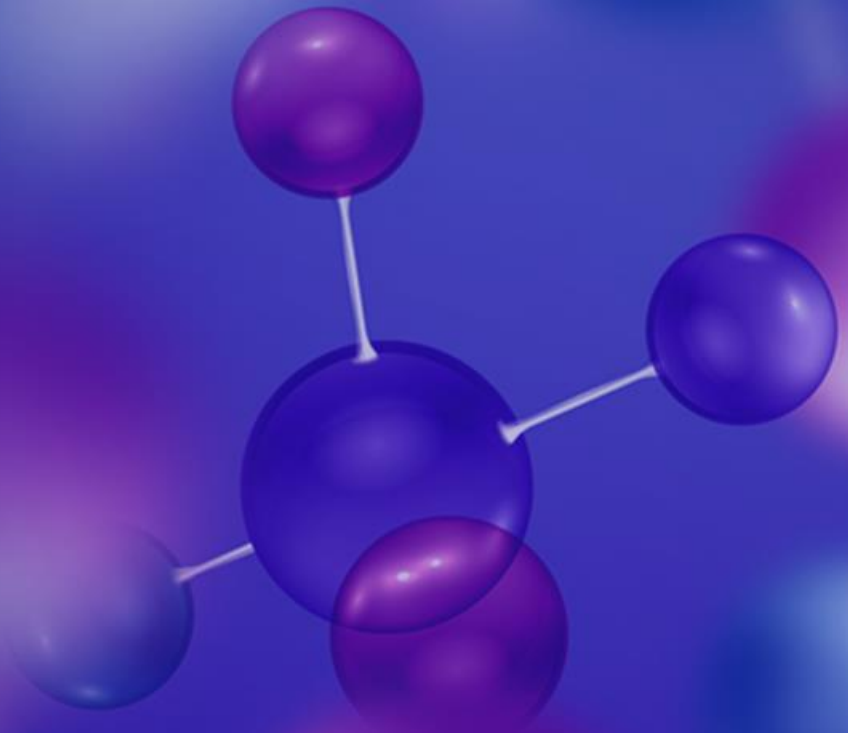
MolGenBio



Company Overview

General Information
What is MGB doing?
Difference & Identity
About the CEO
Co-Founders
SAB

01 General Information

Company name	MolGenBio
CEO	Yoon, Yeo Joon
Established on	March 29, 2021
Business areas	R&D of pharmaceuticals and API
Address	Room 101, Building 141, Seoul National University

02. What is MGB doing?

Genetically encoded small molecules

Higher probability of success compared to synthetic materials

Utilizing microbiomes

Synthetic biology

Microbial genome scanning based on genomic signature

Microbial genome editing

Legoization of biosynthetic genes

High-efficiency Development of Pharmaceuticals Based on Genetically Encoded Small Molecules & Synthetic Biology

MolGenBio

High-efficiency discovery of new active compounds

high-efficiency discovery of new active compounds based on pharmacophores

Efficient mass production

High-efficiency structure-activity modification

High-efficiency structural modification

High-efficiency optimization and activity modification

Creation of new activity and value

03. Difference & Identity

MolGenBio

Global Leading Company in Synthetic Microbial Therapeutics

Top-notch R&D Capabilities

- Synthetic biology, natural product chemistry, and neuroscience research at the highest level
- More than 380 articles listed in SCI(E)

Strong Platform

- Synthetic biology-based mass production and structure-activity modification
- Genomic signature-based genome scanning
- Libraries of 〉5,000 microorganisms, 〉3,000 microbial genomes, and 〉700 small molecules

Pipeline Expandability

- Anti-CNS, anticancer, anti-infective
- Continuous discovery of new active compounds
- Continuous structure-activity modification

High Success Rate

- High success rate of genetically encoded small molecules
- Safety equivalent to that of existing drugs

04. About the CEO

Professor,
College of Pharmacy, Seoul National University

Yoon, Yeo Joon

A world-leading researcher in biosynthesis and synthetic biology of genetically encoded small molecules
First Elucidation of the biosynthetic pathways of FK506, kanamycin, and gentamicin

Awards

- 1988 to 2000 – BS·MS·PhD at Dept. Chem. Technol. at Seoul Nat Univ.
- 1996 to 1998 – Visiting research fellow, University of Wisconsin
- 2000 to 2002 – Postdoctoral fellow, University of Minnesota
- 2002 to 2004 – Assistant professor, Department of Biochemical Engineering, University of Ulsan
- 2004 to 2020 – Professor, Department of Chemistry and Nanoscience, Ewha Womans University
- 2020 to present – Professor, Department of Manufacturing Pharmacy, Seoul National University
- 2014 to present – Fellow of the Royal Society of Chemistry (FRSC)

Career

- Selected as the "Ministry of Education, Science and Technology's Representative Excellent Performance" (2009)
- Selected as "Basic Research Excellent Performance" and "Government R&D Excellent Performance" (2012)
- Awarded as "Best Scientist of the Month" (2012)
- Selected as "Y-KAST Frontier Scientist" (2014)
- Selected as "National R&D Excellent Performance" (2016)
- Selected as "Top 100 Core Future Technologies and Leaders in South Korea" (2017)
- Awarded with the "Ministry of Science, ICT and Future Planning Commendation" (2017)

Achievements

- 〉150 studies published in major journals
- H-index: 39
- Cited more than 5,500 times
- 44/29 domestic patent applications/registrations
- 27/12 international patent applications/registrations
- Six cases of technology transfer (over KRW 350 million)

Publications

- Three studies published in Nature Chemical Biology
- Angewandte Chemie Int. Ed.
- Four studies published in Natural Product Reports
- PNAS
- J Am Chem Soc (First identification of FK506 biosynthesis, quoted more than 150 times)

Editorial Board

- Nat Prod Rep
- Appl Microbiol Biotechnol
- Biomolecules
- J Microbiol Biotechnol
- BioMed Res Int

05. Co-founders

Yoon, Yeo Joon

Seoul National University
College of Pharmacy

Lead/candidate biosynthesis and optimization
Development of mass-produced strains

Oh, Dong-Chan

Seoul National University
College of Pharmacy

Research on discovery of new natural products for over 20 years
“Leading researcher in natural product chemistry”

Discovering new natural products

- Ph.D., University of California, San Diego
- Director of Natural Products Research Institute, Seoul National University
- About 160 studies published
- Achievements: Science , Nat. Chem. Biol, Angew. Chem. Int. Ed. Etc.

Cheong, Eunji

Yonsei University
Department of Biotechnology

Research on physiological activity and signal of brain nerve cells for over 20 years
“Leading researcher in neuroscience”

Efficacy, safety, and mechanism evaluation

- Ph.D., University of Pittsburgh
- About 70 studies published
- Achievements: Neuron, Nat Commun, ACS Nano, PNAS, J. Neurosci. Etc.

06. Scientific Advisory Board

Lee, Phil Hyu

Yonsei University
Severance Hospital
Department of Neurology

Research on neurological diseases for over 20 years

“Renowned for neurological diseases such as Parkinson's disease”

Parkinson's disease specialist

- Doctor of Medicine, Yonsei University (Neuroscience)
- Professor of Neurology at Severance Hospital
- Parkinson's disease · dementia · dyskinesias · EBS Best Doctors
- 2017 Pfizer Medical Research Award
- Achievements: Neurology, Brain, J. Neurochem., etc.

Jo, Eun-Kyeong

Chungnam National University
College of Medicine
Microbiology Lab

Research on control of tuberculosis and infectious inflammation for 25 years

“Leading researcher in the field of tuberculosis immunity”

Tuberculosis Immunization Specialist

- Doctor of Medicine, Chungnam National University
- Director of Infection Control Convergence Medical Research Center (MRC), Chungnam National University
- About 200 studies published
- Achievements: Nat Immunol, Immunity, Cell Host & Microbe, Autophagy, etc.

Shin, Sang Joon

Yonsei University
Severance Hospital
Department of Oncology

Development of big data analysis and decision support system for cancer treatment

“Innovative drug development for cancer treatment”

Cancer treatment specialist

- Doctor of Medicine, Yonsei University (Oncology)
- Professor, Department of Oncology, Cancer Hospital, Severance Hospital
- Director, Medical Information Security Center, Yonsei Medical Center
- Development of new drugs targeting melanoma, big data analysis, and CDSS development
- Achievements: Nature, etc.

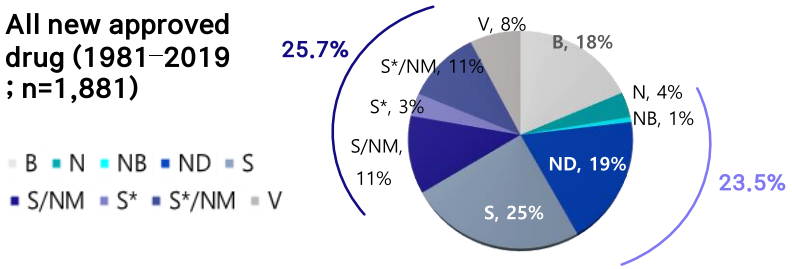
Platform Technology

Importance of Genetically Encoded Small Molecules
Unique New Drug Development Process of MGB
MtG: Drug Development Platform
MtG Expandability
Pipeline Summary

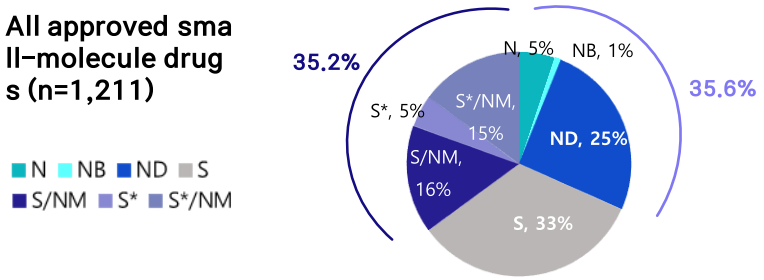
01 Importance of Genetically Encoded Small Molecules (1)

Genetically encoded small molecules: the richest resources for drug development

All new approved drug (1981–2019 ; n=1,881)



All approved small-molecule drugs (n=1,211)



B	Biological; usually a large (>50 residues) peptide or protein
N	Natural product
NB	Natural product "Botanical"
ND	Derived from a natural product and semisynthetic modification
S	Totally synthetic drug
S*	The pharmacophore is/was from a natural product
V	Vaccine

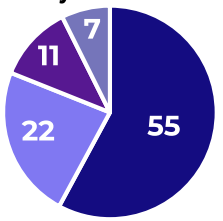
J. Nat. Prod. 2020, 83, 770 / J Antibiot. 2012, 65, 385

Probability of new drug development with genetically encoded small molecules: 0.68%

Classification	Total number of substances	Number of medicines	Probability
Synthetic	~9,000,000	~2,250	0.025%
Natural	~500,000	~1,400	0.28%
Animal-derived	~100,000	~125	0.13%
Plant-derived	~350,000	~800	0.23%
Microorganism -derived	~70,000	~475	0.68%

Mostly derived from streptomycetes/actinomycetes

- Streptomycetes
- Fungi
- Other actinomycetes
- Other bacteria



Case of Lodo Therapeutics

GEN Genetic Engineering & Biotechnology News

Genentech, Lodo Therapeutics Ink Up-to-$969M Metagenomics Drug Discovery Partnership

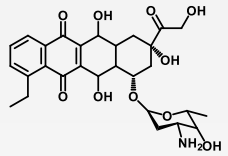
"Genentech signed a broad, open-ended drug discovery collaboration with Lodo Therapeutics that could be worth nearly $1 billion, **focused on deriving unique, natural products from the microbial DNA found in soil**"

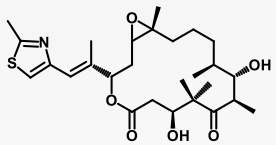
Source: May 9, 2018 | Genetic Engineering & Biotechnology News

01 Importance of Genetically Encoded Small Molecules (2)

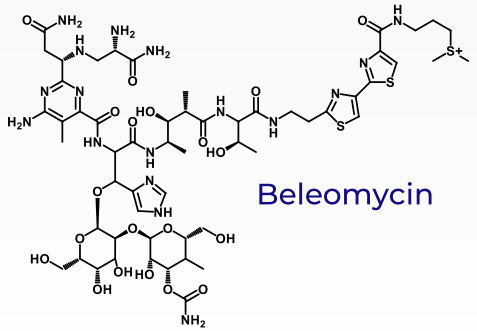
Anticancer

Doxorubicin



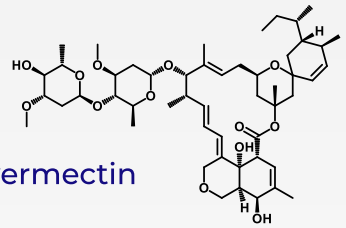


Epothilone

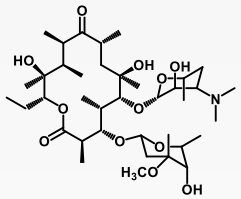


Beleomycin

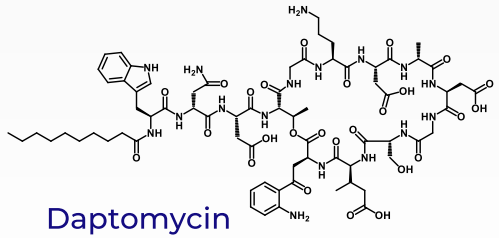
Anti-infective



Avermectin

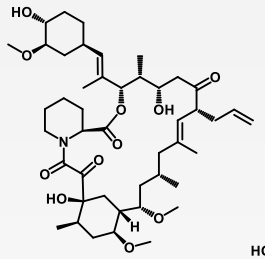


Erythromycin



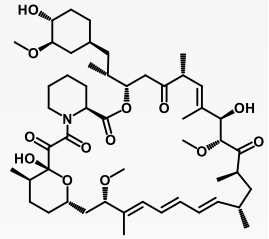
Daptomycin

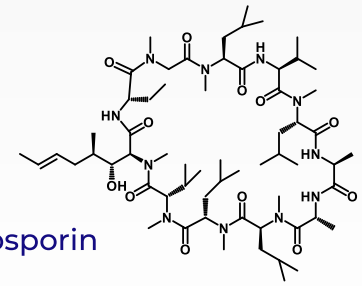
Immunosuppressant



FK506
(tacrolimus)

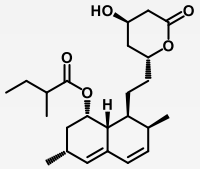
Rapamycin
(sirolimus)





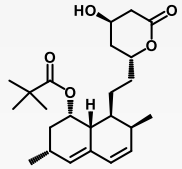
Cyclosporin

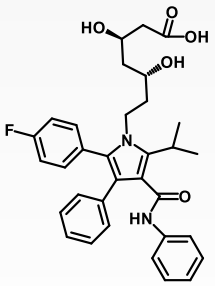
Anti-cholesterol



Lovastatin

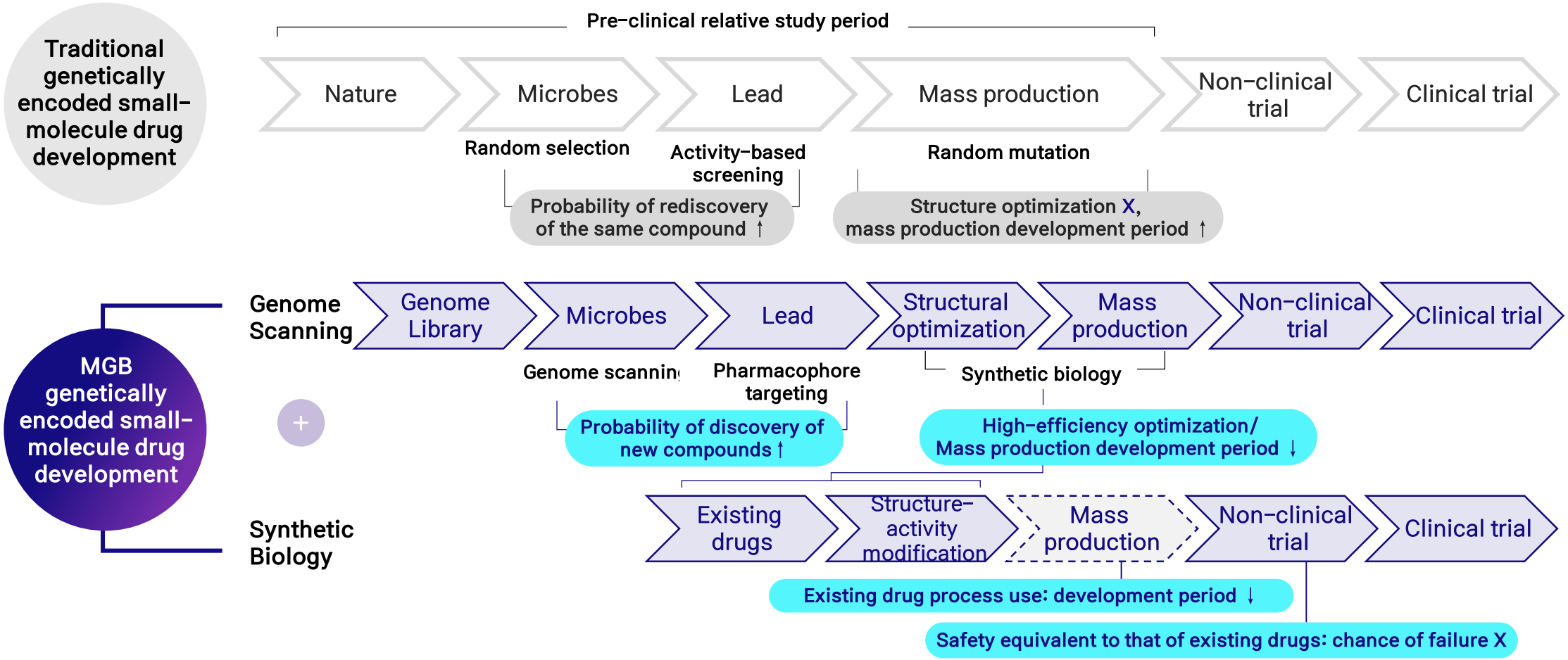
Simvastatin



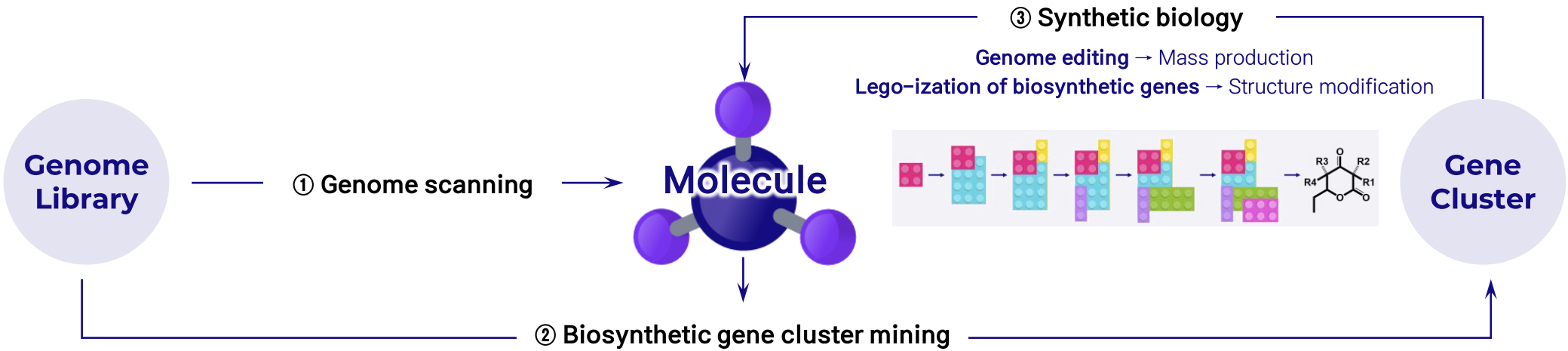


Atorvastatin

02. Unique New Drug Development Process of MGB



03. MGB drug development platform, Molecule through Gene



Molecule through Gene

Efficient lead discovery based on genome scanning

Probability of discovery of new compounds ▲
Probability of discovery of effective activities ▲

Synthetic biological structure-activity modification

Structural modification efficiency ▲
New activity creation ▲
Safety ▲

Synthetic biological massive production

Ease of mass production ▲
Selective production of target substances ▲

04. MtG Scalability

Expansion of pipeline diversity through platform expansion

Expansion of platform infrastructure

Expansion of microbiome/ microorganism library

Expansion of genome library

Expansion of target drugs

[e.g.] Rapamycin

Molecule through Gene

Expansion of platform application

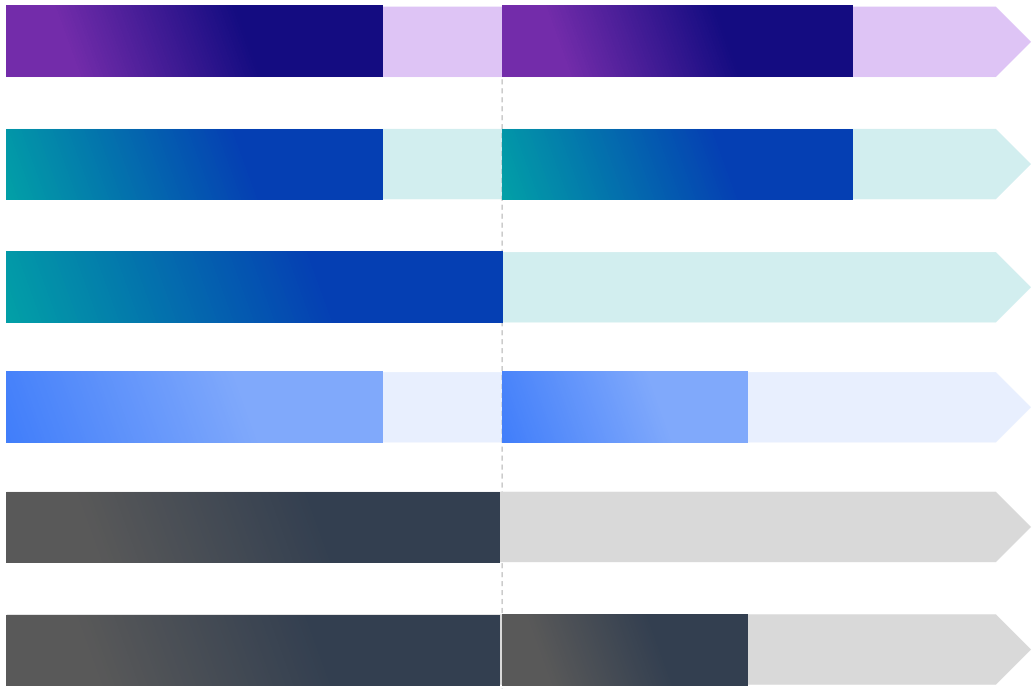
Continuous lead discovery /modification

Expansion of indications by modifying existing drugs

[e.g.] PD, AD, cancer, anti-infectives, stroke, diabetic neuropathy, hair growth, etc.

05. Pipeline Summary

Indication	Development candidate	Exploration/ optimization	Mass production (CMO)	Non-clinical trial
Anti-CNS (PD)	MG-TA			2023
Anti-CNS (AD)	MG-TA			2023
Anti-CNS (AD)	MG-RZ			2024
Anti-hair loss	MG-TA			2024
Anticancer	MG-LZ			2024
Antituberculosis	MG-AR			2024



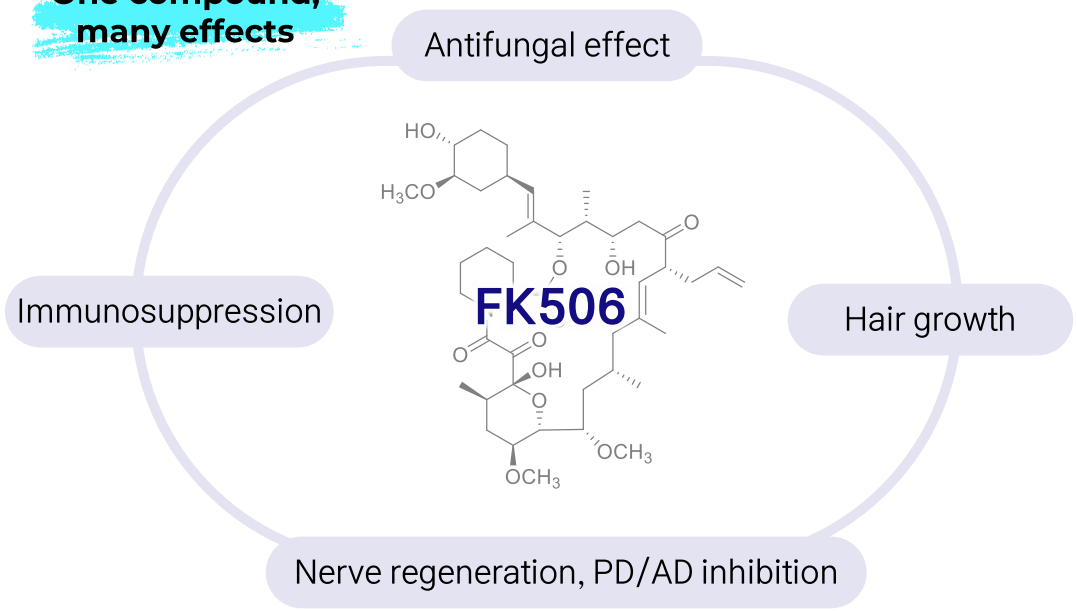
03 Pipeline

- Anti-CNS MG-TA

01 Technology Introduction (1)

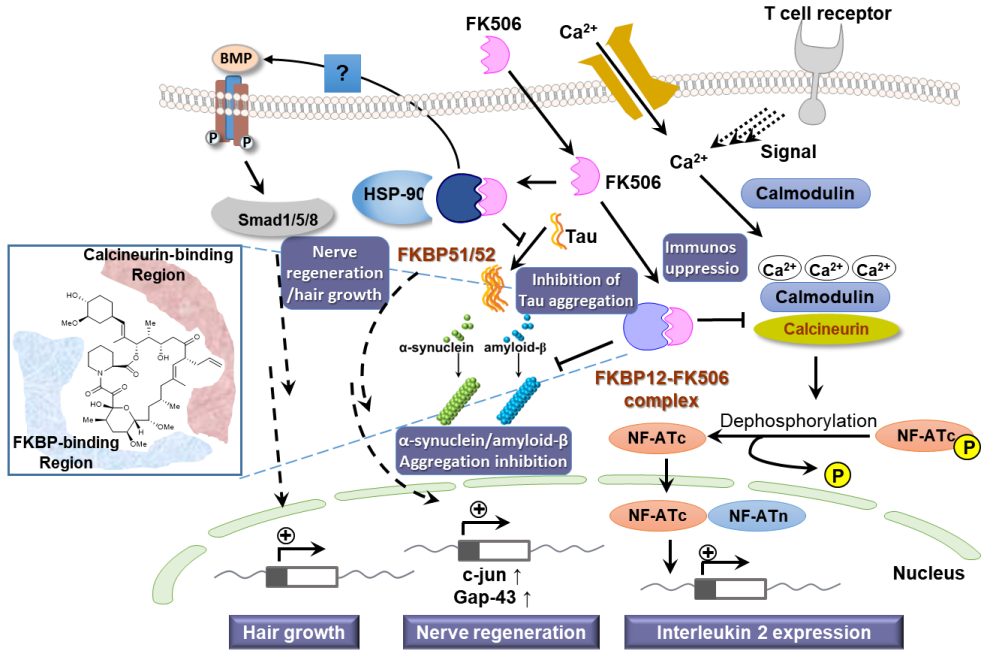
FK506: Immunosuppressants used to prevent the rejection of organ transplant

One compound, many effects



Elimination of immunosuppressive activity of FK506
⇒ Safe nerve regeneration + PD/AD inhibition

FK506 structure modification ⇒ target protein binding regulation ⇒ activity regulation



FK506 + FKBP12 + Calcineurin → NF-ATc dephosphorylation X → IL2 expression ↓ **Immunity ▼**

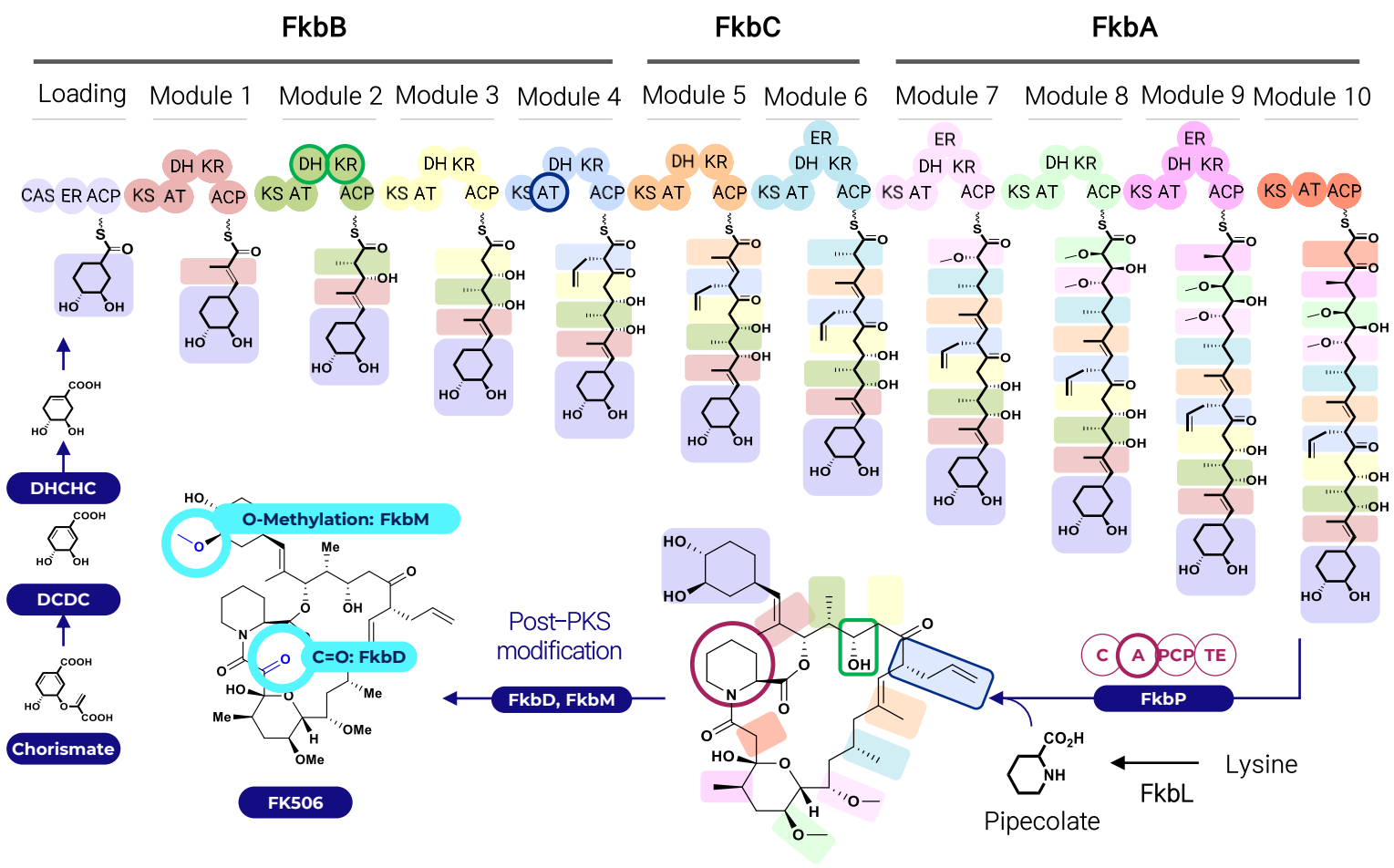
↘ α-synuclein/amyloid-β aggregation▼

FK506 + FKBP51/52 → → → **Neuroregeneration ▲** **Hair growth ▲ (?)**

↘ Tau aggregation ▼, inflammation ▼

01 Technology Introduction (2)

Biosynthetic pathway and synthetic biological modification of FK506



FK506

- ▶ Biosynthesis by *Streptomyces* polyketide synthase (PKS) / nonribosomal synthetase (NRPS) hybrid system
- → Domain composition of each module determining the chemical structure

Complex chemical structure

- ▶ Difficulty in chemical structure modification

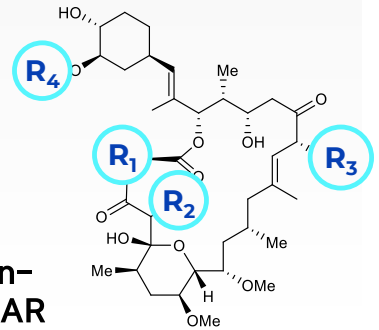
Synthetic biology-based

- ▶ Substitution, insertion, and removal (lego-ization) of domain/module
- → Precise and free modification of FK506 chemical structure

Over 50 new derivatives biosynthesized

▼

Establishment of immunosuppression-neuroregeneration SAR



J. Am. Chem. Soc. 2011, 133, 976
J. Nat. Prod. 2013. 76, 1091

02. Summary of MG303/MG402

Similar hair growth activity at a concentration of 1/50 to minoxidil

Strength & Opportunity

A new paradigm for topical hair growth

Different mode of action compared with minoxidil

Excellent hair growth-promoting efficacy and safety

IP acquisition 10-2019-0086645, PCT/KR2019/017523, US/China/EU patent application

Maintaining/improving excellent Anti-hair loss activity of FK506

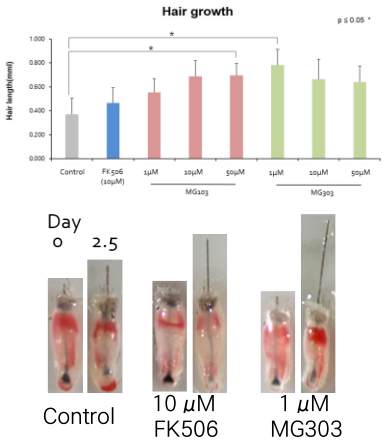
Removal of FK506's immunosuppressive activity (reduction by 10,000-120,000 folds)

Efficacy demonstrated in a mouse model

Efficacy confirmed in ex vivo model

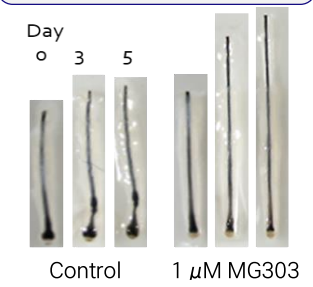
02. Results (1) MG303/MG402 Hair Growth-promoting Activity

Mouse whisker hair follicle cell culture



Increased hair follicle length and anagen induction/elongation

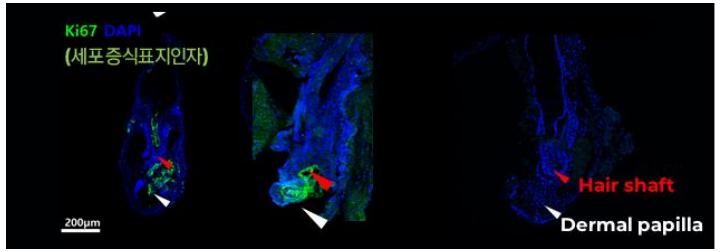
Human hair follicle cell culture



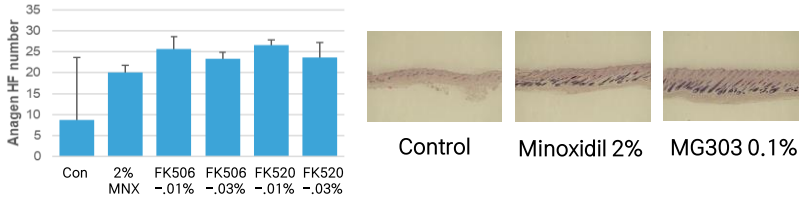
Anagen elongation

Tissue analysis results: Anagen phase extension

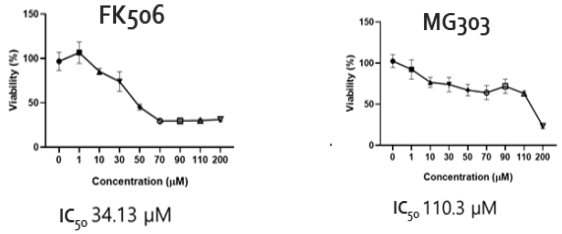
FK506	MG303	Minoxidil	Minoxidil
1 mM	1 mM	1 mM	0.5 mM



Animal model: Increased number of anagen hair follicles



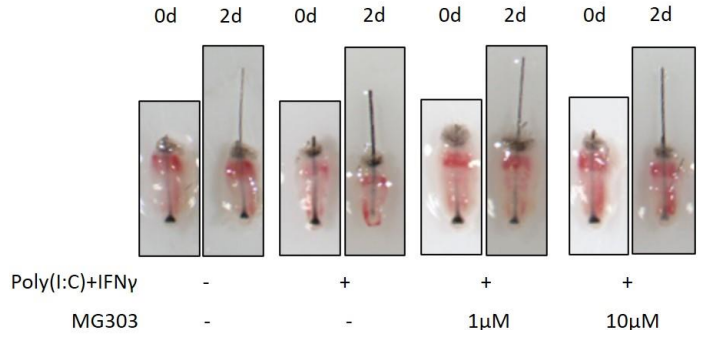
Keratinocyte toxicity test

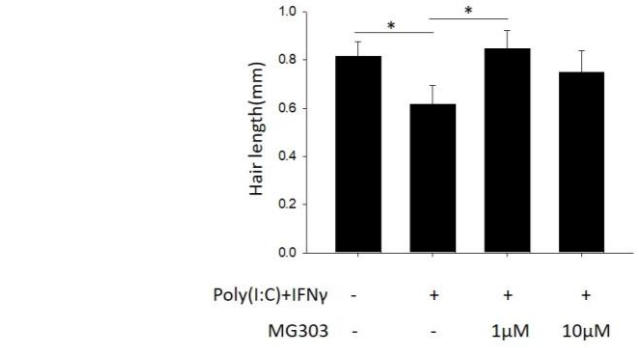


IC_{50} 34.13 μM

IC_{50} 110.3 μM

Alopecia areata ex vivo model: Increase hair length





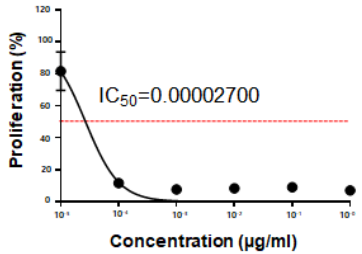
Increased hair follicle length in induced alopecia areata by poly(I:C), interferonχ-treatment

02. Results (2) Safety of MG303/MG402

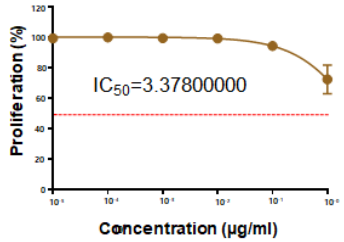
Safety proven to be equivalent to or higher than that of the existing FK506

Immunosuppressive activity:
Reduced by more than 100,000 times

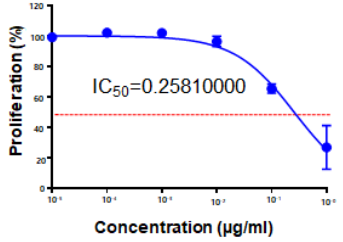
FK506 1



MG402 Reduced by 120,000 times



MG303 Reduced by 10,000 times



Cytotoxicity: No effect at a dose below 1 μM

Genotoxicity (AMES test): No reverse mutation induced

Cardiovascular safety (hERG assay): No potential risk

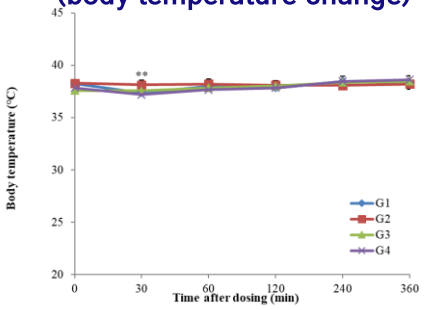
Zebrafish fry safety assessment: No effect at a dose below 100 μM

Mouse liver and kidney tissue assessment: No effect at a dose below 100 mpk (single-dose toxicity test)

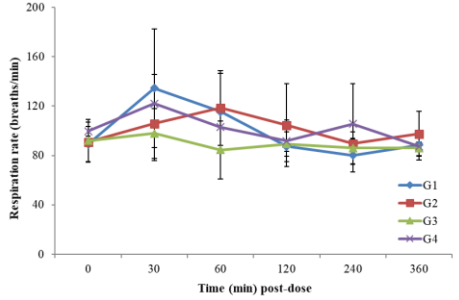
Safety pharmacology test (rodents, single oral administration):
No effect at a dose below 20 mpk

Data are expressed as Mean±S.D.
G1: Vehicle control group (DMSO)
G2: Test article group (5 mg/kg)
G3: Test article group (10 mg/kg)
G4: Test article group (20 mg/kg)

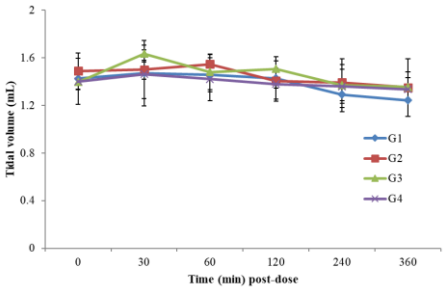
Central nervous system safety pharmacology assay
(body temperature change)



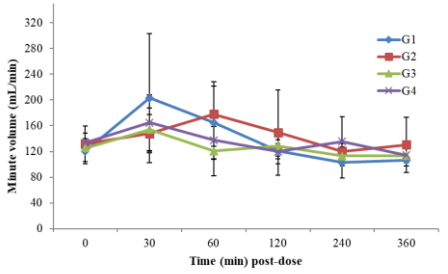
Respiratory system safety pharmacology assay
(respiratory rate)



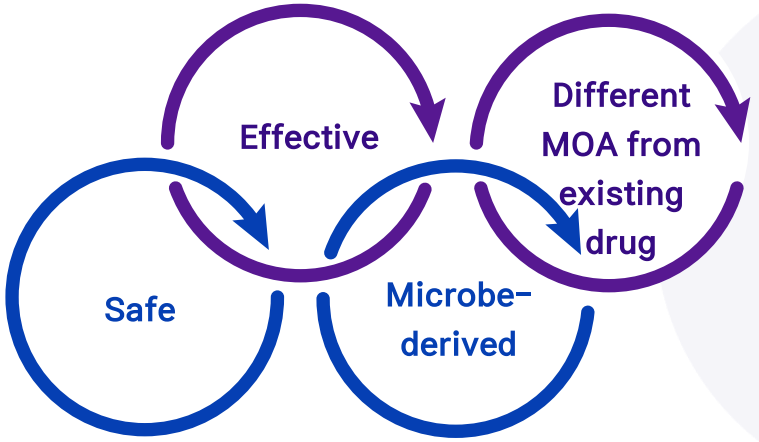
Respiratory system safety pharmacology assay
(tidal volume)

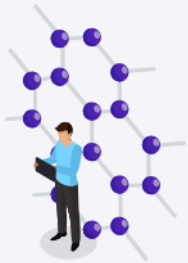


Respiratory system safety pharmacology assay
(respiratory rate per minute)



03. Development Plan





Development plan by year

Indication	2022	2023	2024	2025	2026	2027
Hair growth	Mass production	Optimization/ additional efficacy test	Non-clinical trial	Phase 1 clinical trial	Phase 2 clinical trial	

Thank You