APAC2024
DA-EWG Session
Introduction of Microbiome based drug discovery including recent topics and attractiveness of this modality

April 23, 2024

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（DA-EWG, JPMA, JMBC, Metagen Therapeutics Inc.）

APAC
Asia Partnership Conference of Pharmaceutical Associations

JMBC
JAPAN MICROBIOME CONSORTIUM

Japan Microbiome Consortium, JMBC

We reveal the characteristics of human microbiota to help create the future of medical care and health.

23 Member companies from Pharma, Food, Diagnostics, Analysis, etc.

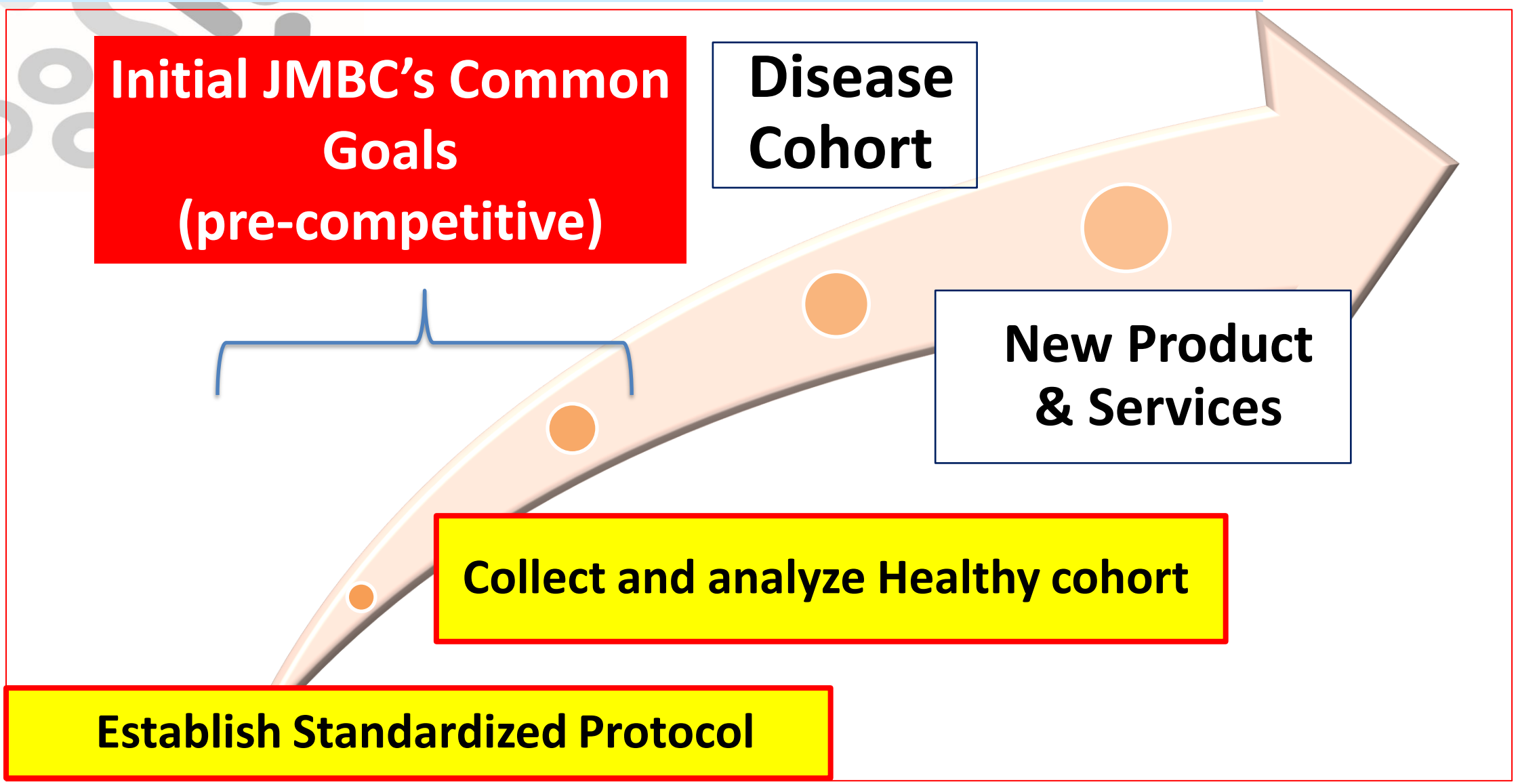
https://jmbc.life/en/index.html

Established April, 2017
Only R&D based industry members in Japan join as member companies.
JMBC is pre-competitive consortium to achieve common goals of healthcare industry.

Mission & Purpose of JMBC

Promotion and Acceleration of Industrialization of Research Achievement and Outcome for Medical and Health Care by Utilizing Human Microbiome Research and Analysis in Japan

JMBC Goals and its Roadmap



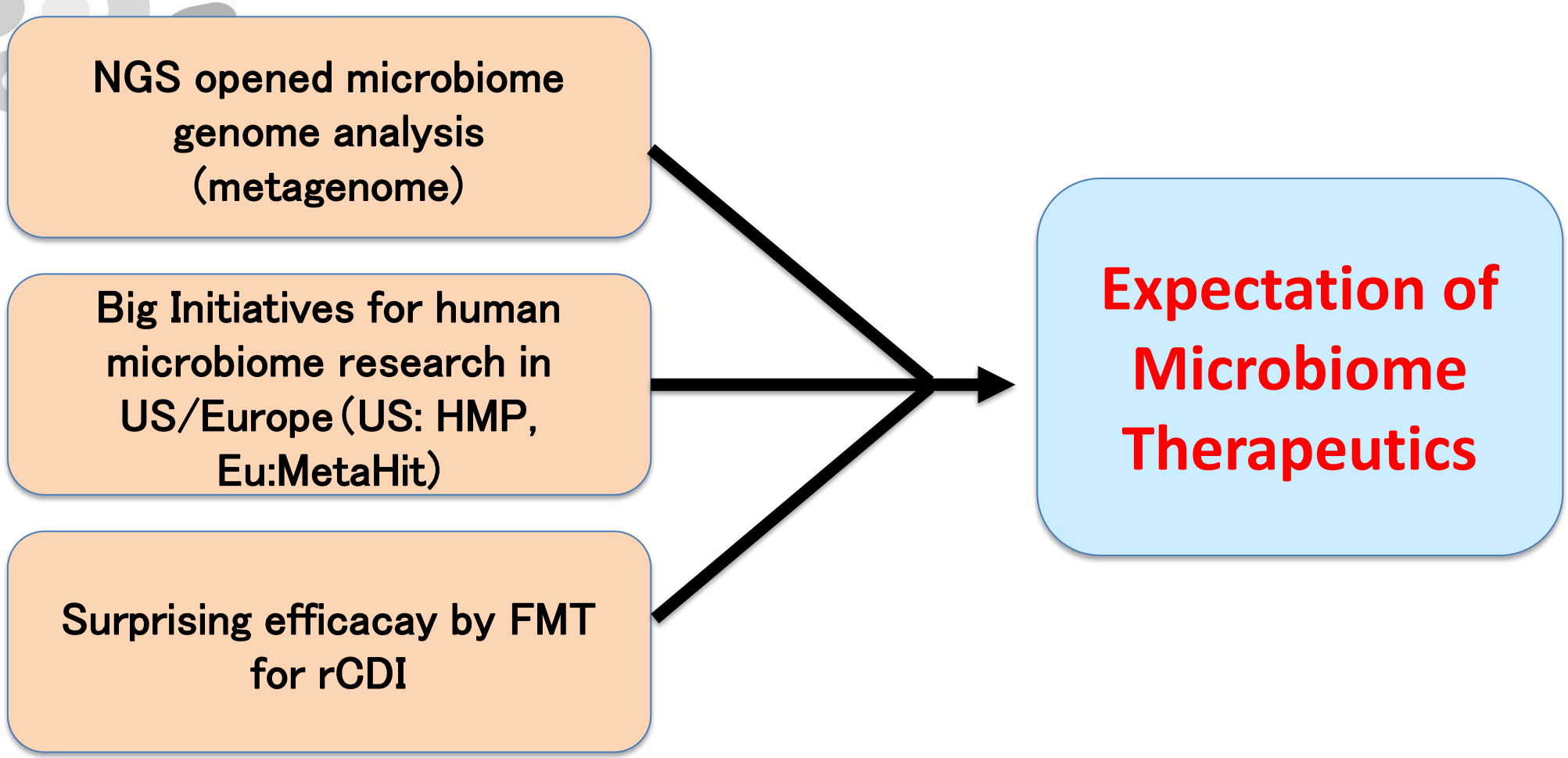
Introduction of Microbiome Based Drug Discovery

- New drugs to modulate gut microbiome are officially approved in 2022 (Australia & USA).
- There are number of indications to be targeted by Microbiome Based Drugs

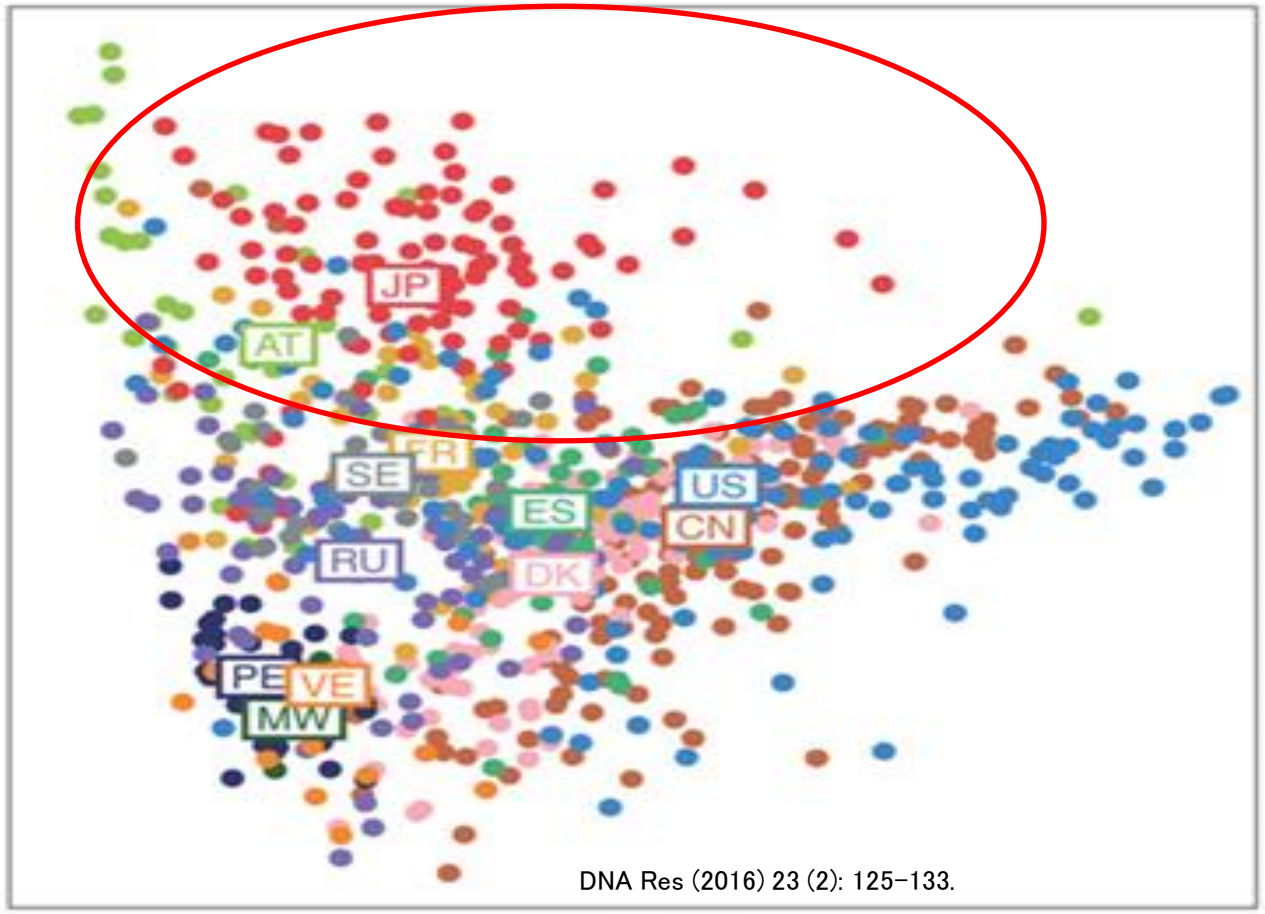
Today's Contents

- Introduction and Recent topics of microbiome Based Drug Discovery
- Pre-competitive Japan Microbiome Consortium (JMBC) activities

Expectation of Microbiome Therapeutics



Regional differences of gut microbiome



DNA Res (2016) 23 (2): 125–133.

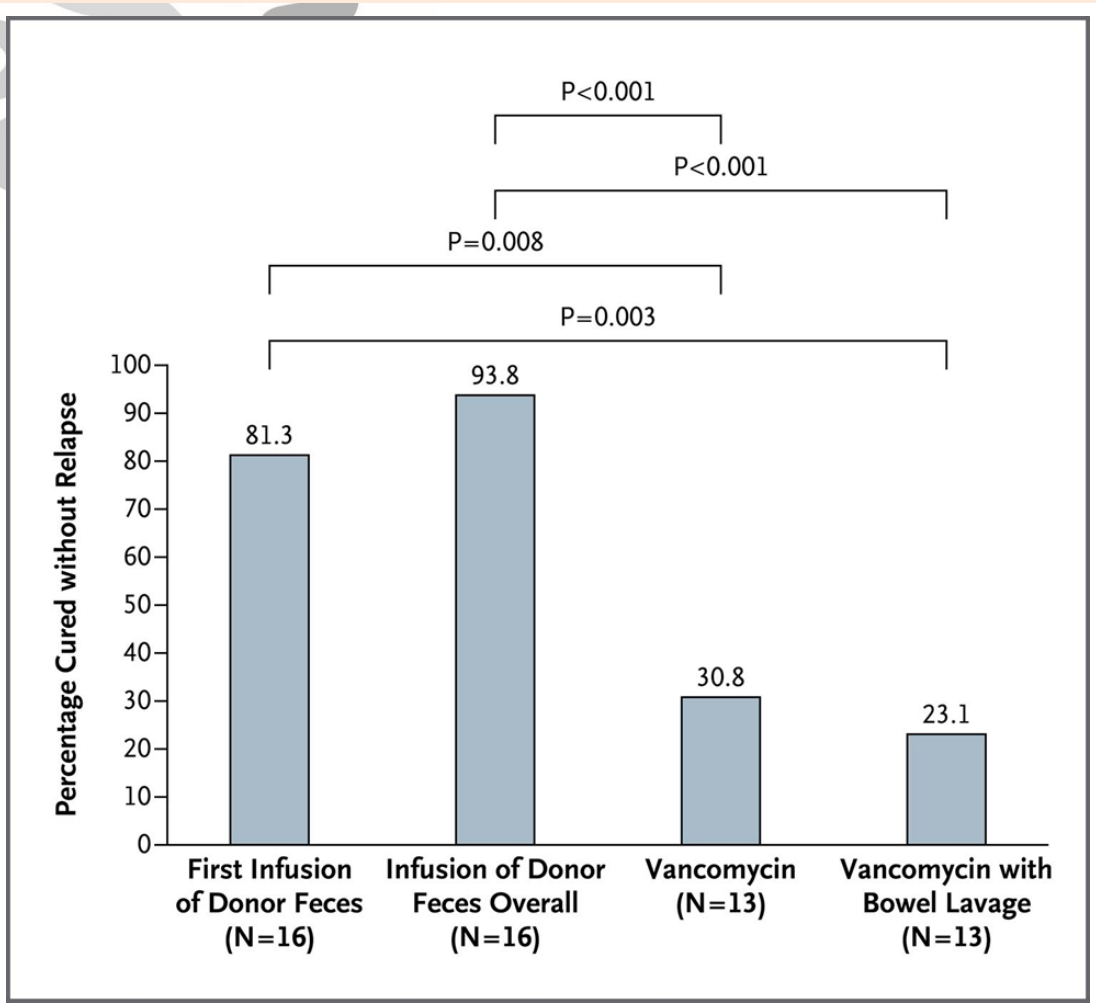
Gut microbiome in Japan shows unique distribution compared to other countries.

Food? Environment?

Need to understand and capture the gut microbiome distribution in Asia.

Unique Microbiome Based Drug Discovery approach to people in Asia may be required by understanding the uniqueness of gut microbiome in Asian people.

Fecal Microbiota Transplantation (FMT) efficacy to recurrent C. Difficile Infection



van Nood E et al. N Engl J Med 2013;368:407-415

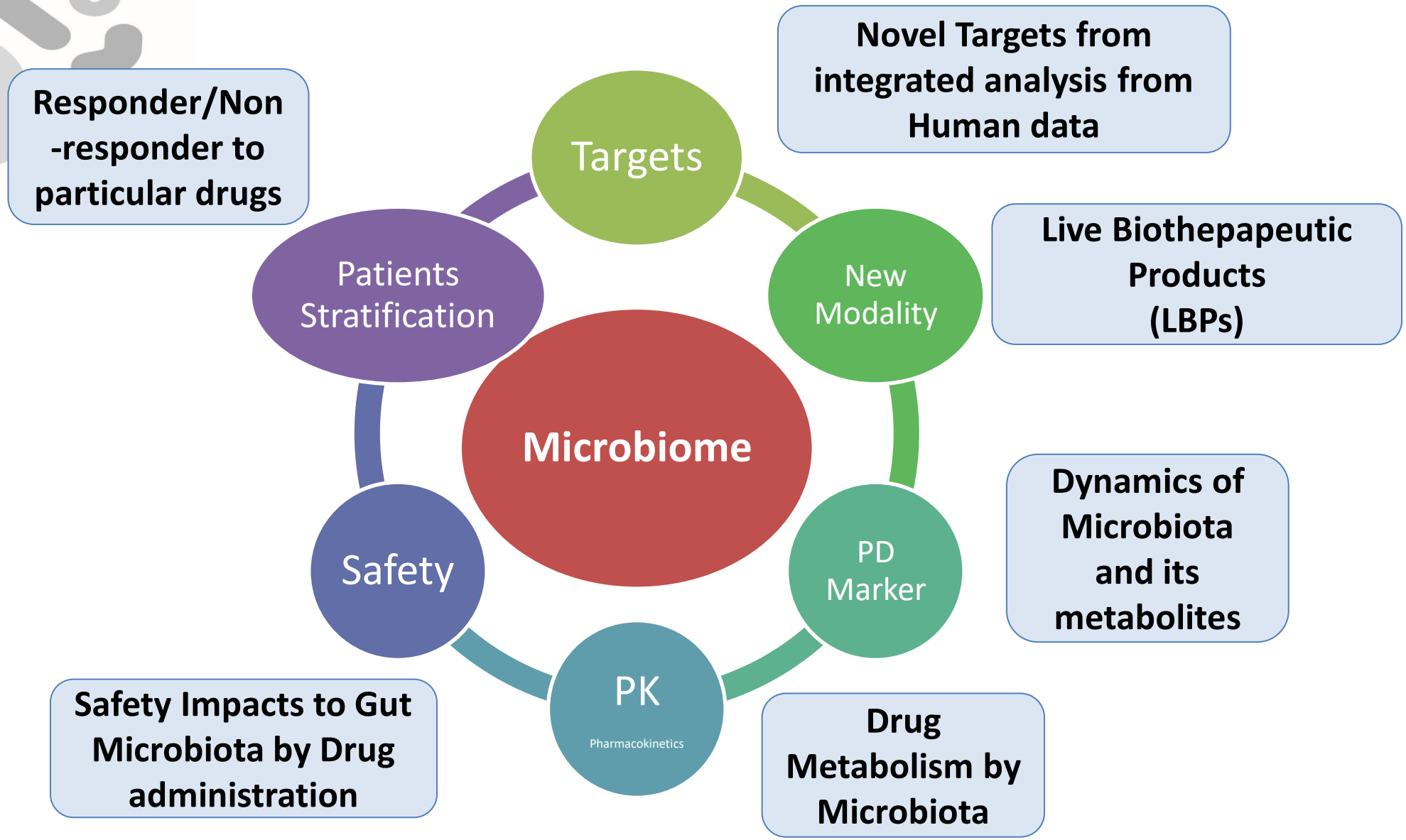
FMT using healthy donor stool showed surprisingly high efficacy compared to SOC (15/16).

- **1st 13/16**
- **2nd 2/3**

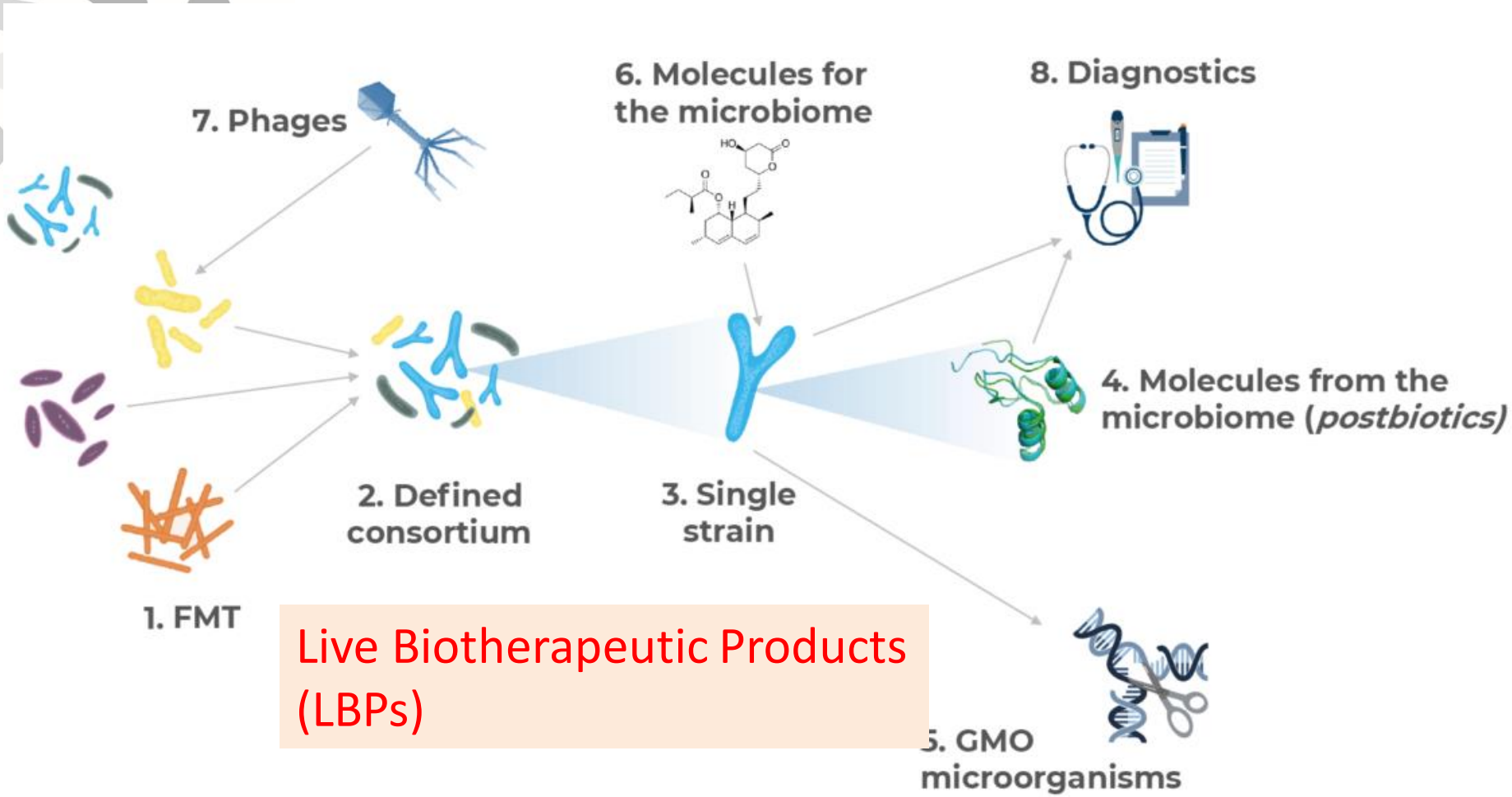
Modulating only gut showed efficacy

Paradigm Shift!

Implications of microbiome for drug discovery



Various Microbiome related drug discovery approach

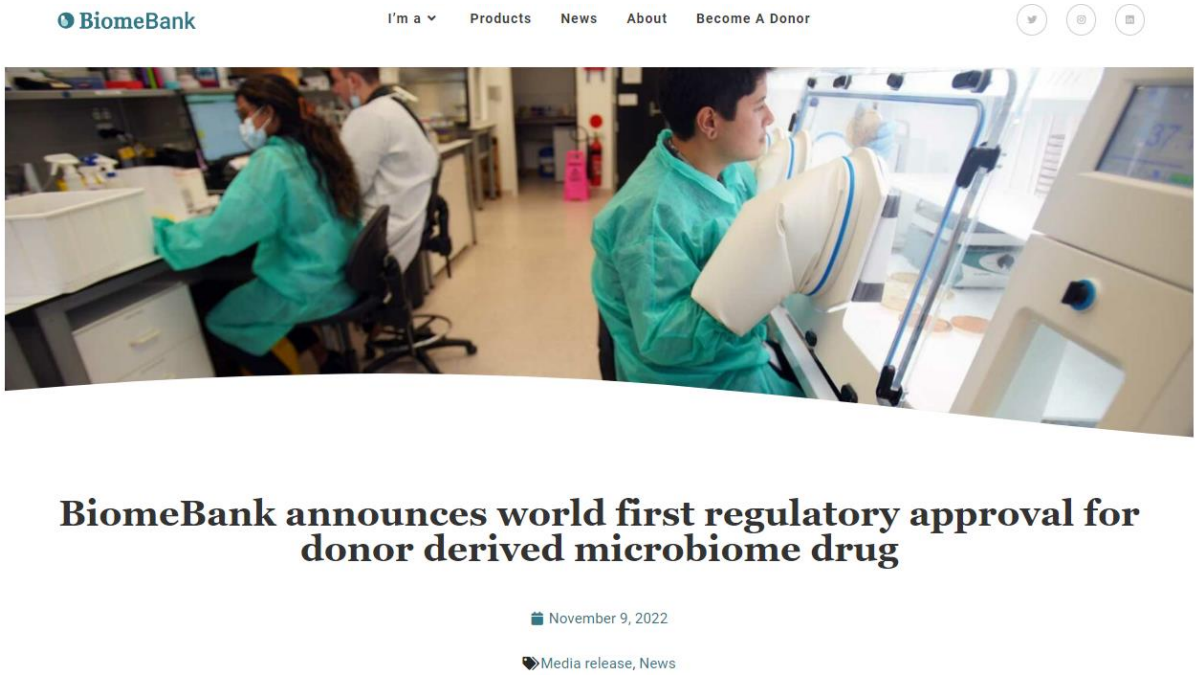


Live Biotherapeutic Products (LBPs)

https://www.sandwalkbio.com/microbiome-drug-database

World First Official Approval as a drug (2022)

BiomeBank announces world first regulatory approval for donor derived microbiome drug



Australian BiomeBank obtained from TGA official approval of BIOMICTRA（FMT）for rCDI（2022/11/9）

First Approval in USA by FDA (2022)

FERRING PHARMACEUTICALS

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PRESS RELEASE 2022 > Ferring receives U.S. FDA approval for REBYOTA™ (fecal microbiota, live-jslm) – A novel first-in-class microbiota-based live biotherapeutic

30 November 2022

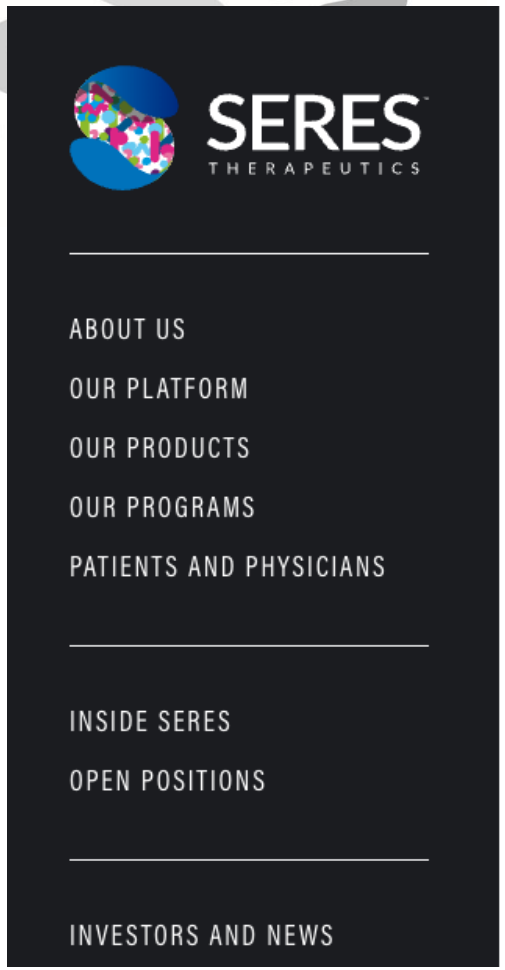
PRESS RELEASE 2022

Ferring receives U.S. FDA approval for REBYOTA™ (fecal microbiota, live-jslm) – A novel first-in-class microbiota-based live biotherapeutic

- *Ferring's novel first-in-class REBYOTA is indicated for the prevention of recurrence of Clostridioides difficile (C. difficile) infection in individuals 18 years of age and older, following antibiotic treatment for recurrent CDI*
- *The safety and efficacy of REBYOTA was studied in the largest clinical trial program in the field of microbiome-based therapeutics, including five clinical trials with more than 1,000 participants*
- *Recurrent CDI represents a significant burden for patients, caregivers and the healthcare system*

FDA approved Rebyota from Ferring（2022/11/30）

Oral drug is approved (2023)



SERES THERAPEUTICS AND NESTLÉ HEALTH SCIENCE ANNOUNCE FDA APPROVAL OF VOWST™ (FECAL MICROBIOTA SPORES, LIVE-BRPK) FOR PREVENTION OF RECURRENCE OF C. DIFFICILE INFECTION IN ADULTS FOLLOWING ANTIBACTERIAL TREATMENT FOR RECURRENT CDI

Apr 26, 2023 at 7:46 PM EDT

– First and only FDA-approved orally administered microbiota-based therapeutic, validating Seres' microbiome platform –

Download PDF

– Phase 3 ECOSPOR III study demonstrated that 88% of treated individuals were recurrence-free at 8 weeks –

– Opportunity to address prevention of recurrence of C. difficile infection in adults with rCDI, including first recurrence, following antibacterial treatment –

– VOWST product availability expected in June –

– Conference call at 8:30 a.m. ET tomorrow –

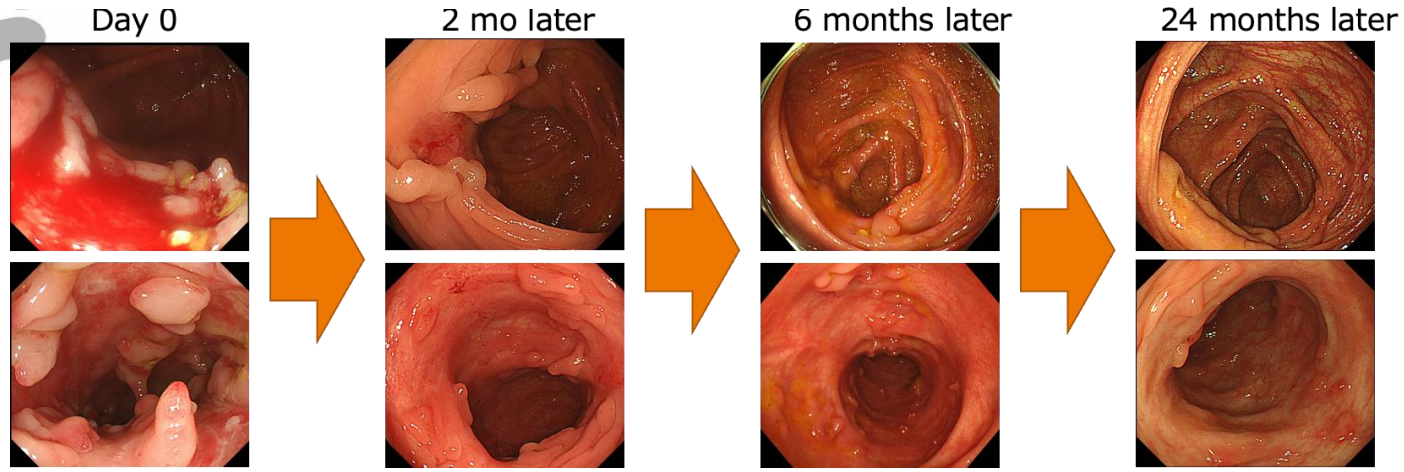
CAMBRIDGE, Mass. & HOBOKEN, N.J.--(BUSINESS WIRE)--Apr. 26, 2023-- Seres Therapeutics, Inc. (Nasdaq: MCRB) and Nestlé Health Science today announced the U.S. Food and Drug Administration (FDA) approval of VOWST™ (fecal microbiota spores, live-brpk), formerly called SER-109, an orally administered microbiota-based therapeutic to prevent recurrence of *C. difficile* Infection (CDI) in adults following antibacterial treatment for recurrent CDI (rCDI). VOWST is not indicated for the treatment of CDI.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20230426006066/en/

FDA approved first oral drug, Vowst of Seres（2023/4/26）

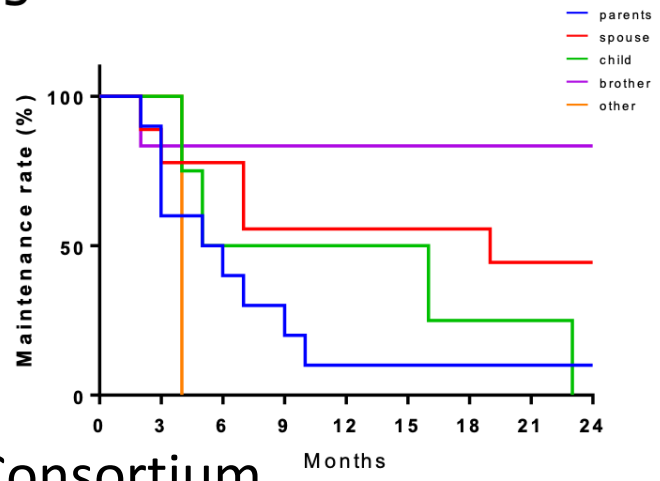
FMT for Ulcerative Colitis (Japan)

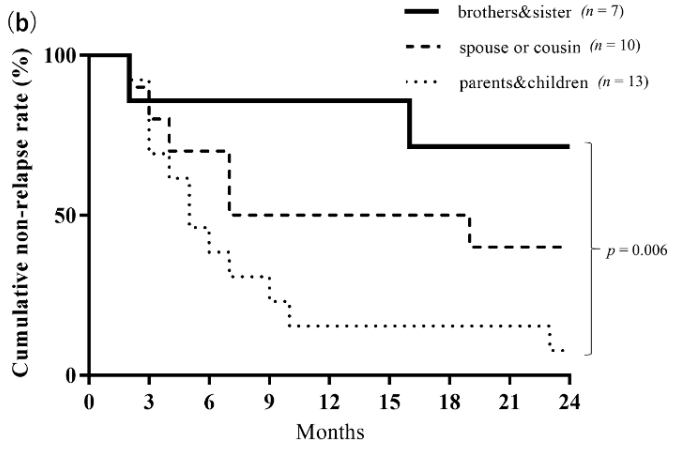
Case study: A-FMT treatment with 2 years+ followup



Advanced Care Program B
(先進医療B)
Is ongoing

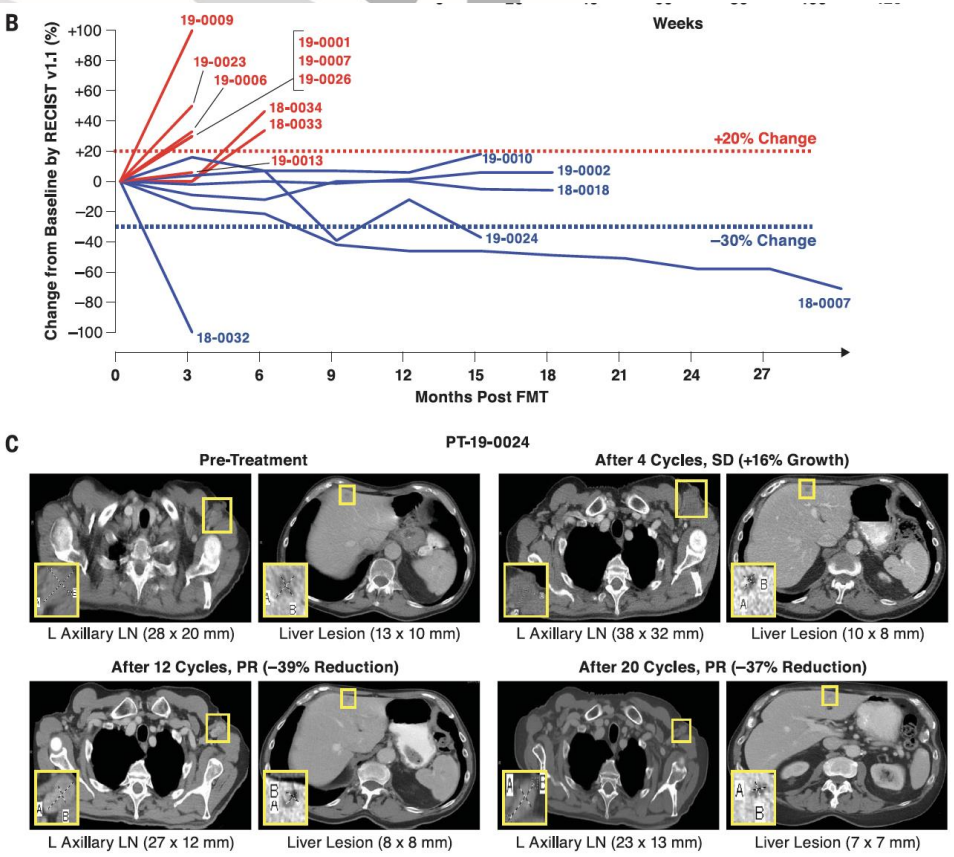
Clinical remission is better if a donor is your siblings or same generation



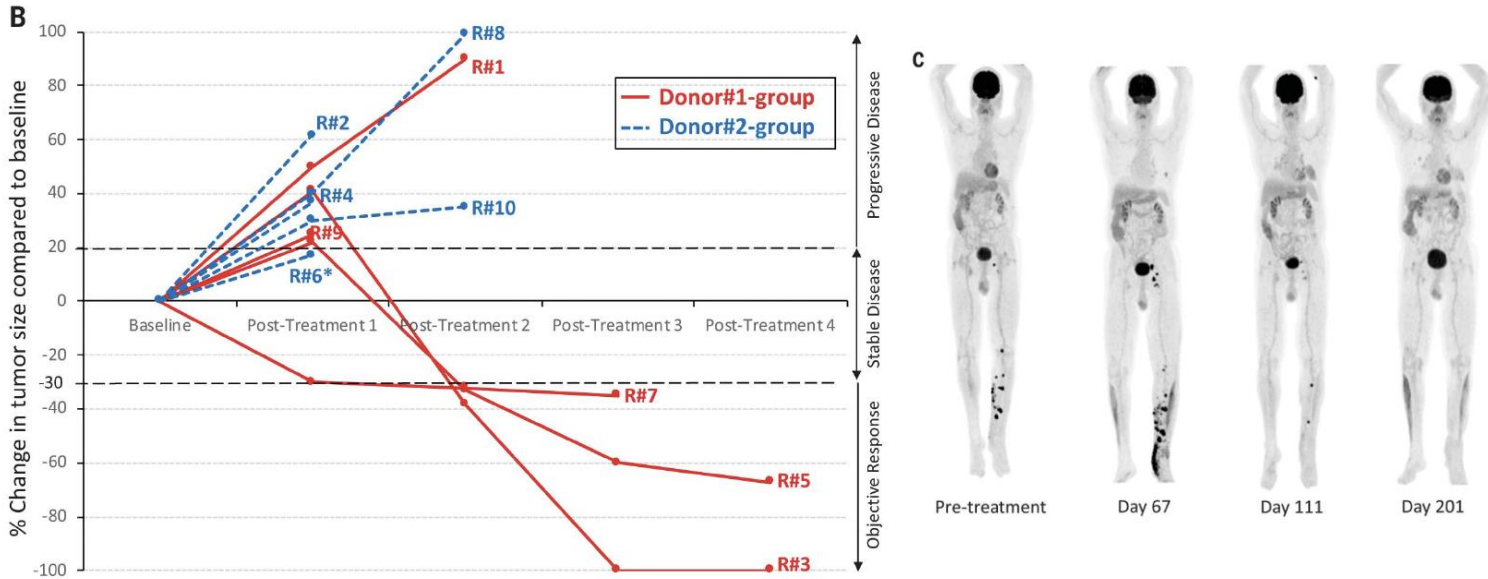


Okahara K, Ishikawa D et al., J Clin Med (2020)

FMT for Oncology



Science . 2021 Feb 5;371(6529):595-602.



Science . 2021 Feb 5;371(6529):602-609.

Combination with Immunocheckpoint Inhibitor showed efficacy in refractory patients!!

FMT for Parkinson's disease

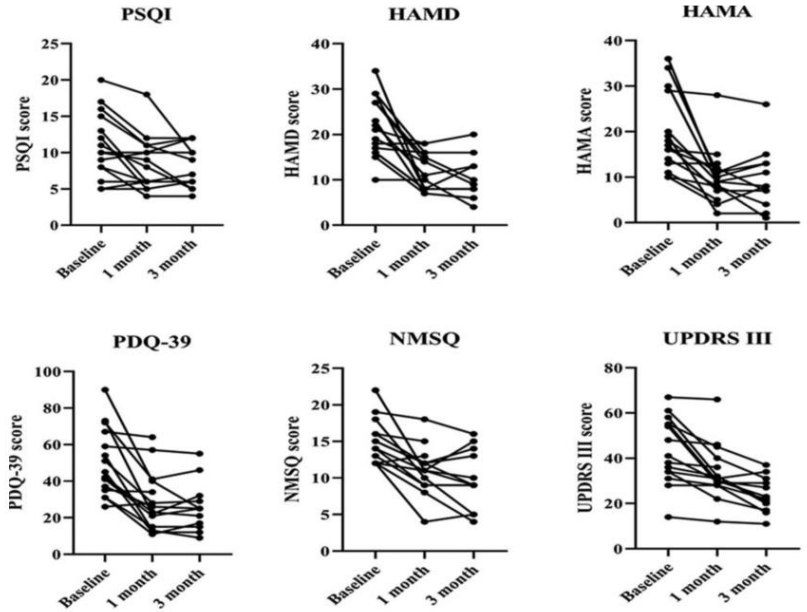


Figure 2. The motor and non-motor symptoms were evaluated by scale scores during the 3-mo follow-up. The score of PSQI, HAMD, HAMA, PDQ-39, NMSQ and UPDRS-III significantly decreased at 1 and 3 mo after FMT.

Table 2

The changed score of PSQI, HAMD, HAMA, PDQ-39, NMSQ and UPDRS-III at 1 mo after FMT.

Items (n=15)	Baseline	1 mo	Change from baseline	*P* value
PSQI	11.00±4.50	8.47±3.68	2.53±2.72	.003
HAMD	21.53±6.57	11.86±4.13	9.66±7.56	<.001
HAMA	19.53±8.62	10.13±6.02	9.40±8.49	.001
PDQ-39	50.26±18.63	29.00±15.86	21.26±17.18	<.001
NMSQ	14.80±3.00	11.06±3.15	3.73±3.21	.001
UPDRS III	43.60±14.64	33.80±12.25	9.80±9.77	.002

Data are expressed as mean (standard deviation).

Table 3

The changed score of PSQI, HAMD, HAMA, PDQ-39, NMSQ and UPDRS-III at 3 mo after FMT.

Items (n=12)	Baseline	3 mo	Change from baseline	*P* value
PSQI	12.41±3.84	8.16±3.01	4.25±3.27	.001
HAMD	22.41±7.11	10.08±4.62	12.33±6.42	<.001
HAMA	21.08±8.96	9.58±6.77	11.50±7.29	<.001
PDQ-39	52.16±18.37	25.91±13.48	26.25±17.10	<.001
NMSQ	15.16±3.12	9.83±3.99	5.33±3.28	<.001
UPDRS III	41.75±14.66	24.00±7.76	17.75±11.29	<.001

Various scores (UPDRS-III, PSQI, etc) are improved in 3 month!

Xue LJ, Yang XZ, Tong Q, et al.: Fecal microbiota transplantation therapy for Parkinson's disease: a preliminary study . Medicine (Baltimore). 2020, 99:e22035. 10.1097/MD.0000000000022035

Why FMT is important?

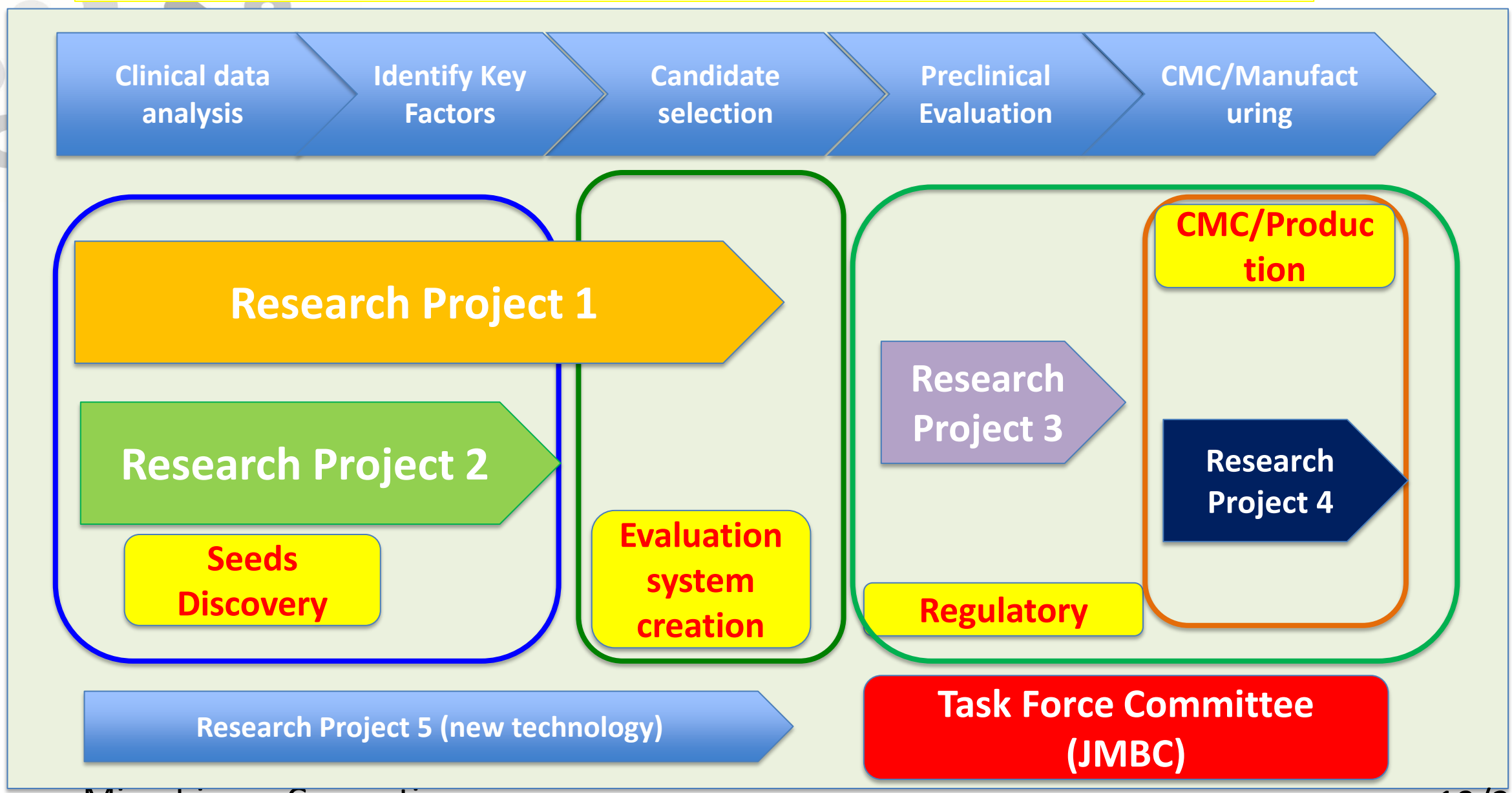
- FMTs is a new treatment option.
- From successful FMT, we can expect following new drug discovery activities
  - From analysis of donor stool, we can extract relevant bacteria as **Live Biotherapeutics Products (LBPs)**
  - From data analysis of FMT clinical studies, we can identify **novel drug targets, biomarkers and new findings** about diseases from **effective human data set**.

Drug Discovery Initiative (AMED*)

- In order to accelerate the drug discovery based on microbiome research/science, creating **an effective and collaborative infrastructure** is crucial to connect diverse expertise , strength and background as a **Microbiome Based Drug Discovery Ecosystem.**
- The project named "NeDDTrim" (The Next generation Drug Discovery and Development Technology on Regulating Intestinal Microbiome) is started in 2021 with more than 30 research organizations including academic institutes, hospital and companies. JMBC takes an important role to unify this project teams and members as one team with effective project management skill set.
- Project duration: 2021-2027
- Budget Size (estimation): 10 billion yen ($700M)

*: AMED: Japan Agency for Medical Research and Development

Drug Discovery Process and Research Theme (image)



Research Team 1 Project: Reverse Translational Aproach

JMBC 一般社団法人日本マイクロバイオームコンソーシアム

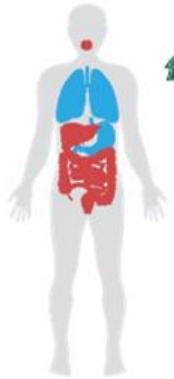
Disease Axis

Platform Axis

Seeds Discovery Platform

Evaluation Platform

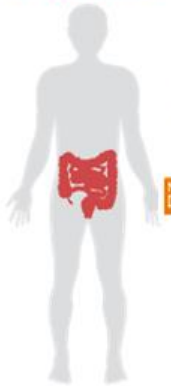
1-3a Oncology



名古屋大学

国立がん研究センター

1-3b IBD



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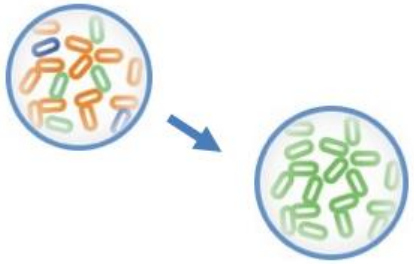
Metagen Therapeutics

1-1a Microbiome Analysis

1-1b High Throughput Bacteria Isolation and Culture



産総研

1-2a in vitro system

課題1-2b in vivoシステム

神戸大学

1-4 Candidate Selection

JMBC

Ecosystem

Summary

- Multiple microbiome drugs are officially approved by regulatory authorities in the world as one of new modalities.
- **FMT is the leading approach** to expand possible indications, such as oncology and neuroscience in addition to infectious diseases and gastrointestinal diseases.
- **A national project** to create a unique **Microbiome Based Drug Discovery Ecosystem** is started in 2021 by the support of AMED.
- **More collaborations** and precompetitive activities seem to accelerate the industrialization in **Asian region**.