Lab of Data Pharmacognosy

- Novel source & Technology -

동국대학교 약학대학 생약학 연구실

조교수 김현우

hwkim8906@dongguk.edu

생약·천연물화학 연구실 (김현우 교수)

KIM, MYEONG JI

Integrated PhD course (2022.09 - Present)

KANG, YOUNG HOON

Master course (2024.03 - Present)

WEN, JINGXUAN

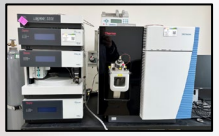
Master course (2024.09 - Present)

LEE, OJU

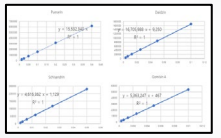
Master course (2024.09 - Present)

천연물 성분 분석 및 함량평가

- 천연물 기반 건강기능식품, 화장품, 한약제제 및 의약품 소재의 분석 및 지표성분 도출
- 지표 및 구성 성분 동정 및 분리 정제를 통한 표준물질 확보 지표 및 함량 평가

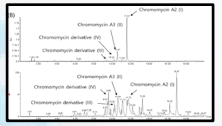


LC-MS/MS

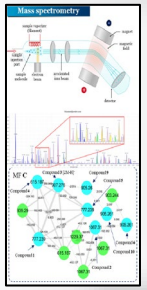


함량 평가

UPLC-QTOF-MS



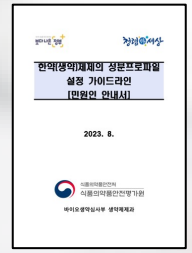
구성 성분 규명



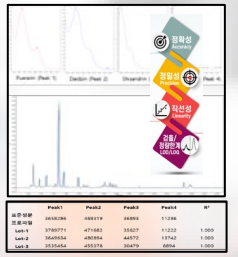
Tentative ID

기준 및 시험법 개발

- 식약처 가이드라인에 기반한 기준 및 시험법 개발 (Method validation)
- GMP 생산시설 환경에 맞는 분석법 개발을 통한 소재 표준화 및 배치간 동등성 확보



성분프로파일

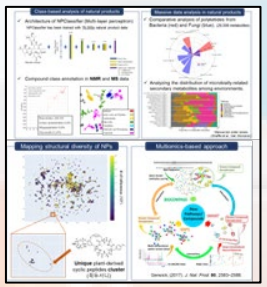


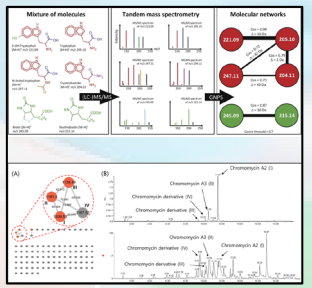
Method validation

확인시험

신규 및 대체 소재 도출

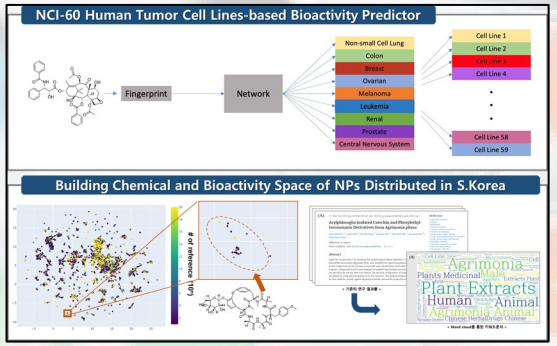
- 인포매틱스 기반 화학적 다양성 평가를 통한 신규 소재 도출
- 대사체 프로파일링 기반의 대체 천연물 소재 도출





A.I. 기반 *in-silico screening*

- 인공지능 및 딥뉴럴넷을 활용한 소재 활성 예측 및 발굴



숭실대학교 약학대학 생약학 연구실 김현우

Academic Career of Prof. Hyunwoo Kim

2012-2018

서울대학교 약학대학
박사 (생약학)

2018-2019

서울대학교 약학대학
박사후 연구원

2019-2022

Scripps Institution of Oceanography
University of California San Diego
Postdoctoral fellow

동국대학교 약학대학
생약학 연구실 김원우

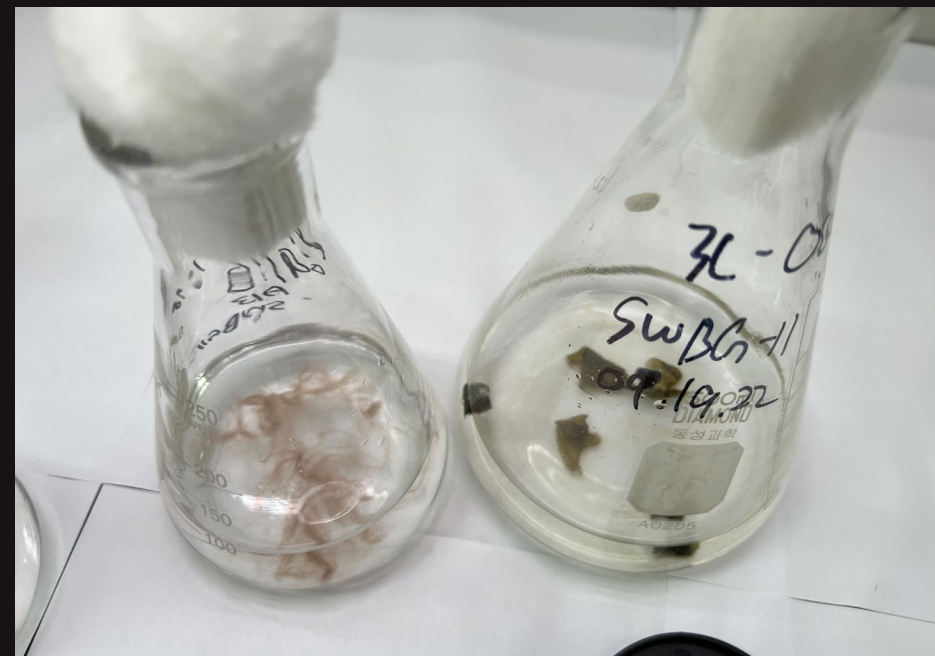
02

소재: Novel source
- Filamentous Cyanobacteria

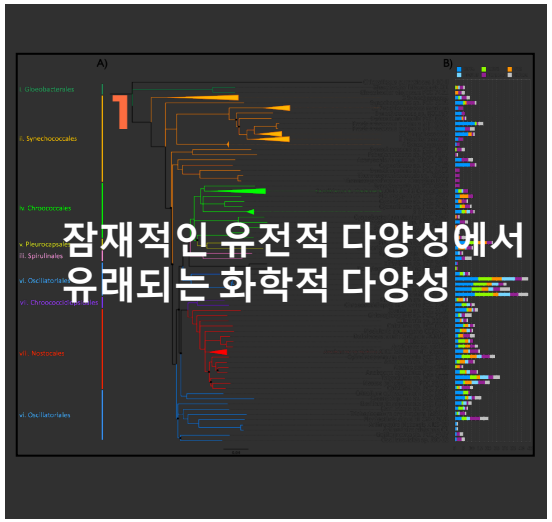
Photosynthetic prokaryotes, only bacterial group that produce molecular oxygen.

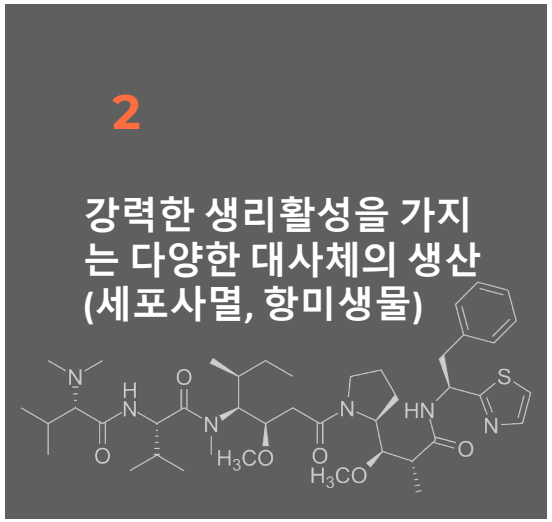
Chemodiversity of Cyanobacteria is still veiled, but various results including genomic research promise the potential of the Cyanobacteria as a producer of unique and bioactive secondary metabolites.

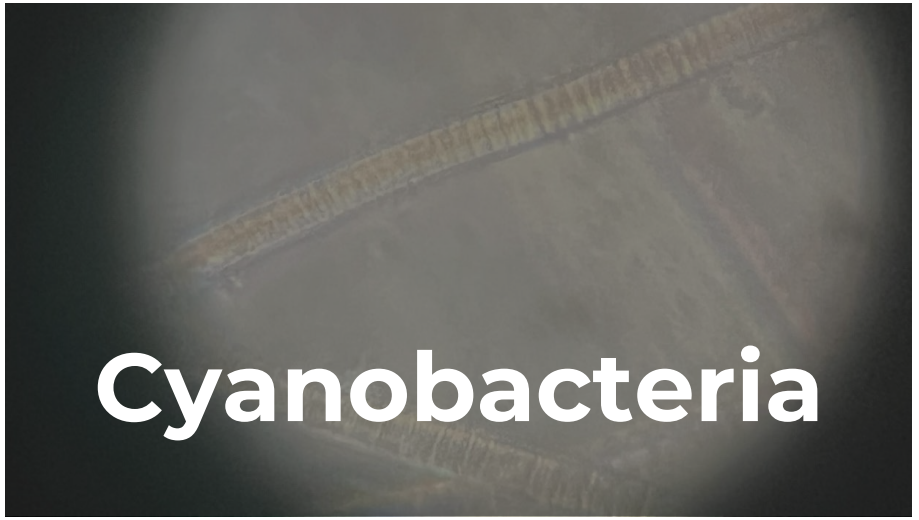
Leptolyngbya

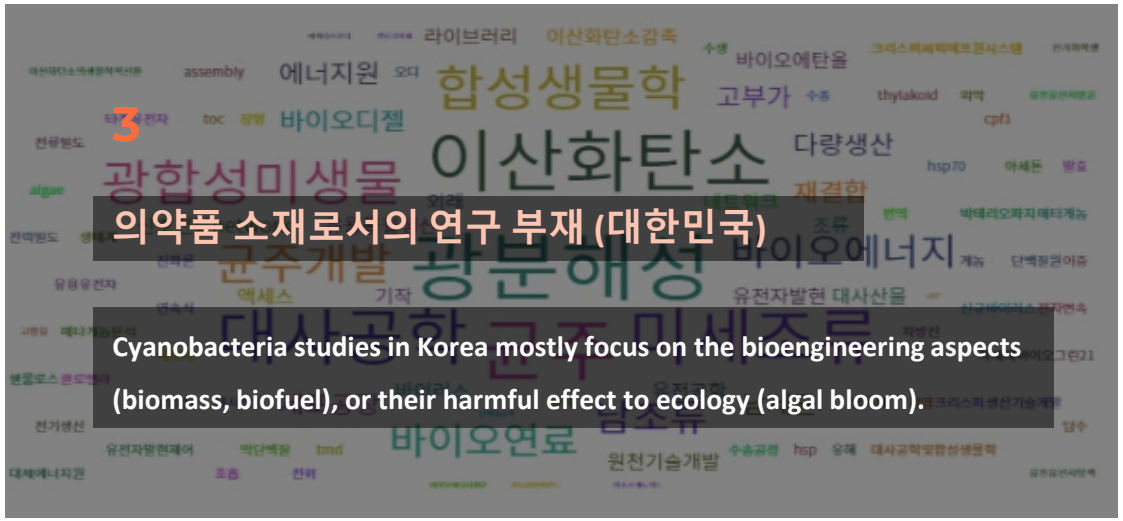


Cyanobacteria culture









저희 연구실에서는
시아노박테리아의 배양 및
대사체의 분리 분석을 수행하고 있습니다

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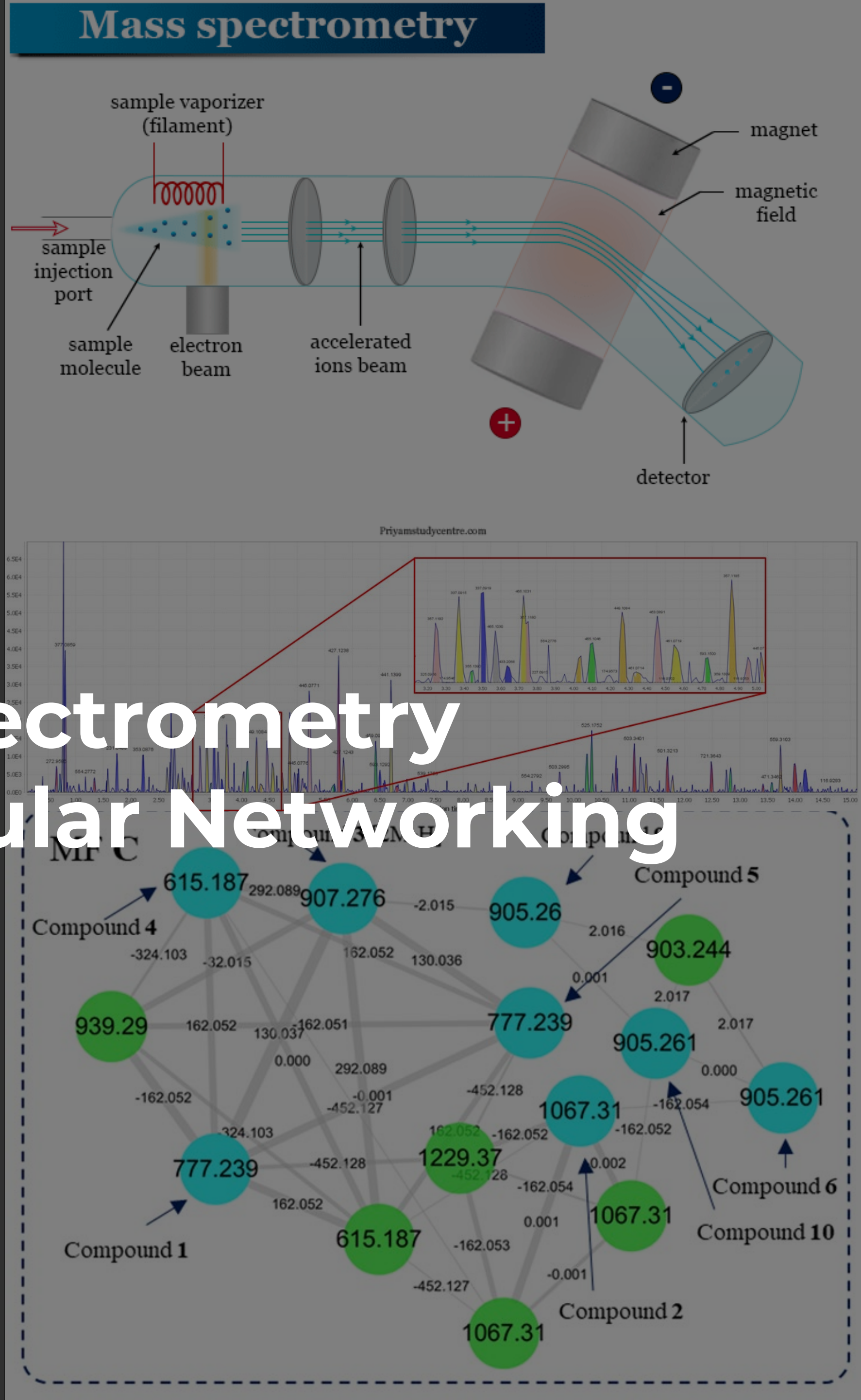
04

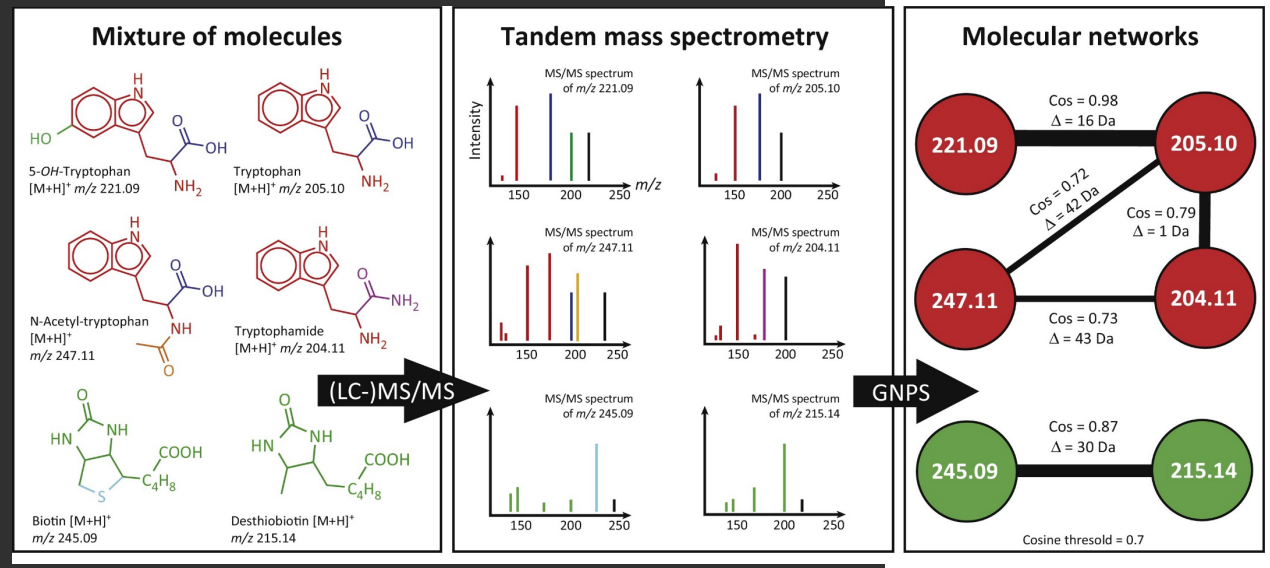
Mass spectrometry is the most appropriate analysis technology to explore the complexity of natural products.

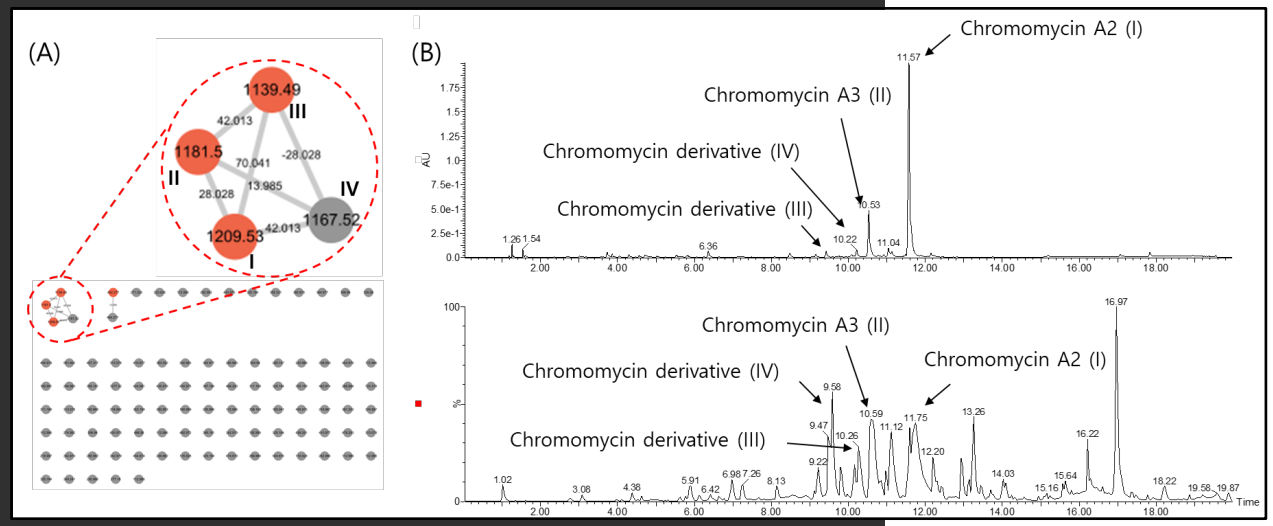
Along with informatics and AI, mass spectrometry is getting powerful to identify secondary metabolites in natural products.

기술:
Mass spectrometry & Molecular Networking



생약학 연구실 김현우





Strength of MS²-based Molecular Network

A. Holistic analysis of secondary metabolites

B. Facile identification of metabolites

C. Discovery of novel structures

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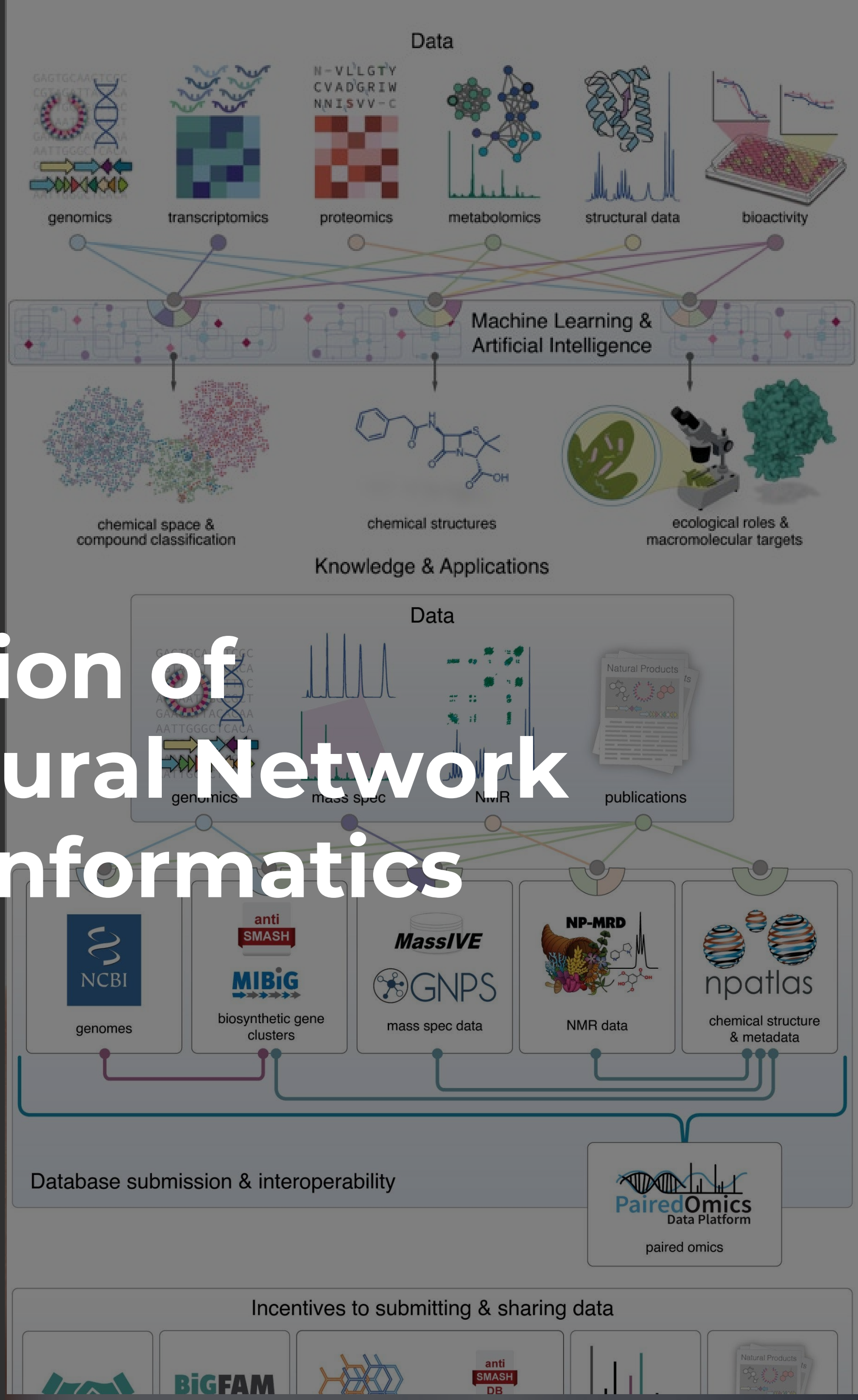
06

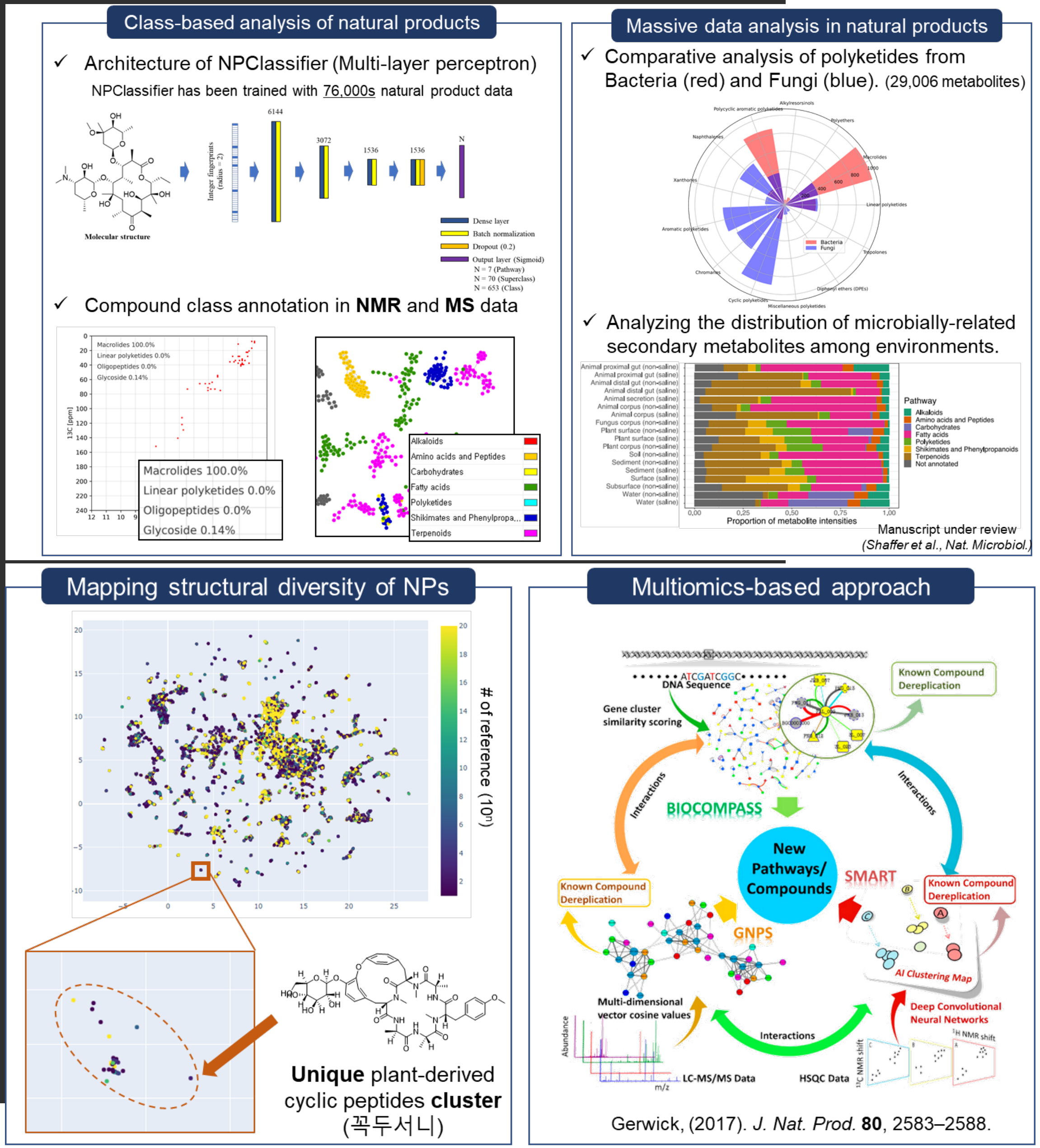
Expanding the natural product research using A.I.

A.I. and informatics allow efficient natural product discovery by new dereplication methodology and natural product repositioning.

기술: Application of Deep Neural Network & Cheminformatics



생약학 연구실 김현우


Class-based analysis of natural products
✓ Architecture of NPClassifier (Multi-layer perceptron)
NPClassifier has been trained with 76,000s natural product data
Molecular structure
Dense layer
Batch normalization
Dropout (0.2)
Output layer (Sigmoid)
✓ Compound class annotation in NMR and MS data
Macrolides 100.0%
Linear polyketides 0.0%
Oligopeptides 0.0%
Glycoside 0.14%
Alkaloids
Amino acids and Peptides
Carbohydrates
Fatty acids
Polyketides
Terpenoids
Massive data analysis in natural products
✓ Comparative analysis of polyketides from Bacteria (red) and Fungi (blue). (29,006 metabolites)
✓ Analyzing the distribution of microbially-related secondary metabolites among environments.
Pathway
Proportion of metabolite intensities
Manuscript under review
(Shaffer et al., Nat. Microbiol.)
Mapping structural diversity of NPs
# of reference (10ⁿ)
Unique plant-derived cyclic peptides cluster (꼭두서니)
Multiomics-based approach
DNA Sequence
Gene cluster similarity scoring
Known Compound Dereplication
BIOCOMPASS
New Pathways/ Compounds
SMART
GNPS
Interactions
AI Clustering Map
Deep Convolutional Neural Networks
Multi-dimensional vector cosine values
LC-MS/MS Data
HSQC Data
Gerwick, (2017). J. Nat. Prod. 80, 2583–2588.

Recently, AI changes the natural product research.

A. Structure elucidation of NPs.

B. Bigdata analysis of NP databases

C. Discovery of novel structures

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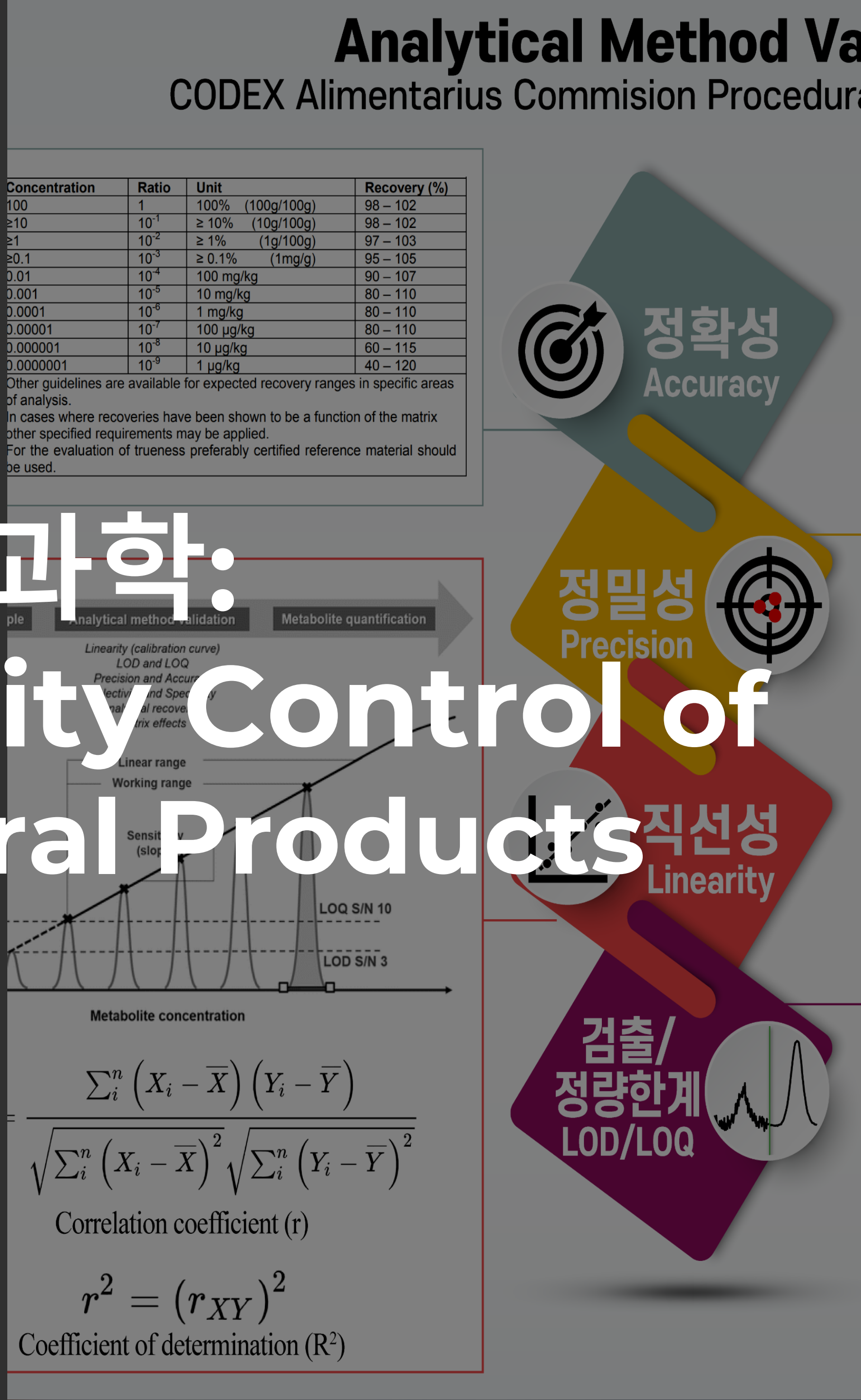
08

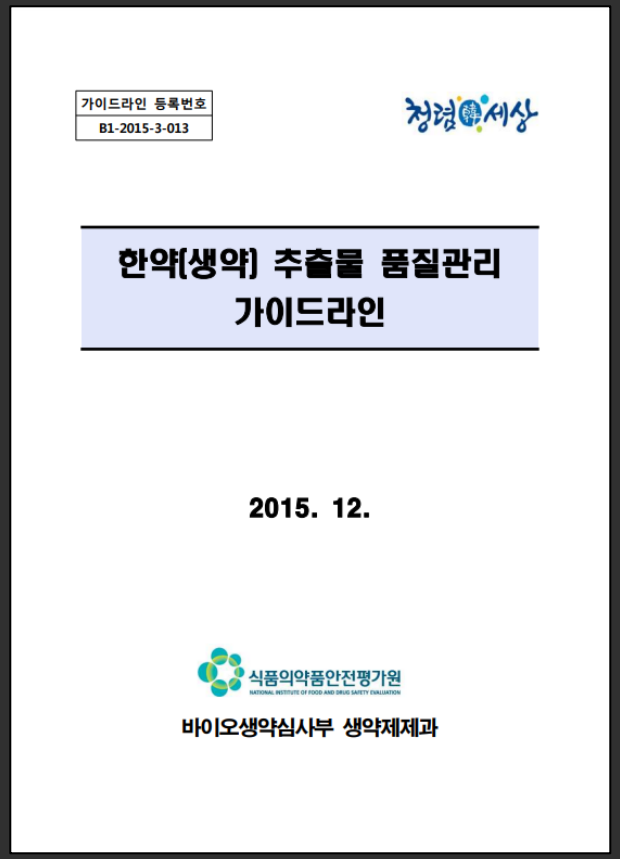
Standardization of Natural Products & Botanical Drugs

Quantitative and Qualitative analysis using HPLC, UPLC-qTOF-MS, and NMR allows to control the quality of natural products and botanical drugs scientifically.

규제 과학: Quality Control of Natural Products



생약학 연구실 김현우


가이드라인 등록번호
B1-2015-3-013

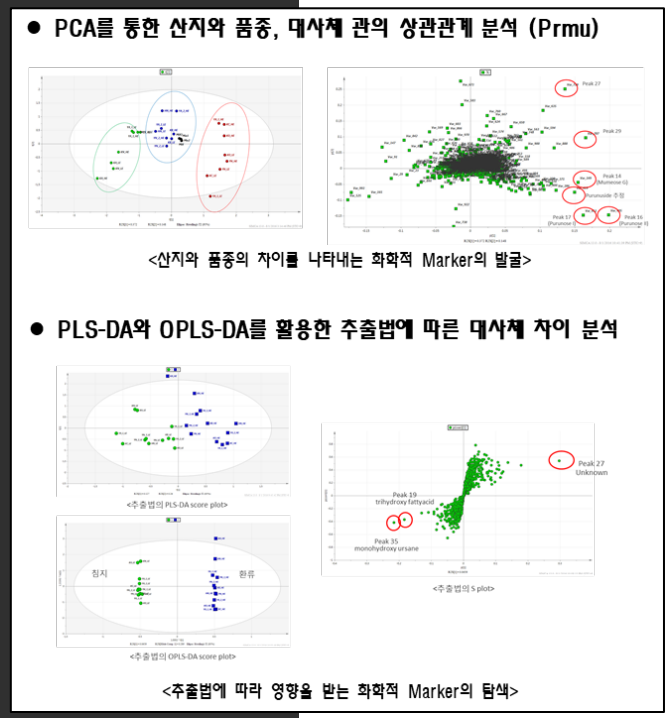
청렴세상

한약(생약) 추출물 품질관리 가이드라인

2015. 12.

식품의약품안전평가원
NATIONAL INSTITUTE OF FOOD AND DRUG SAFETY EVALUATION

바이오생약심사부 생약제제과


● PCA를 통한 산지와 품종, 대사체 관의 상관관계 분석 (Prmu)

<산지와 품종의 차이를 나타내는 화학적 Marker의 발굴>

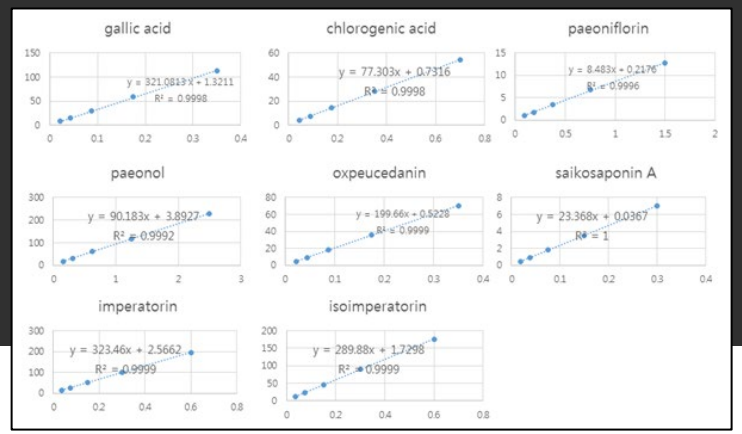
● PLS-DA와 OPLS-DA를 활용한 추출법에 따른 대사체 차이 분석

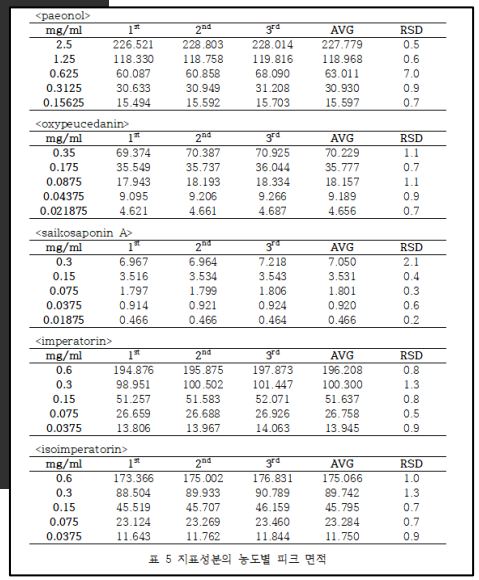
<추출법의 PLS-DA score plot>

<추출법의 S plot>

<추출법의 OPLS-DA score plot>

<주출법에 따라 영향을 받는 화학적 Marker의 탐색>




<paeonol>

mg/ml	1st	2nd	3rd	AVG	RSD
2.5	226.521	228.803	228.014	227.779	0.5
1.25	118.330	118.758	119.816	118.968	0.6
0.625	60.087	60.858	68.090	63.011	7.0
0.3125	30.633	30.949	31.208	30.930	0.9
0.15625	15.494	15.592	15.703	15.597	0.7

<oxypeucedanin>

mg/ml	1st	2nd	3rd	AVG	RSD
0.35	69.374	70.387	70.925	70.229	1.1
0.175	35.549	35.737	36.044	35.777	0.7
0.0875	17.943	18.193	18.334	18.157	1.1
0.04375	9.095	9.206	9.266	9.189	0.9
0.021875	4.621	4.661	4.687	4.656	0.7

<saikosaponin A>

mg/ml	1st	2nd	3rd	AVG	RSD
0.3	6.967	6.964	7.218	7.050	2.1
0.15	3.516	3.534	3.543	3.531	0.4
0.075	1.797	1.799	1.806	1.801	0.3
0.0375	0.914	0.921	0.924	0.920	0.6
0.01875	0.466	0.466	0.464	0.466	0.2

<imperatorin>

mg/ml	1st	2nd	3rd	AVG	RSD
0.6	194.876	195.875	197.873	196.208	0.8
0.3	98.951	100.502	101.447	100.300	1.3
0.15	51.257	51.583	52.071	51.637	0.8
0.075	26.659	26.688	26.926	26.758	0.5
0.0375	13.806	13.967	14.063	13.945	0.9

<isoimperatorin>

mg/ml	1st	2nd	3rd	AVG	RSD
0.6	173.366	175.002	176.831	175.066	1.0
0.3	88.504	89.933	90.789	89.742	1.3
0.15	45.519	45.707	46.159	45.795	0.7
0.075	23.124	23.269	23.460	23.284	0.7
0.0375	11.643	11.762	11.844	11.750	0.9

표 5 지표성분의 농도별 피크 면적

Quality control technology is the basic, but the most important in the drug development

A. Quality control of raw material

B. Method validation

C. Metabolomics-based guidline

JU YEONG NS 케이팜스 비체담

Basic technique & Infrastructure

1. Isolation and purification of small molecules

Isolation and purification of secondary metabolites from natural products was set up and now available.

2. Application of UPLC-Q-TOF MS/MS & UPLC-QQQ-MS/MS

Parameters and method was set up and modified for MS2 based MN.

Qualitative and quantitative analysis of chemical substances in natural products

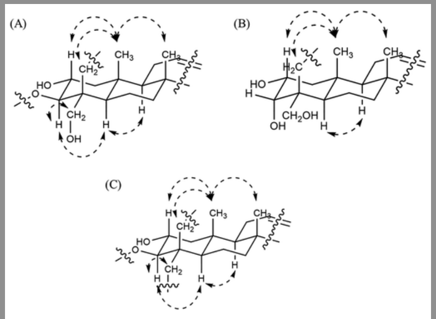
3. Structure elucidation of molecules using NMR, MS, and ECD

Full assignment of molecular structure and absolute configuration from isolation and purification process.

4. Cheminformatic approaches for natural products discovery

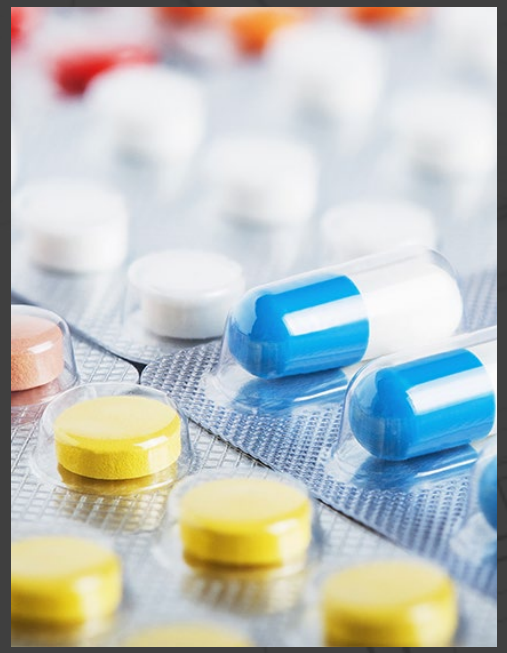
Application of AI and informatics to discover bioactive natural products.

< Preparative HPLC system >



< Structure elucidation >

< UPLC-QTOF-MS system >



Pharmaceutics
(제약회사)

Research Institute
(연구소)

Academia & Faculty
(교수 및 연구자)

- 제약회사:
  원료의약품 품질관리, 천연물 의약품 개발
- 연구소:
  천연물 연구 기술 개발, 의약품 후보물질 도출
- 학계:
  교수 및 연구원

Career


TOGETHER
RECRUITMENT
QUALIFICATION
30%
Benefits
Bonus
dates

Thanks!!