U.S. FDA GRAS Notification

Global immune modulation company based on microbiome

Microbiome research based on *Bifidobacterium*

BIFIDO

BIFIDO
microbiome leader

BIFIDO Co., Ltd. was founded in 1999, in a spirit of challenge to pursue the best biotechnology and try to be the best in the field of human microbiome.

Among various intestinal microbiome, *Bifidobacterium* is considered to be the most beneficial bacteria to maintain healthy intestinal microbial balance. BIFIDO has focused on research and development of *Bifidobacterium spp*. since 1999. Over 178 of concerning scientific papers and 70 patents prove that BIFIDO is the top-tier company with the greatest experience and expertise in microbiome industry.

Recently, BIFIDO started microbiome research on rheumatoid arthritis(RA), a chronic inflammatory disease. We analyzed the microbiota of RA patients and tried to find a way to treat even those who were less responsive to treatment. We have selected novel *Bifidobacterium* strains which can improve the symptoms of RA animal model and we expect a new pharmabiotics from those strains. We are now expanding our pipelines for other immune related diseases including cancer.

Competitiveness

30	52	30	74	178
Years know-how (research)	Research Projects	Export Countries	Patents	SCI Papers

Certification

U.S. FOOD & DRUG ADMINISTRATION

WORLD CLASS PRODUCT OF KOREA 세계일류상품

글로벌 강소기업 Small Giant Company of Korea

KOSDAQ LISTED COMPANY

우수건강기능식품제조기준 GMP 식품의약품안전처

건강기능식품 식품의약품안전처

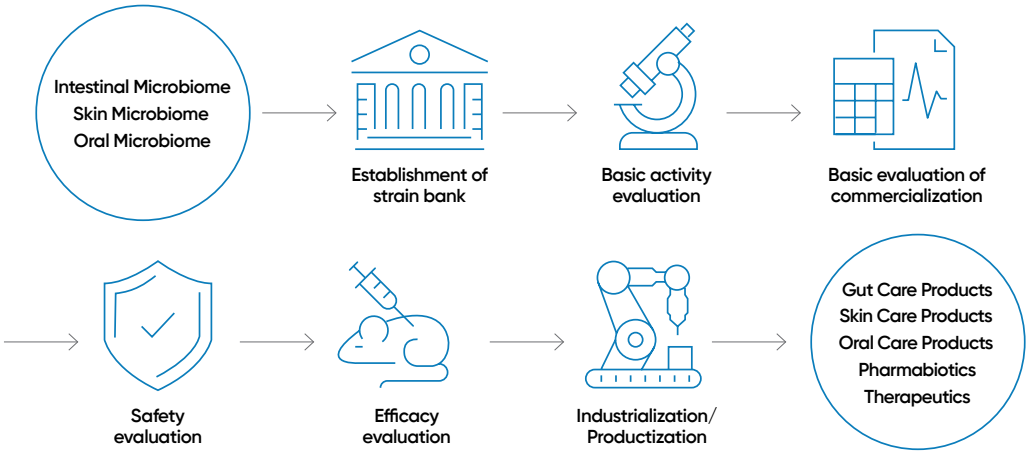
과학기술부 국가지정연구실

Korea Muslim Federation Halal Committee HALAL

BIFIDO EXPRESS PLATFORM

BIFIDO Express Platform

From the selection of pharmabiotics candidates to the production of finished products with various formulations, we have our own R&D and industrialization platform and we are expecting to create mutual profit by BIFIDO Express Platform based collaboration.



Manufacturing Facilities

CORE STRAIN

Bifidobacterium bifidum BGN4

Immune Modulator

- **Prevention of Allergy**
- **Improve IBS**
- **Anti-tumor**
- **High Adhesion Ability**
- **US FDA GRAS & NDI Notification**
  GRN814 / NDI 1079

Bifidobacterium bifidum BGN4 found to produce chiroinositiol containing polysaccharide (BB-pol) which showed anti-tumor activity on human colon cancer cell line.

Bifidobacterium longum BORI

Pathogen Inhibitor

- **Suppression of Pathogens**
- **Improve Constipation**
- **Anti-rotavirus**
- **Inhibit Diarrhea**
- **US FDA GRAS & NDI Notification**
  GRN813 / NDI 1082

Bifidobacterium longum BORI showed 99% inhibition of the rotavirus infection in the experimental model. It was identified to be a single protein named BORI by our research group.

Bifidobacterium lactis AD011

Bowel Helper

- **Improve Bowel Health**
- **Prevention of Allergy**
- **Improve IBS**
- **Improve Constipation**
- **US FDA NDI Notification**
  NDI 1118

Prenatal and postnatal supplementation with *Bifidobacterium lactis* AD011 is an effective approach in prevention the development of eczema in infants at high risk of allergy during the first year of life.

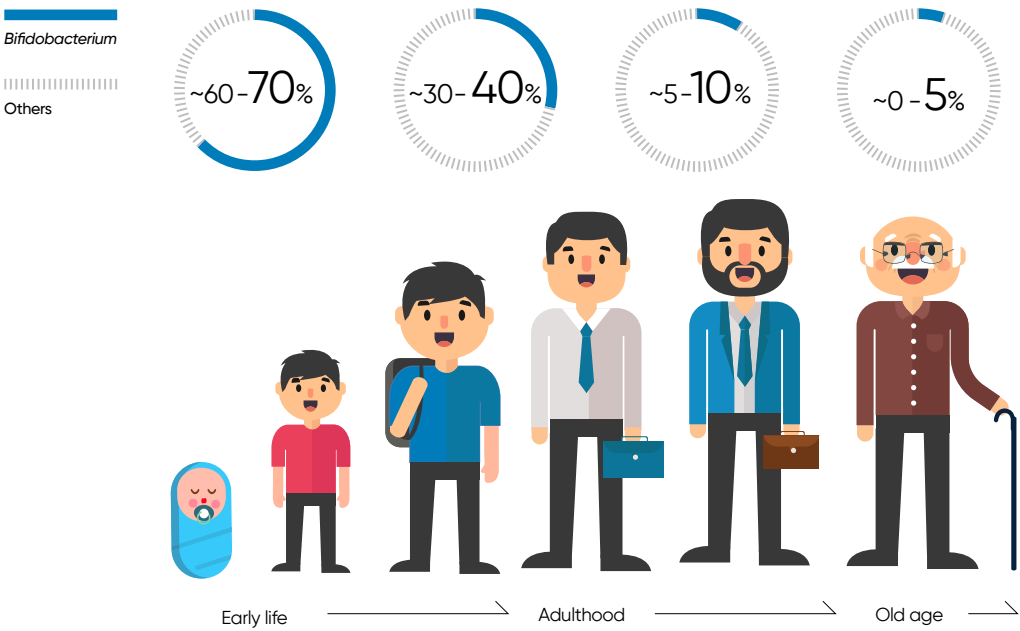
NGS (Illumina Miseq)

Over 100 kinds of BIFIDO strains have been established through cutting edge technologies including NGS. In addition, this technology can also be used to analyze the distribution of human intestinal microorganisms, so as to better diagnose the intestinal environmental status and provide a reliable basis for subsequent prevention and treatment.

WHY *BIFIDOBACTERIUM* IMPORTANT ?

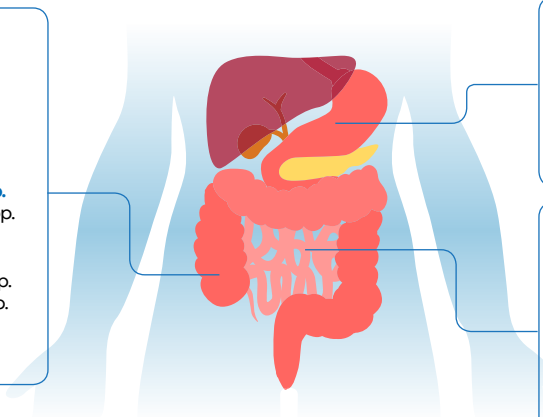
Bifidobacterium is one of the most abundant genera in the gut of healthy adults, but its predominance is even more pronounced in infants, especially during breast feeding, when they can constitute the majority of the total bacterial population. They are one of the pioneering colonizers of the early gut microbiota, and they are known to play important roles in the metabolism of dietary components, otherwise indigestible in the upper parts of the intestine, and in the maturation of the immune system.

Adopted from
Front Microbiol. 2016 Aug 19;7:1204.
Gut Bifidobacteria Populations in
Human Health and Aging.



Colon
>10^{11} bacteria mL^{-1}

Alistipes spp.
Anaerostipes spp.
Bacteroides spp.
***Bifidobacterium* spp.**
Clostridium cluster spp.
Dorea spp.
Eubacterium spp.
Faecalibacterium spp.
Parabacteroides spp.
Roseburia spp.
Ruminococcus spp.



Stomach
10^{2}–10^{4} bacteria mL^{-1}

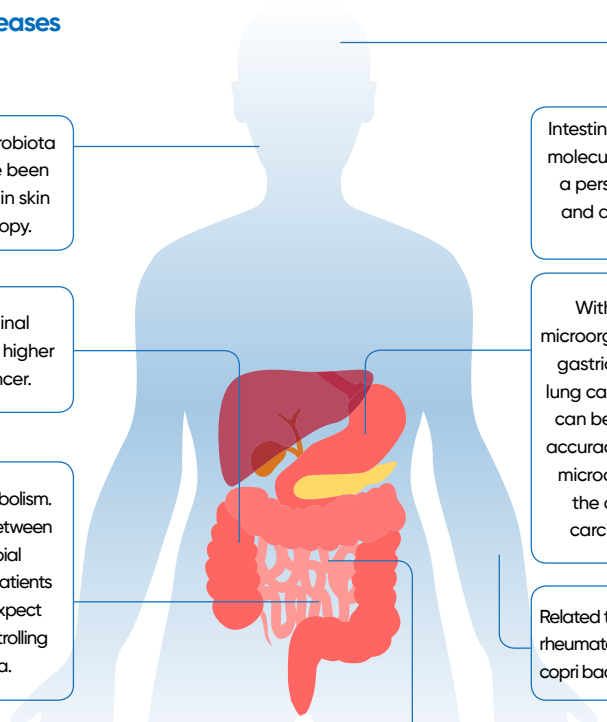
Lactobacillus spp.
Propionibacterium spp.
Streptococcus spp.
Staphylococcus spp.

Small intestine
10^{7}–10^{8} bacteria mL^{-1}

Escherichia spp.
Bacteroides spp.
Clostridium cluster XIVa spp.
***Lactobacillus* spp.**
Streptococcus spp.
Veillonella spp.

Data resource*
Front Microbiol. 2016;7:979

Microbiome & Diseases



Some specific gut microbiota and metabolites have been shown to be effective in skin diseases such as atopy.

Intestinal microorganisms use molecular signals to influence a person's appetite, mood, and decisions about what foods to eat.

The lower the intestinal microbial diversity, the higher the risk of colon cancer.

With the distribution of microorganisms in the intestine, gastric cancer, liver cancer, lung cancer and colon cancer can be diagnosed with 90% accuracy. The more beneficial microorganisms, the higher the anticancer effect of carcinostatis substance.

Regulate the lipid metabolism. There are differences between the intestinal microbial composition of obese patients and healthy people. Expect to treat obesity by controlling intestinal microflora.

Related to the development of rheumatoid arthritis by Prebotella copri bacteria etc.

Beneficial gut microorganisms activate immune cells to boost immunity. If the intestinal microbial balance is broken, the development of metabolic diseases such as diabetes and enteritis is at risk.

Stroke, dementia, Parkinson's disease, depressive disorder

Lung cancer, asthma, chronic obstructive pulmonary disease

Myocardial infarction, cardiomyopathy, variant angina pectoris

Gastric cancer

Liver cirrhosis, liver cancer

Pancreatic cancer

Obesity

Colitis, colon polyp, colorectal cancer

Diabetes mellitus, chronic kidney disease

Bladder cancer, prostate cancer

Data resource*

Innovating Data into Strategy and Business. 2018 Sep; Issue 12.

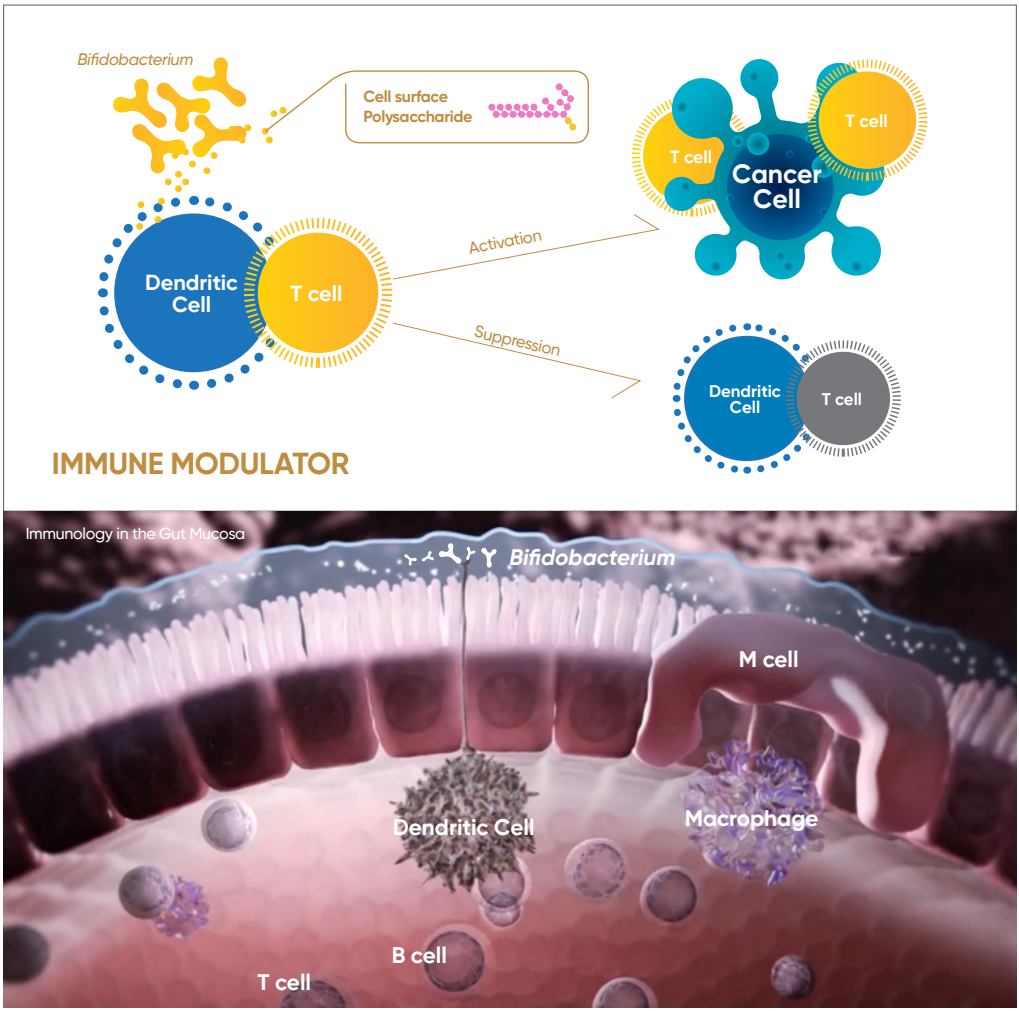
Two-way Immune Modulation based on *Bifidobacterium* spp.

Activation

Bifidobacterium-derived signals modulate the activation of DC(Dendritic Cell) in the steady state, which in turn supports improved effector function of tumor-specific CD8+ T cells.

Inactivation

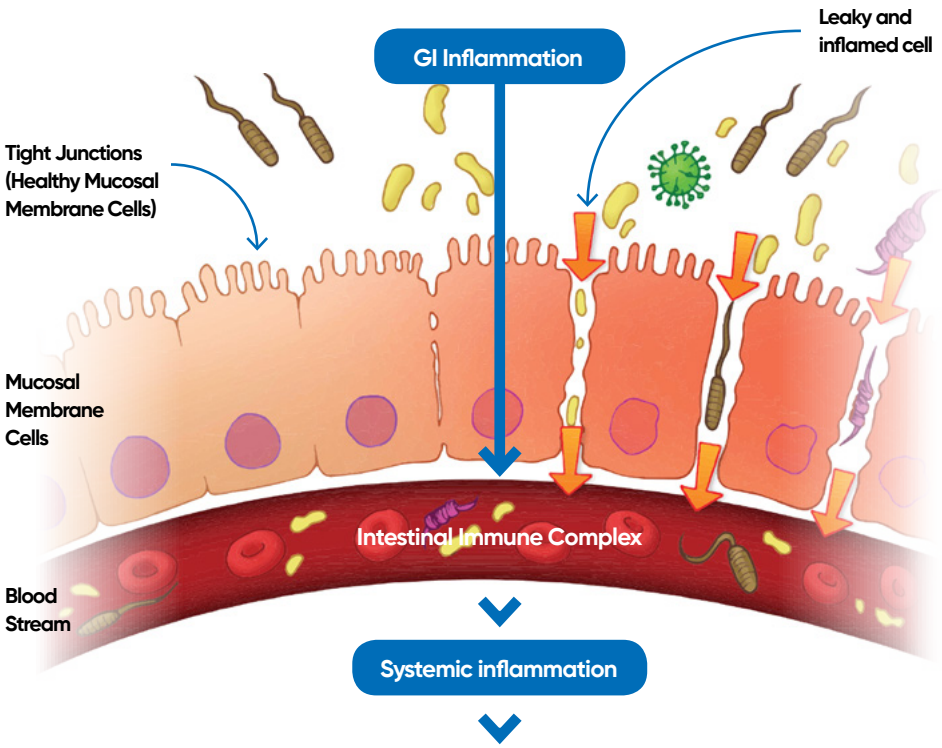
Cell Surface β-glutan/galactan (CSGG) polysaccharides produced by *Bifidobacterium* as the key effector component able to induce Treg cells via a DC(Dendritic Cell)-dependent mechanism with the capacity to ameliorate intestinal inflammation.



Data resource*

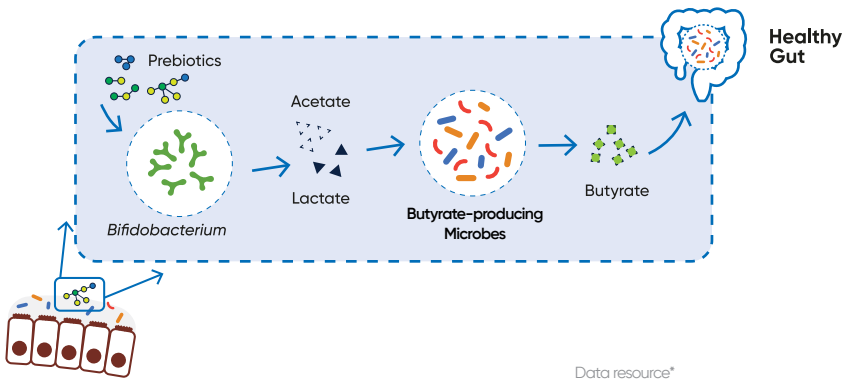
1. Science Immunology 19 Oct 2018: Vol.3, Issue 28, Cell surface polysaccharide of *Bifidobacterium* bifidum induce the generation of Foxp3+ regulatory T cell.
2. Science 2015 November 27; 350(6264): Commensal Bifidobacterium promotes immunity and facilitates anti-PD-L1 efficacy.

BIFIDOBACTERIUM & LEAKY GUT



Brain : Depression, Anxiety, ADHD
Skin : Acne, Rosacea, Eczema, Psoriasis
Colon : Constipation, Diearrhea, IBD
Adrenals : Fatigue

Sinus and Mouth : Frequent Colds Food Sensitivities
Joints : Rheumatoid Arthritis, Fibromyalgia, Headaches
Thyroid : Hashimotos, Hypothyroidism, Graves



Data resource*
FEMS Microbiology Letters, 2015, Vol.362, No. 21.

CLINICAL STUDY
BIFIDO MAIN FORMULA (THERAPY)

MAIN INGREDIENTS LIST	STRAIN	
Bifidobacterium spp.	*Bifidobacterium bifidum* BGN4 *Bifidobacterium longum* BORI *Bifidobacterium lactis* AD011 *Bifidobacterium breve* BH12 *Bifidobacterium infantis* BH07	
IMT Immune Therapy	*Bifidobacterium bifidum* BGN4 *Bifidobacterium longum*BORI *Bifidobacterium lactis* AD011	
ECZEMA	*Bifidobacterium bifidum* BGN4 *Bifidobacterium longum*BORI *Lactobacillus acidophilus* AD031	Clinical Study
IBS Irritable Bowel Syndrome	*Bifidobacterium bifidum* BGN4 *Bifidobacterium longum* BORI *Lactobacillus acidophilus* AD031 *Lactobacillus casei* IBS041	Clinical Study
Ulcerative Colitis	*Bifidobacterium bifidum* BGN4 *Lactobacillus acidophilus* *Lactobacillus salivarius*	Clinical Study
RA Rheumatoid Arthritis	*Bifidobacterium bifidum* ATT *Bifidobacterium longum* RAPO	Clinical Study
RI Rotavirus Infection	*Bifidobacterium longum* BORI *Lactobacillus acidophilus* AD031	Clinical Study
Kidney Inflammation	*Bifidobacterium bifidum* BGN4 *Bifidobacterium longum* BORI	Clinical Study
Cognitive function of the elderly	*Bifidobacterium bifidum* BGN4 *Bifidobacterium longum* BORI	Clinical Study
Constipation	*Weissella confuse* VP30	Clinical Study
Acne	*Bifido probiotics ferment lysate*	Clinical Study
Rhinitis	*Bifidobacterium bifidum* BGN4 *Bifidobacterium longum*BORI *Bifidobacterium lactis* AD011	Clinical Study

RESEARCH BASED ON *BIFIDOBACTERIUM* – RHEUMATOID ARTHRITIS

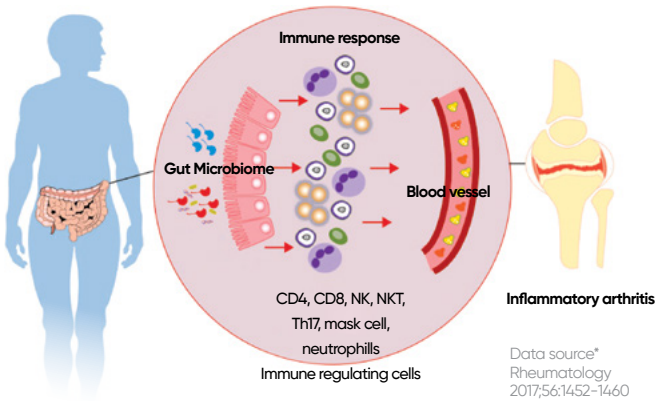
Rheumatoid Arthritis (RA)

Co-work with the Catholic University of Korea Seoul St. Mary's Hospital

***Bifidobacterium* Therapy**	• *Bifidobacterium bifidum* ATT • *Bifidobacterium longum* RAPO

Mechanism

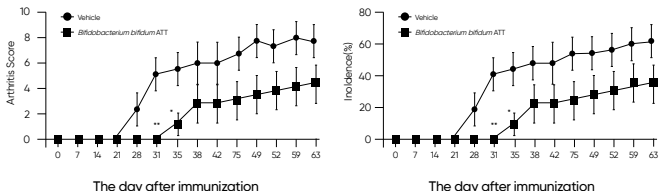
Microbiome dysbiosis



Data source*
Rheumatology 2017;56:1452-1460

Animal Experiment

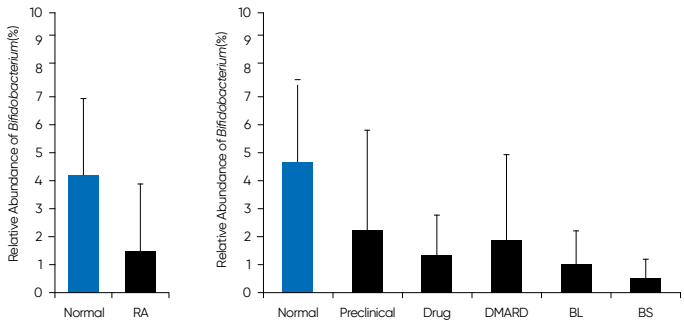
BIFIDO treated a selected novel strain of *Bifidobacterium* to RA in vivo model mice and observed the suppressive effect of RA related symptoms and immunologic criteria. Our results can shed light on the development of RA targeted pharmabiotics.



Human Clinical Experiment (Underway)

Microbiome profiling of RA patients with different therapeutic agents implicated a novel *Bifidobacterium* Strain as one of the way to overcome severe RA

US Patent Application :
A composition comprising *Bifidobacterium* for the treatment or prevention of rheumatoid arthritis (Patent Application No.10-2018-0012354



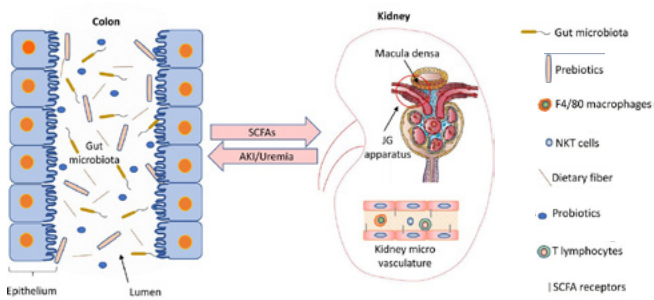
RESEARCH BASED ON *BIFIDOBACTERIUM* - KIDNEY HEMODIALYSIS

Kidney Inflammation

Co-work with Korea University Anam Hospital

***Bifidobacterium* Therapy**	• *Bifidobacterium bifidum* BGN4 • *Bifidobacterium longum* BORI

Mechanism



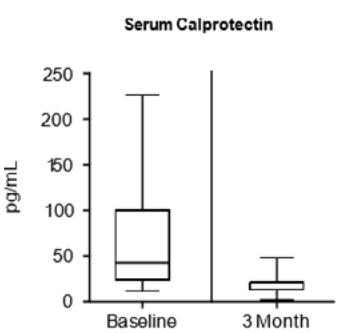
Animal Experiment

Effect of *Bifidobacterium* therapy in Acute Kidney Injury(AKI) model (bilateral ischemia reperfusion injury model)

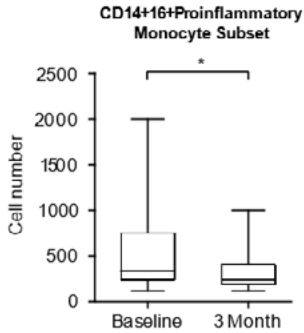
- Improved renal function and structure
- Decreased proteinurea, Restored claudin-1, occluding, and HSP 70
- Increased Foxp3 Tregs in colon and kidney

Human Clinical Experiment

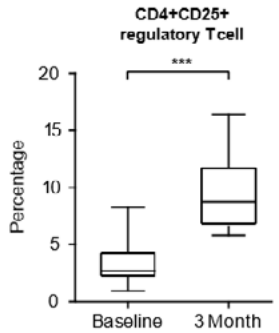
Effect of *Bifidobacterium* therapy in 21 Hemodialysis patients



Reduced inflammatory calprotectin



Reduced CD14+CD16+inflammatory monocyte count



Increased CD4+CD25+Treg count

RESEARCH BASED ON *BIFIDOBACTERIUM* – INTESTINE HEALTH

Intestine Health

Co-work with IRB of Seoul National University and Bundang Jesaeng Hospital

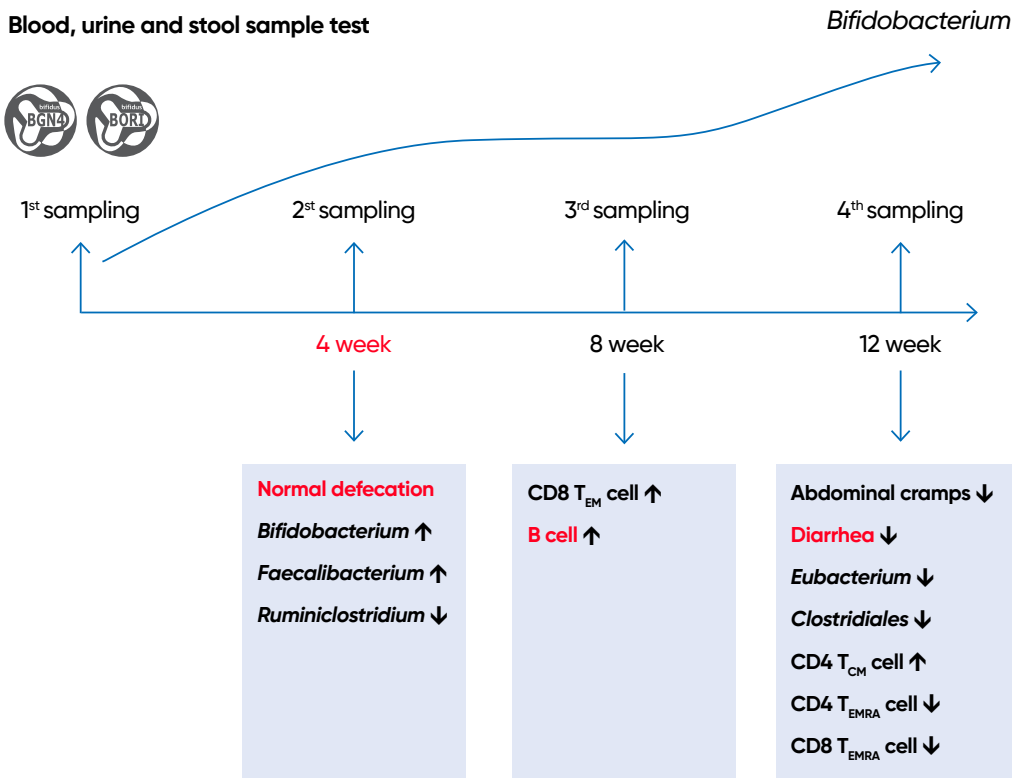
***Bifidobacterium* Therapy**

- *Bifidobacterium bifidum* BGN4
- *Bifidobacterium longum* BORI

Human Clinical Experiment

Effect of *Bifidobacterium* therapy in the age over 65.

Blood, urine and stool sample test



The defecation showed to become normal at 4th week. During 12 weeks of test period, the viable cell number of *Bifidobacterium* and *Faecalibacterium* increased, whereas that of *Eubacterium* and *Clostridiales* decreased, which were tracked by Next Generation Sequencing(NGS). In addition, Abdominal cramps, diarrhea and inflammatory biomarkers were improved.

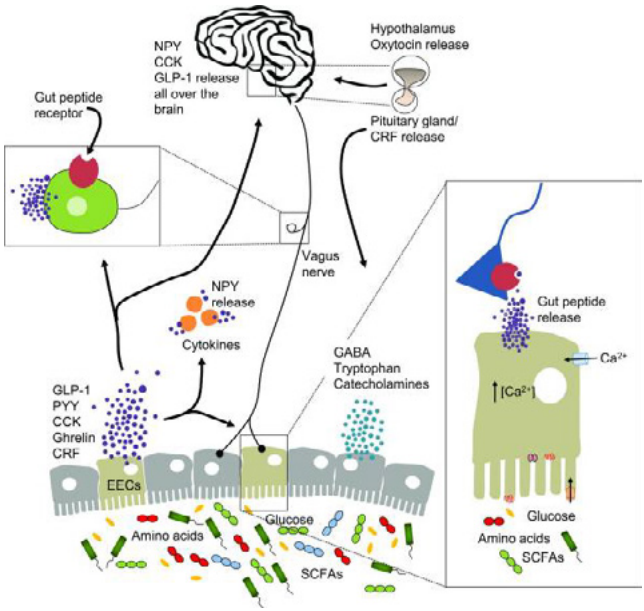
RESEARCH BASED ON *BIFIDOBACTERIUM* – COGNITIVE FUNCTION

Cognitive Function

Co-work with
Seoul National University

***Bifidobacterium* Therapy**	• *Bifidobacterium bifidum* BGN4 • *Bifidobacterium longum* BORI

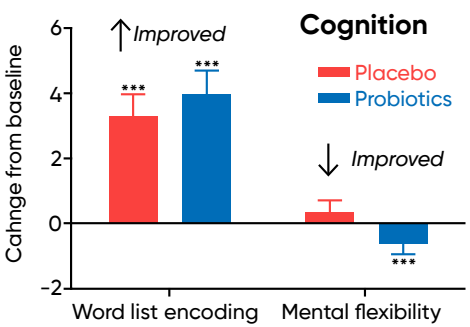
Mechanism



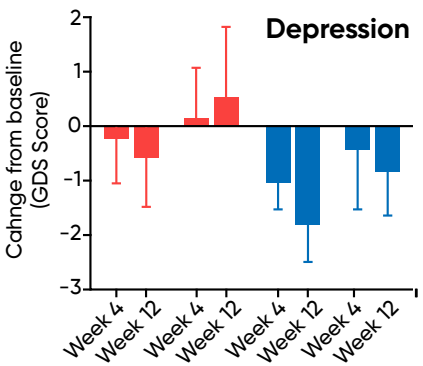
*Neurotherapeutics. 2018 Jan; 15(1): 36–59. Published online 2017 Nov 13. doi: 10.1007/s13311-017-0585-0

Human Clinical Experiment

Effect of *Bifidobacterium* therapy in the elderly.



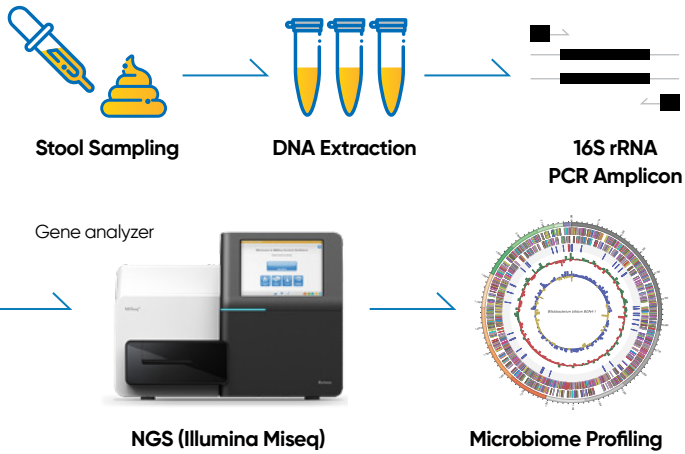
Improved memory ability to focus attention and mental flexibility.



Reduced score of depression.

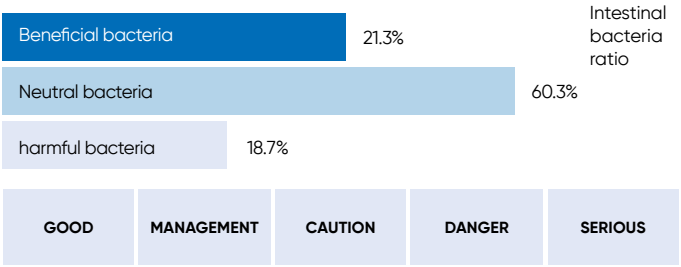
CUSTOMIZED SERVICE

Analysis Process



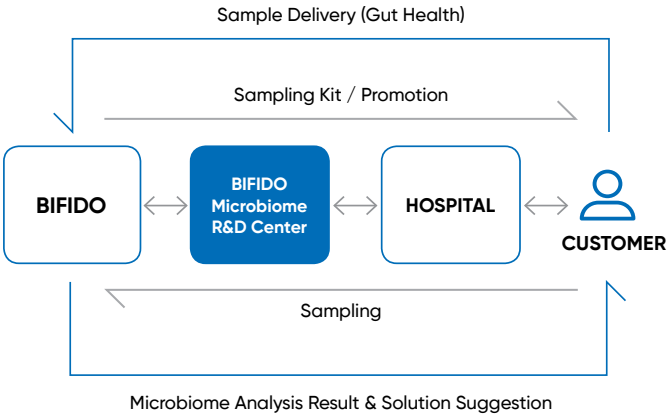
Microbiome Analysis Report

As a result, beneficial bacteria are 21.3% and harmful bacteria are 18.7%



Health Solution

Gut care
Oral care
Skin care



BIFIDO BRAND PRODUCT

Gut & Immune Care

ZIGUNUK
BIFIDUS PREMIUM
Probiotics

ZIGUNUK
BIFIDUS BABY PREMIUM
Probiotics + VitB complex

ZIGUNUK BIFIDUS Pro G
Probiotics + Prebiotics

ZIGUNUK BIFIDUS HYO
Probiotics +Zn

Oral care

ZIGUNUK BIFIDUS
DENTI

ZIGUNUK BIFIDUS
DENTI FRESH

Skin care

BIFIDOLAB
CALMING & ERASING
SERUM

BIFIDOLAB
pH CALMING
CLEANSER

BIFIDOLAB
AQUA PROJECT

BIFIDOLAB
AGING PROTECT
MASK

BIFIDO
microbiome leader

CONTACT US

HEAD OFFICE
23-16 Nonggongdanji-gil,
Hongcheon-eup,
Hongcheon-gun Gangwon-do
25117, Republic of Korea

SEOUL OFFICE
639 Seolleung-ro
Gangnam-gu, Seoul,
Republic of Korea

FAX. +82-33-435-4963
TEL. +82-33-435-4962
E-MAIL bgn4@bifido.com

www.bifido.com