



U.S. FDA GRAS Notification

Global immune modulation company based on microbiome

Microbiome research based on *Bifidobacterium*

 **BIFIDO**

INTRODUCTION



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



Certification



**U.S. FOOD & DRUG
ADMINISTRATION**



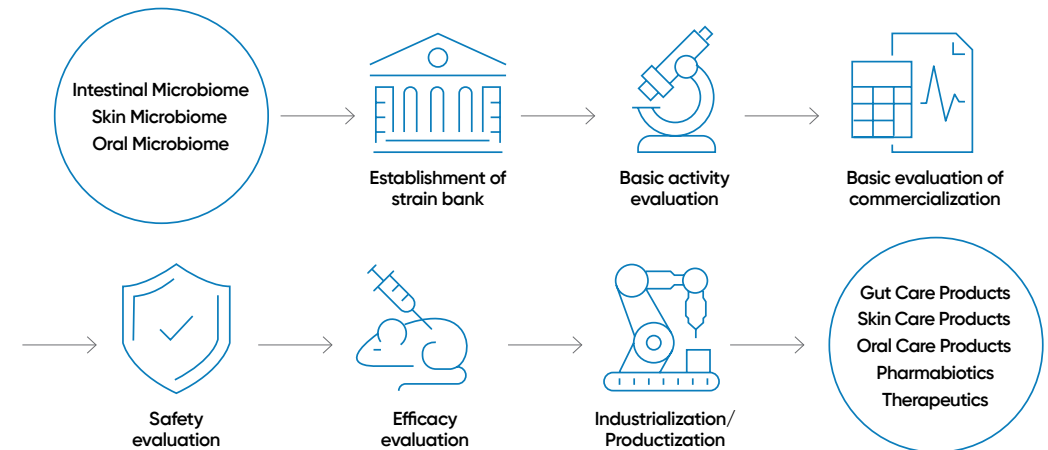
KOSDAQ
LISTED COMPANY



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 chiroinositol 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.

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.

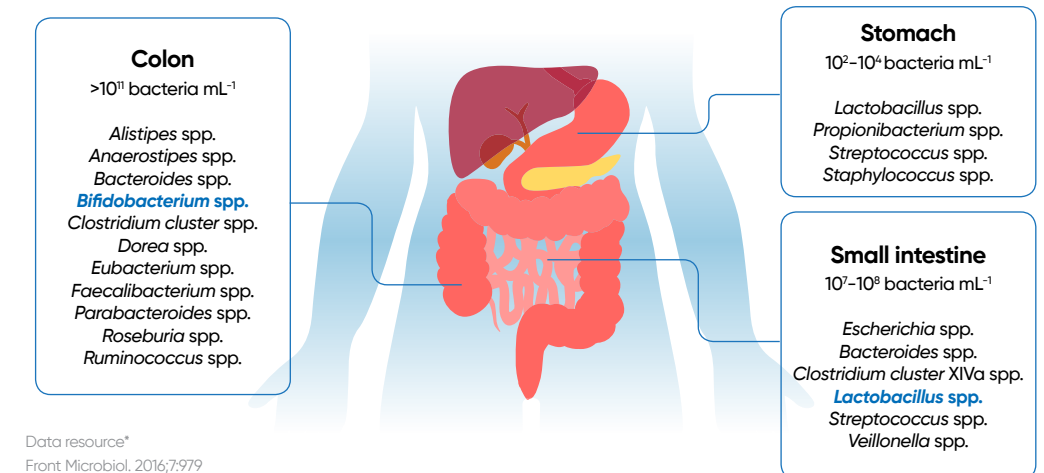
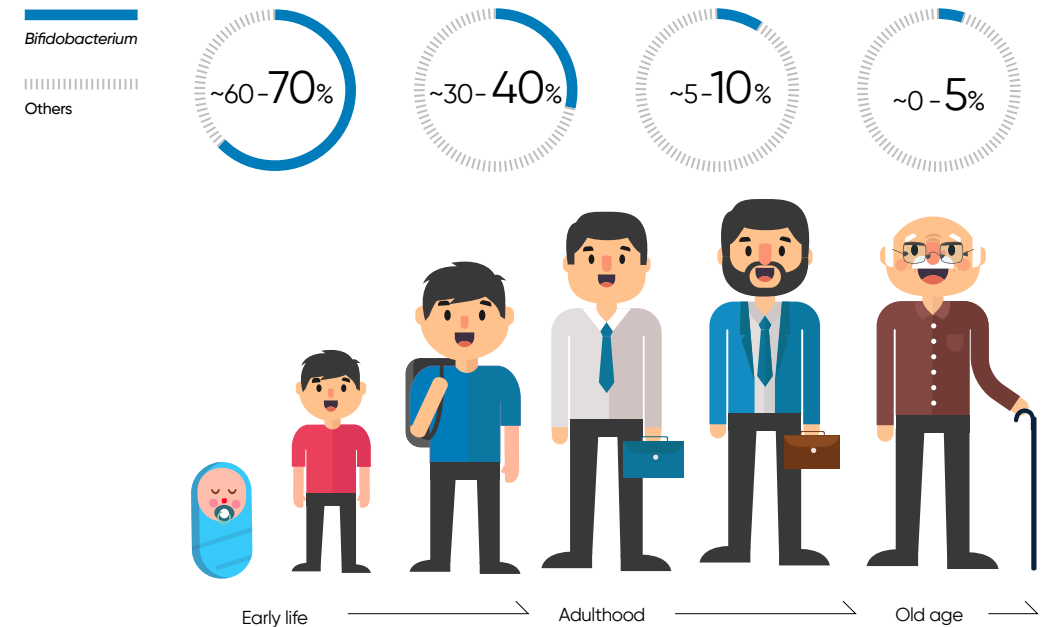


NGS (Illumina Miseq)

WHY BIFIDOBACTERIUM IMPORTANT ?

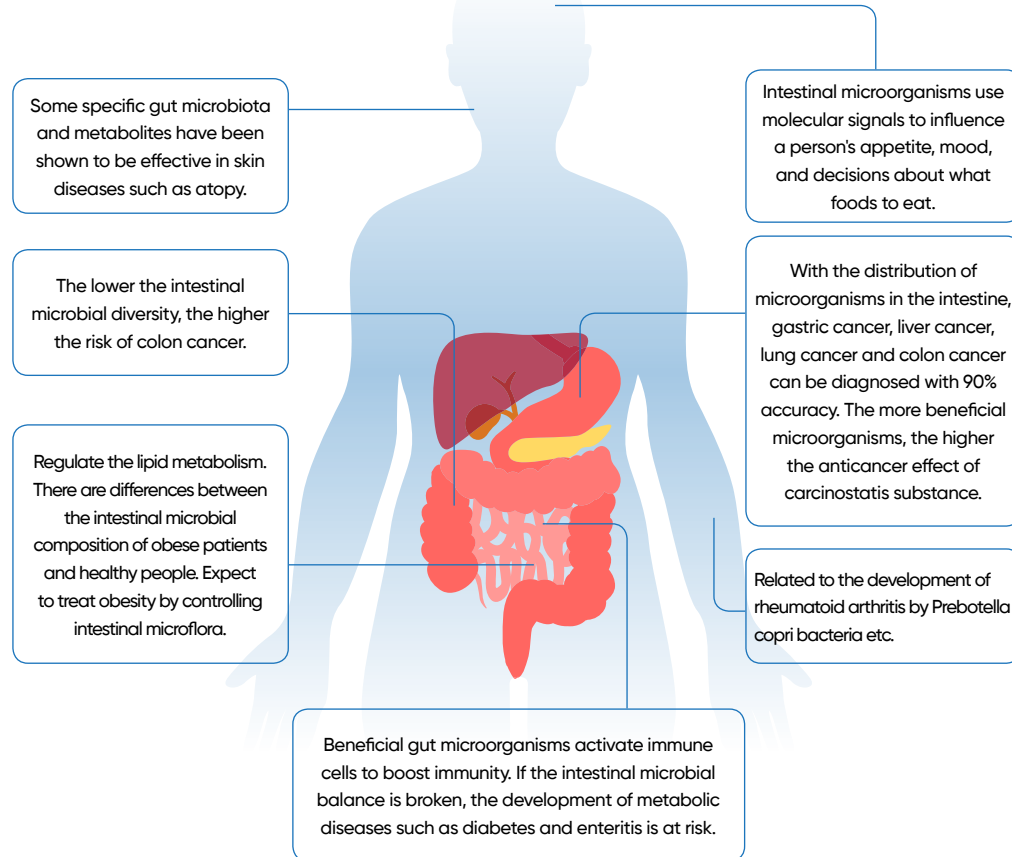
Bifidobacterium is one of the most abundant genera in the gut of healthy adults, but its predominance is even more pronounced in infants, especially during breast feeding, when they can constitute the majority of the total bacterial population. They are one of the pioneering colonizers of the early gut 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.



Data resource*
Front Microbiol. 2016;7:979

Microbiome & Diseases



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.

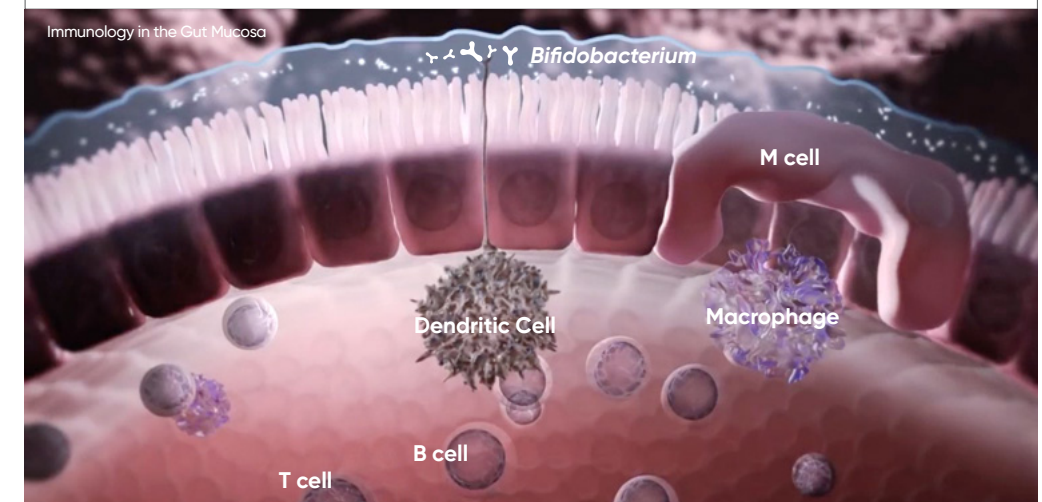
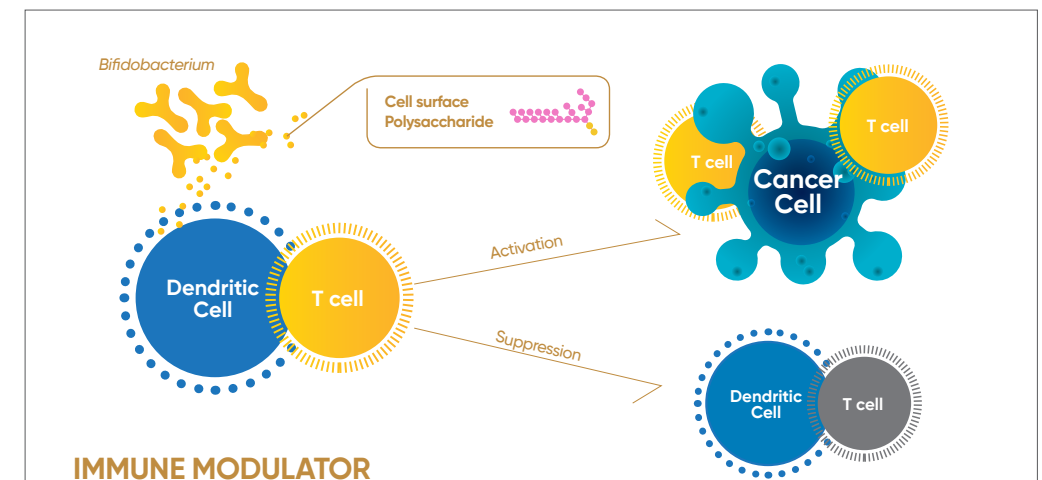
Two-way Immune Modulation based on *Bifidobacterium* spp.

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

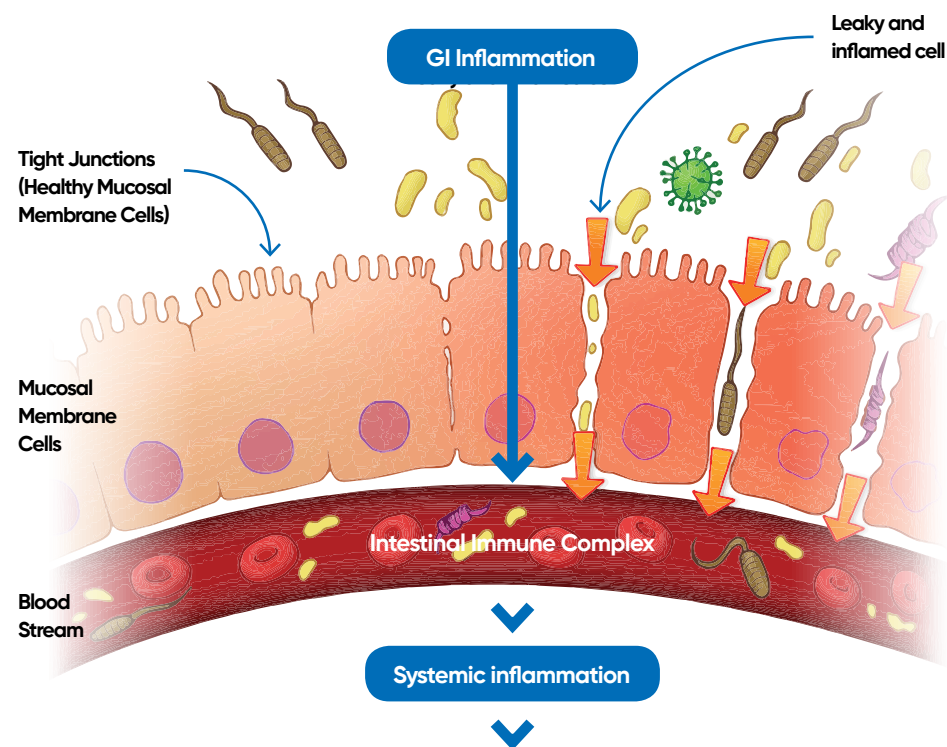
Cell Surface β -glucan/galactan (CSGG) polysaccharides produced by *Bifidobacterium* as the key effector component able to induce Treg cells via a DC(Dendritic Cell)-dependent mechanism with the capacity to ameliorate intestinal inflammation.



Data resource*

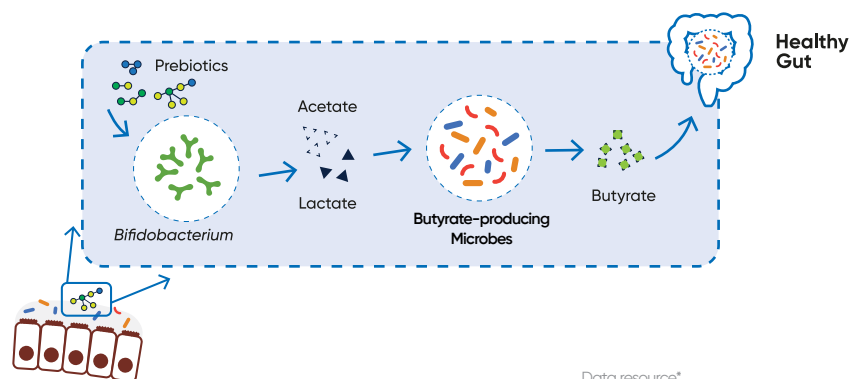
1. Science Immunology 19 Oct 2018; Vol.3, Issue 28, Cell surface polysaccharide of *Bifidobacterium bifidum* induce the generation of Foxp3+ regulatory T cell.
2. Science 2015 November 27; 350(6264): Commensal *Bifidobacterium* promotes immunity and facilitates anti-PD-L1 efficacy.

BIFIDOBACTERIUM & LEAKY GUT



Brain - Depression, Anxiety, ADHD
Skin : Acne, Rosacea, Eczema, Psoriasis
Colon : Constipation, Diarrhea, 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.	<i>Bifidobacterium bifidum</i> BGN4 <i>Bifidobacterium longum</i> BORI <i>Bifidobacterium lactis</i> AD011 <i>Bifidobacterium breve</i> BH12 <i>Bifidobacterium infantis</i> BH07	
IMT Immune Therapy	<i>Bifidobacterium bifidum</i> BGN4 <i>Bifidobacterium longum</i> BORI <i>Bifidobacterium lactis</i> AD011	
ECZEMA	<i>Bifidobacterium bifidum</i> BGN4 <i>Bifidobacterium longum</i> BORI <i>Lactobacillus acidophilus</i> AD031	Clinical Study
IBS Irritable Bowel Syndrome	<i>Bifidobacterium bifidum</i> BGN4 <i>Bifidobacterium longum</i> BORI <i>Lactobacillus acidophilus</i> AD031 <i>Lactobacillus casei</i> IBS041	Clinical Study
Ulcerative Colitis	<i>Bifidobacterium bifidum</i> BGN4 <i>Lactobacillus acidophilus</i> <i>Lactobacillus salivarius</i>	Clinical Study
RA Rheumatoid Arthritis	<i>Bifidobacterium bifidum</i> ATT <i>Bifidobacterium longum</i> RAPO	Clinical Study
RI Rotavirus Infection	<i>Bifidobacterium longum</i> BORI <i>Lactobacillus acidophilus</i> AD031	Clinical Study
Kidney Inflammation	<i>Bifidobacterium bifidum</i> BGN4 <i>Bifidobacterium longum</i> BORI	Clinical Study
Cognitive function of the elderly	<i>Bifidobacterium bifidum</i> BGN4 <i>Bifidobacterium longum</i> BORI	Clinical Study
Constipation	<i>Weissella confuse</i> VP30	Clinical Study
Acne	<i>Bifido probiotics ferment lysate</i>	Clinical Study
Rhinitis	<i>Bifidobacterium bifidum</i> BGN4 <i>Bifidobacterium longum</i> BORI <i>Bifidobacterium lactis</i> AD011	Clinical Study

RESEARCH BASED ON *BIFIDOBACTERIUM* – RHEUMATOID ARTHRITIS

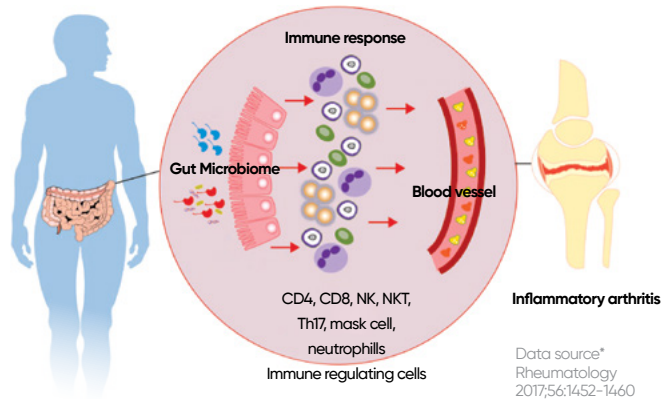
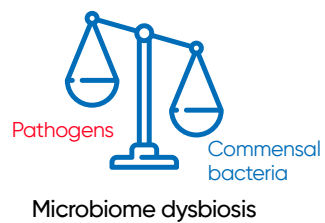
Rheumatoid Arthritis (RA)

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

***Bifidobacterium* Therapy**

- *Bifidobacterium bifidum* ATT
- *Bifidobacterium longum* RAPO

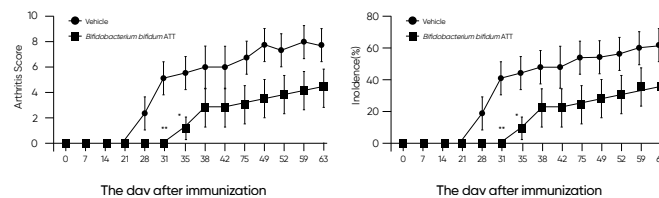
Mechanism



Data source*
Rheumatology
2017;56:1452-1460

Animal Experiment

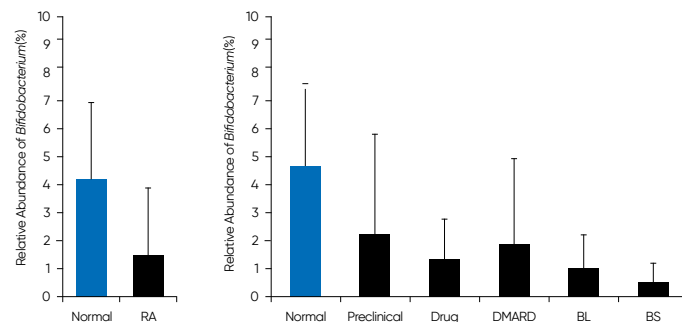
BIFIDO treated a selected novel strain of *Bifidobacterium* to RA in vivo model mice and observed the suppressive effect of RA related symptoms and immunologic criteria. Our results can shed light on the development of RA targeted pharmabiotics.



Human Clinical Experiment (Underway)

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

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



RESEARCH BASED ON *BIFIDOBACTERIUM* – KIDNEY HEMODIALYSIS

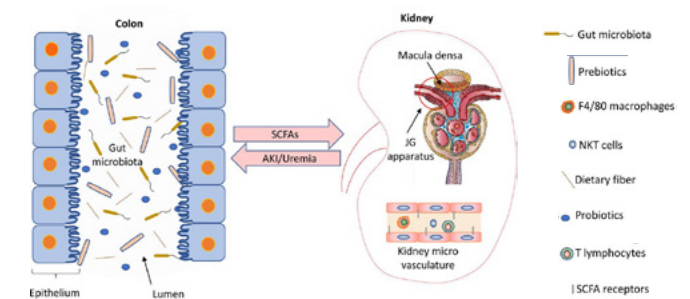
Kidney Inflammation

Co-work with Korea University Anam Hospital

***Bifidobacterium* Therapy**

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

Mechanism



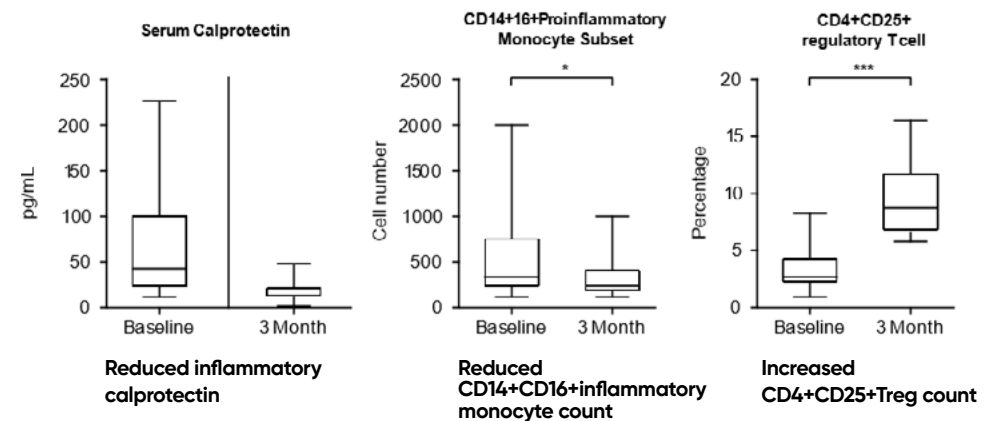
Animal Experiment

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

- Improved renal function and structure
- Decreased proteinuria, 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



RESEARCH BASED ON *BIFIDOBACTERIUM* – INTESTINE HEALTH

Intestine Health

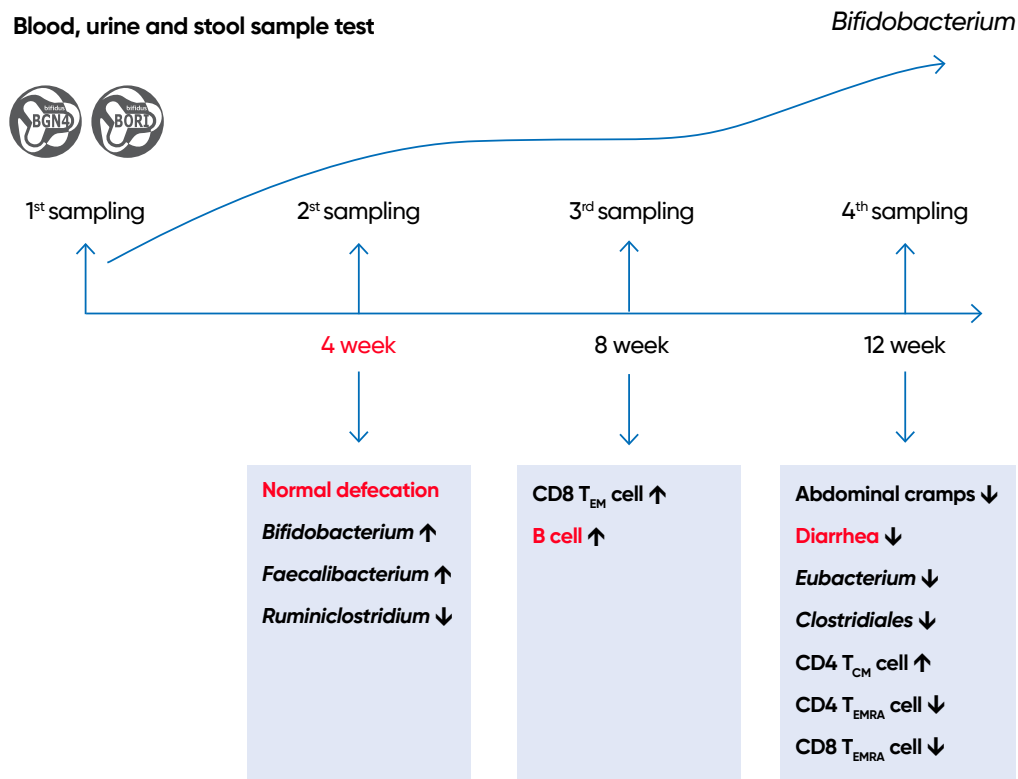
Co-work with IRB of Seoul National University and Budang Jesaeng Hospital

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

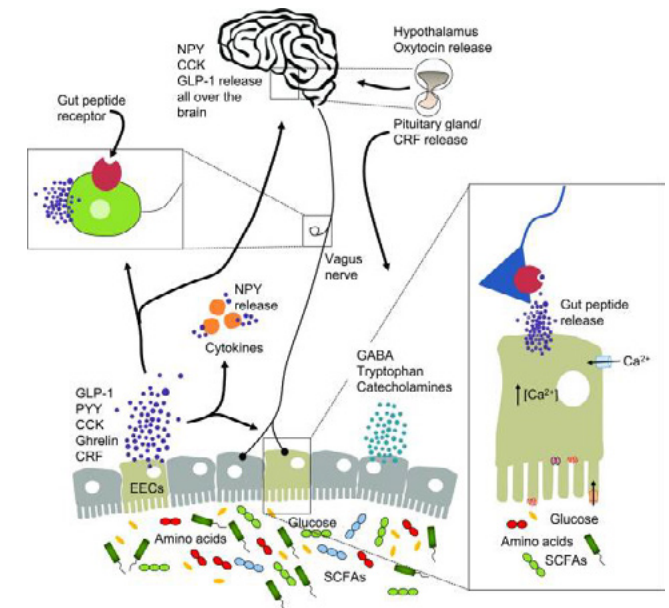
Co-work with Seoul National University

Bifidobacterium Therapy

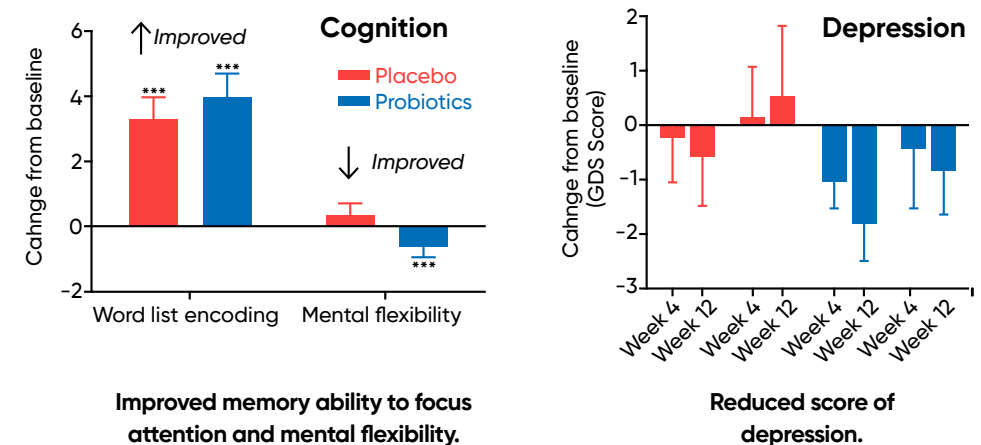
- *Bifidobacterium bifidum* BGN4
- *Bifidobacterium longum* BORI

Mechanism

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

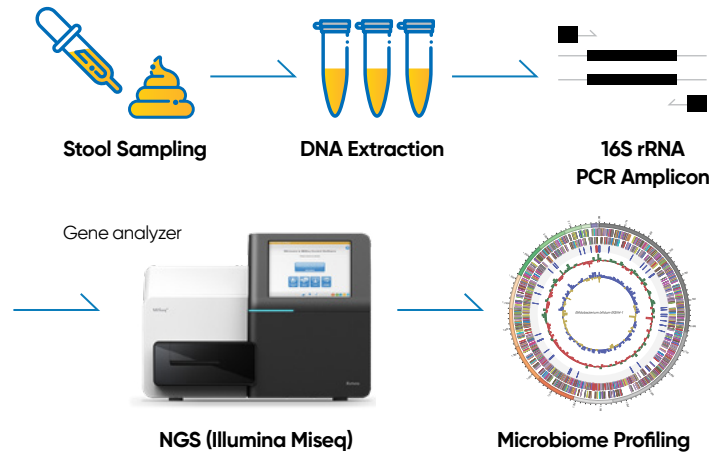


Human Clinical Experiment Effect of *Bifidobacterium* therapy in the elderly.

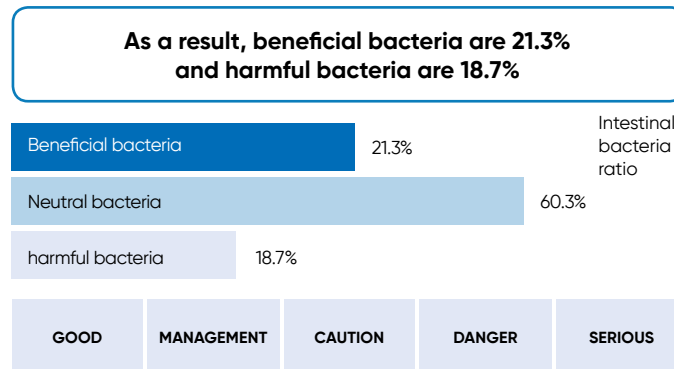


CUSTOMIZED SERVICE

Analysis Process

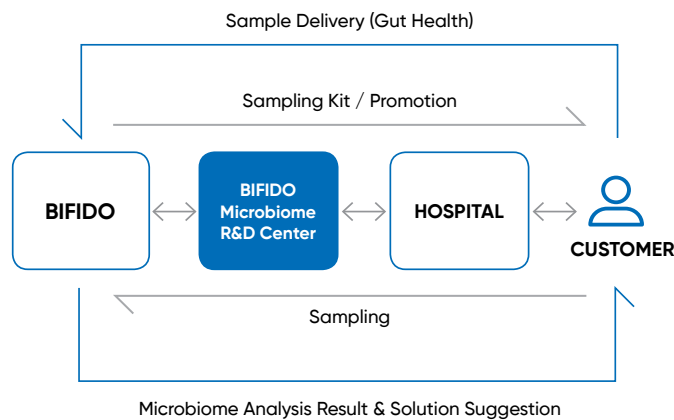


Microbiome Analysis Report



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 HYDRO
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



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