# 목차

# 회사 소개

| | |
|---|---|
| 설립일 | 2015년 9월 24일 설립 |
| 주소 | 판교 테크노밸리, 이노밸리 A동 801호, 806호  |
| 구성원 | Total 30 People<br>4 MD's<br>8 PhD's<br>13 MA's<br>3 MBA's |

# Team (1/2): Leadership

## Leadership

### Jisoo Pae, MD, MBA (CEO)

- Seoul National University, Medical School, MD
- Duke Univ., MBA
- Bain & Company, Consultant
- MSD, Associate Director

### Hansoo Park, MD, PhD (CTO)

- Seoul National University, Medical School, MD
- Seoul National University, Biochemistry, PhD
- Harvard Medical School, Post Doc
- The Jackson Laboratory, Research Associate

### Kyoung Wan Yoon, PhD

- Korea University, Molecular and Cellular Biology, PhD
- Harvard Medical School / Massachusetts General Hospital, Post Doc

### Sujin Hwang, MBA

- Seoul National University, Pharmacy, BA
- Duke Univ., MBA
- Pfizer, MR
- AstraZeneca, Brand Manager
- Eli Lilly, Business Development, Associate Director

### Sohyun Won, MBA

- Yonsei Univ., Business, BA
- USC, MBA
- Accenture, Consultant
- IBM, Consultant
- LG Chem, General Manager
- AT Kearney, Subject Matter Expert

## Team

4 MD's, 8 PhD's, 13 MA researchers, 3 MBA's, Total 30 people

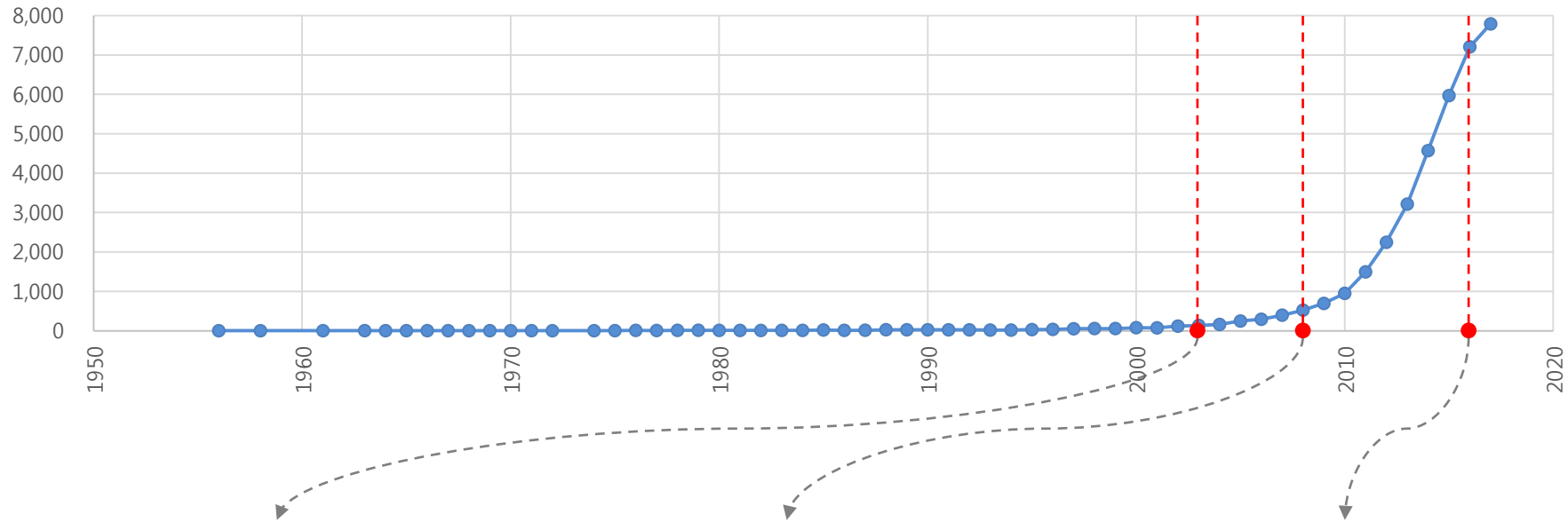
## Partners

SAMSUNG MEDICAL CENTER
SNUH SEOUL NATIONAL UNIVERSITY HOSPITAL
ASAN Medical Center
National Cancer Center
SNUH 서울대학교병원운영 서울특별시보라매병원 SMG-SNU BORAMAE MEDICAL CENTER
GIMS Gachon University Gil Medical Center International Medical Service
Seoul National University
우리아이 마음클리닉 Seoul Our Child Psychiatric Clinic
WELL'S Dermatology & Medical SPA
GIST Gwangju Institute of Science and Technology
연세대학교 YONSEI UNIVERSITY
CHA 의과학대학교 차병원 CHA University College of Medicine
코슬립수면클리닉 KOSLEEP CLINIC

# 목차

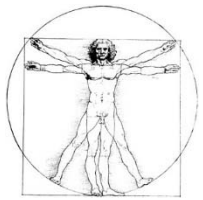
# 마이크로바이옴 산업의 태동

Pubmed Number of articles




US Government Initiatives

## Human Genome Project



- 1990~2003년
- US Government
- total budget of $3 billion

## Human Microbiome Project

NIH HUMAN MICROBIOME PROJECT

- 2008년
- National Institutes of Health (NIH) initiative
- total budget of **$115 million**

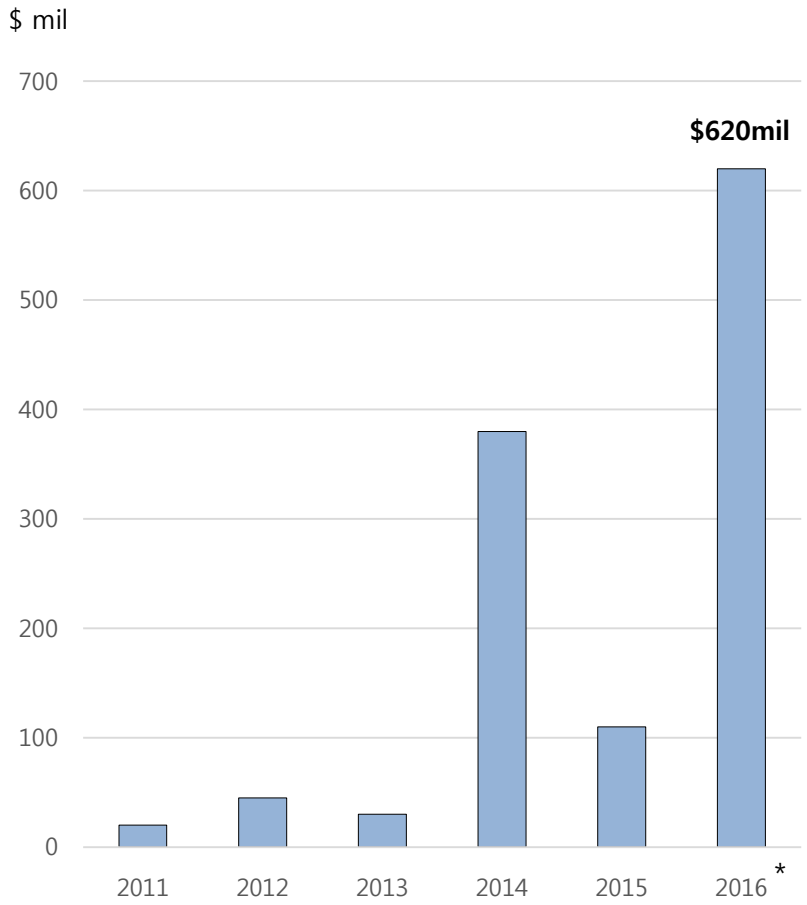
## National Microbiome Initiative

THE NATIONAL MICROBIOME INITIATIVE

- 2016년 5월 13일
- White House, President Obama
- 미국 정부 **$121million**
- 미국 민간 **$191million**

# Venture capital 의 마이크로바이옴에 대한 투자

## VC 들의 Microbiome Venture 에 투자 현황*




## 2017년 Microbiome 투자 뉴스

**고바이오랩**, **100억** 시리즈 B 투자 유치

*"4일 바이오업계에 따르면 **고바이오랩**은 에이티넘인베스트먼트·컴퍼니케이파트너스·스톤브릿지캐피탈 등 벤처캐피탈 3곳으로부터 총 **100억 원**의 투자를 유치했다."*

2017-08-07, 더벨

미래에셋, 이스라엘 바이오 벤처에 투자

*"미래에셋금융그룹 계열사인 미래에셋캐피탈과 미래에셋벤처투자는 미국의 유명 바이오 VC인 오비메드와 다케다벤처스, 존슨앤존슨 이노베이션과 함께 **바이옴X**에 투자했다.*

*총 투자 규모는 **270억원**이다."*

2017-06-11, 한국경제

**Evolve BioSystems** Completes **$20Million** Series B Financing

2017-05-30, www.evolvebiosystems.com/news

Seventure debuts in Japan with microbiome investment

*"Venture capitalist Seventure Partners announced that it has participated in a **US$13m** financing of **Japanese biotech company Anaeropharma Science.***

*The investment is made from Seventure's Health for Life Capital investment vehicle."*

2017-05-07, European Biotechnology

**Inocucor** raises **$38.8 million** series B to invest in R&D, US expansion

2017-03-29, betakit.com

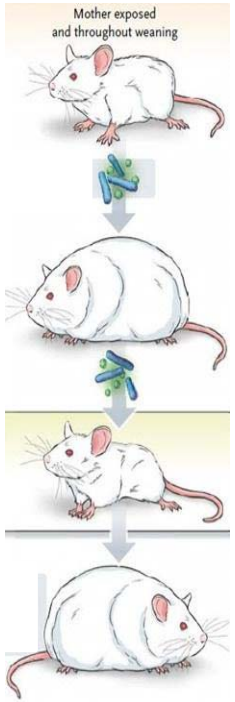
* 2016년은 9월까지의 투자액임
Source: Dow Jones Venture Sources; Securities and Exchange Commissions, The companies
https://www.wsj.com/articles/microbiome-companies-attract-big-investments-1474250460

# 마이크로바이옴의 건강증진 효과

## 1 건강기능식품 및 화장품

### 비만 치료*


2014




어릴 적 항생제에 노출됨

성인이 되어서 비만이 됨

비만 쥐의 장내 세균을 정상 쥐에 이식

정상 쥐가 비만이 됨

### 피부건강 증진**

AMI American Microbiome Institute

21명의 자원자

S. epidermidis 제거

실험군

대조군

S. epidermidis 동결건조 겔

플라세보

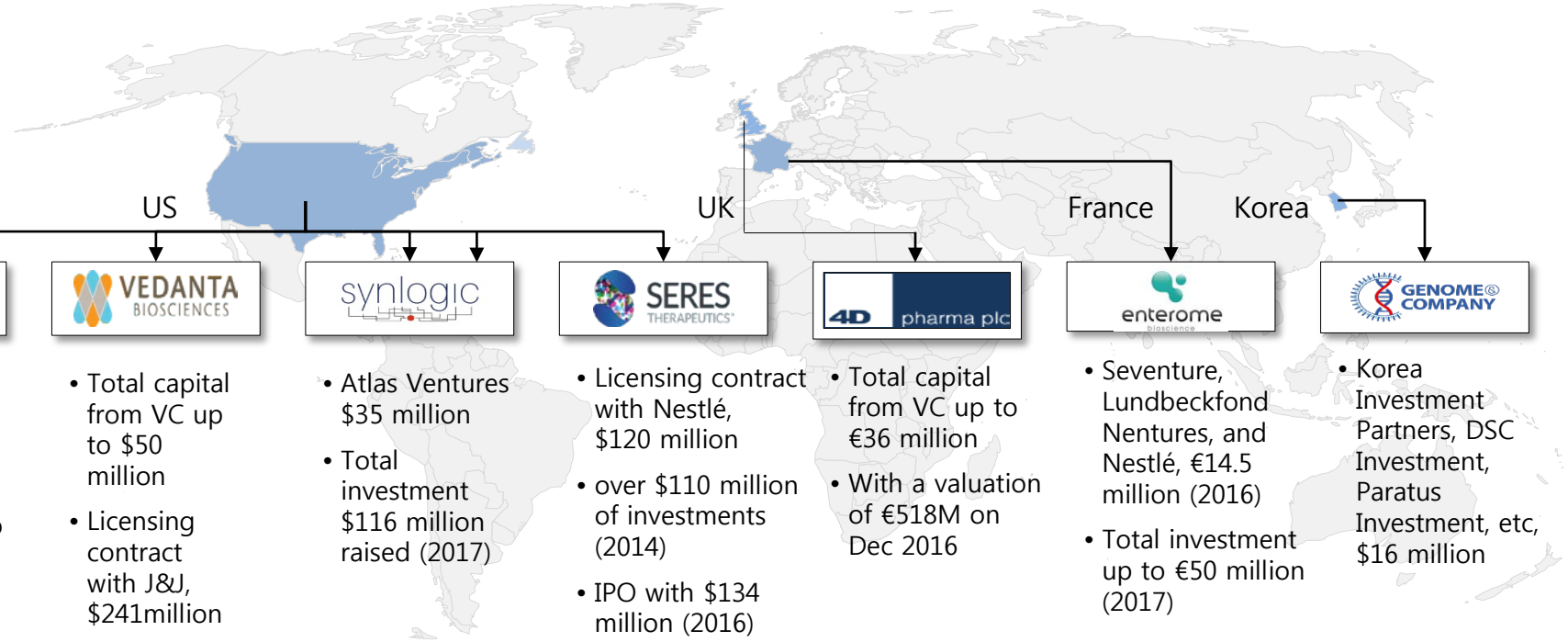
피부 건강도 높음
- 수분 함량이 많음 (대조군의 1.4배)
- 지질 함량이 높아 수분 증발을 억제함
- 피부 표면 산도가 낮음

피부 건강도 낮음
- 수분 함량이 적음
- 지질 함량이 낮아 수분 증발이 많음
- 피부 표면 산도가 높음

Source: * NEJM, 2014, ** AMI: American Microbiome Institute

# 마이크로바이옴 면역항암제 경쟁 현황

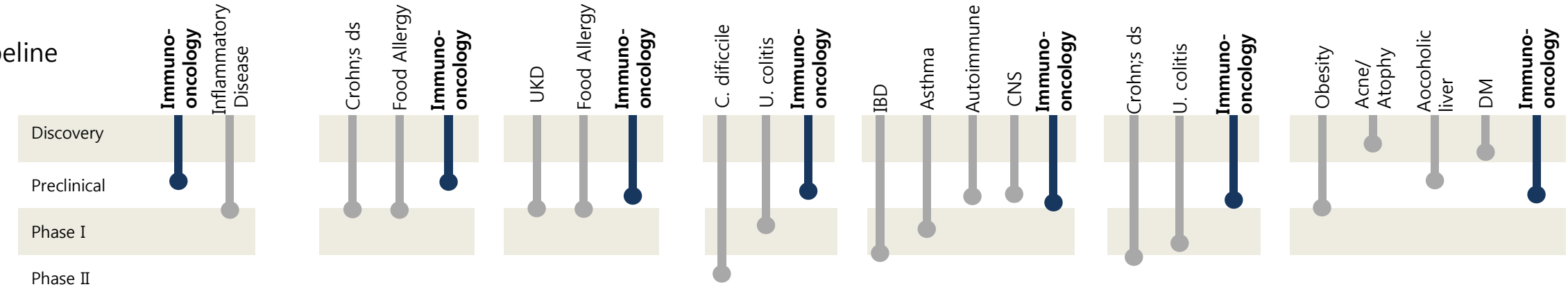
## 2 면역항암제




**Investment**

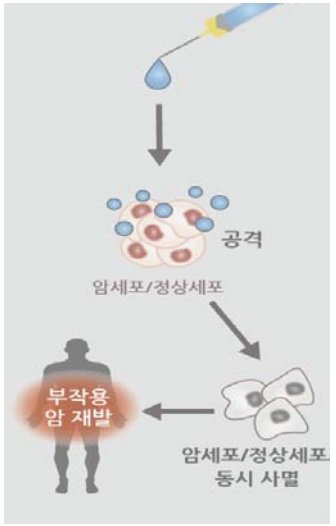
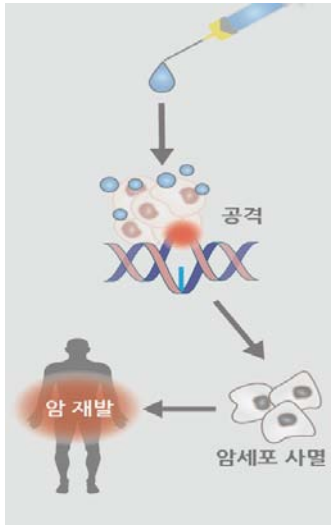
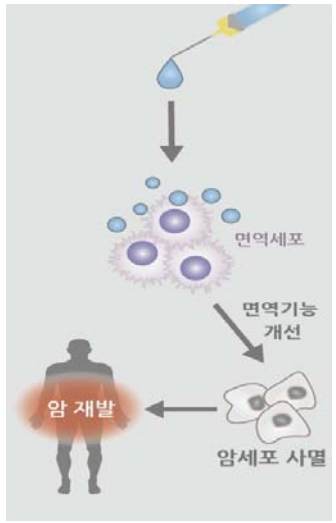
| EVELO THERAPEUTICS | VEDANTA BIOSCIENCES | synlogic | SERES THERAPEUTICS | 4D pharma plc | enterome | GENOME & COMPANY |
|---|---|---|---|---|---|---|
| • Flagship Ventures, $35 million<br>• Total capital from VC up to $50 million<br>• IPO with $140 million (2016) | • Total capital from VC up to $50 million<br>• Licensing contract with J&J, $241million | • Atlas Ventures $35 million<br>• Total investment $116 million raised (2017) | • Licensing contract with Nestlé, $120 million<br>• over $110 million of investments (2014)<br>• IPO with $134 million (2016) | • Total capital from VC up to €36 million<br>• With a valuation of €518M on Dec 2016 | • Seventure, Lundbeckfond Nentures, and Nestlé, €14.5 million (2016)<br>• Total investment up to €50 million (2017) | • Korea Investment Partners, DSC Investment, Paratus Investment, etc, $16 million |

**Pipeline**

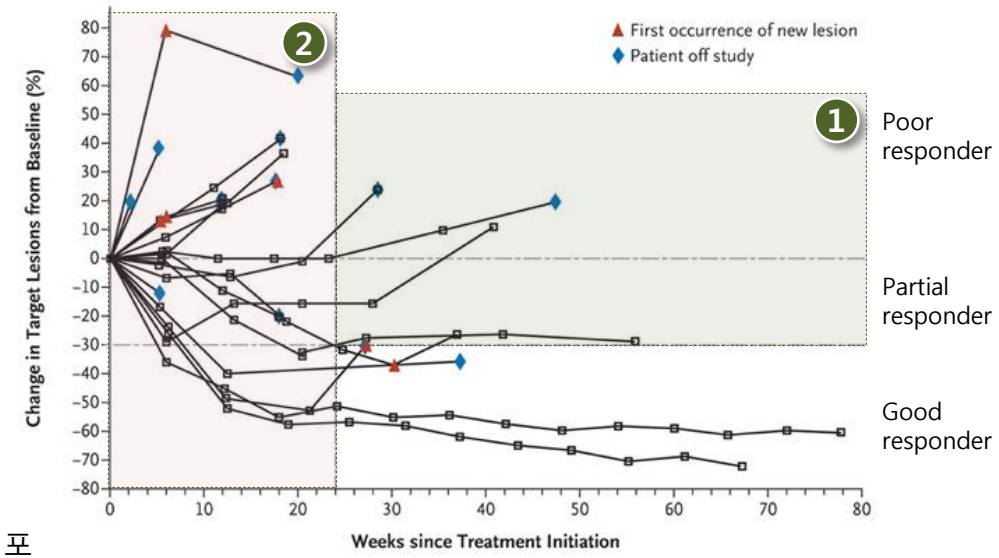


# 마이크로바이옴 면역항암제의 unmet needs

## 2 면역항암제

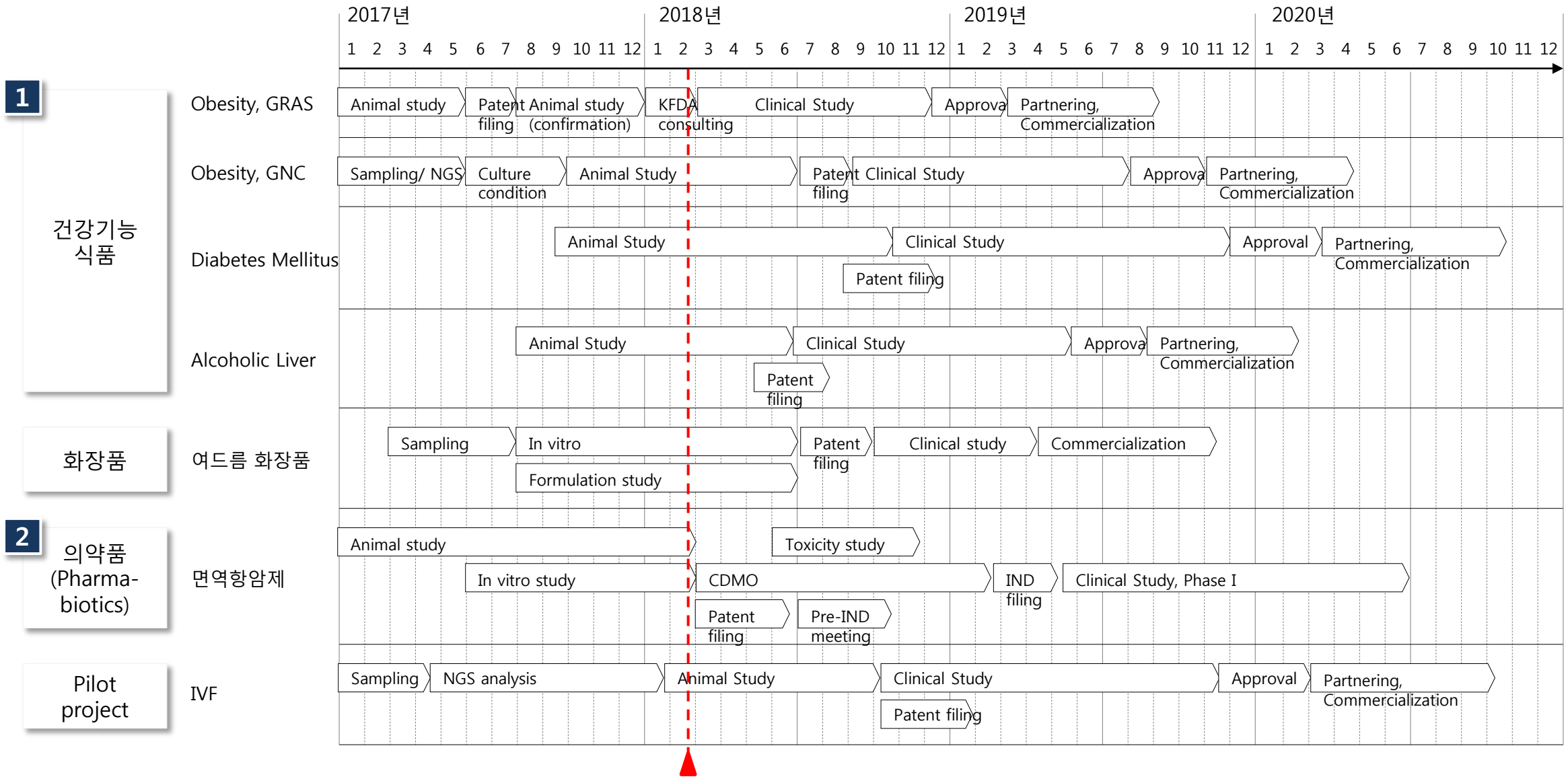
| | 1세대: 화학항암제 | 2세대: 표적항암제 | 3세대: 면역항암제 |
|---|---|---|---|
| | 2000년 이전 | 2000년 ~ 현재 | 2010년 ~ 현재 |
| |  |  |  |
| **MoA** | • 빨리 분화하는 세포 증식 억제 | • 암을 유발하는 Mutation을 해결 | • 면역 활성화를 통한 암세포 공격 |
| **Unmet needs** | • 정상 세포도 함께 공격<br>➔ 심각한 부작용 | • 종양내 제2 유전변이 발생<br>➔ 획득 내성 발행<br>➔ 2~3년 내 종양 재발 가능성 | • 타겟 환자 중 20%~45%만이 면역항암제에 반응<br>- 특히 PD1 발현이 50% 이하인 환자에서는 반응율이 현저히 떨어짐 ①<br>• 일부 암종에서는 유효성 입증하지 못함<br>• 폐렴, 장내 천공, 간염 등 면역 매개 약물 이상반응 (5~10%) ② |

Response to anti-PD1 treatment in NSCLC



# 목차

# Pipeline



# Mouse Obesity model: 총 7차에 걸친 동물실험을 진행함

**1** 건강기능식품 (항비만)

## Animal study schedule


**8주 실험**

- Normal Diet(ND) — Control (ND)
- High Fat Diet(HFD) — Control (HFD)
- HFD + Probiotics A — Probiotics A with HFD
- HFD + Probiotics B — Probiotics B with HFD

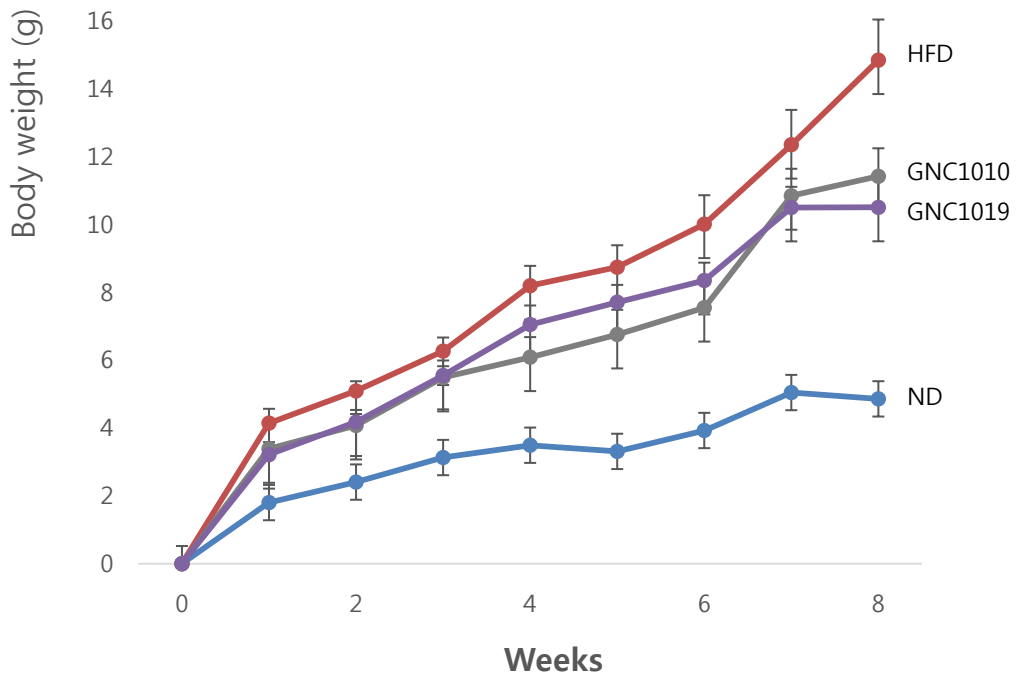
**12주 실험**

- Normal Diet(ND) — Prevention 2W → Control (ND)
- High Fat Diet(HFD) — Prevention 2W → Control (HFD)
- HFD + Probiotics C — Prevention 2W → Probiotics C with HFD
- HFD + Probiotics D — Prevention 2W → Probiotics D with HFD
- HFD + Probiotics D+A — Prevention 2W → Probiotics D+A with HFD
- HFD + Probiotics D+A+B — Prevention 2W → Probiotics A+B+D with HFD

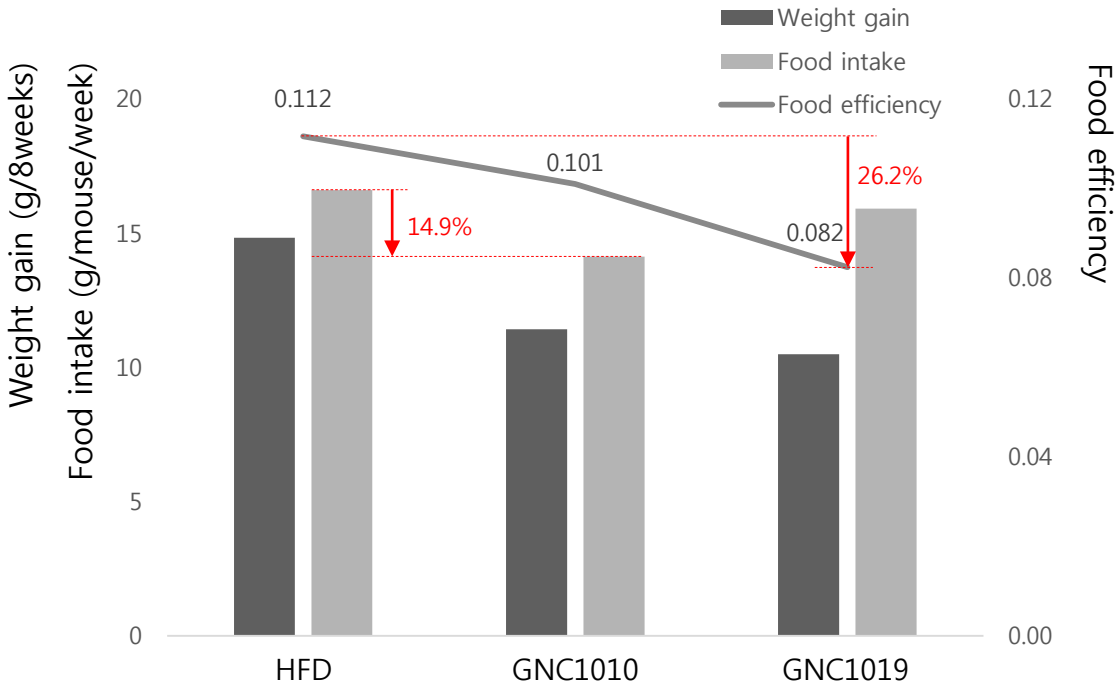
# Mouse Obesity model: 실험 결과

## 1 건강기능식품 (항비만)

### Weight Changes




### Food Intake Analysis




- Food intake reduced by 14.9% with GNC 1010
- Food efficiency reduced by 26.2% with GNC 1019

# 항비만 건강기능식품의 임상연구: 3월 시작 예정

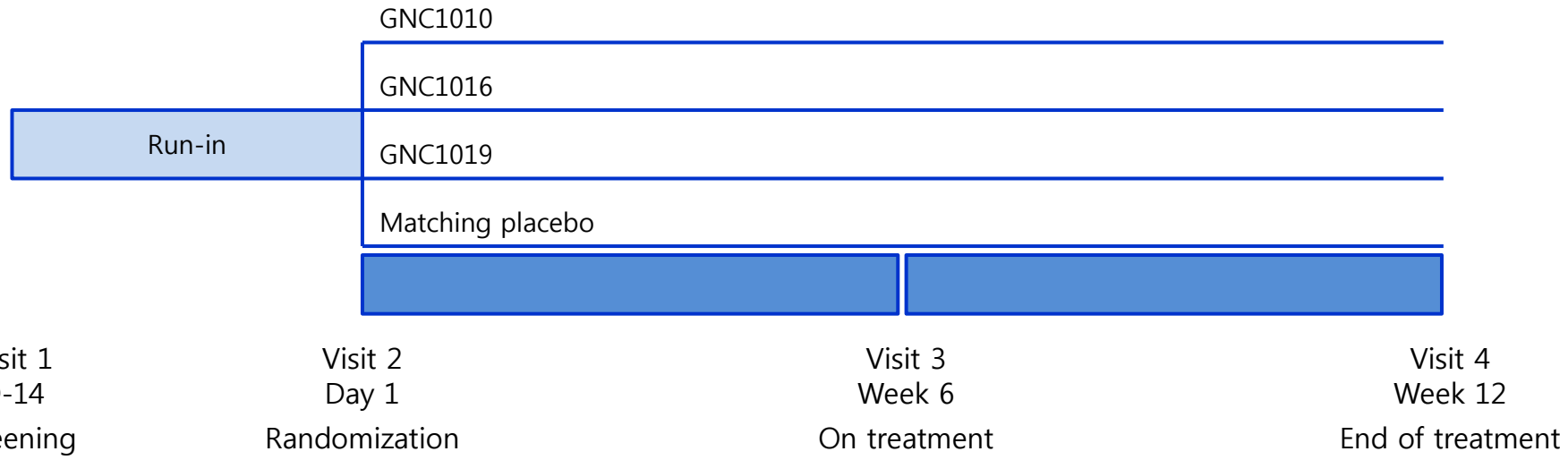
## 1 건강기능식품 (항비만)

**연구 진행팀**

- 서울대병원 가정의학과, 조비룡 교수, 박진호 교수, 권혁태 교수

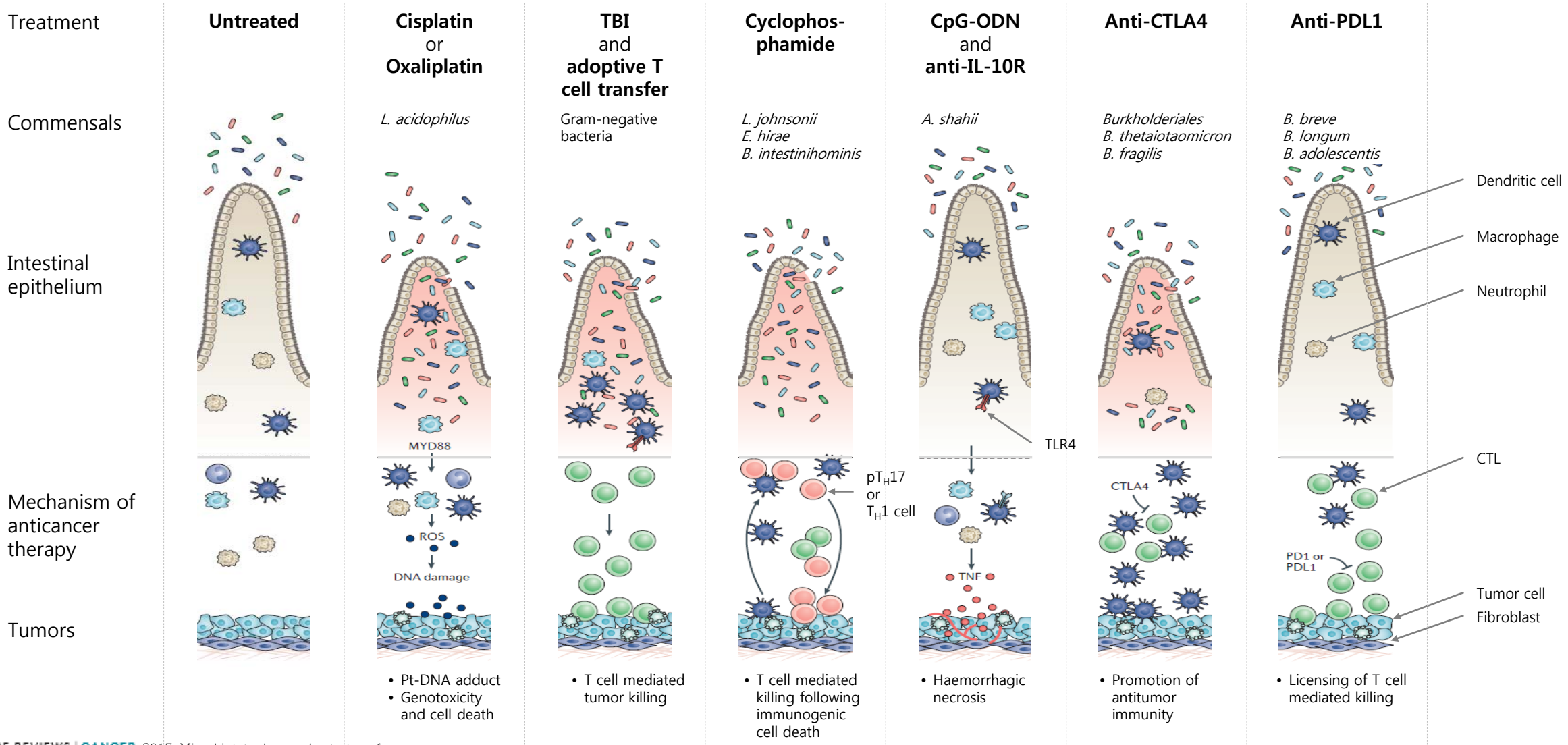
**연구 디자인**

- 19~65세, BMI 27~30 kg/m$^2$
- 단일기관, 무작위배정, 이중눈가림, 평행설계
- 총 48명 (군당 10명, 탈락률 10%)
  - 최소한의 수로 10 명의 시험대상자를 우선 배정하여 그 결과를 분석 (Interim analysis)
  - 중간분석을 통하여 각 시험군의 지속/중단 결정 및 샘플사이즈 재산정



# 마이크로바이옴 면역항암제: Mode of Action

## 2 면역항암제

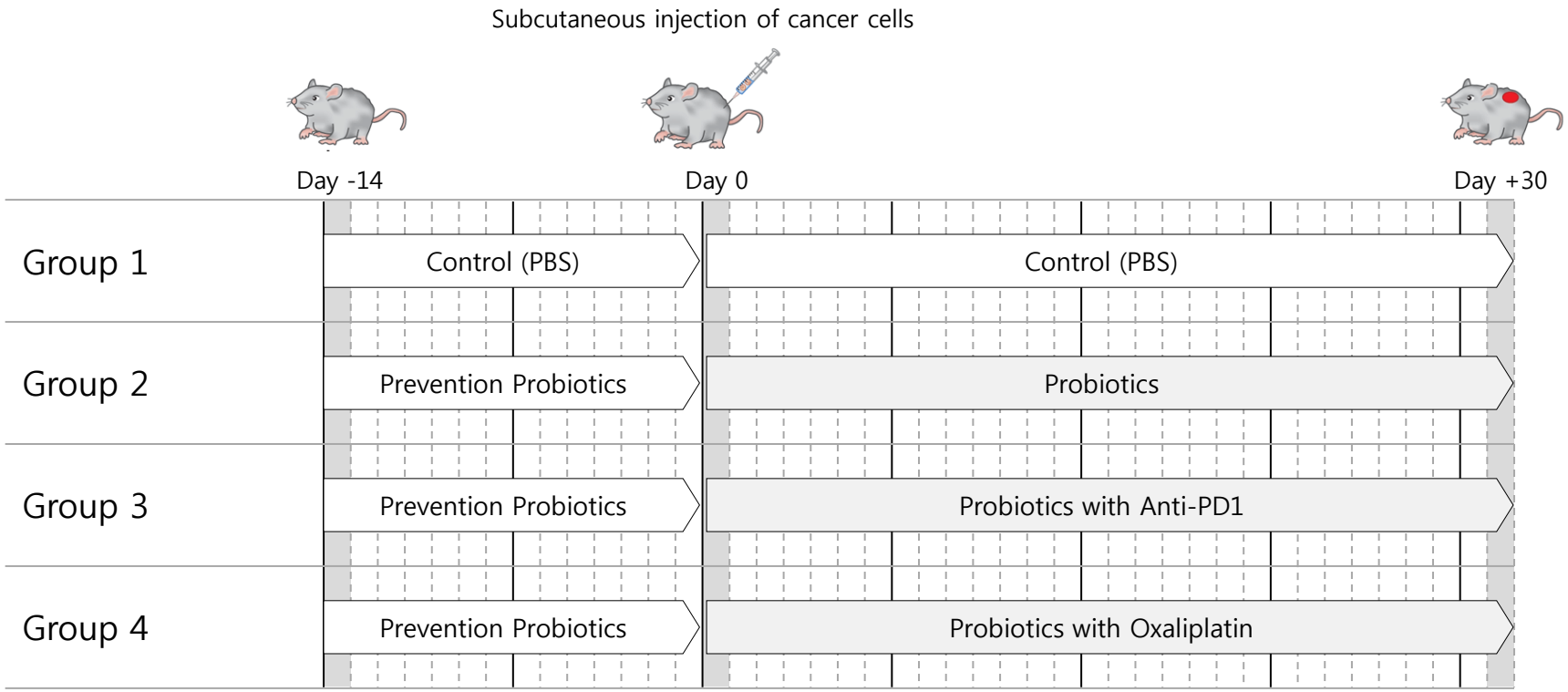



NATURE REVIEWS | CANCER 2017, Microbiota: a key orchestrator of cancer therapy

# 동물실험: Syngeneic tumor model

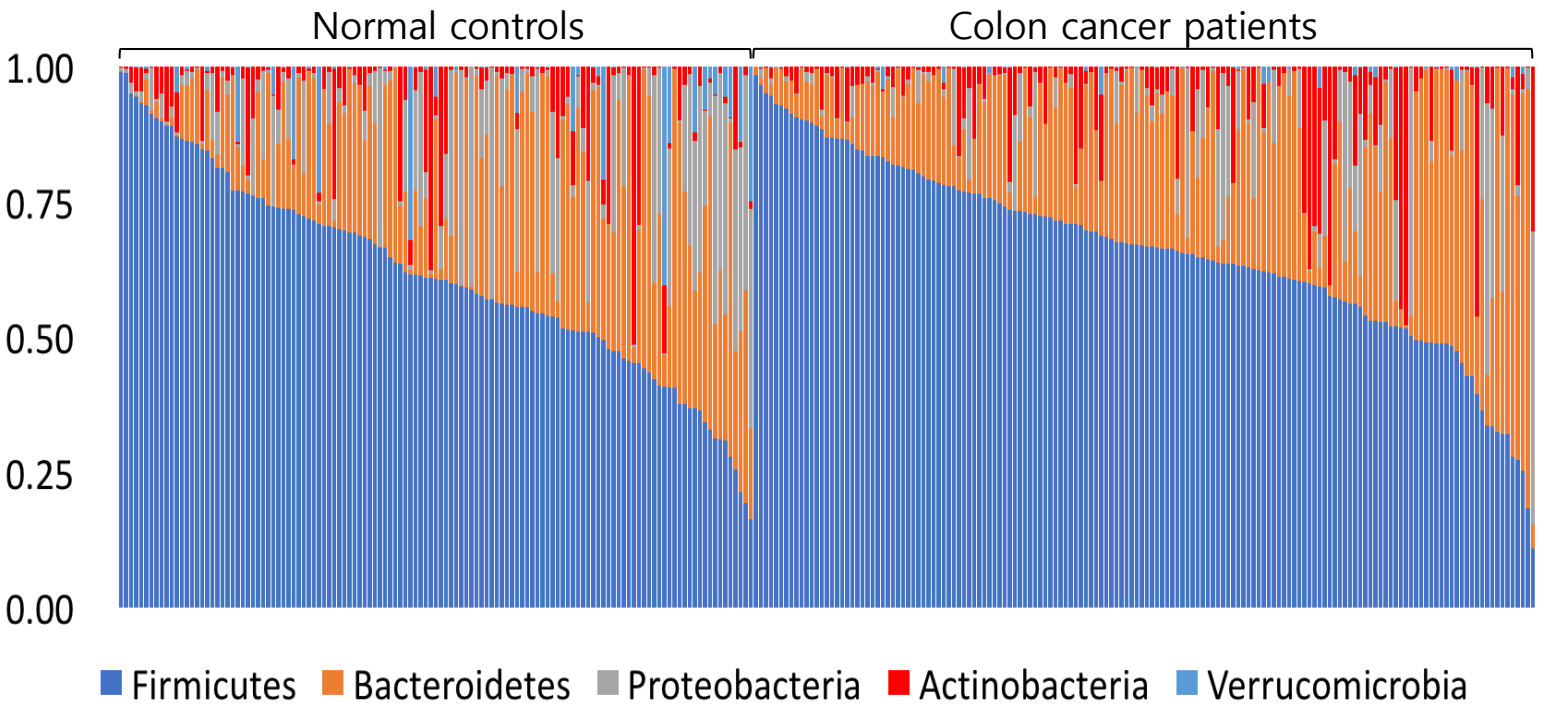
## 2 면역항암제

### Animal study schedule

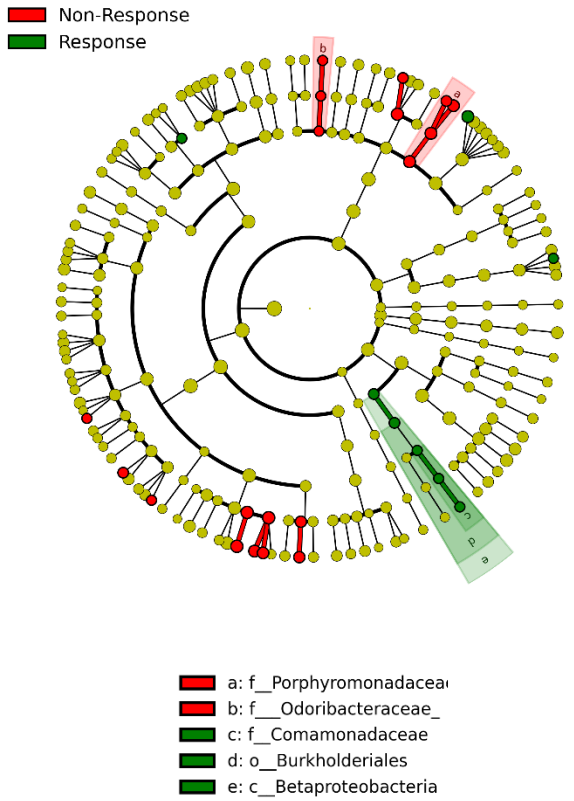



PBS: Phosphate-buffered saline

## Taxonomic analysis at phylum level

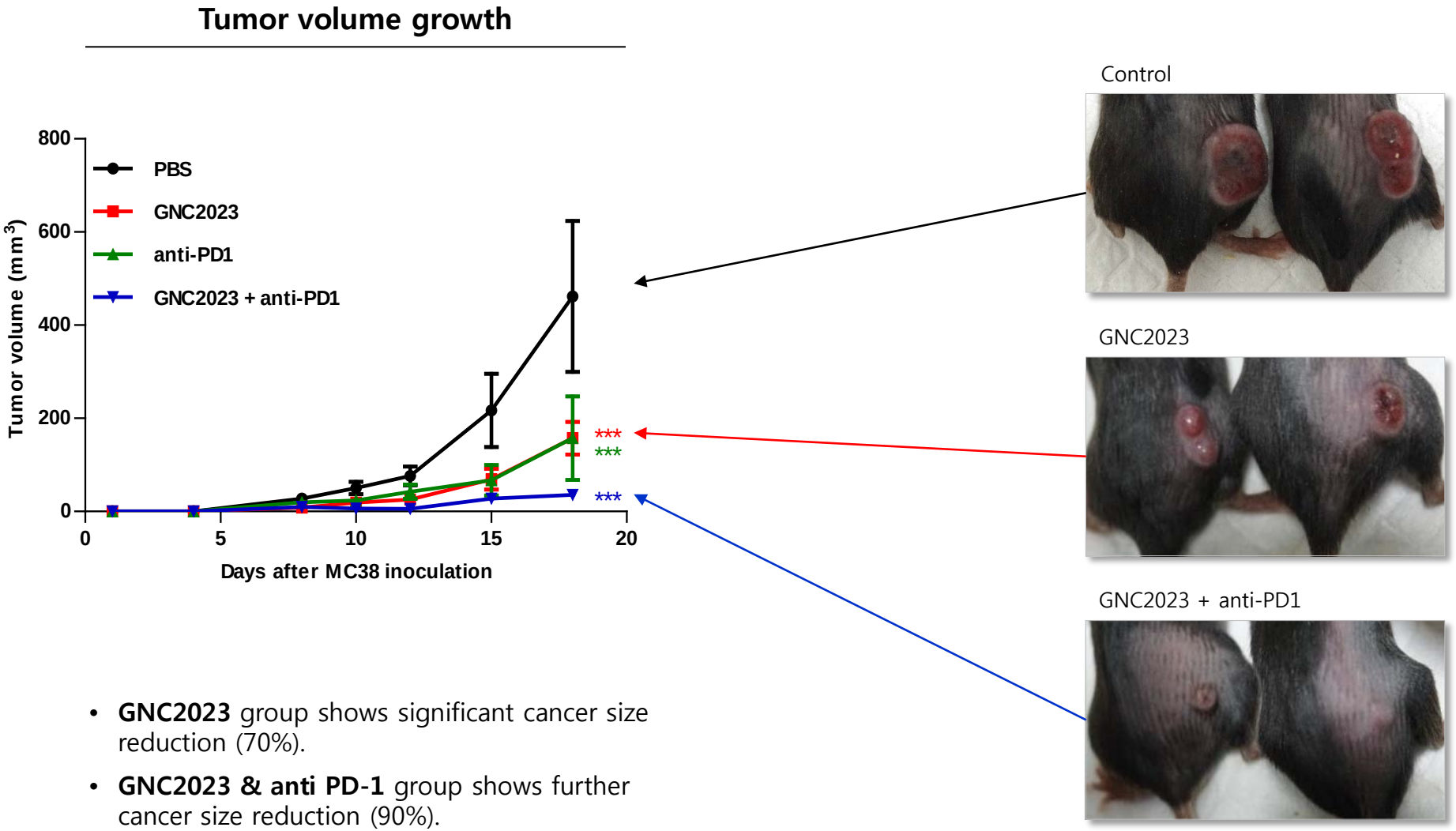



## LEfSe analysis



# 동물실험: Anti-cancer effects

## 2 면역항암제

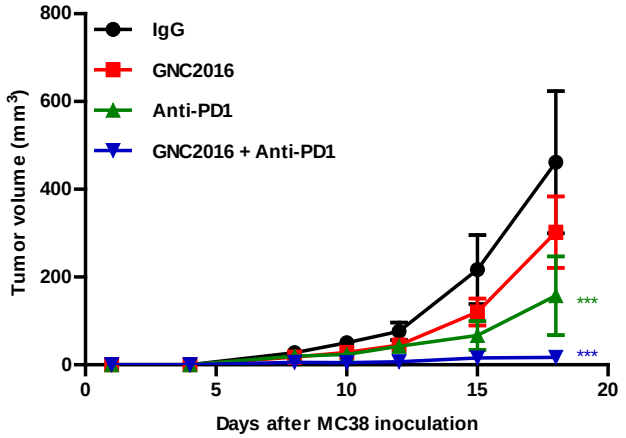


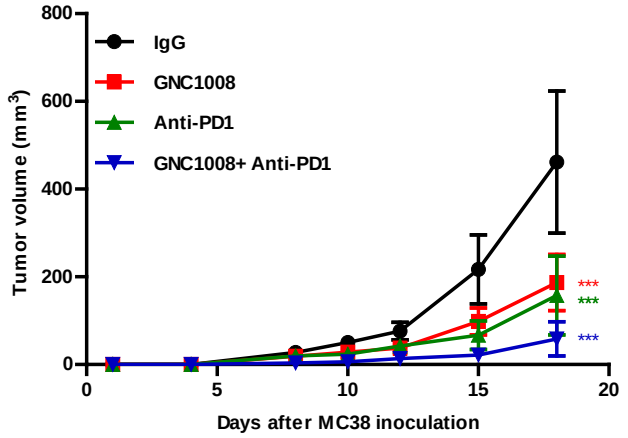

- **GNC2023** group shows significant cancer size reduction (70%).
- **GNC2023 & anti PD-1** group shows further cancer size reduction (90%).

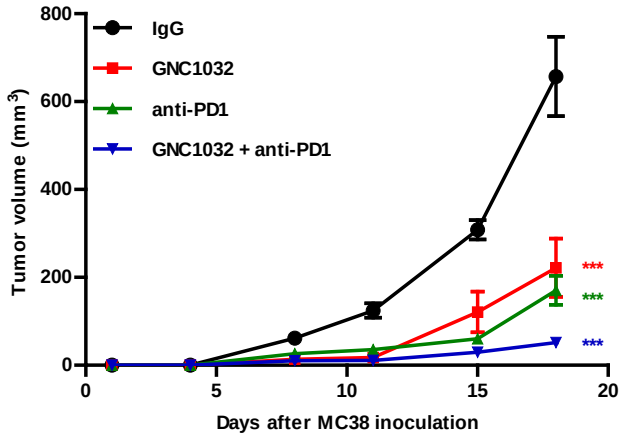
* P<0.05, ** P<0.005, *** P<0.001

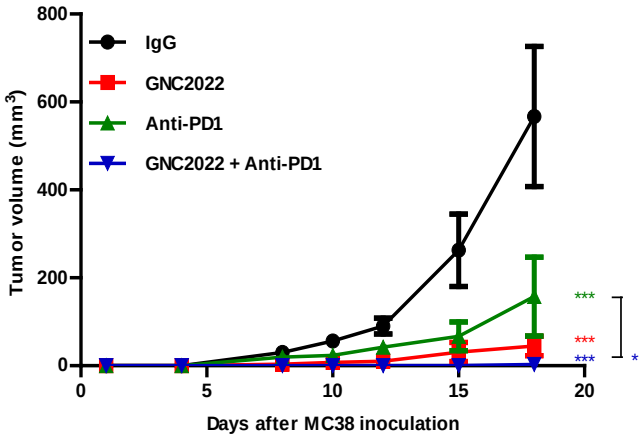
# 동물실험 결과: 항암효과를 보이는 균주 15개 strain 확보

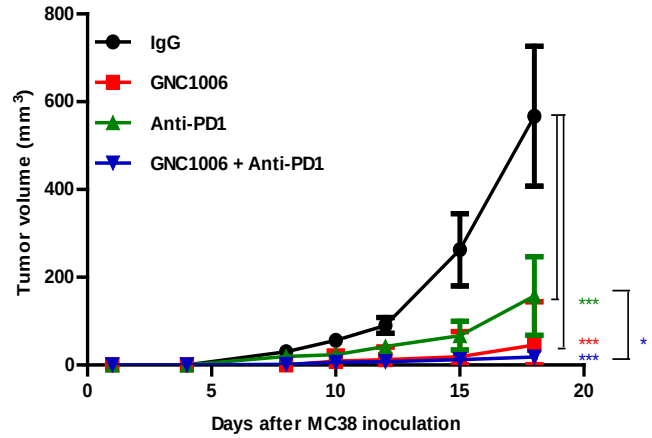
## 2 면역항암제

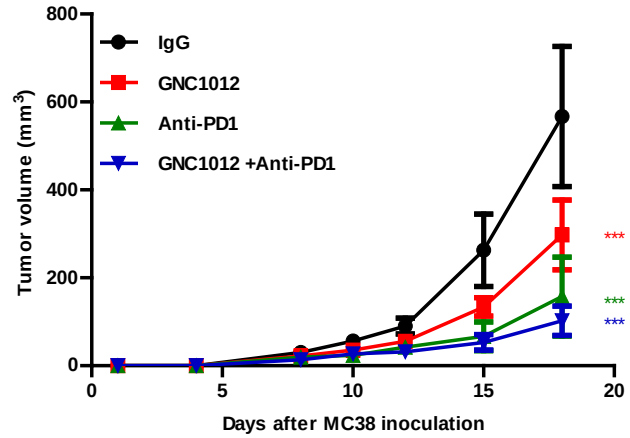


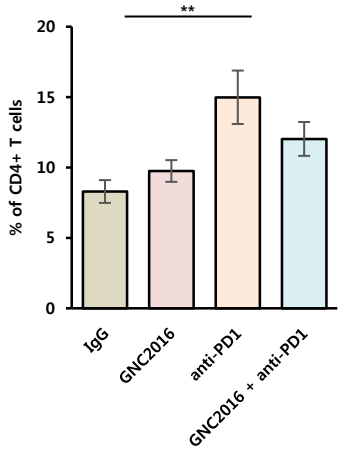

* P<0.05, ** P<0.005, *** P<0.001

# 세포실험: 암세포에서 면역세포의 활성화 관찰

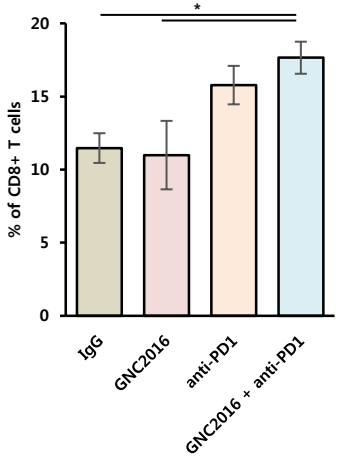
## 2 면역항암제

**Tumor**

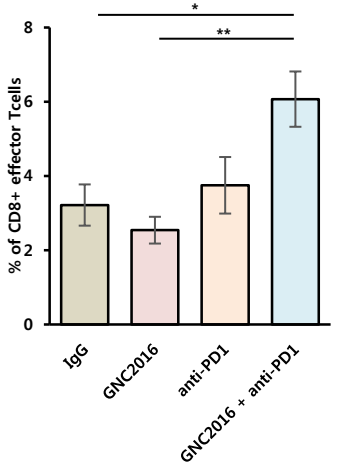
### 1 CD4+ T cells



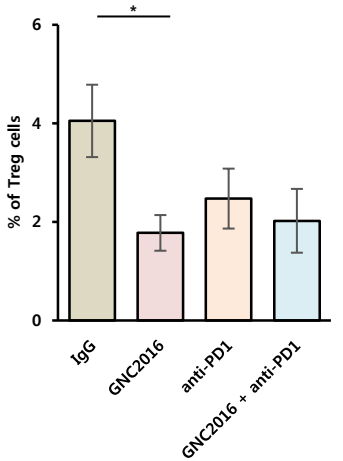

### 2 CD8+ T cells



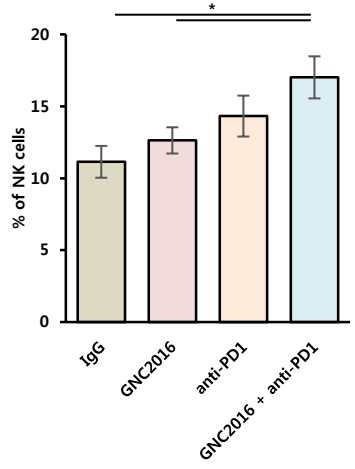

### 3 CD8+ effector T cells

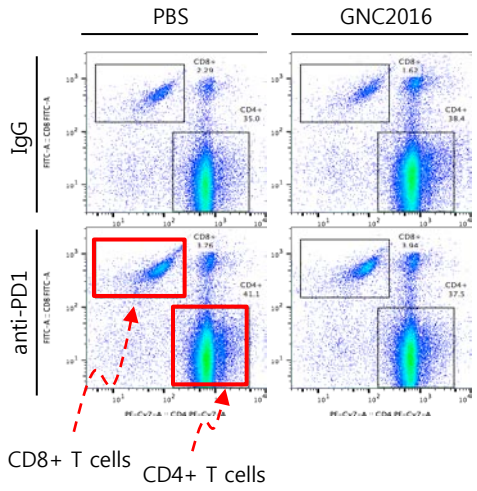


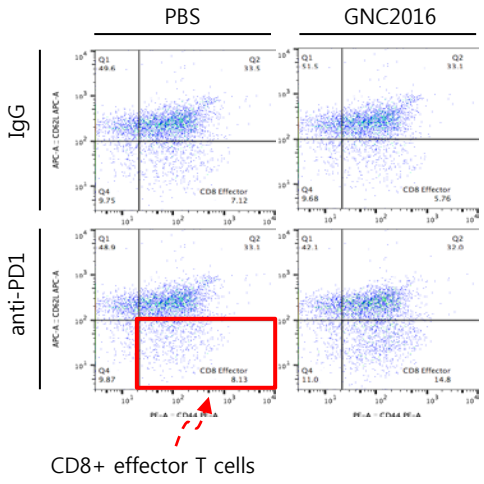

### 4 Treg cells

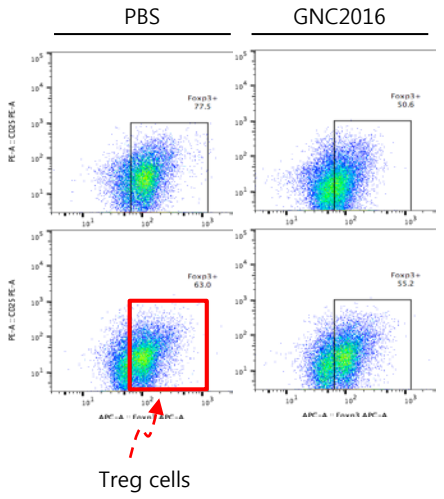


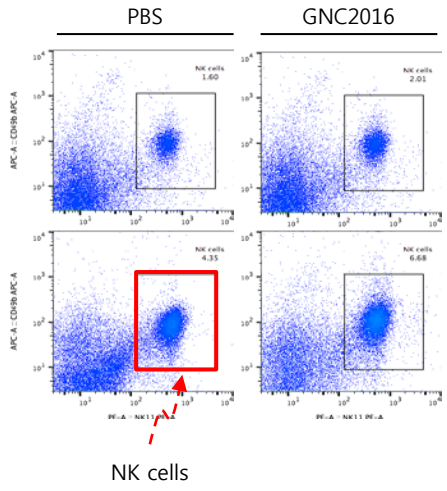

### 5 NK cells



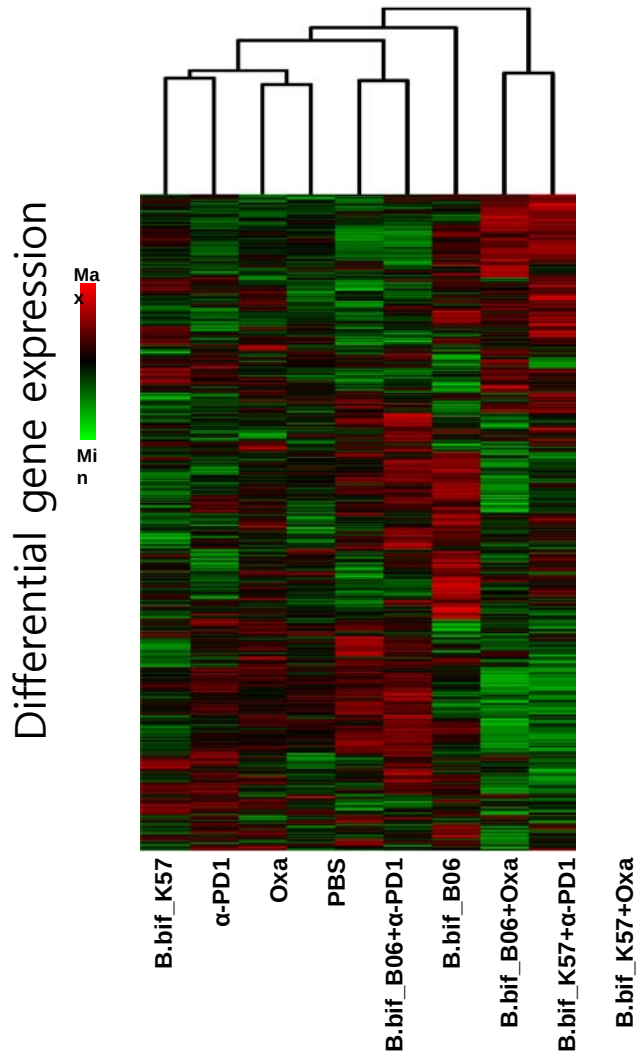



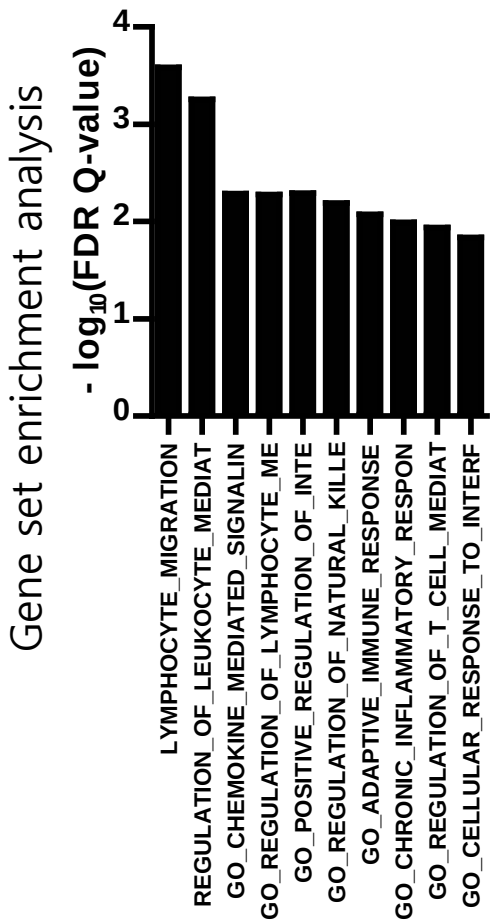



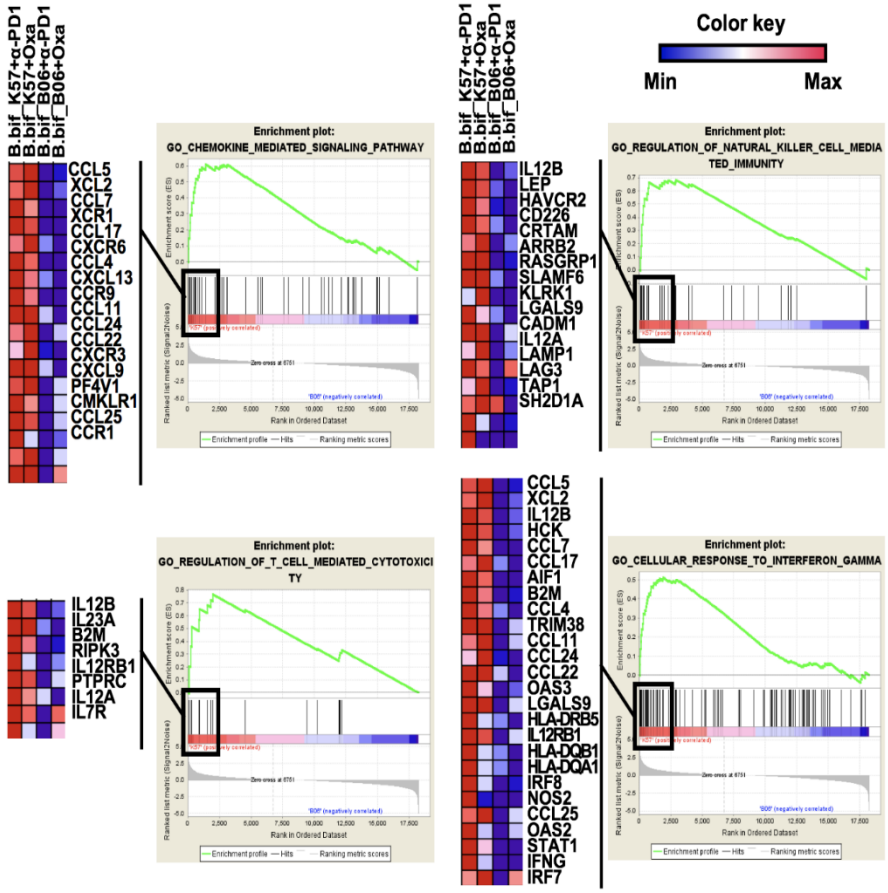




* P<0.05, ** P<0.01

# Intestinal tissue RNA sequencing



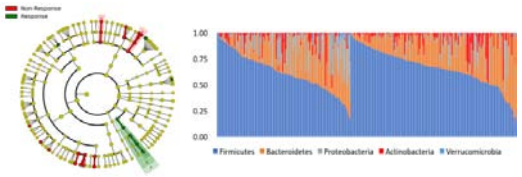



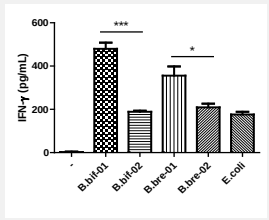



# Conclusion of the Oncoprobiotics Project

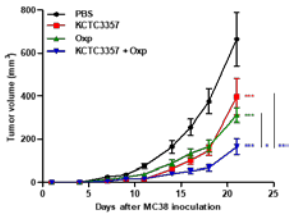
***Clinical Trial****

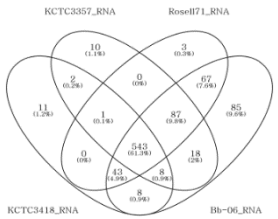
Cancer patients
Stool 16s rRNA seq



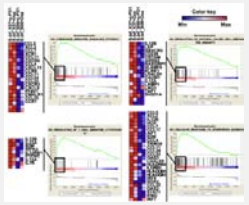



**Immune Fxn!**



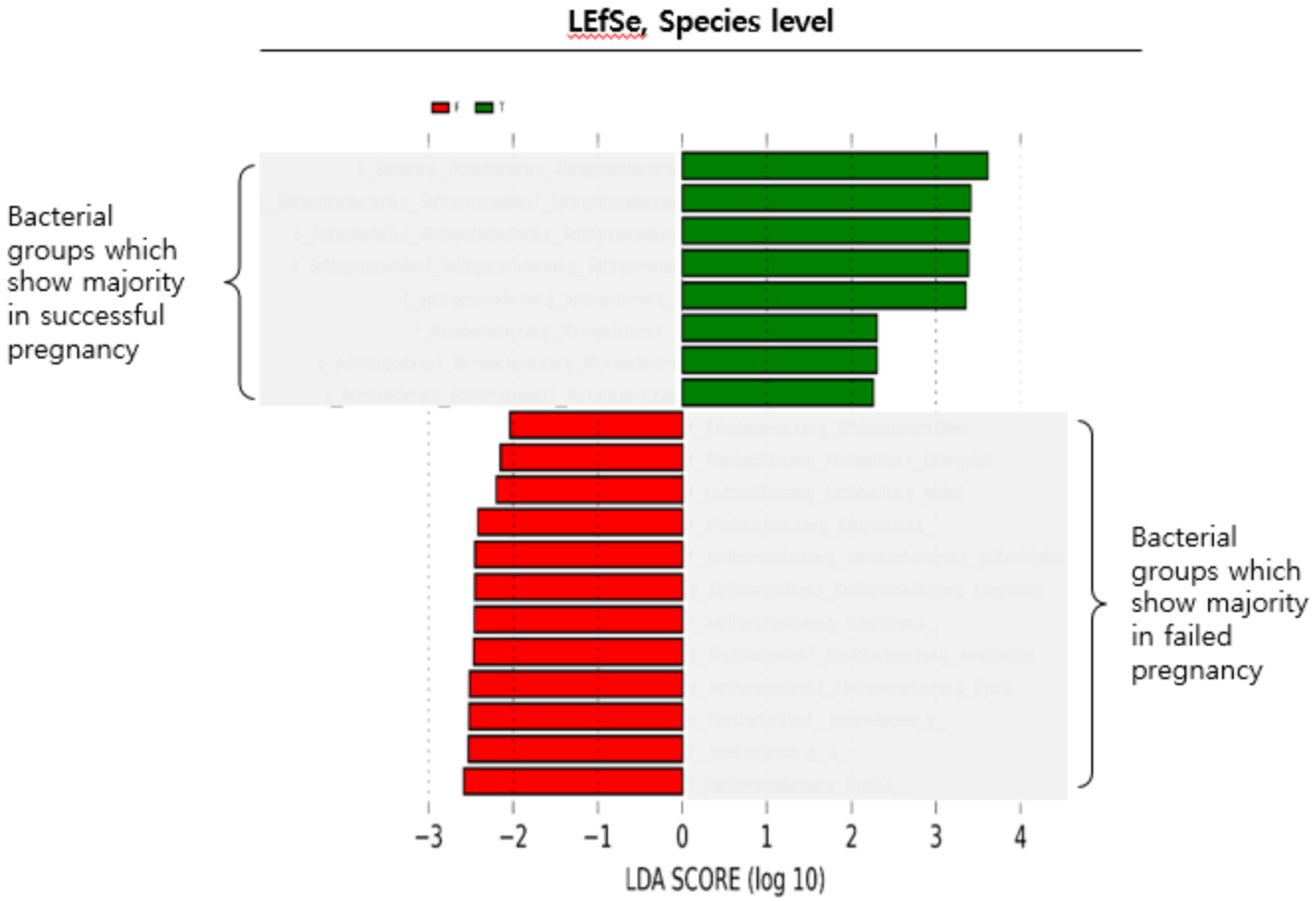



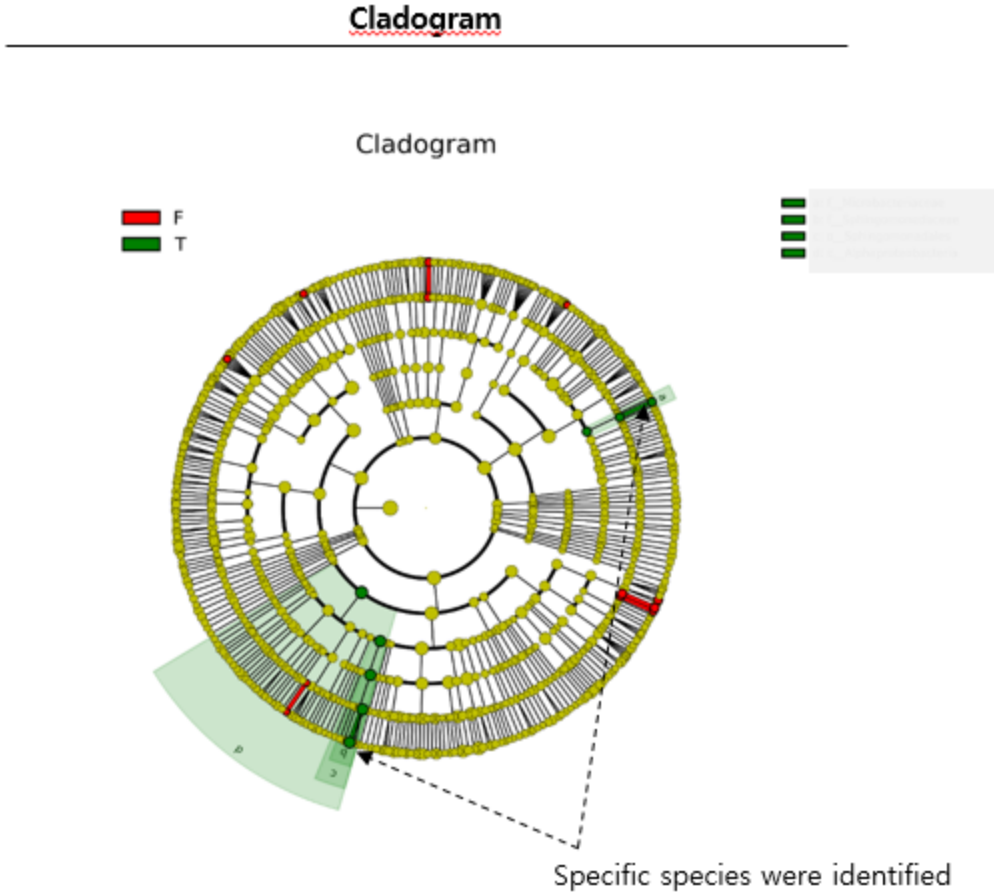

Active Microbiome
Whole genome shotgun seq
RNA seq
IFN-γ stimulation assay
Metablomics data
Proteomics



Syngenic mice model
Blood & tumor immune profiling
Serum cytokine
Stool 16s rRNA seq
Intestine RNA seq
Serum Metabolomics data

# Metagenome Sequencing

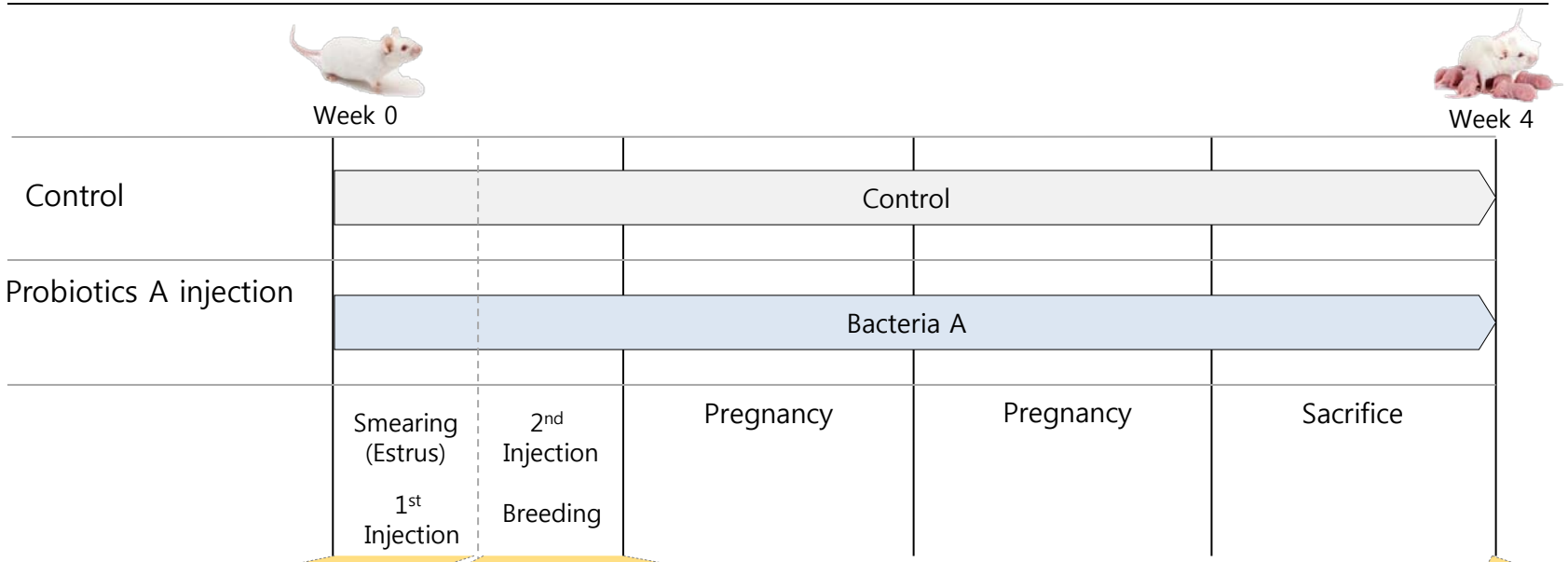


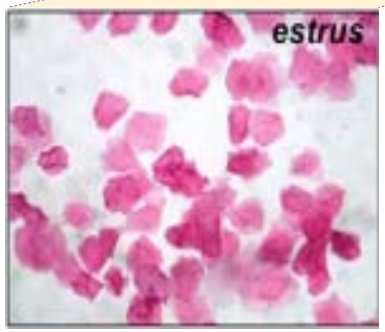




Sample: 36 , Positive Pregnancy(True) 21 , Negative Pregnancy(False)15

# Mouse IVF model

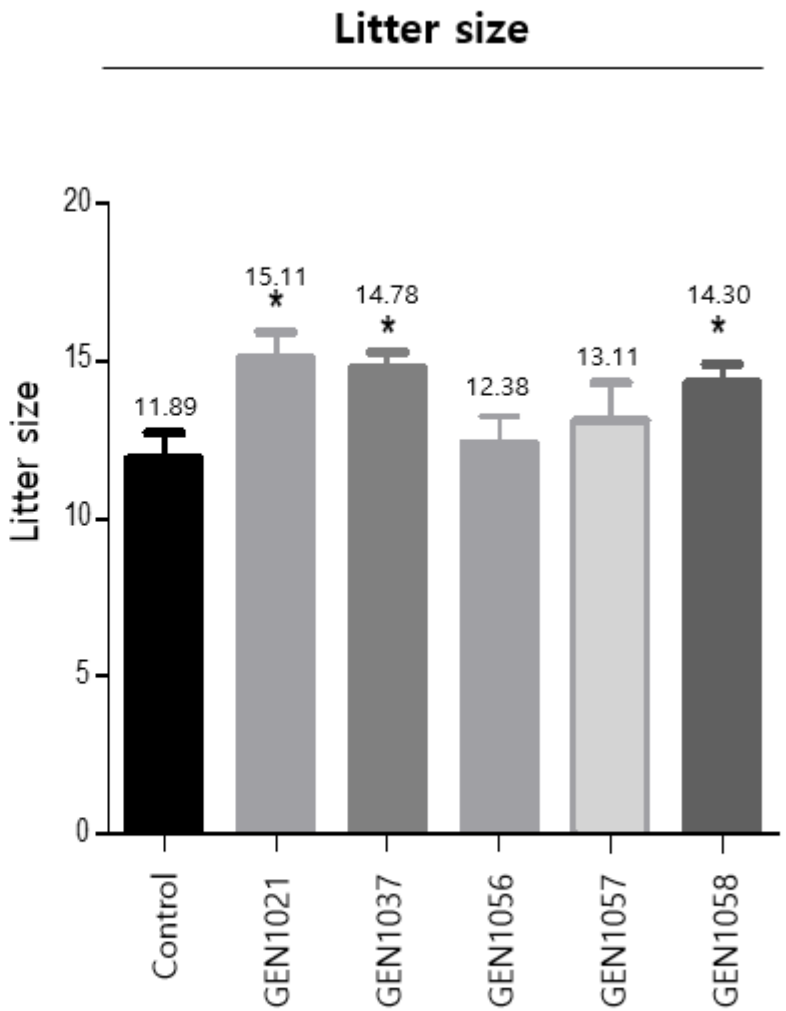
## Animal study schedule



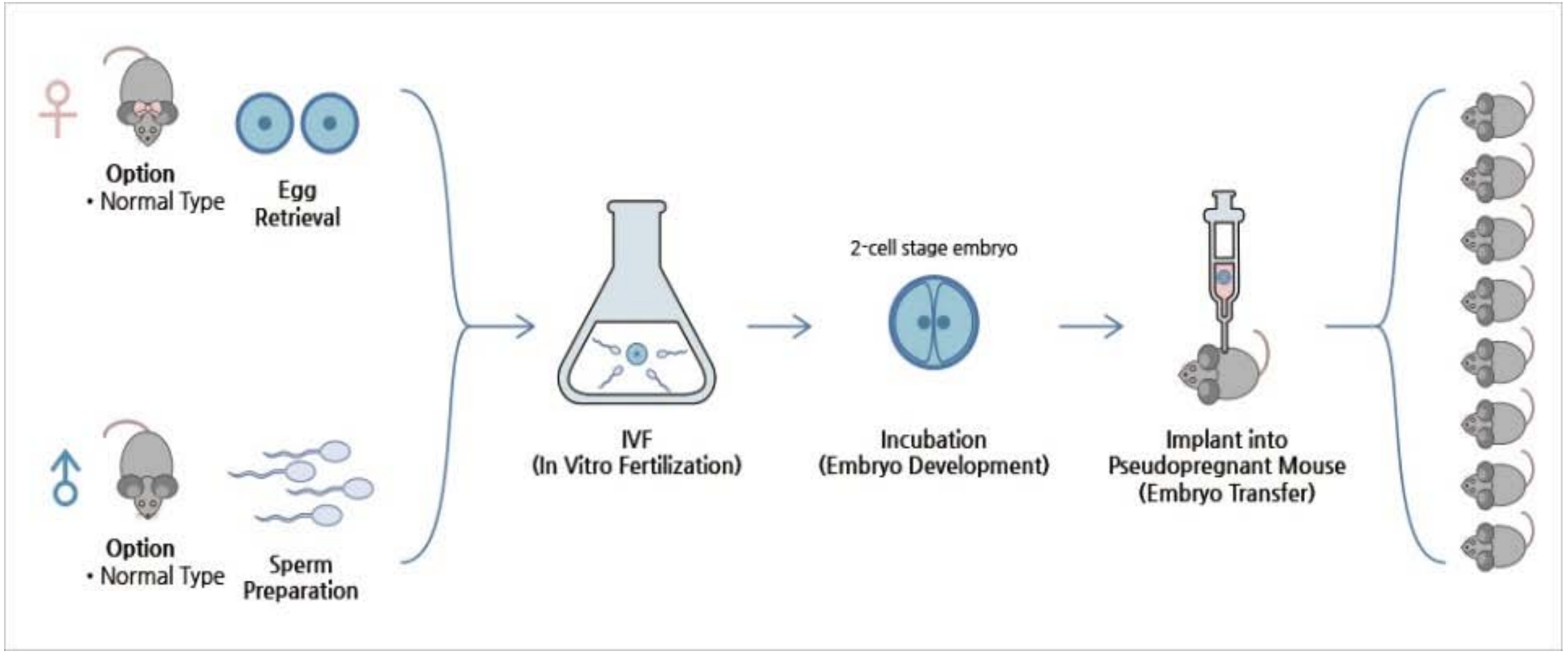




Non-Surgical Embryo Transfer Device

# Litter size increase in mouse study

# Mouse IVF



# 목차

# “With Bugs As Drugs!”: 마이크로바이옴으로 의약품을 개발한다

## Chemical

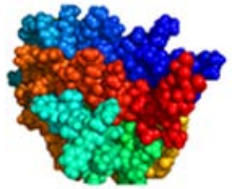
Aspirin

180

## Biologics

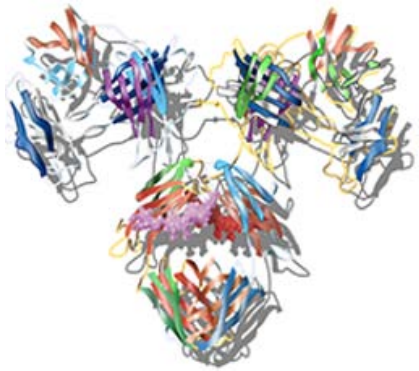
Insulin

~5,800



Erythropoietin

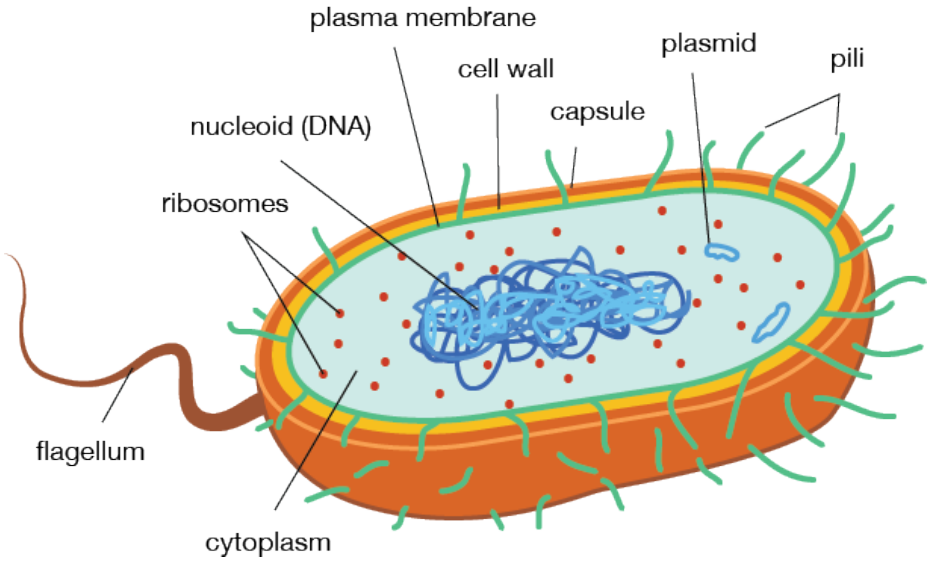
30,400



mAb

~150,000

## Microbiome

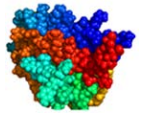
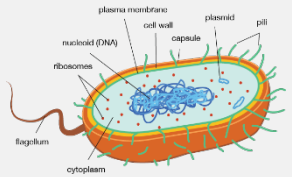



Bacteria

# Technical Feasibility

● 난이도 높음
◑ 난이도 중간
○ 난이도 낮음

## Challenges in Drug Discovery

| | ADME | PK,PD/ 투여경로 | 안전성 | 대량 생산 | CMC | Patent | MoA | Antibiotics 취약성 |
|---|---|---|---|---|---|---|---|---|
| **Chemical**  | ● | ● | ● | ◑ | ◑ | ○ | ○ | ○ |
| | • Lead optimization 에 많은 시간과 자원 필요 | • pH에 따른 용해도, 안정성 및 selectivity, affinity 고려 | • 체내에 존재하지 않던 물질이므로, 간, 신장으로 대사<br>• 유사 타겟에 작용가능 | • 최적의 합성 경로 도출 필요 | • 순도 유지 및 확인 필요 | • 새로운 물질이므로 비교적 단순 | • 새로운 물질이므로 비교적 단순 | • Antibiotics 와 무관 |
| **Biologics**  | ● | ◑ | ◑ | ● | ● | ◑ | ○ | ○ |
| | • Lead optimization 에 많은 시간과 자원 필요 | • pH에 따른 용해도, 안정성 및 selectivity, affinity 고려 | • 체내 유래인 경우 우호적<br>• 아닌 경우 심각한 부작용 | • 대량 생산 어렵고, 비교적 고가 | • 생산방법에 따라 동일 단백질 합성 확인 필요 | • 변종 옵션이 다양 | • Chemical 과 큰 차이 없음 | • Antibiotics 와 무관 |
| **Microbiome**   | ○ | ○ | ○ | ○ | ◑ | ◑ | ◑ | ◑ |
| | • 생산된 유효물질이 자연 경로를 따라 작용 | • 경구투여 후 장에 도달 | • 인체 유래<br>• Homeostasis 성향 | • 적정 조건에서 자체번식 | • 오염 혹은 변이 통제 필요<br>• 미국 FDA 최신 guideline | • 한국/유럽은 균주 특허 가능<br>• 미국의 경우 방법, 용법 특허를 활용 | • 복잡성이 높음 | • Antibiotics 치료 환자에서 효능 저하 우려 |

# US FDA 의 마이크로바이옴 신약 개발에 대한 입장

## Seres 의 임상연구 관련 기사 내용

With **FDA's Blessing,** Seres Preps New **"Pivotal" Microbiome Drug Trial**

- Frank Vinluan, March 16th, 2017

If successful, Seres CEO Roger Pomerantz says **the FDA agreed that this larger study would be a "pivotal" trial**, another way of saying that it should provide enough data for Seres to file for FDA approval.

"One of the reasons a Phase 2 trial can be considered pivotal is that this is **a breakthrough drug**, and we believe, and the **FDA believes, the first microbiome drug,"** Pomerantz says.

To date, Seres has **not reported signs of "safety signals"**—indications that the drug is causing dangerous side effects.


## 본사의 해외 컨설팅 내용

It appears that these products are currently **considered to be quite safe by FDA** and other regulators.

It appears that **a Maximum Tolerated Dose (MTD) has not been reached** in various first-in-human (FIH) dose escalation safety and tolerability studies.

4D Pharma's phase 1 study for pediatric Crohn's disease.
This study follows a first in adult (IBS) safety and tolerability study but still seems to **point towards FDA feeling comfortable with such products even in a pediatric setting.**

Another indication that **FDA is comfortable** with the evolving safety profile of these products is the fact that *Seres Therapeutics received Breakthrough Therapy (BTT) designation in June 2015* for its SER-109.

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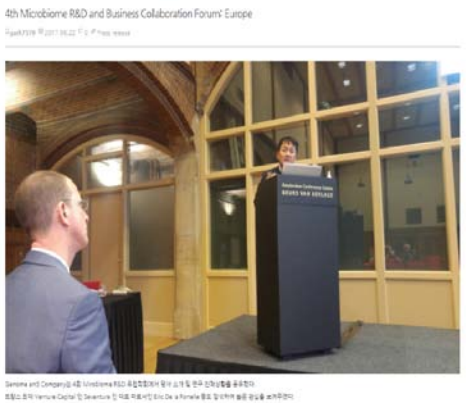
# 파트너링 (해외)

## Microbiome R&D and Business Collaboration Forum

Amsterdam
2017.04.03




Seventure

## BIO International Conference

SanDiego
2017.06.20


Pfizer
abbvie
NOVARTIS
Boehringer Ingelheim
Takeda

## Microbiome R&D and Business Collaboration Forum

SanDiego
2017.11.04

Seventure

## BIO International Conference

Berlin
2017.11.07


Johnson & Johnson
Boehringer Ingelheim
AMGEN
Genentech
Bayer
AstraZeneca
Bristol-Myers Squibb

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