future was uncertain.

"It was about this time that BioGaia contacted us, inquiring about our research," Ivan Casas recalls.

"They were interested in natural products. Since we had evidence that Reuteri had a probiotic effect, more studies were conducted on stress in birds. In repeated tests chickens and turkeys were subjected to cold or heat stress, which normally impedes growth. Reuteri helped them survive the challenge."

At the outset, the company focused on controlling *Salmonella* in poultry production. Ivan Casas: "A group of professors – of whom I was one – was trying to persuade people in the industry to let us conduct large-scale tests with Reuteri. We succeeded in demonstrating that early administration (spraying) of Reuteri reduced

mortality in newly-hatched turkey chicks and that they quickly increased their weight."

It was already believed that Reuteri bacteria strains could be specific to individual species. Bacteria strains from mice, hamsters, poultry and pigs all had different morphology. Researchers also knew that Reuteri from a human source did not colonize mice and vice versa. What was needed at this point was a human Reuteri strain from a population, which had been living a natural lifestyle.

During his vacation time, Ivan Casas travelled to Peru, obtained the help of friends and relatives in contacting local doctors, and was advised that a particular hospital would be prepared to help. Of seven women tested, three of them had Reuteri in their breast milk. At an altitude of 3,200m Ivan Casas secured a sample of the breast milk. The sample was transported to the United States – and became the basis of production for Reuteri for human use.

Research has revealed that Reuteri is active against pathogens and stimulates the development of intestinal villi. Immunologists have demonstrated in studies of mice that the bacteria boosts production of cyto-



Dr. Ivan Casas

kines, and the results indicate that the production of antibodies is also increased.

"My honest opinion is that Reuteri can travel far," says Ivan Casas. "We know that Reuteri is specific to each particular animal species and can colonize its host species."

At BioGaia it is generally believed that during the course of its evolution Reuteri has developed with animals and plays an increasingly important role in the protection of its host thus other lactobacilli.

Ivan Casas: "There are many positive arguments for future development. With more research and more resources Reuteri will really take off."

Clinical studies with all BioGaia probiotics - per age group

266 completed clinical studies in 22 634 individuals



L. reuteri improves sociability in ASD

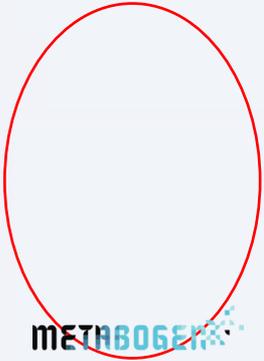


Clinical and Translational Report

Highlights

- *L. reuteri* (6475 + 17938) improves social functioning in children with autism
- *L. reuteri* does not improve overall autism severity or repetitive behaviors
- *L. reuteri* does not significantly alter microbiome composition or immune profile
- Only the 6475 strain reverses the social deficits in a mouse model for autism

More than 30 years of probiotic innovation



Opportunities, regulatory context, choices...



Food supplements
Probiotics



IBP-9414



LBP

NEC prevention in preterm infants
Granted Orphan Drug & Rare Pediatric Disease designations by FDA

Still recruiting for Phase 3:
"The Connection Study"



LBP

STRAIN SELECTION	PRECLINICAL	DEVELOPMENT	PHASE I	PHASE II
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Next-generation
Probiotics (?)



Article

Synergy and oxygen adaptation for development of next-generation probiotics

<https://doi.org/10.1038/s41586-023-06378-w> Muhammad Tanweer Khan^{1,2*}, Chinmay Dwivedi^{1,2,3*}, Daniel Sundh^{1,2*}, Meenakshi Pradhan¹, Jamie D. Kraft¹, Robert Caesar¹, Valentina Tremaroli^{1,2*}, Mattias Lorentzon^{1,2,3,4*} & Fredrik Bäckhed^{1,2,3,4*}

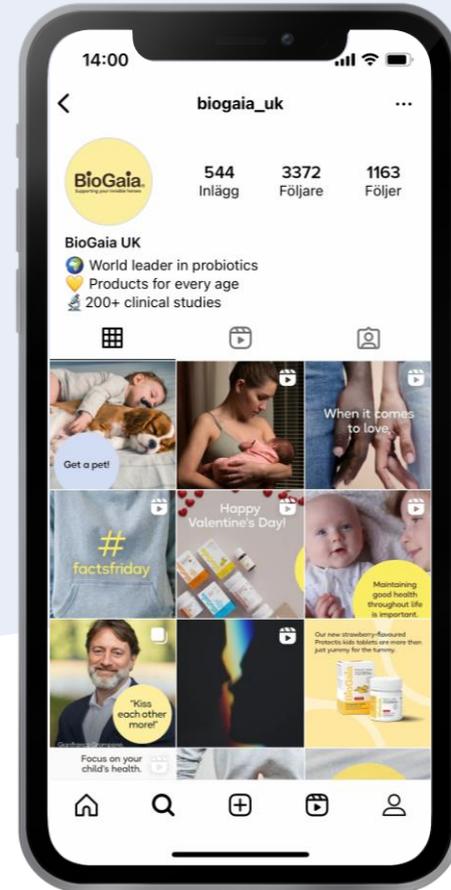
Received: 30 June 2021
Accepted: 27 June 2023
Published online: 02 August 2023
Open access

The human gut microbiota has gained interest as an environmental factor that may contribute to health or disease¹. The development of next-generation probiotics is



Thank you

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The logo for BioGaia is centered on a light blue background with white curved lines. The text "BioGaia" is written in a bold, dark brown, sans-serif font. The "Bio" part is in a slightly smaller font size than "Gaia". A registered trademark symbol (®) is located to the right of the "a" in "Gaia".

BioGaia®