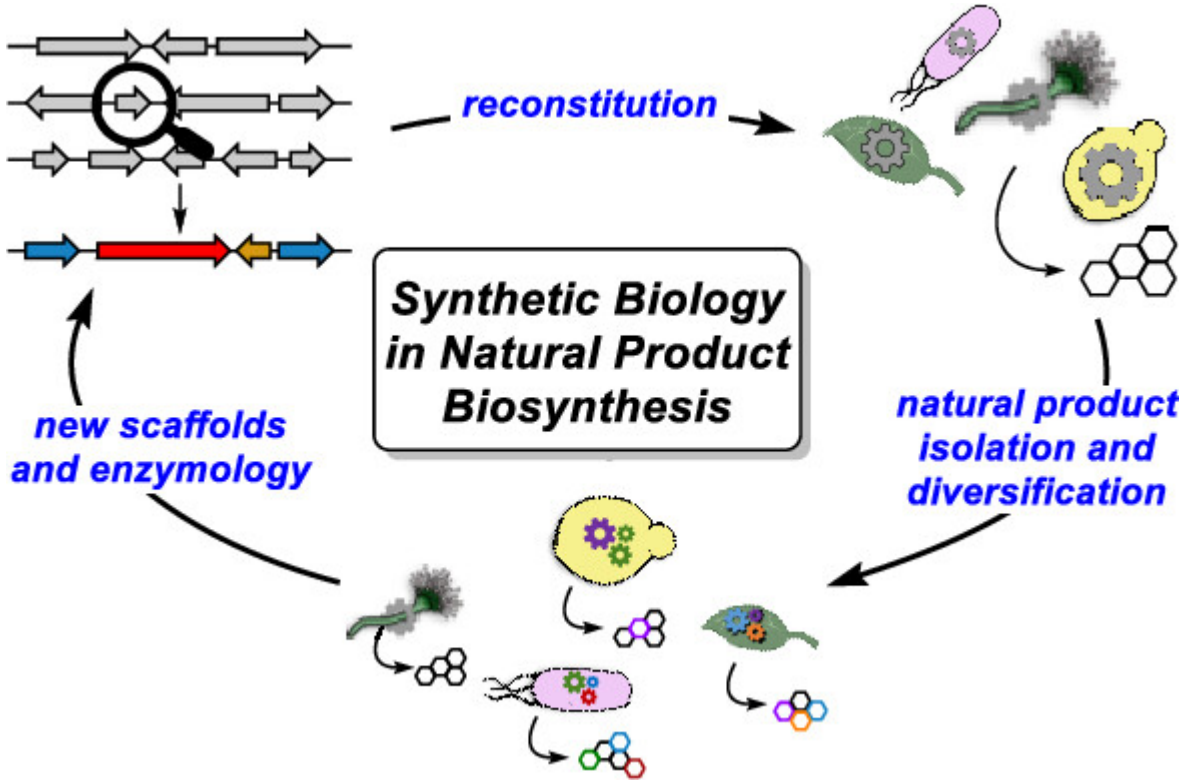
A Brief Overview of Synthetic Biology in Natural Product Biosynthesis



Grace Fleury

Literature Presentation

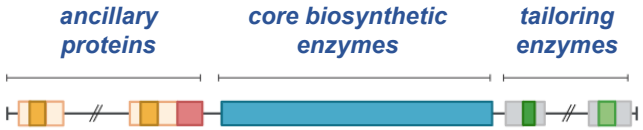
October 31st, 2025

Chem. Rev., **2025**, *125* (7), 3814–3931

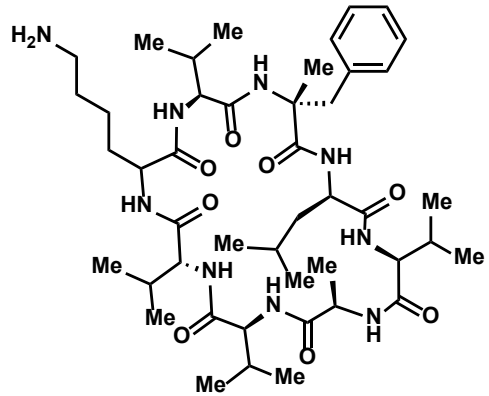
Synthetic Biology in Natural Product Biosynthesis

Advances in Tools for Natural Product Discovery

- **Bioinformatics and Machine Learning**



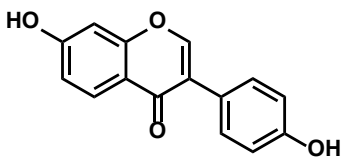
- **Synthetic Biology Tools for Mining Silent BGCs**



surugamide I

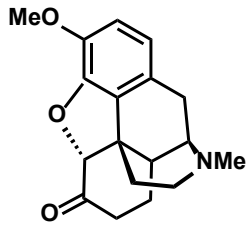
Heterologous Expression Natural Product Pathways

- **Bacteria**



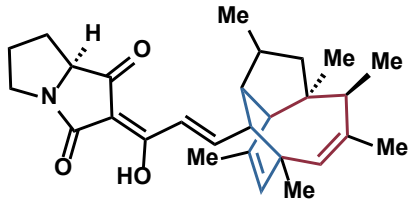
Daidzein

- **Yeast**



hydrocodone

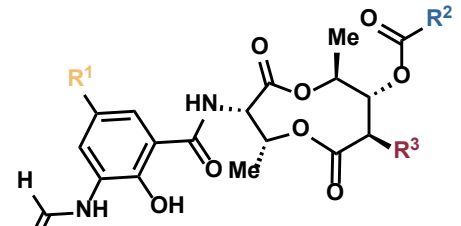
- **Fungi**



(-)-PF-1018

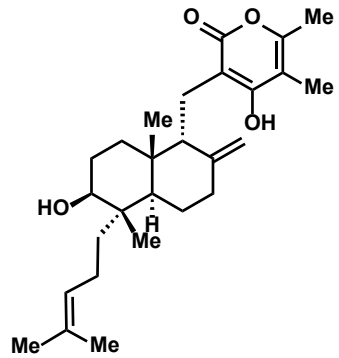
Structural Diversification of Natural Products

- **Redirecting Biosynthesis**



antimycins
380 derivatives

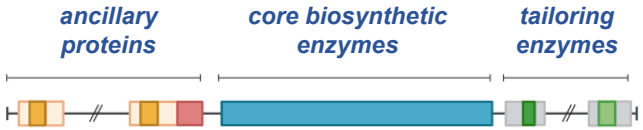
- **Combinatorial Biosynthesis**



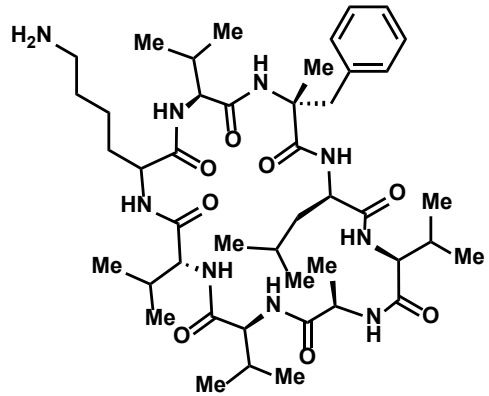
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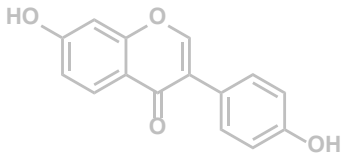
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surugamide I

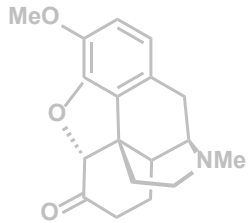
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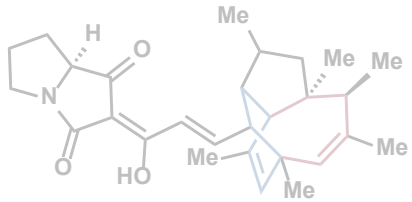
Daidzein

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hydrocodone

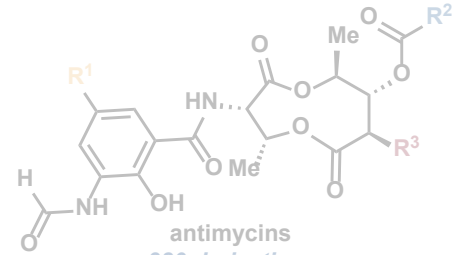
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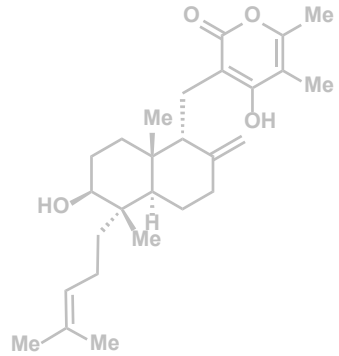
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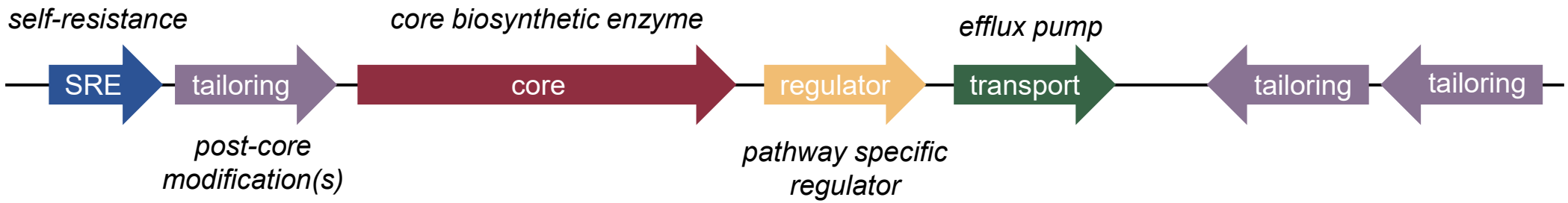


antimycins
380 derivatives

- **Combinatorial Biosynthesis**



Advances in Tools in Natural Product Discovery:
Biosynthetic Gene Clusters



- Biosynthetic gene clusters (BGCs) are comprised of genes responsible for biosynthesis of natural products
  - Core enzymes:
    - Polymerizing (e.g. PKSs, NRPSs, TSs, TCs)
    - Class-defining reaction catalysts (e.g. CDPSs, PALs, RiPP)
  - Tailoring enzymes:
    - transferases, cyclases, hydrolases, redox-neutral & redox-active enzymes

Chem. Rev., **2025**, *125* (7), 3814–3931

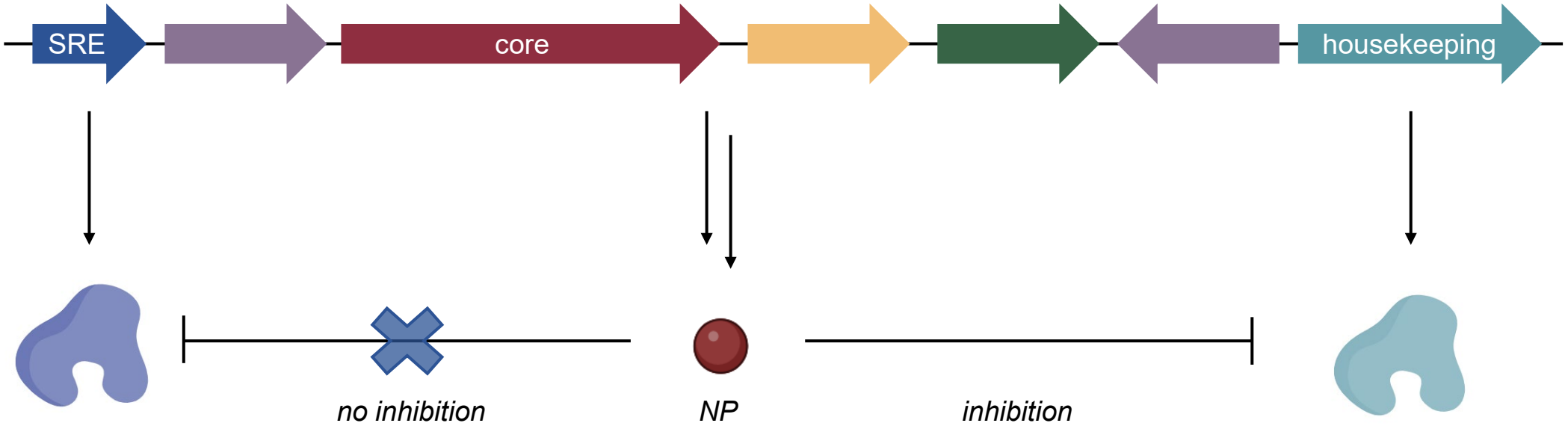
Advances in Tools in Natural Product Discovery:
Genome Mining Tools

tool	*natural product classes*	*kingdoms*
SMURF	**nonribosomal peptides, polyketides, NRP-PK hybrids, indole alkaloids**	**fungal**
antiSMASH	**most major NP classes (81 BGC types)**	**bacteria, fungal, plant**
PRISM	**NRP, PK, RiPPs, β-lactams, alkaloids, phosphonates, cyclodipeptides, bisindoles, aminoglycosides**	**fungal, bacterial**
ClusterFinder	**NRP, PK, NRP-PK hybrides, terpenes, saccharides**	**bacterial**
BAGEL	**RiPPs**	**bacterial**
RiPPMiner	**RiPPs (including lasso peptides)**	**n/a**
RODEO	**lasso peptides**	**dependent on known RiPPs**
DeepRIPP	**RiPPs**	**bacterial**
GECCO	**NRP, PK, RiPPs, terpenes, alkaloids, saccharides**	**bacterial**
DeepBGC	**NRP, PK, RiPPs, terpenes, alkaloids, saccharides**	**bacterial**
BiGCARP	**NRP, PK, RiPPs, terpenes, alkaloids, saccharides**	**bacterial**

Chem. Rev., **2025**, *125* (7), 3814–3931: *Fungal Genetics and Biology*, **2010**, *47* (9), 736−741: *Nucleic Acids Res.*, **2015**, *43* (20), 9645−9662: *Cell*, **2014**, *158* (2), 412−421: *Nucleic Acids Res.*, **2023**, *51* (W1), W46− W50: *Nucleic Acids Res.*, **2011**, *39* (suppl_2), W339−W346

Advances in Tools in Natural Product Discovery:

Predicting Bioactivity from Self Resistance

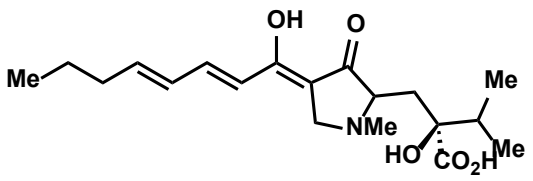


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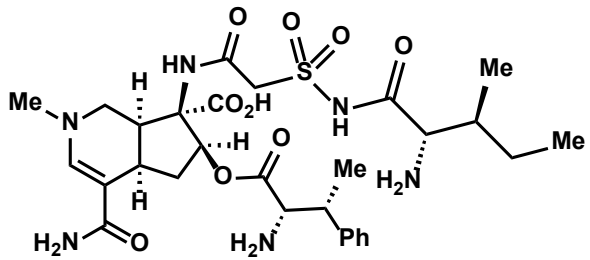
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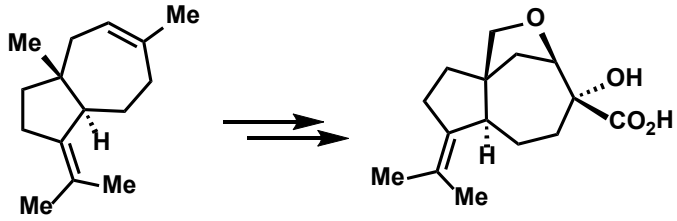
- Assign biological activity of natural products with known BGCs
- Discover BGCs of known natural products with known bioactivity
- Find new natural products or rediscover known compounds with biological activity against a desired target



harzianic acid
herbicide/fungicide
(acetohydroxyacid synthase)



SB-203208
antibiotic
(Ile-tRNA synthetase)



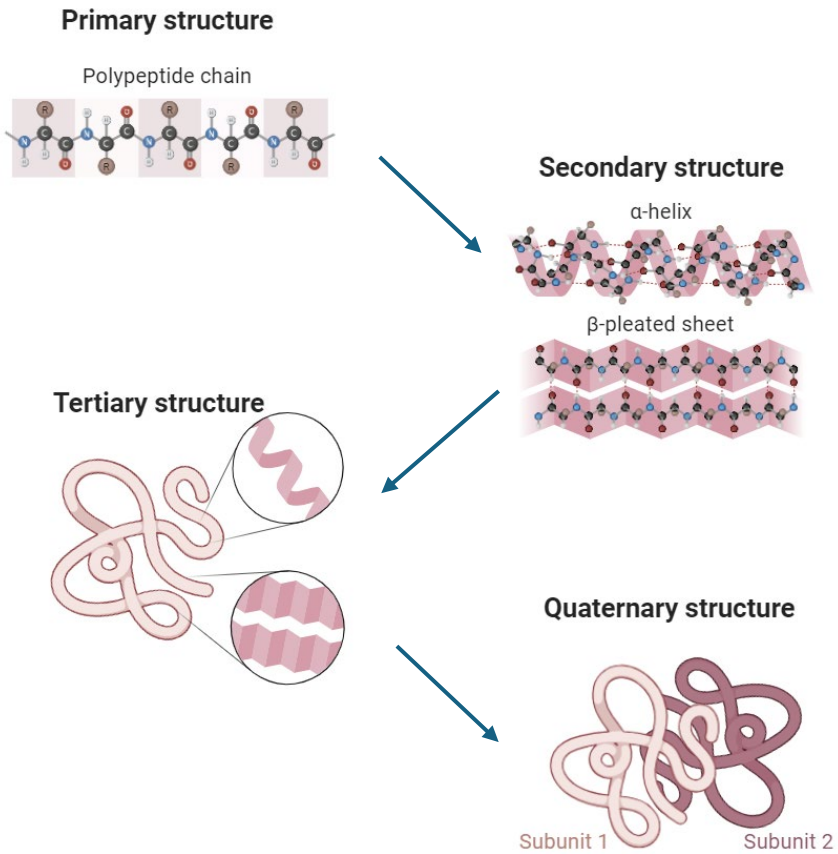
(-)-dauccane
(new sesquiterpene)

aspterric acid
herbicide
(dihydroxy-acid dehydratase)

J. Am. Chem. Soc. 2021, 143, 25, 9575–9584: *Nature Commun.*, **2019**, *10*, 184: *Nature*, **2018**, *559*, 415-418

Advances in Tools in Natural Product Discovery:
Prediction of Protein Function

- Proteins in BGCs are often assessed for functions using characterized enzyme sequences
  - Various databases of similar sequences
  - *can often be inaccurate*
- If can't be predicted then labeled hypothetical proteins or domains of unknown function
  - *can mislead or impede biosynthetic studies*
  - can discover catalysts of new reactions or novel mechanisms

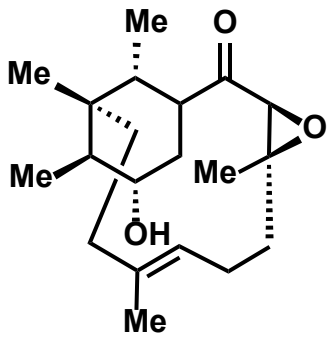


Nat. Commun., **2018**, *9* (1), 1963: *Angew. Chem. Int. Ed.*, **2023**, *62* (47), e202312996: *Nat. Chem. Biol.*, **2017**, *13* (8), 836– 838: *Sci. Adv.*, **2020**, *6* (20), eaba0721

Advances in Tools in Natural Product Discovery:

Prediction of Protein Function -Phomactin





phomactin B4

- Phomactin-producing fungus *Phoma* sp. ATCC 74077 whole gene sequencing yielded 35.53 Mb of genomic data

- antiSMASH narrowed to 25 BGCs (3 related to known cyclases)
  - probe searching revealed no new cyclases with sequence homology to characterized terpene cyclases

- GGPP synthase as new target in genome search
  - 1 GGPP found clustered with putative TC and cytochrome P450 monooxygenase (PhmC)

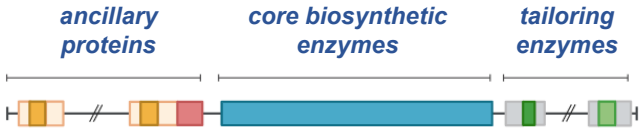
- GGPP synthase and TC tested in *Aspergillus nidulans* A1145
  - found phomactatriene thus enzyme role of TC confirmed

Angew. Chem. Int. Ed., **2023**, *62* (47), No. e202312996

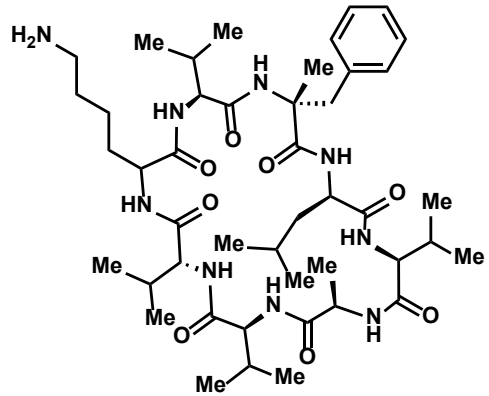
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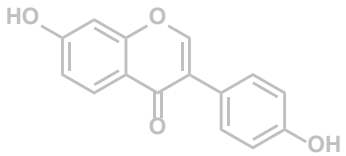
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surugamide I

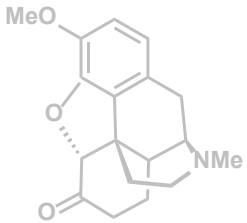
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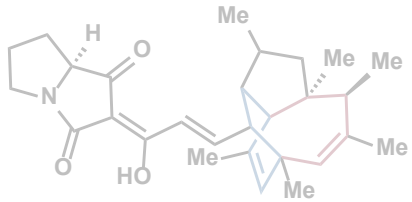
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hydrocodone

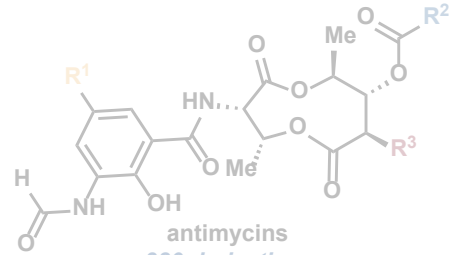
- **Fungi**



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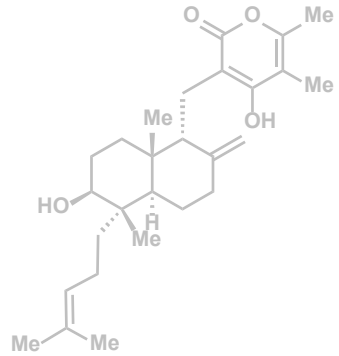
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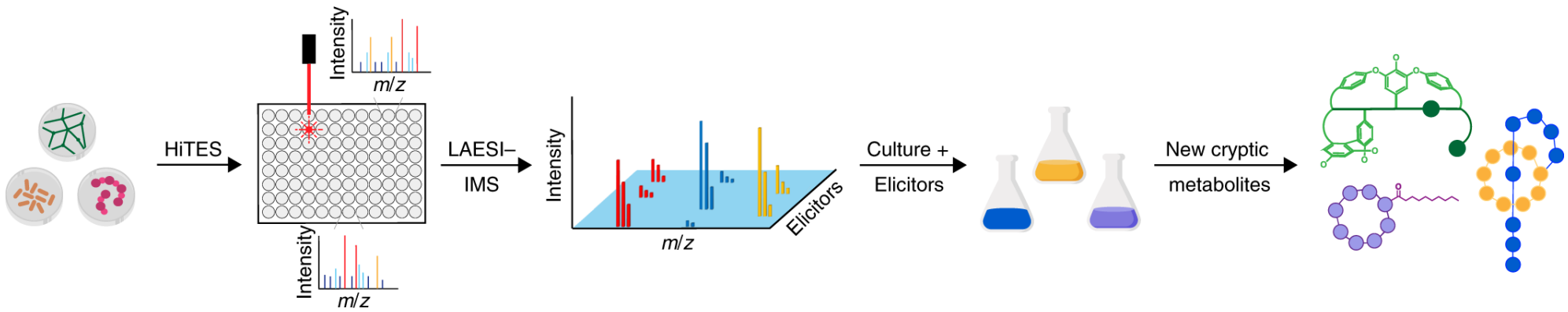
- **Combinatorial Biosynthesis**



Advances in Tools in Natural Product Discovery:

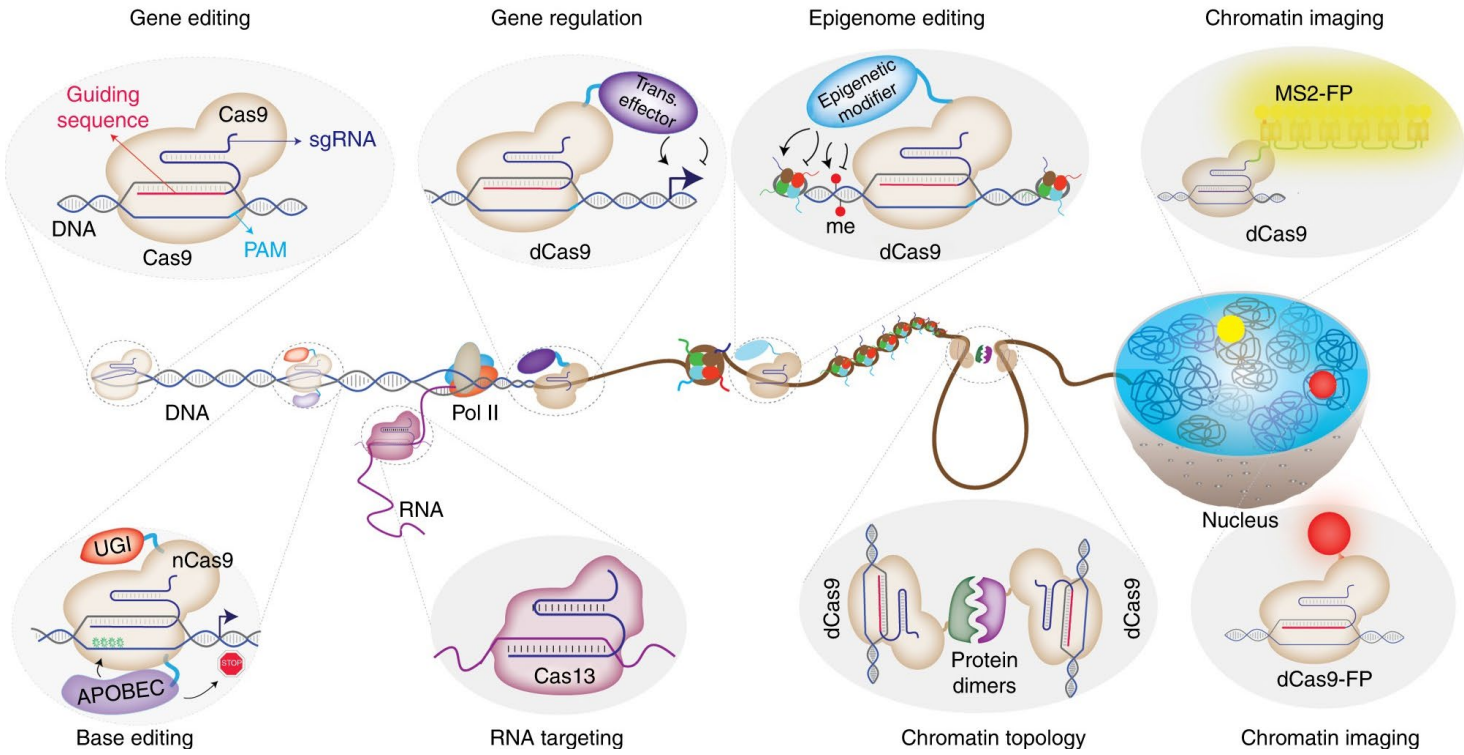
Synthetic Biology Tools for Mining Silent BCGs

- Genetic manipulation of BGC activation in native hosts via artificial control of BGC transcription
  - High Throughput Elicitor Screening
    - Screens for upregulation of BGCs in presence of small molecule activators/elicitor



Advances in Tools in Natural Product Discovery:
Synthetic Biology Tools for Mining Silent BCGs

- Genetic manipulation of BGC activation in native hosts via artificial control of BGC transcription
  - CRISPR interference & CRISPR activation
    - Precise repression and activation of BGCs

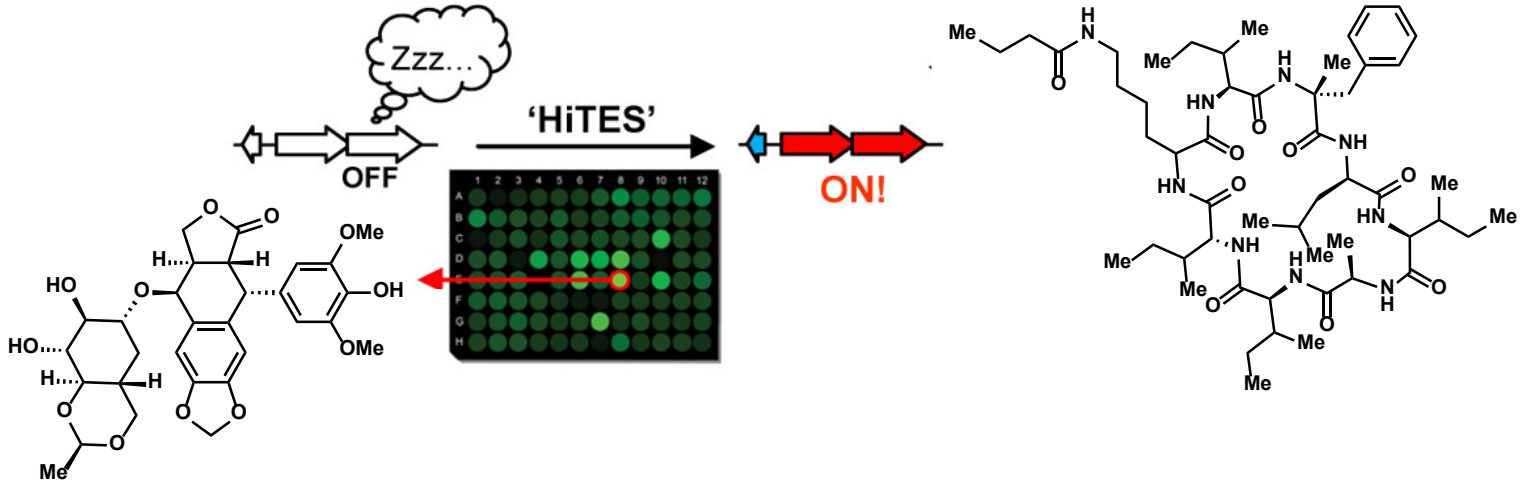


Chem. Rev., **2025**, *125* (7), 3814–3931: *Nature Commun.*, **2018**, *9*, 1911

Advances in Tools in Natural Product Discovery:

Mining Silent BGCs: HiTES

- **H**igh-**T**hroughput **E**licitor **S**creening (HiTES) by Seyedsayamdost
  - Genetic reporter fusions on gene cluster of interest yields activation read out
  - High-throughput screening of diffusible small molecules as potential inducers
  - No heterologous expression required

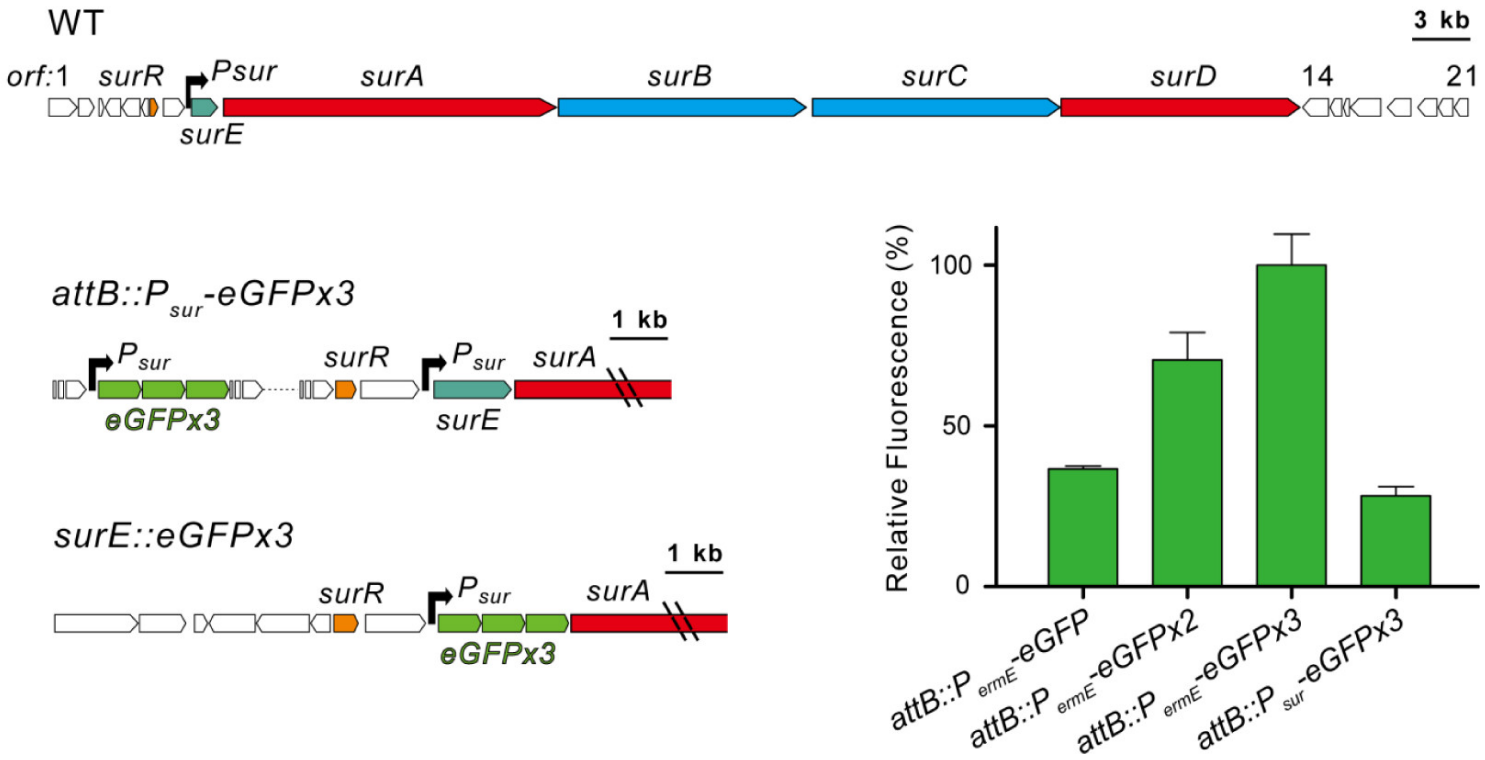


J. Am. Chem. Soc. **2017**, *139* (27), 9203–9212: *Proc. Natl. Acad. Sci. U. S. A.* **2014**, *111* (20), 7266–7271: *Nat. Chem. Biol.*, **2019**, *15* (2), 161–168: *Nat. Chem. Biol.*, **2024**, *20* (7), 924–933: *ACS Chem. Biol.*, **2023**, *18* (8), 1854–1862

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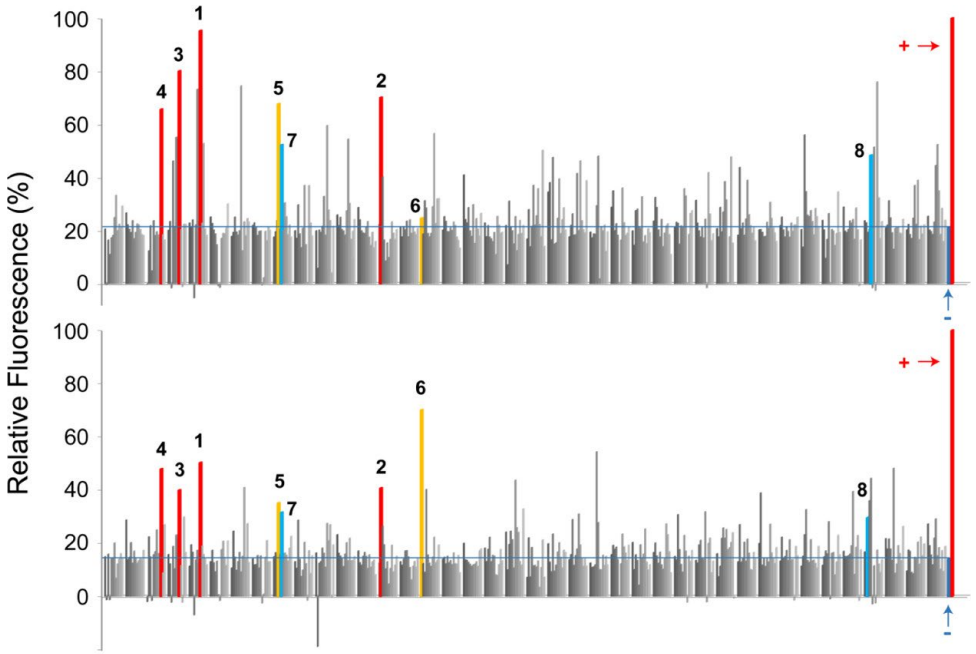
- HiTES in *Streptomyces* spp. (*S. albus* J1074)
- Large nonribosomal peptide synthetase (NRPS) cluster activated
  - Previously no compound associated with it
- eGFP x3 reporter inserted into chromosome

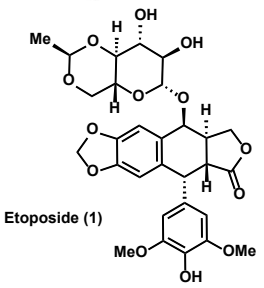


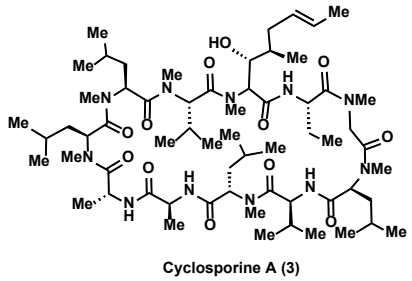
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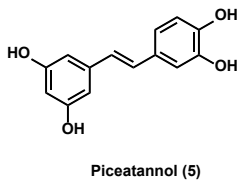
Advances in Tools in Natural Product Discovery:

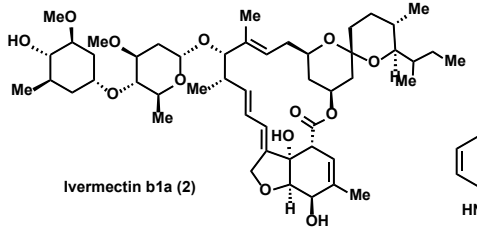
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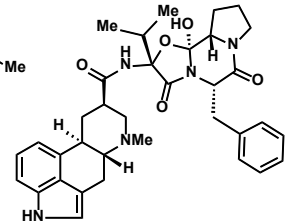


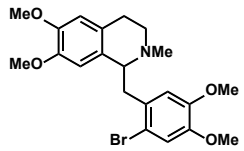

Etoposide (1)


Cyclosporine A (3)


Piceatannol (5)


Ivermectin b1a (2)


Dihydroergocristine (4)

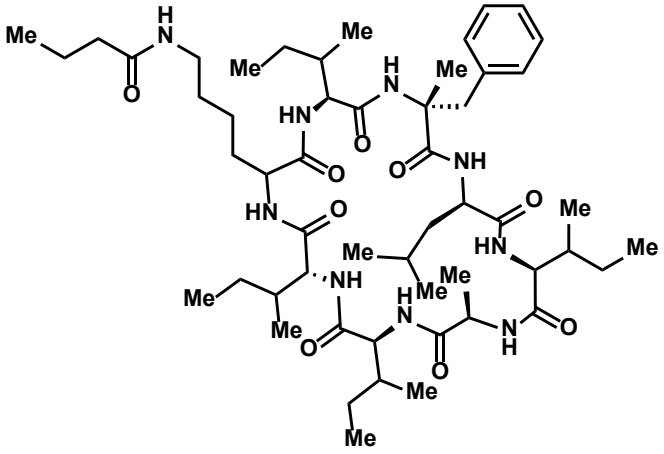

6-Bromolaudanosine (6)

- ~500 natural products screened as elicitors in 96-well plates
- eGFP derived fluorescence analyzed
- Up to 5-fold induction of expression observed

J. Am. Chem. Soc. **2017**, *139* (27), 9203–9212

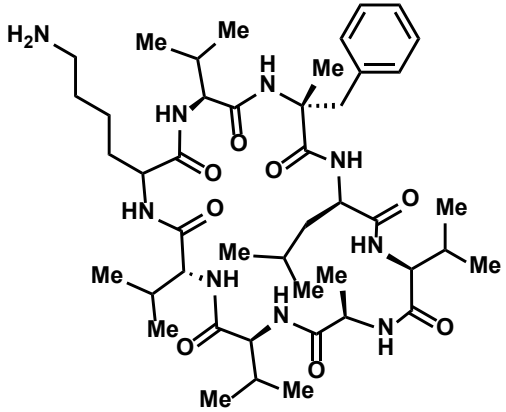
Advances in Tools in Natural Product Discovery:

Mining Silent BGCs: HiTES



acyl-surugamide A

3.5 μM IC_{50} against *Saccharomyces cerevisiae*



surugamide I

9.0 μM IC_{50} against cathespin B

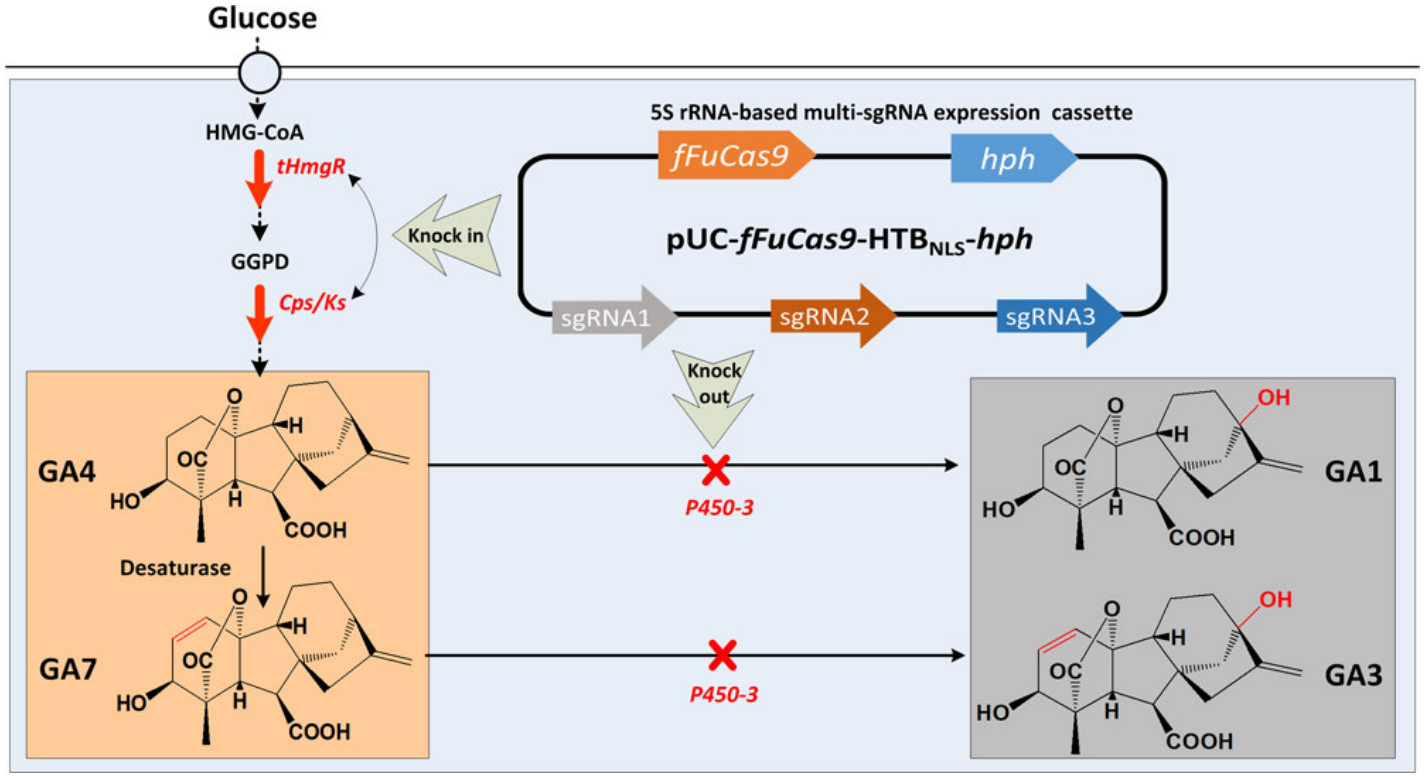
- ~500 natural products screened as elicitors in 96-well plates
- eGFP derived fluorescence analyzed
- Up to 5-fold induction of expression observed
- Several new surugamides isolated

J. Am. Chem. Soc. **2017**, *139* (27), 9203–9212

Advances in Tools in Natural Product Discovery:
Mining Silent BGCs: CRISPR

- Importing, activating, or interfering with CRISPR can lead to BGC activation in native hosts

- *F. fujikuroi* known to produce plant growth hormones gibberellic acids (GAs)
  - promote plant growth and fruit production
  - inefficient and difficult to produce tailor-made GAs

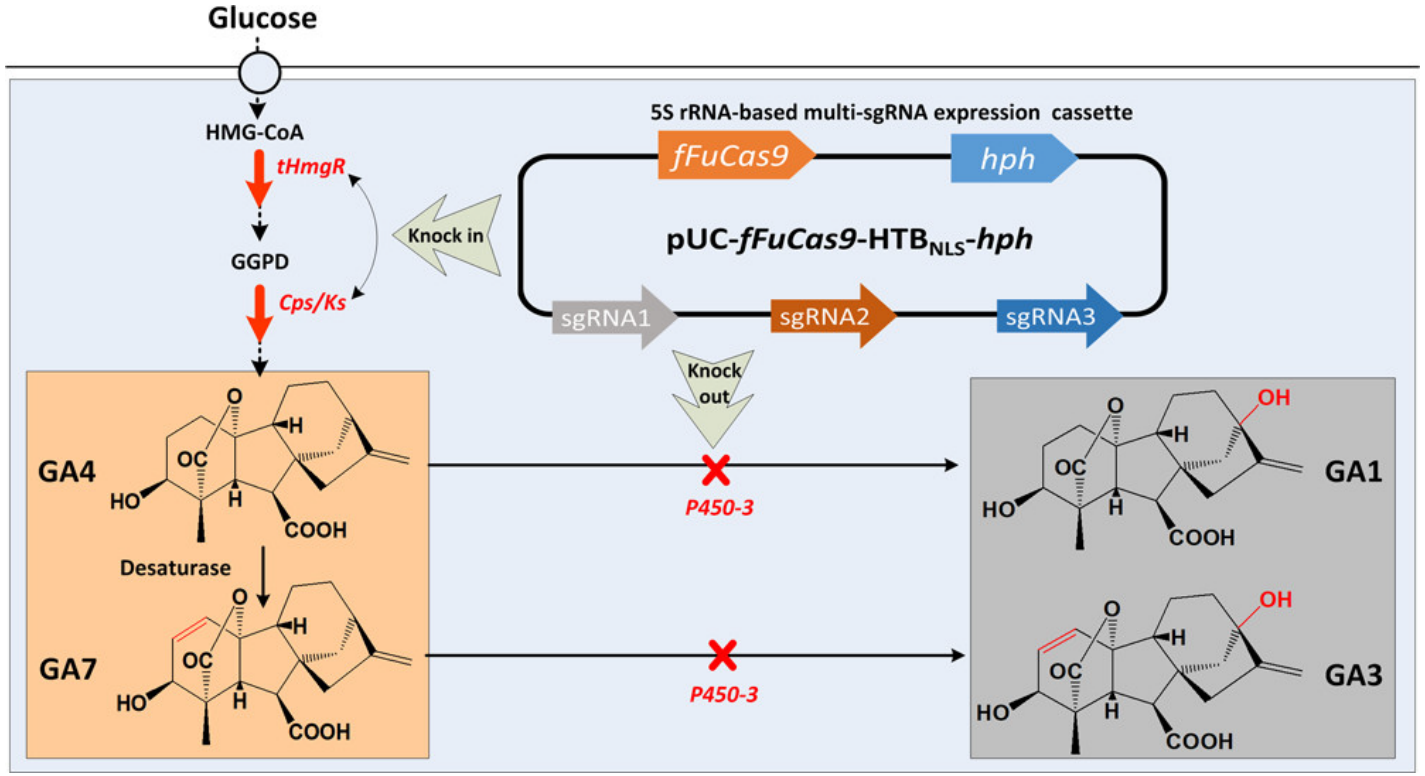


ACS Synth. Biol. **2019**, *8* (2), 445–454

Advances in Tools in Natural Product Discovery:

Mining Silent BGCs: CRISPR

- CRISPR/Cas-9 inertion to fungal nucleus of *F. fujikuroi* to insert *5S rRNA* (RNA polymerase promoter) in proximity to the BGC
  - 79.2% genome editing efficiency
- Additional gene mutations led to 8 fold increase in metabolic flux through the pathway
- Further modifications yielded mixtures of GA products



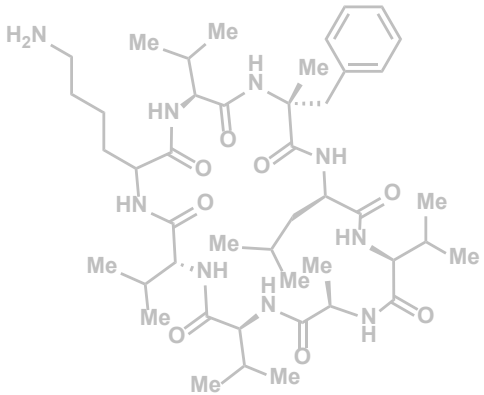
ACS Synth. Biol. **2019**, *8* (2), 445–454

Synthetic Biology in Natural Product Biosynthesis

Advances in Tools for Natural Product Discovery

- Bioinformatics and Machine Learning

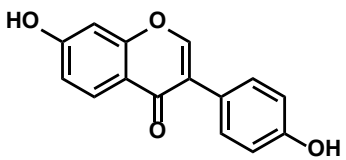
- Synthetic Biology Tools for Mining Silent BGCs



surugamide I

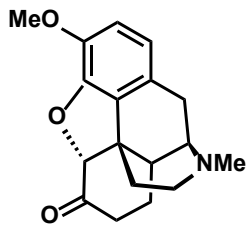
Heterologous Expression Natural Product Pathways

- Bacteria



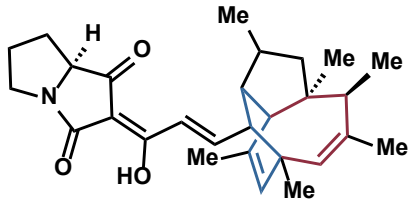
Daidzein

- Yeast



hydrocodone

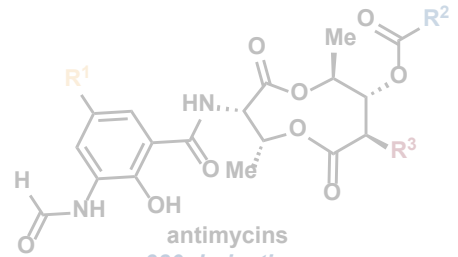
- Fungi



(-)-PF-1018

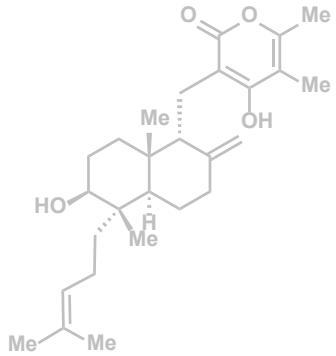
Structural Diversification of Natural Products

- Redirecting Biosynthesis



antimycins
380 derivatives

- Combinatorial Biosynthesis

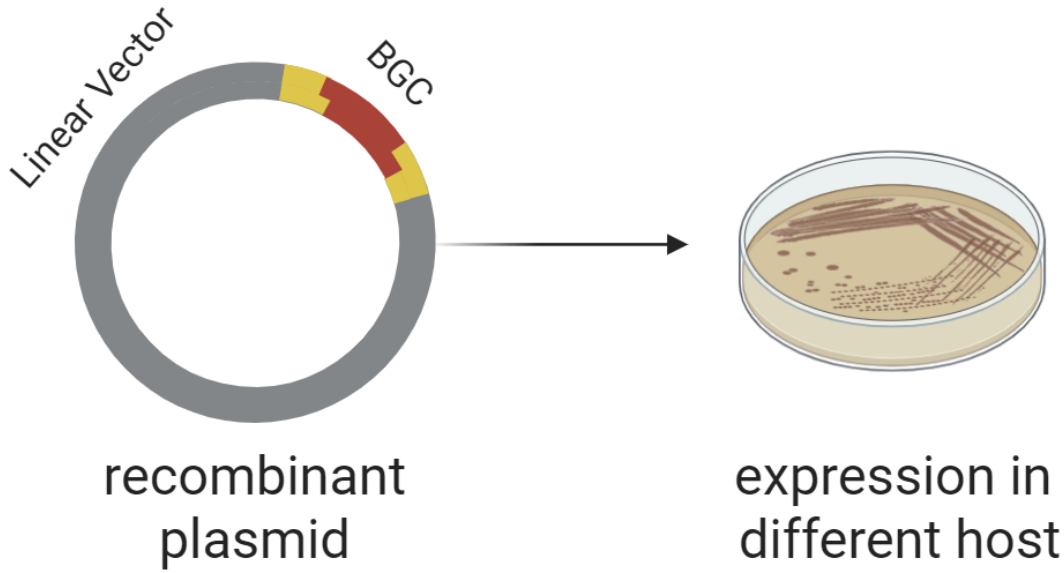


Synthetic Biology in Natural Product Biosynthesis

Heterologous Expression

Heterologous Expression:

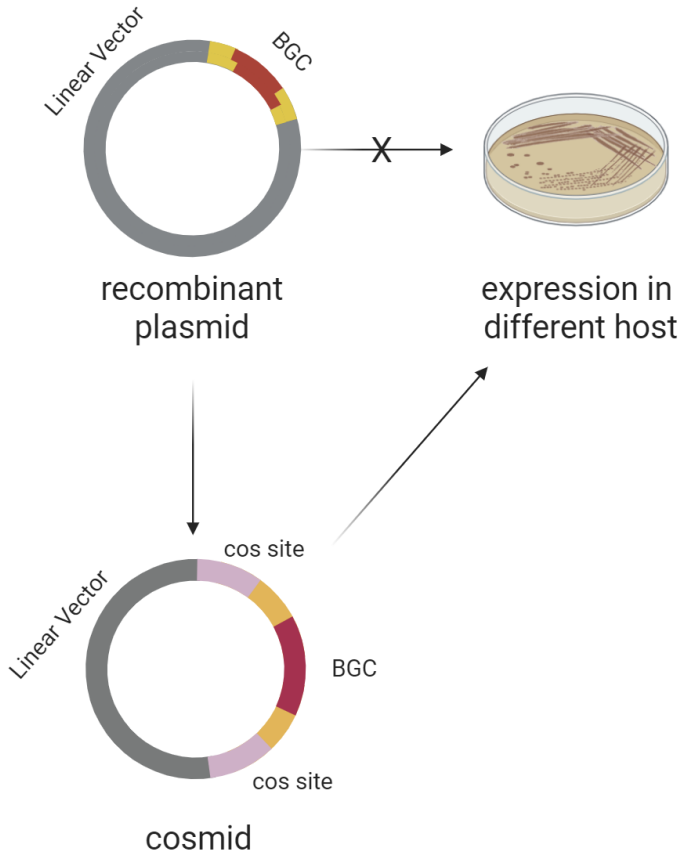
- Analyze biosynthetic pathways and enzymes
- Renewable and increased production of valuable natural products
- Design and production of analogs
- New natural product discovery from cryptic pathways



Chem. Rev., **2025**, *125* (7), 3814–3931

Heterologous Expression:
Cloning Bacterial BGCs into Hosts

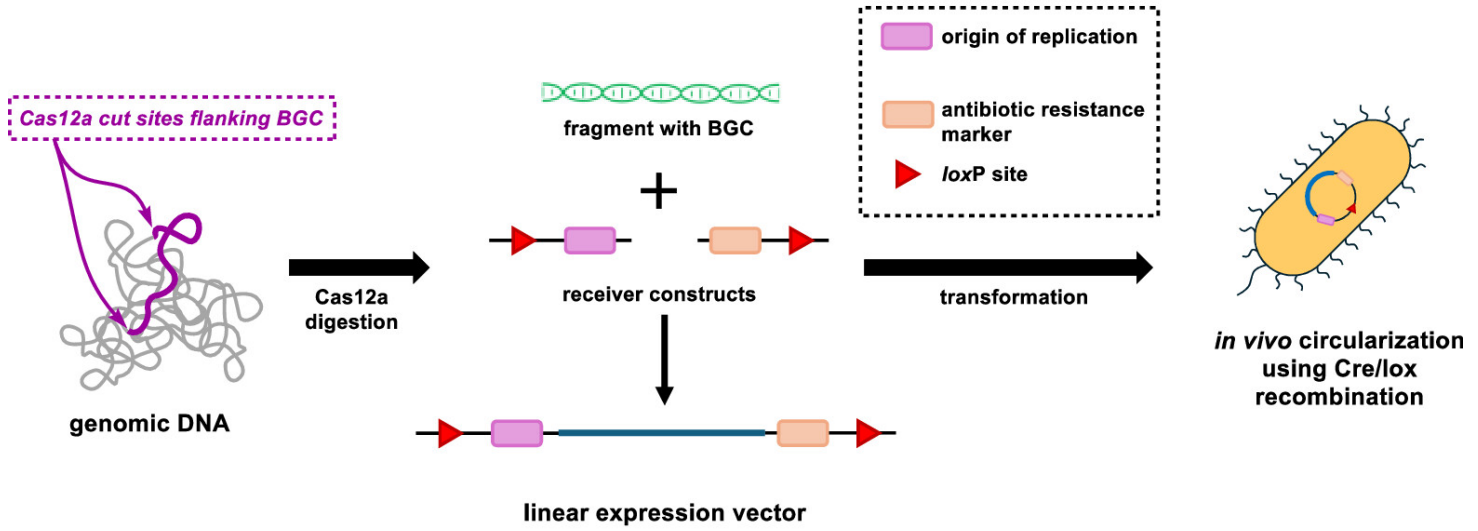
- Cosmids hold ~45 kilobases compared to ~1 to 20 in plasmids
  - libraries exist to screen in hosts
- Bacterial BGCs can be quite large (>100 kb)
  - challenge to get into the host for expression
- Bacterial artificial chromosomes preferred with even greater capacity than cosmids (~80 to 300 kilobases)



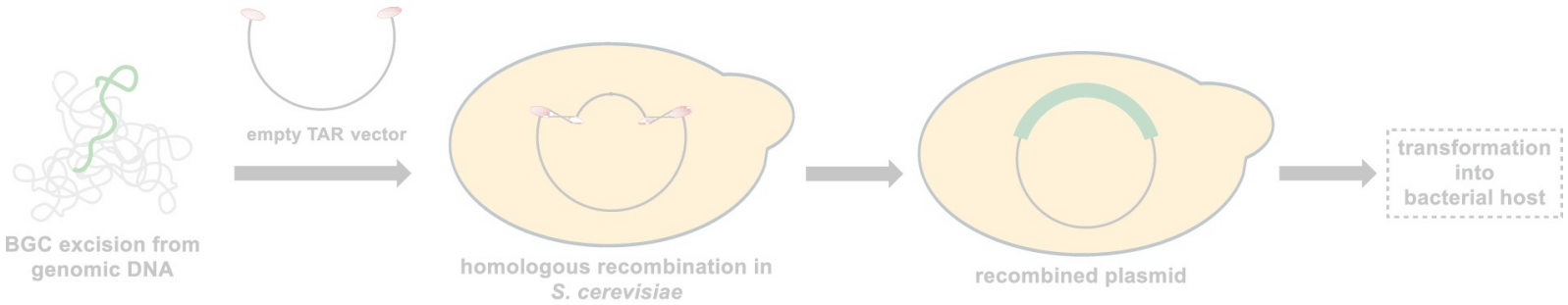
Chem. Rev., **2025**, *125* (7), 3814–3931: *Nature Prot.*, **2007**, *2*, 1297-1305: *Org. Lett.*, **2018**, *20* (24), 7996–7999

Heterologous Expression:
Cloning BGCs into Hosts

CAPTURE



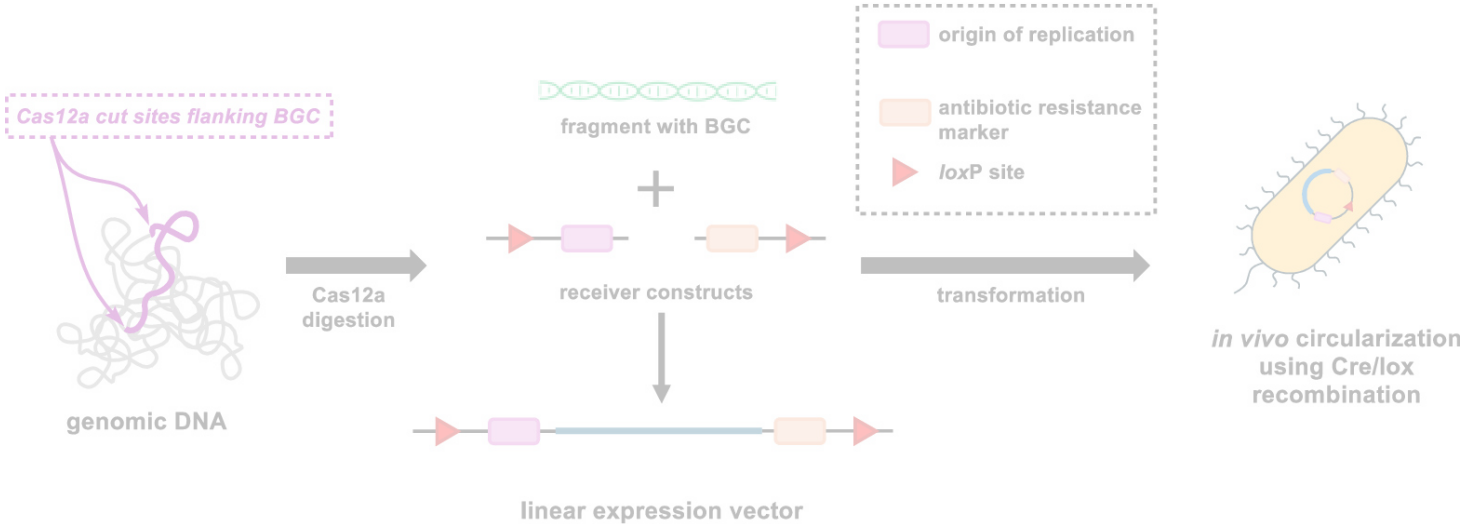
TAR



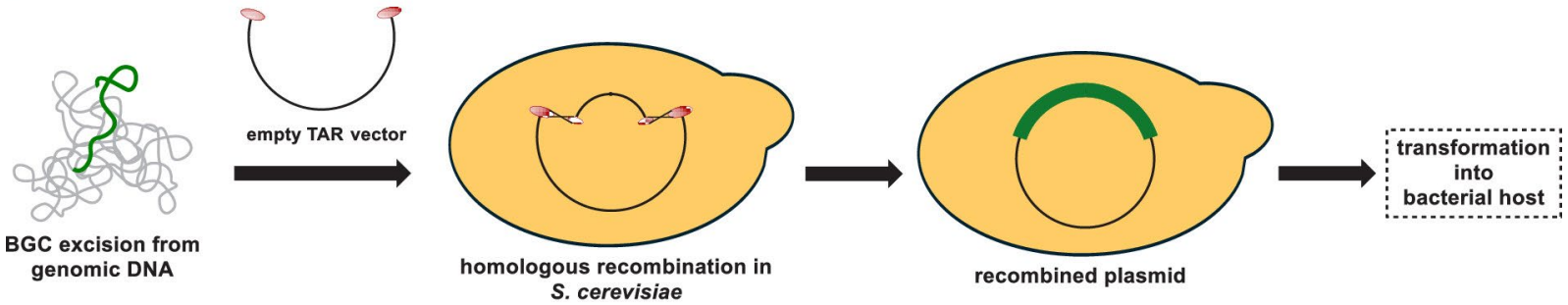
Chromosoma, **2016**, *125* (4), 621– 632: *Nat. Commun.*, **2021**, *12* (1), 1171: *Chem. Rev.*, **2025**, *125* (7), 3814–3931

Heterologous Expression:
Cloning BGCs into Hosts

CAPTURE



TAR

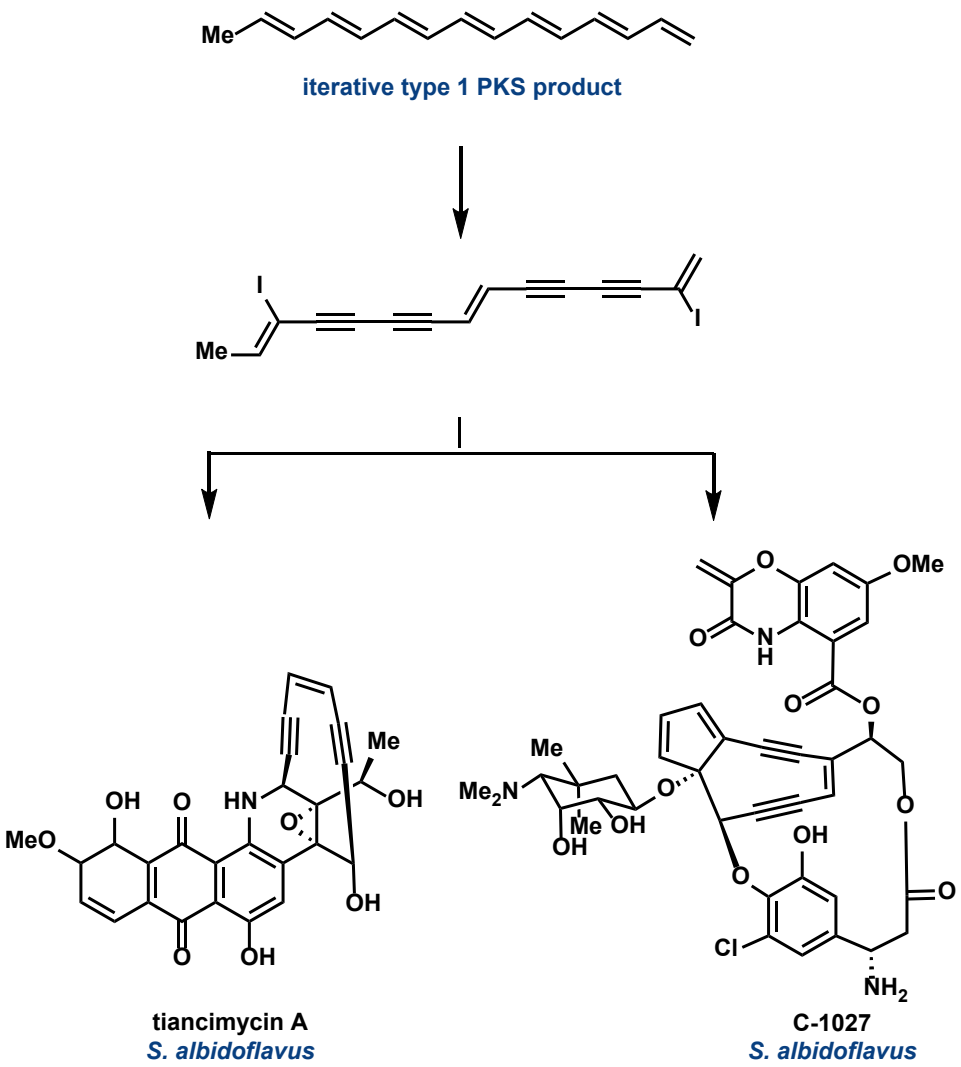


Chromosoma, **2016**, *125* (4), 621– 632: *Nat. Commun.*, **2021**, *12* (1), 1171: *Chem. Rev.*, **2025**, *125* (7), 3814–3931

Heterologous Expression:

BGC Expression in Bacteria

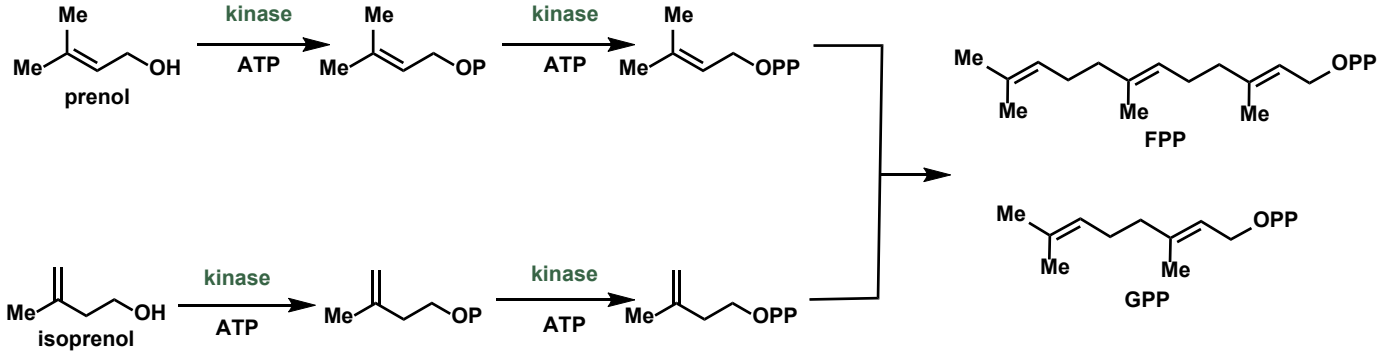
- Thousands of enediyne BGCs sequenced
- Conserved polyketide synthase gene and regulator
- Identified the vinyl iodide as the final common product of the conserved enzymes
  - Previously unknown link between heptaene and all known enediynes
- Exploited cryptic iodination to increase titers in cells
  - supplemented cells with NaI to give 4.6 g/L of C-1027

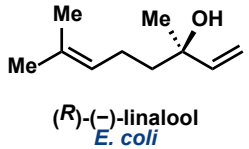


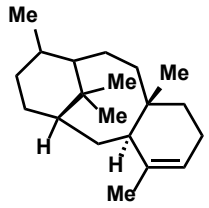
Proc. Natl. Acad. Sci. U. S. A., **2023**, *120* (9), e2220468120: *Nat. Chem. Biol.* **2024**, *20* (9), 1210– 1219

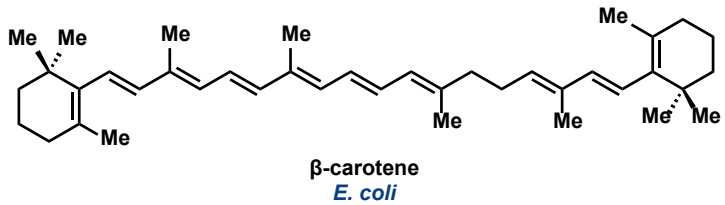
Heterologous Expression:

Terpene Biosynthesis via BGC Expression in Bacteria









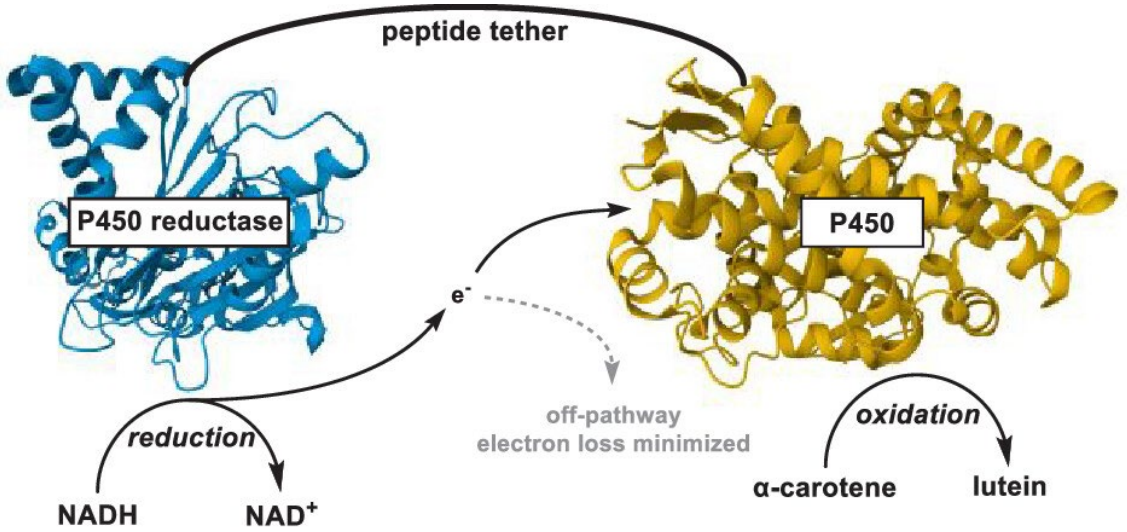
- Isopentenol Utilization Pathway (IUP)
  - Introduce an overexpressed isopentenyl phosphate kinases via inducible promoter and terpene BGC to host

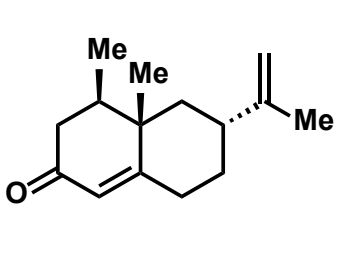
J. Agric. Food Chem., **2022**, *70* (11), 3512– 3520: *Org. Lett.*, **2024**, *26* (8), 1640– 1644: *ACS Synth. Biol.*, **2019**, *8* (2), 232– 238:
Proc. Natl. Acad. Sci. U. S. A., **2019**, *116* (2), 506– 511

Heterologous Expression:

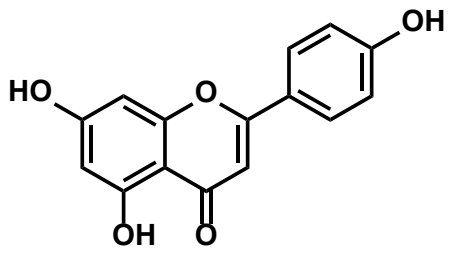
Biosynthesis Utilizing P450 via BGC Expression in Bacteria

- Terpenoid BGCs often include P450 enzymes
  - Difficult to express in *E. coli*
- Tether P450 monooxygenase and P450 reductase partners via synthetic proteins scaffolds

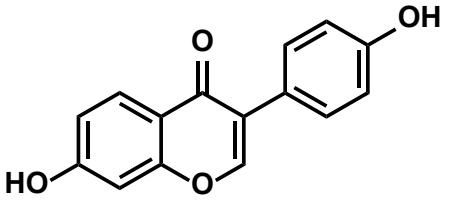




(+)-nootkatone
E. coli



apigenin
E. coli

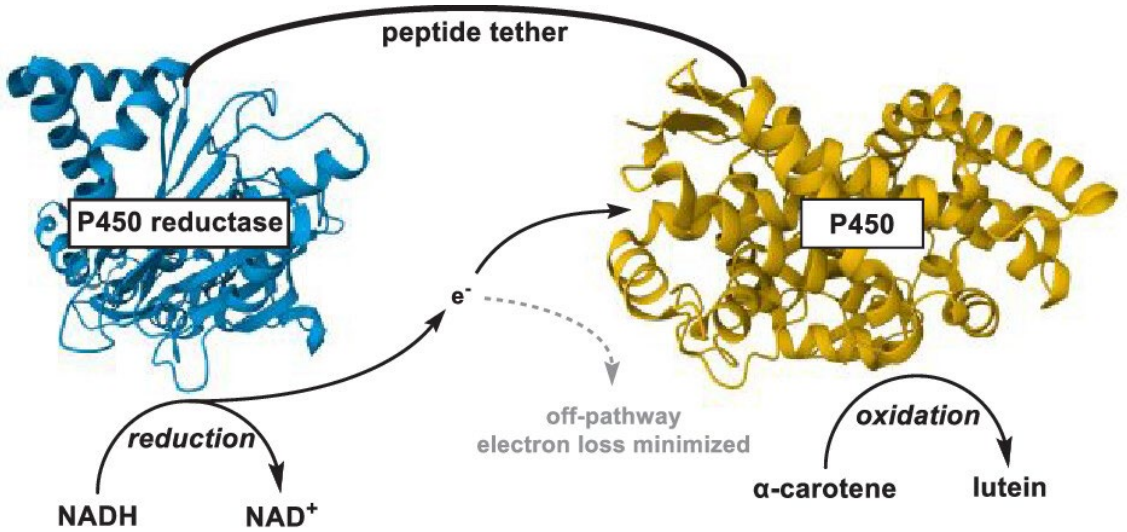


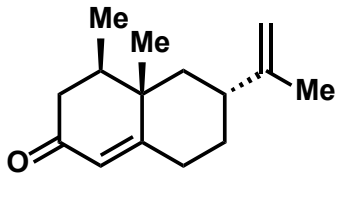
daidzein
E. coli

Chem. Rev., **2025**, *125* (7), 3814–3931: *J. Agric. Food Chem.*, **2024**, *72* (11), 5849–5859

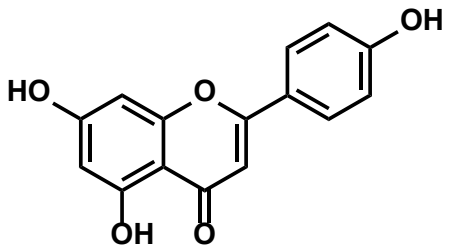
Heterologous Expression:

Biosynthesis Utilizing P450 via BGC Expression in Bacteria

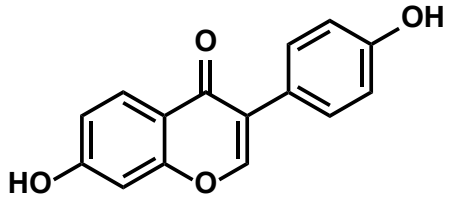




(+)-nootkatone
E. coli



apigenin
E. coli

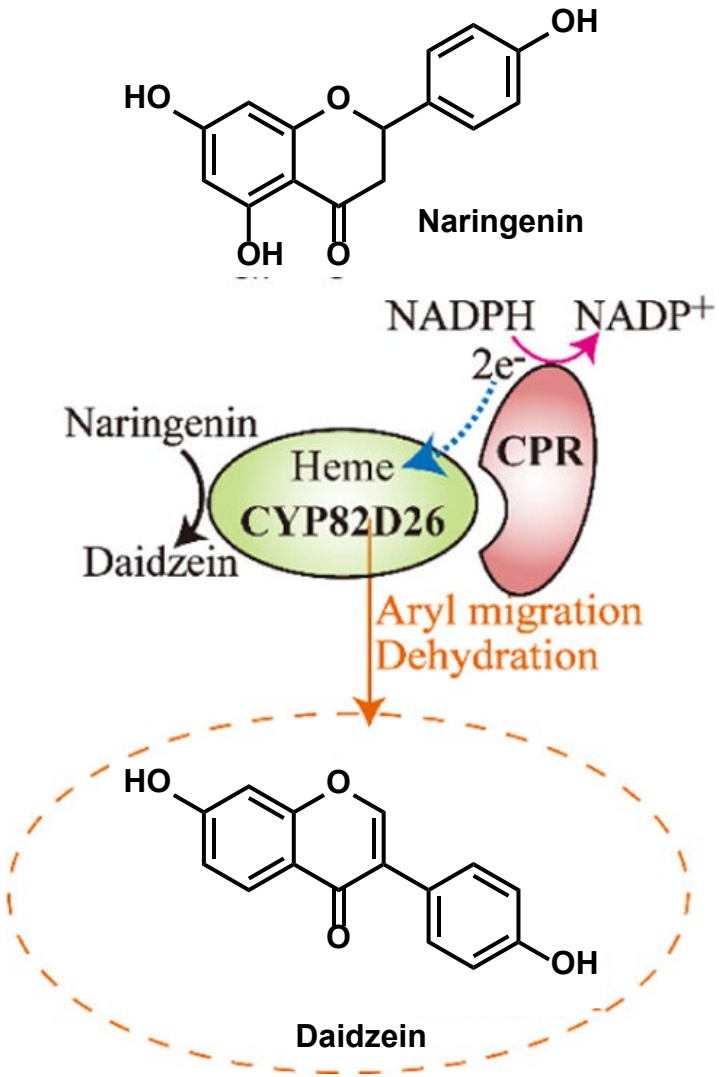


daidzein
E. coli

Chem. Rev., **2025**, *125* (7), 3814–3931: *J. Agric. Food Chem.*, **2024**, *72* (11), 5849–5859

Heterologous Expression:

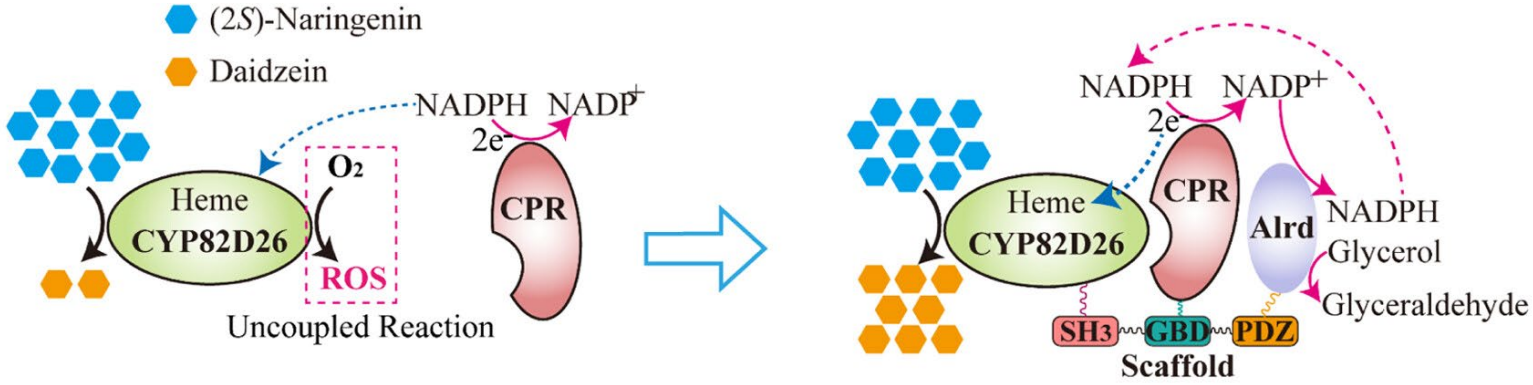
Biosynthesis Utilizing P450 via BGC Expression in Bacteria



J. Agric. Food Chem., **2024**, *72* (11), 5849–5859

Heterologous Expression:

Biosynthesis Utilizing P450 via BGC Expression in Bacteria

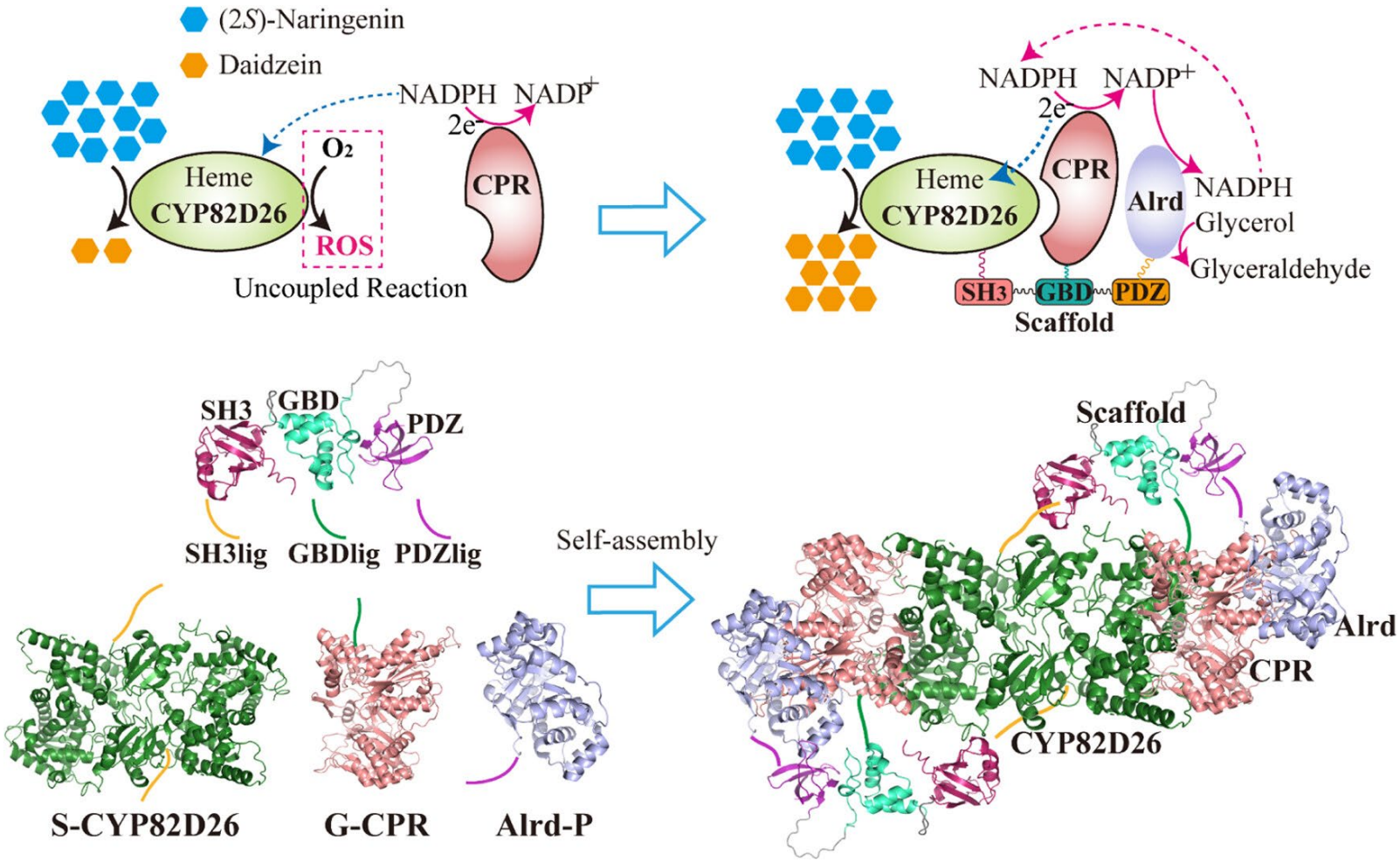


titer increased to 240.5 mg/L with 86% conversion
(9-fold increase)

J. Agric. Food Chem., **2024**, *72* (11), 5849–5859

Heterologous Expression:

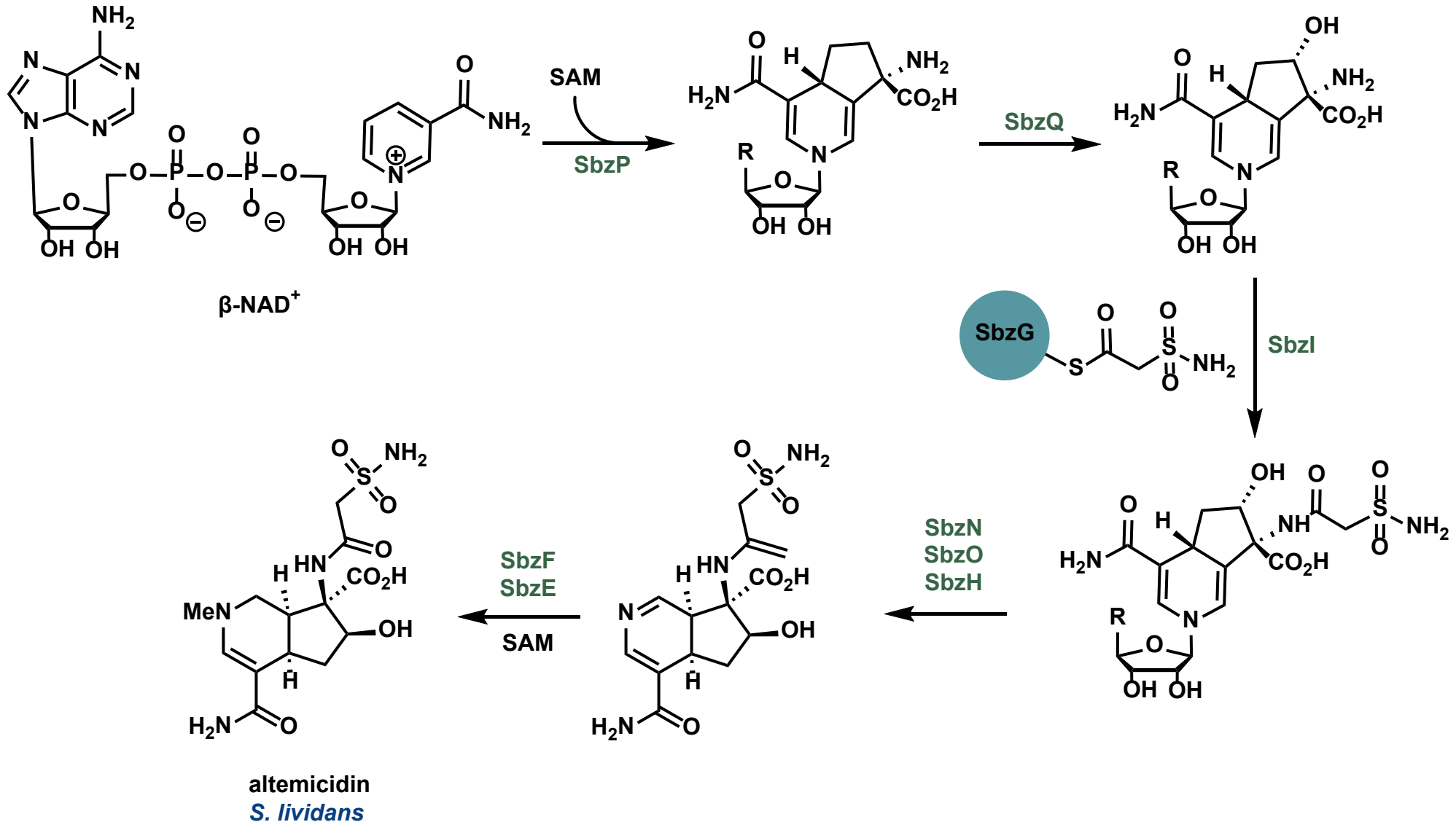
Biosynthesis Utilizing P450 via BGC Expression in Bacteria



J. Agric. Food Chem., **2024**, *72* (11), 5849–5859

Heterologous Expression:

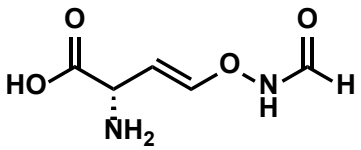
BGC Expression in Bacteria without Known Core Enzymes



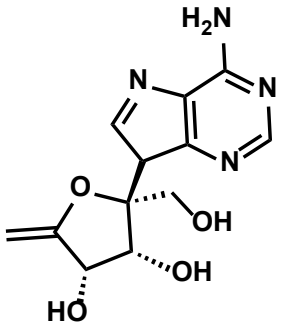
Nature, **2021**, *600* (7890), 754−758

Heterologous Expression:

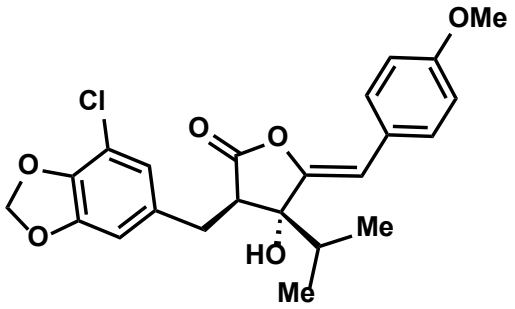
BGC Expression in Bacteria without Known Core Enzymes



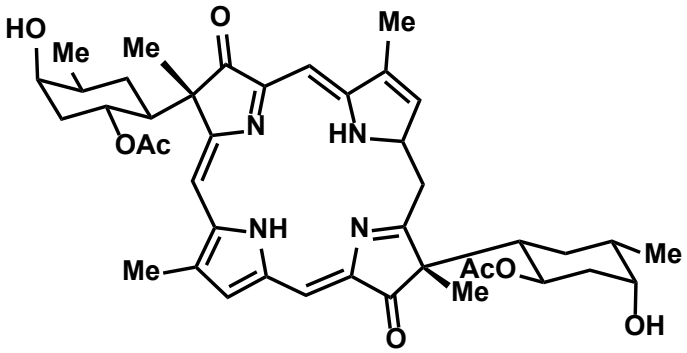
4-formylaminooxyvinylglycine
P. fluorescens



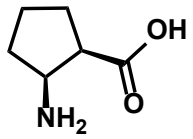
angustmycin A
E. coli, S. albus



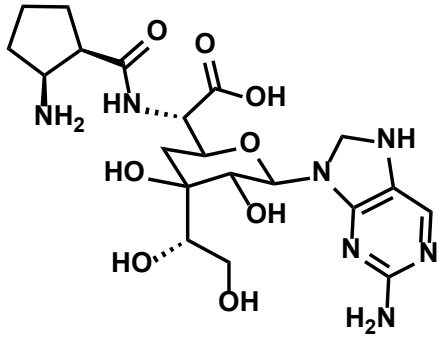
cyanobacterin
E. coli



tolyporphin A
E. coli



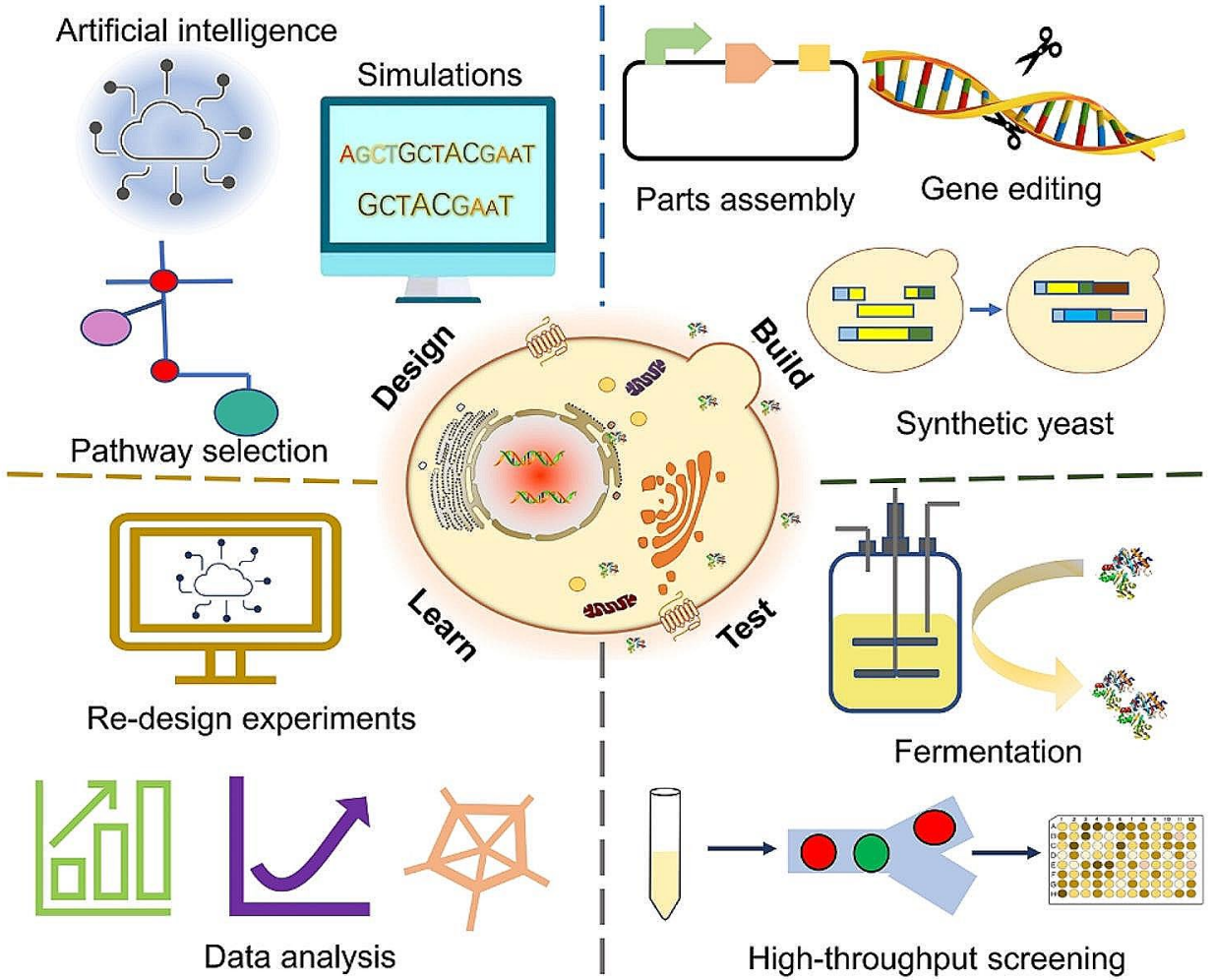
(-)-cispentacin
S. albus



amipurimycin
S. albus

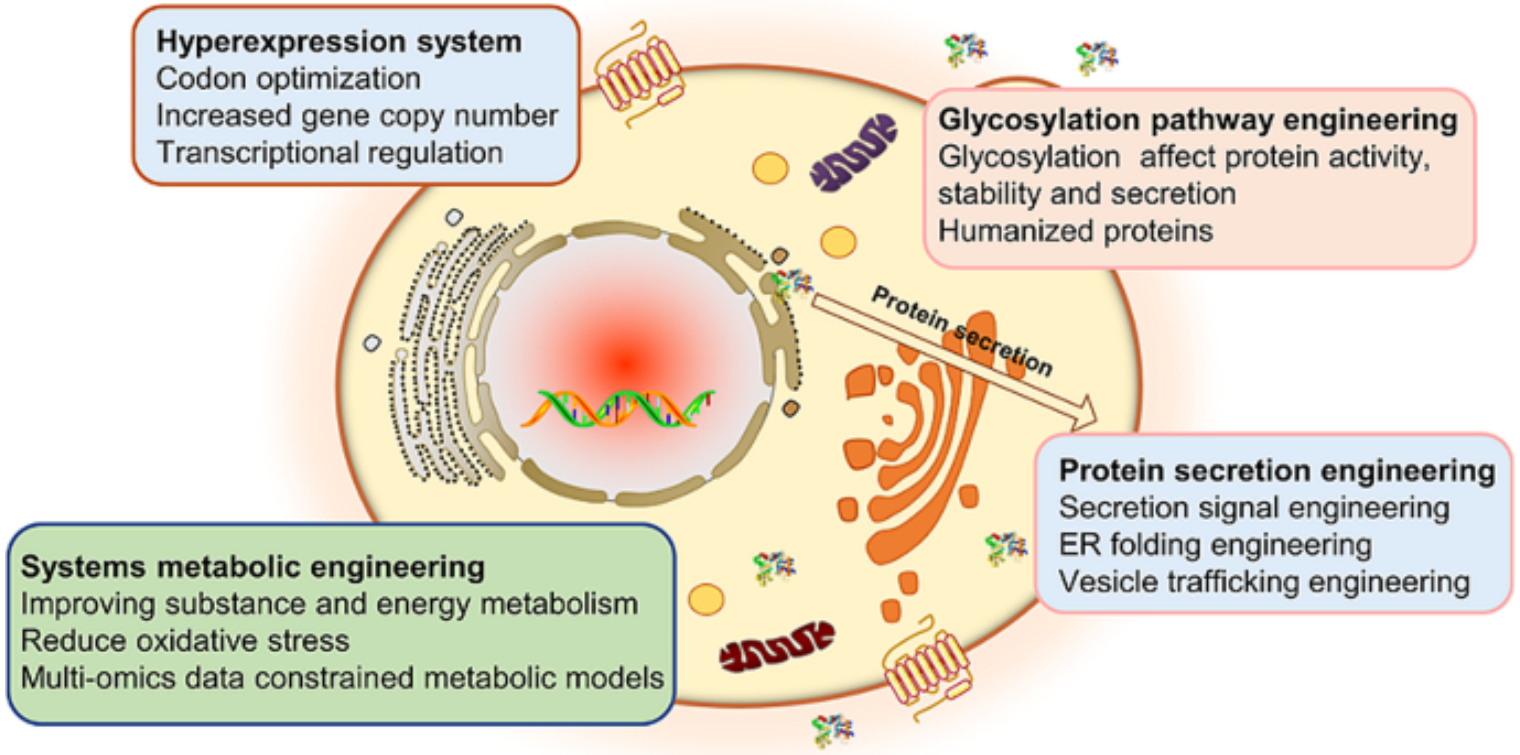
Biochemistry, **2022**, *61* (19), 2159– 2164: *Nat. Chem. Biol.,* **2021**, *17* (7), 794– 799: *Nat. Commun.,* **2021**, *12* (1), 6633: *Nat. Chem. Biol.*, **2022**, *18* (6), 652– 658: *J. Am. Chem. Soc.*, **2023**, *145* (17), 9834– 9839: *Nat. Commun.*, **2023**, *14* (1), 8065

Heterologous Expression:
Natural Product Production in Yeast



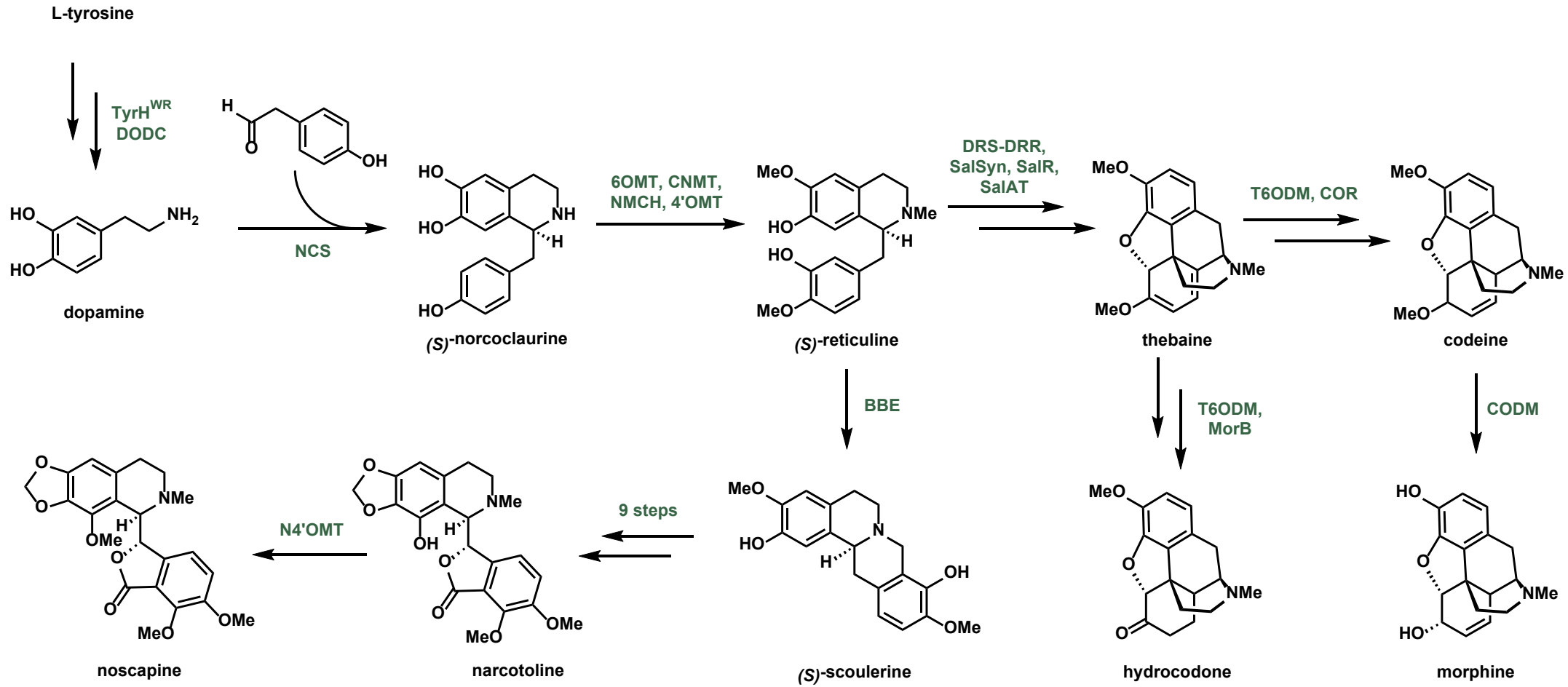
Microb. Cell Fact, **2024**, *23* (32)

Heterologous Expression:
Natural Product Production in Yeast



Microb. Cell Fact, **2024**, *23* (32)

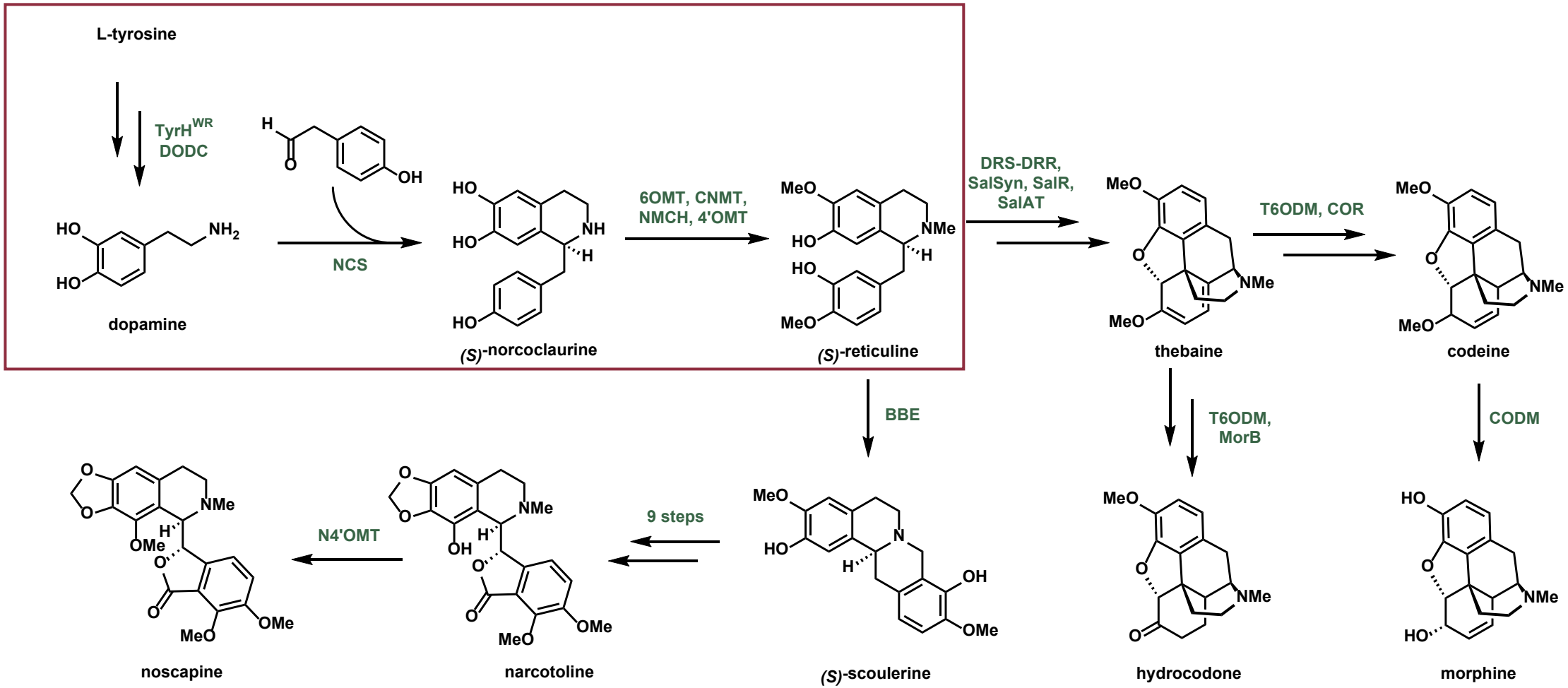
Heterologous Expression:
Biosynthetic Reconstitution in Yeast



Science, **2015**, *349* (6252), 1095-1100

Heterologous Expression:

Biosynthetic Reconstitution in Yeast

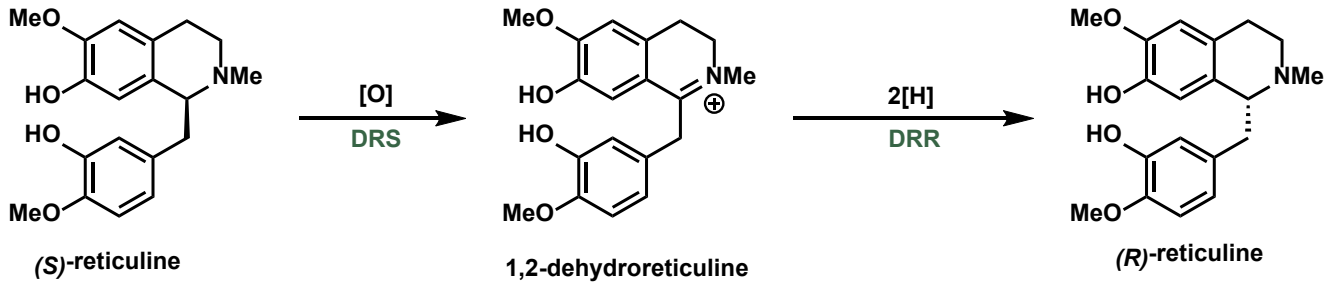


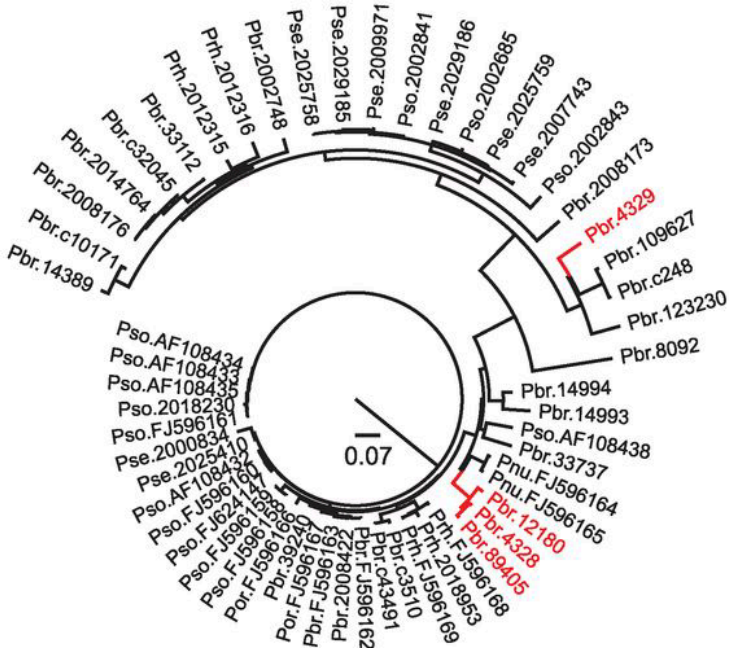
Science, **2015**, *349* (6252), 1095-1100

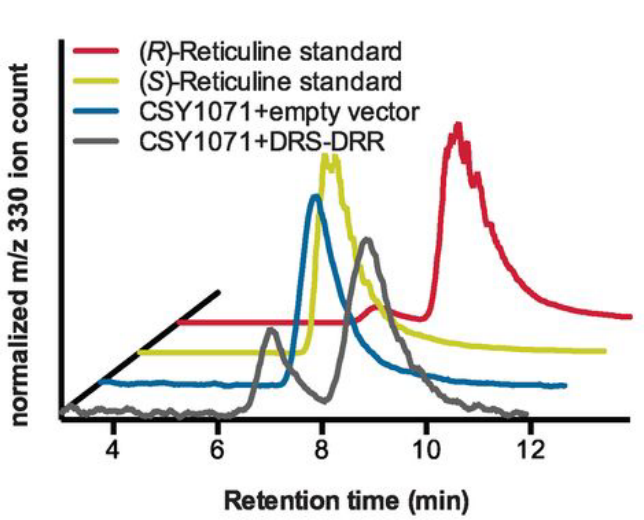
Heterologous Expression:
Biosynthetic Reconstitution in Yeast

- (*S*)-reticuline to (*R*)-reticuline\
  - yeast strain produced *S* but *R* is the desired precursor

- BLAST search for genes
  - Looking for proximally encoded enzymes to catalyze oxidation and reduction
  - Codeinone reductase and cytochrome P450 found together







Science, **2015**, *349* (6252), 1095-1100: *Proc. Natl. Acad. Sci. U. S. A.* **2018**, *115* (17), E3922-E3931

Heterologous Expression:

BGC Expression in Yeast vs Fungi

Yeast:

- Robust for fungal BGC terpene biosynthesis
- Inconsistent expression of membrane bound proteins (ex: P450)
- Minimal intron splicing applicable to introns from other fungi
  - Requires intron-free genes from synthetic DNA (expensive!!)

Fungi:

- Challenging to perform genetic knockouts or overexpression for the natural fungi
- Heterologous expression in closely related fungal hosts solves native fungi and yeast issues

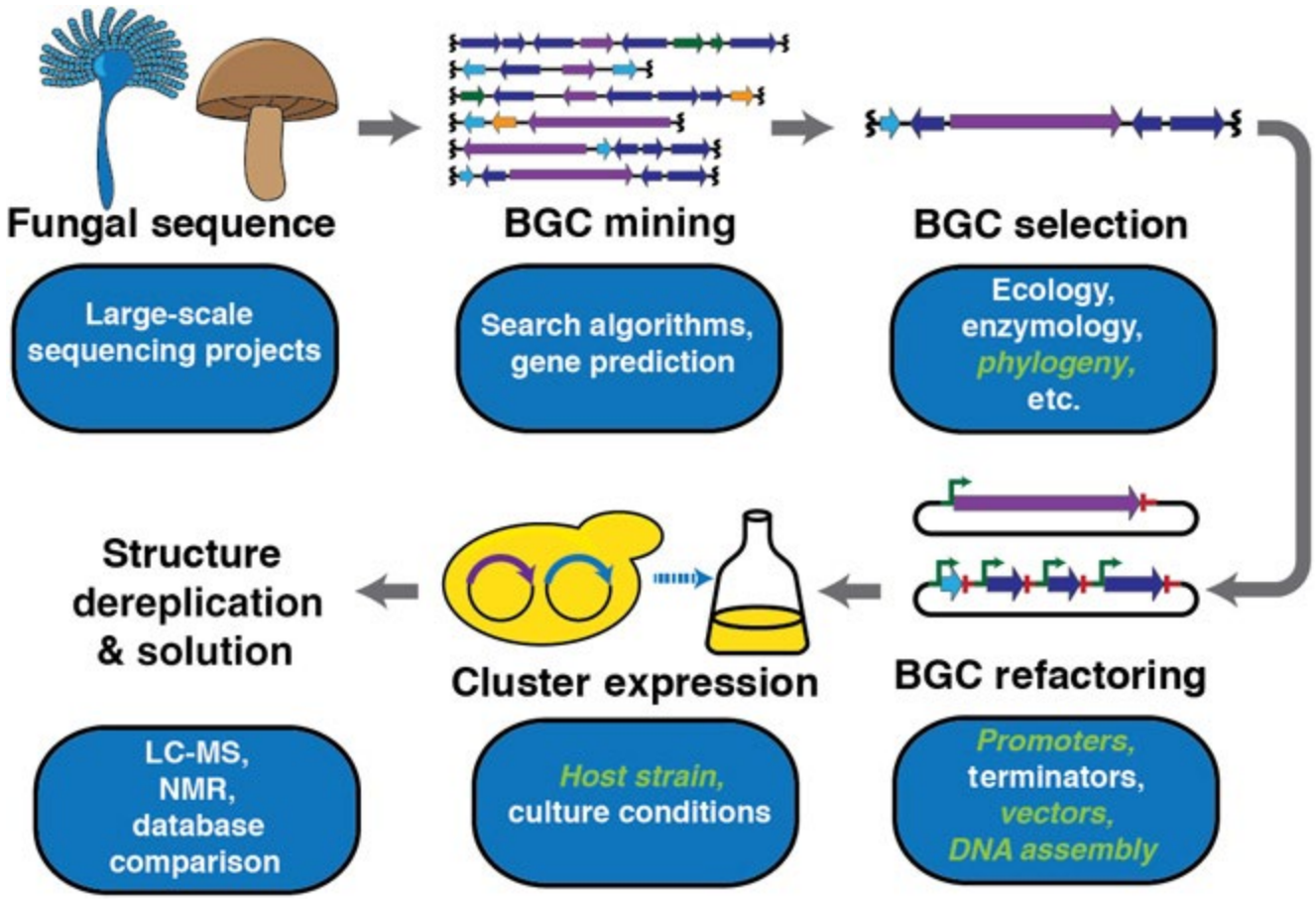


S. cerevisiae *native host* *A. nidulans*

FEMS MicroBio. Lett., **2021**, *368* (19), fnab135

Heterologous Expression:

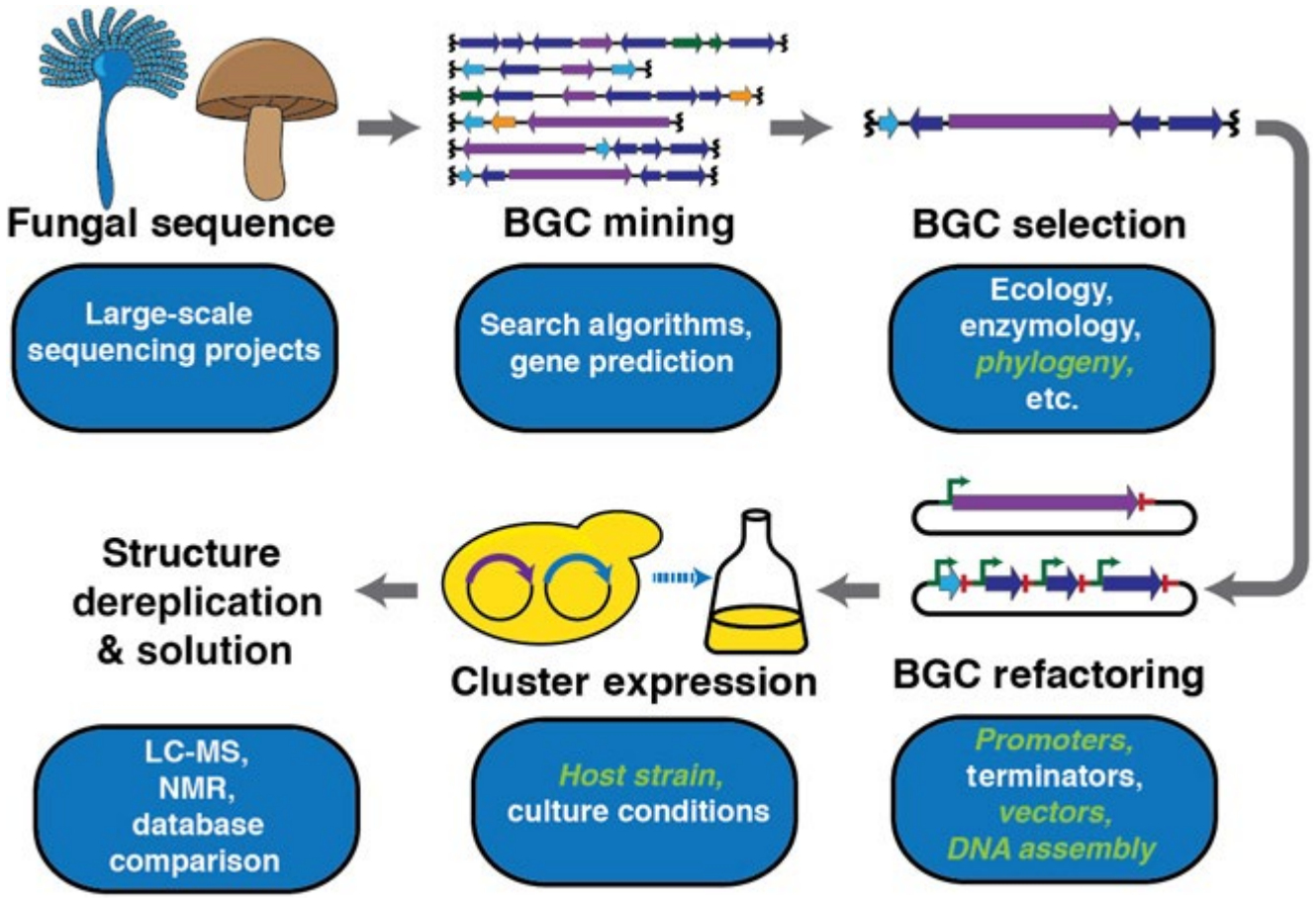
HEx in Fungi



Sci. Adv., **2018**, *4* (4), eaar5459

Heterologous Expression:

HEx in Fungi

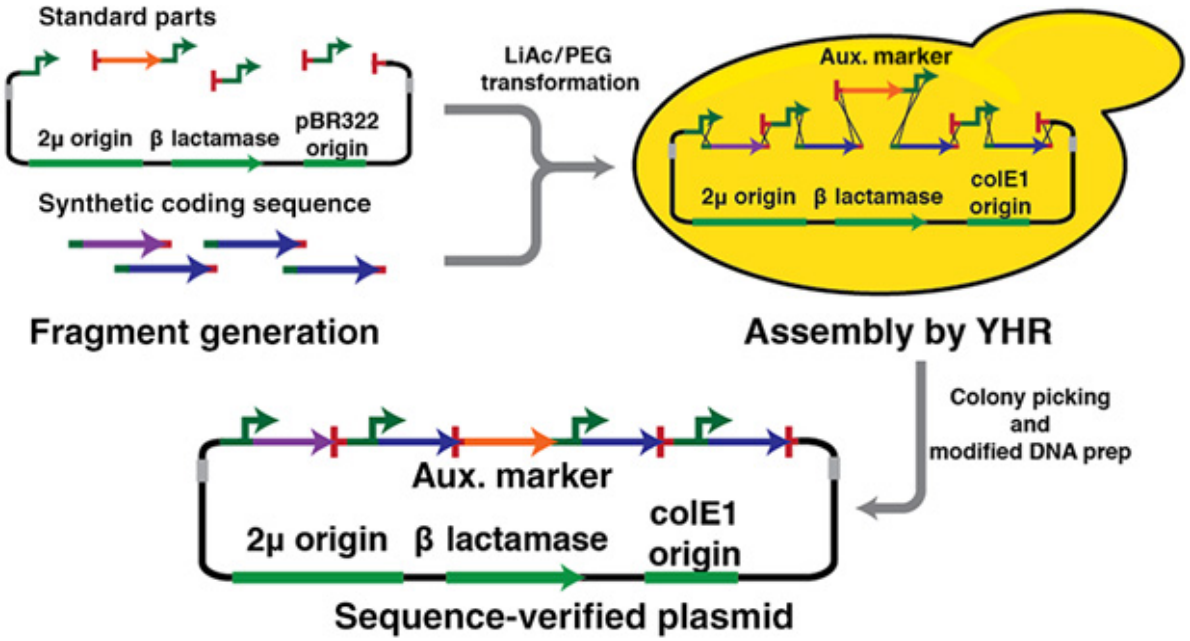


- Applied to 41 fungal BGCs
  - 22 produced detectable compounds
  - Novel natural products found
  - Unexpected biosynthetic origins studied

Sci. Adv., **2018**, *4* (4), eaar5459

Heterologous Expression:

HEx in Fungi

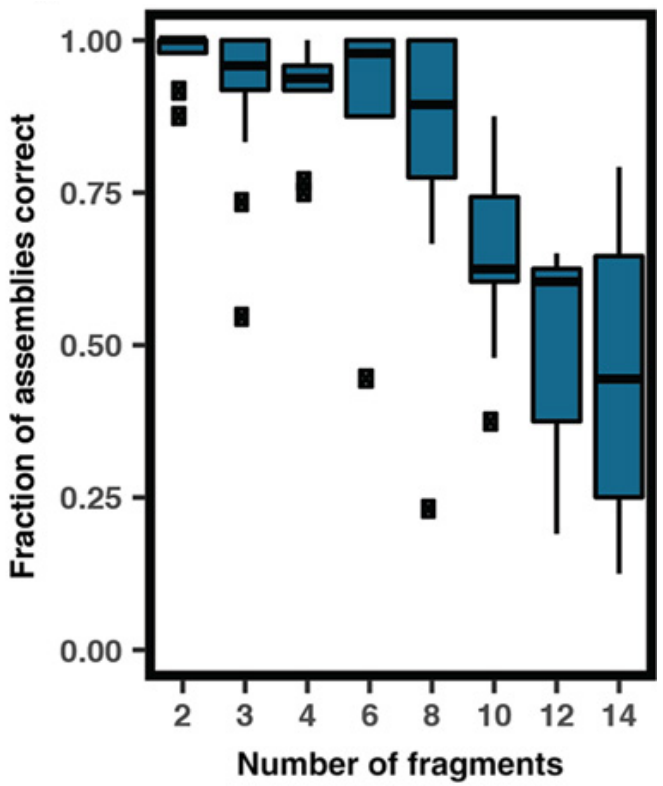


- Yeast homologous recombination assembles DNA from commercially synthesized fragments
- Plasmid extracted and ready for insertion into new host

Sci. Adv., **2018**, *4* (4), eaar5459

Heterologous Expression:

HEx in Fungi

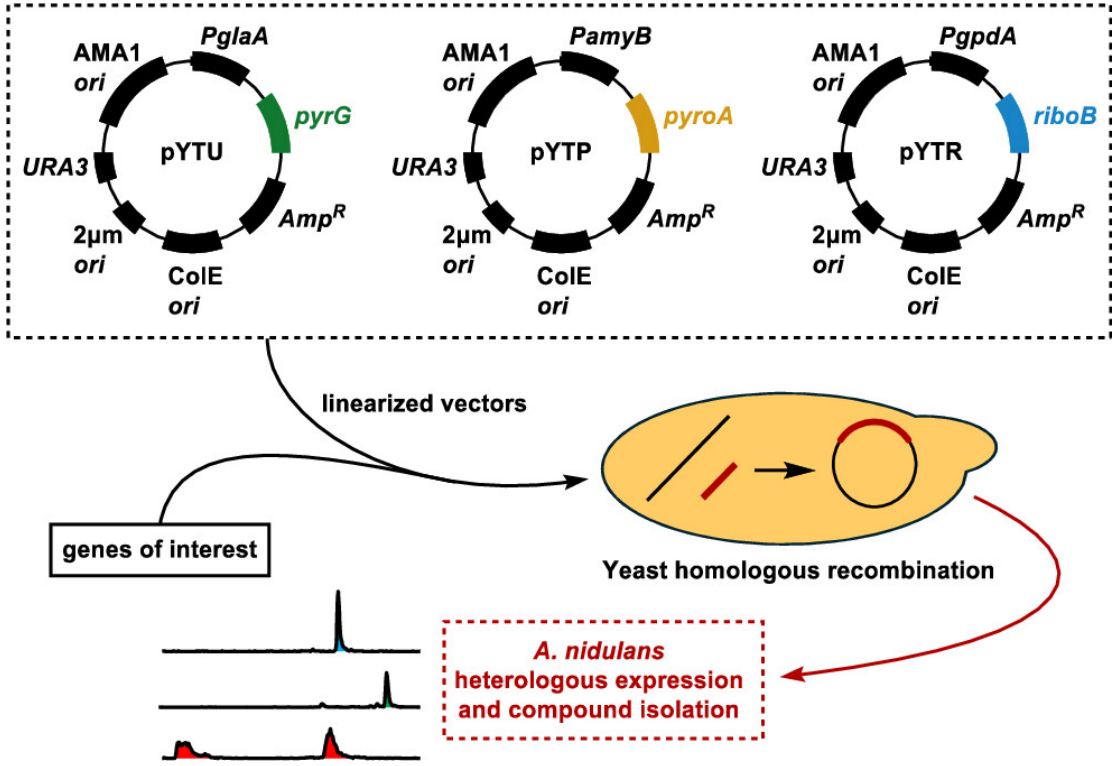


- Yeast homologous recombination assembles DNA from commercially synthesized fragments
- Plasmid extracted and ready for insertion into new host
- Up to 14 unique DNA fragments assembled together

Sci. Adv., **2018**, *4* (4), eaar5459

Heterologous Expression:
Three Plasmid System

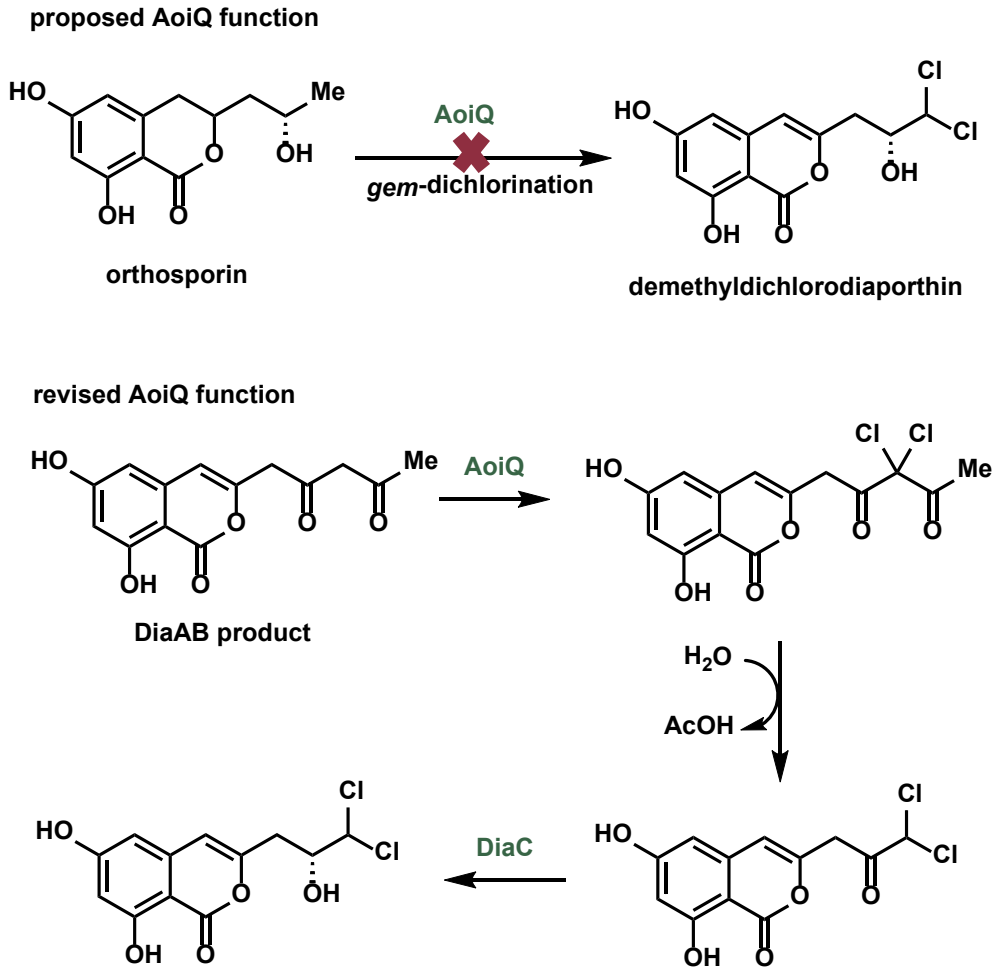
- Each gene given new promoters and terminators
- Each vector carries 4 to 5 genes (up to 15 genes for a BGC)



Chem. Rev., **2025**, *125* (7), 3814–3931

Heterologous Expression:

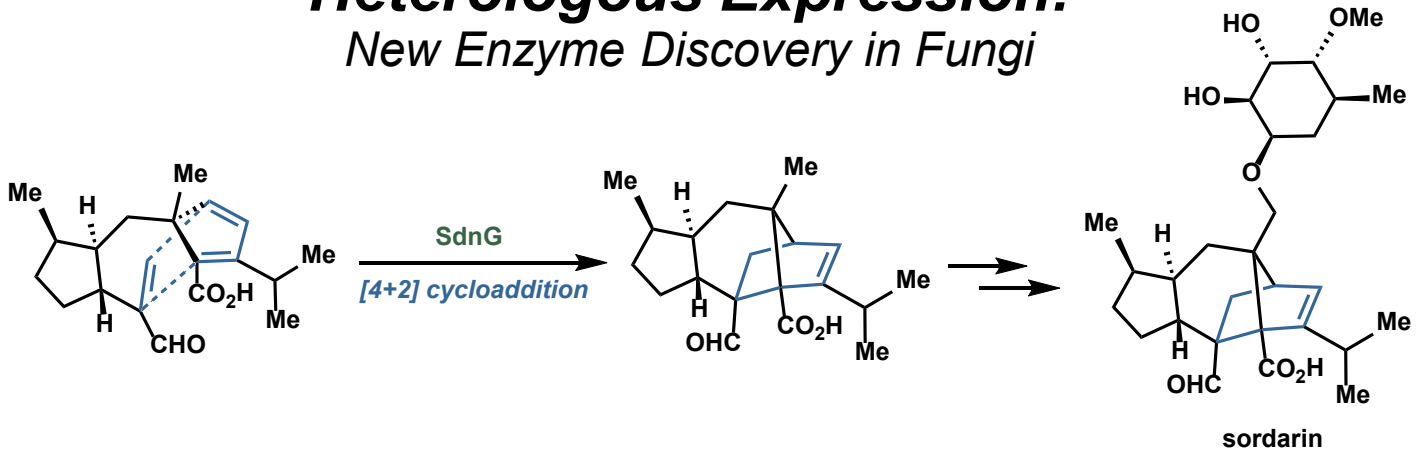
Revision of Enzyme Function in Fungi



J. Am. Chem. Soc., **2021**, *143* (19), 7267– 727: *Angew. Chem., Int. Ed.*, **2016**, *55* (39), 11955– 11959

Heterologous Expression:

New Enzyme Discovery in Fungi



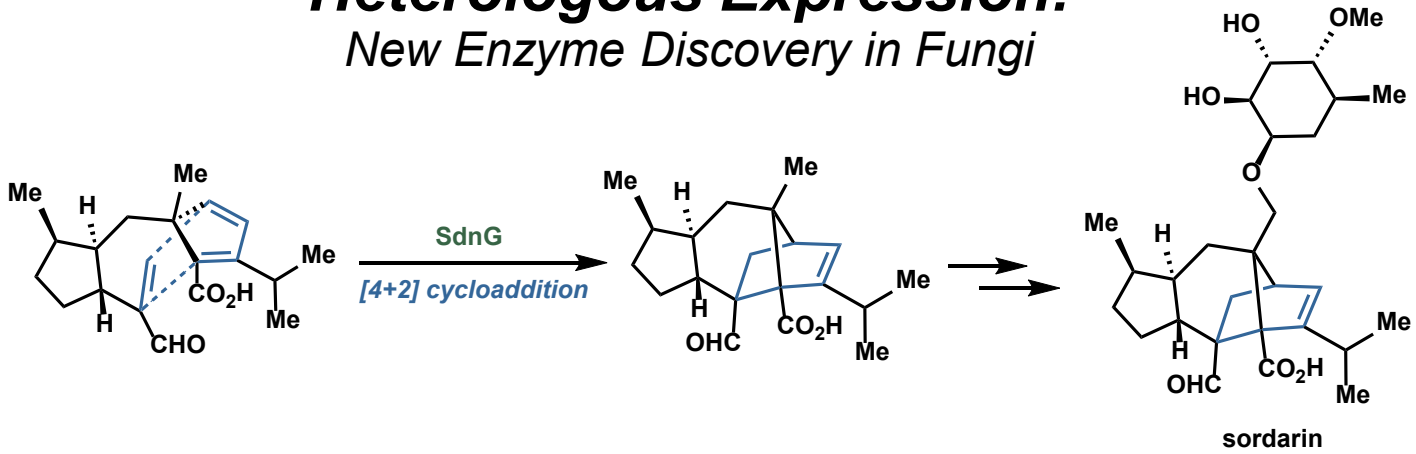
- Reconstituted biosynthesis of various natural products lead to discovery of pericyclase enzymes
  - Genome mining beacon

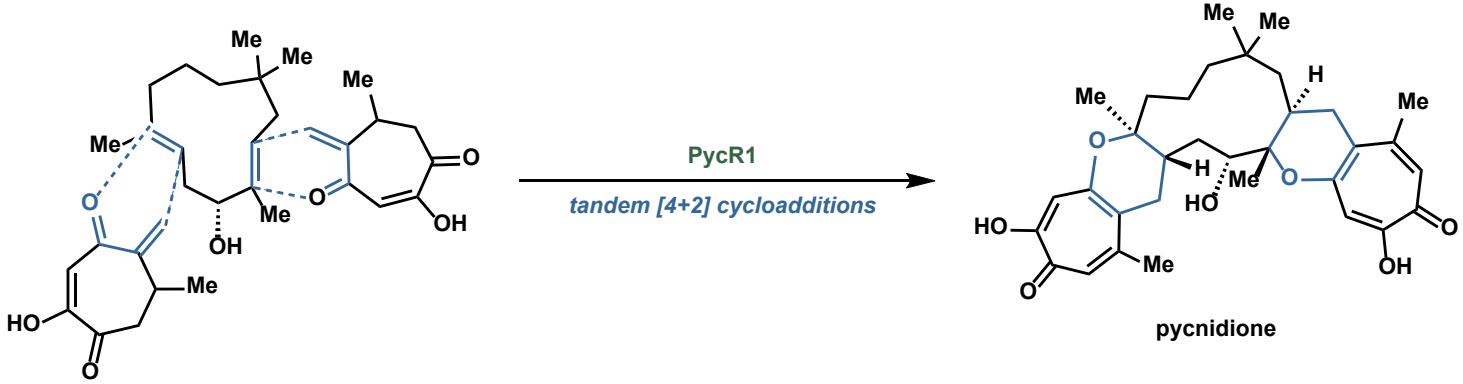
- SdnG was a protein of unknown function in sordarin BGC
  - Heterologous expression without it lead to significantly decreased natural product production

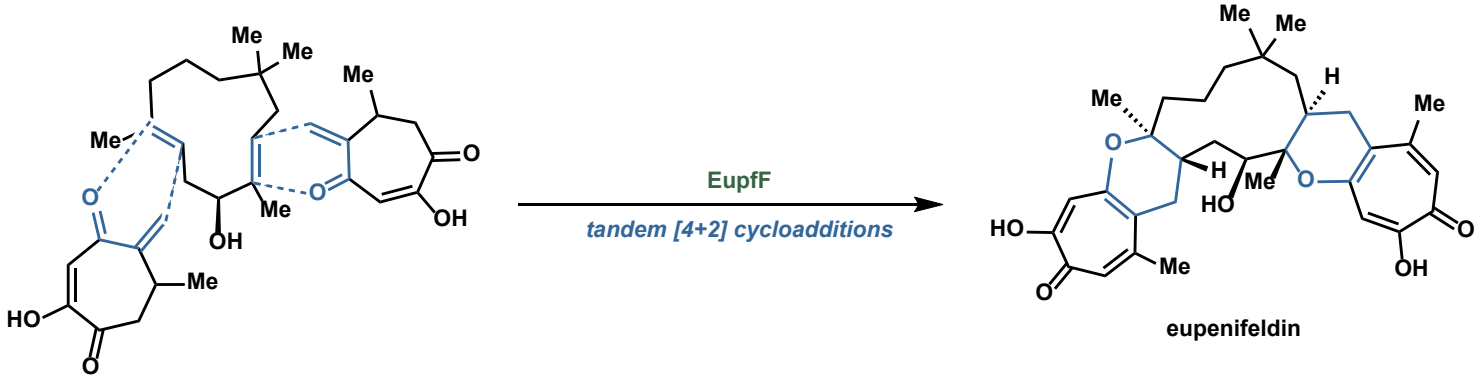
Nat. Chem., **2023**, *15* (8), 1083– 1090: *J. Am. Chem. Soc.* **2022**, *144*, 8, 3580–3589

Heterologous Expression:

New Enzyme Discovery in Fungi



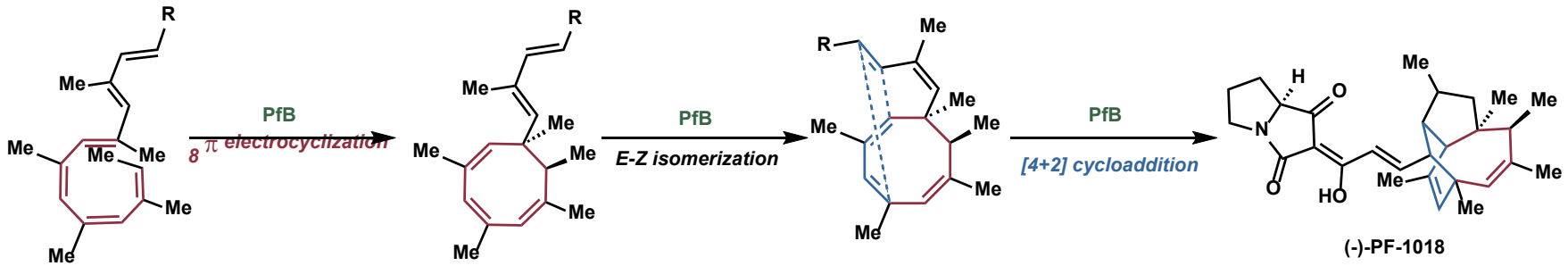




Nat. Chem., **2023**, *15* (8), 1083– 1090: *J. Am. Chem. Soc.* **2022**, *144*, 8, 3580–3589

Heterologous Expression:

New Enzyme Discovery in Fungi

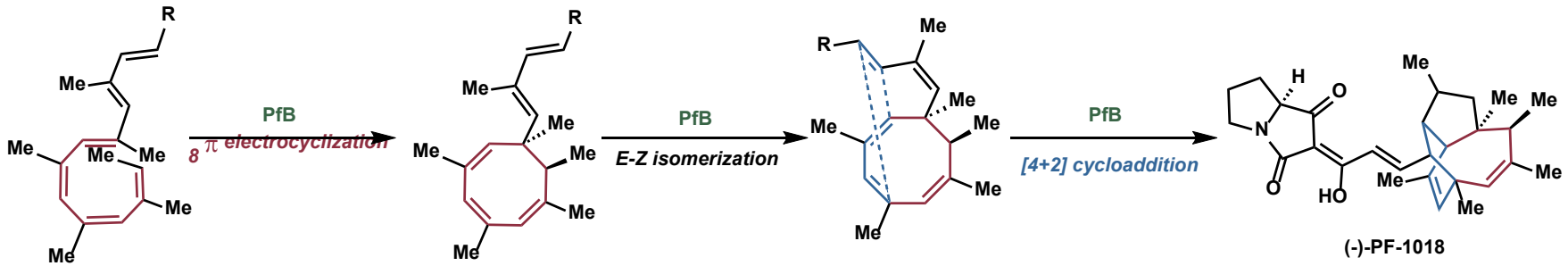


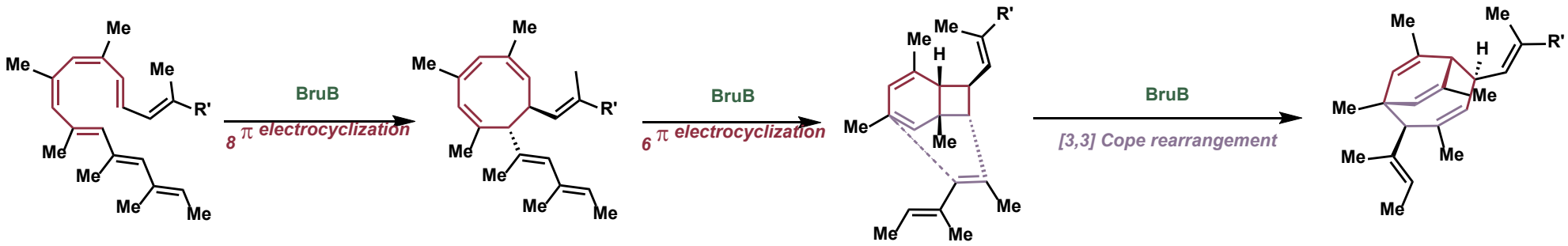
- PfB and BruB characterized from homologous BGCs
  - catalyze regioselective and stereoselective electrocyclization of polyene products
- (-)-PF-1018 isolated as single diastereomer
- PfB role confirmed in facilitating a stereoselective 8 π electrocyclization (helical conrotatory transition state)

J. Am. Chem. Soc., **2023**, *145* (25), 13520– 13525

Heterologous Expression:

New Enzyme Discovery in Fungi





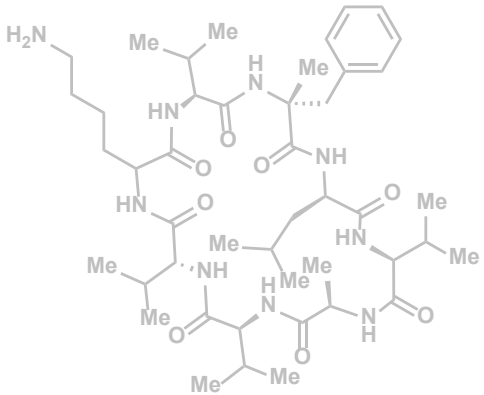
J. Am. Chem. Soc., **2023**, *145* (25), 13520– 13525

Synthetic Biology in Natural Product Biosynthesis

Advances in Tools for Natural Product Discovery

- Bioinformatics and Machine Learning

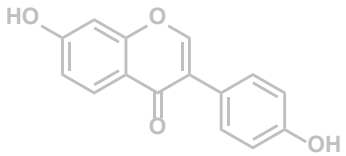
- Synthetic Biology Tools for Mining Silent BGCs



surugamide I

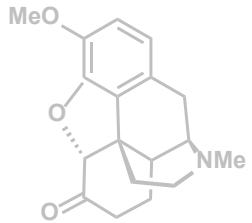
Heterologous Expression Natural Product Pathways

- Bacteria



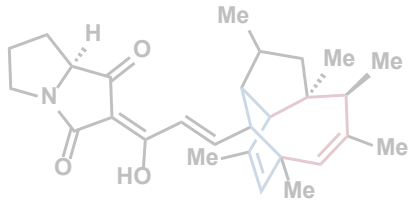
Daidzein

- Yeast



hydrocodone

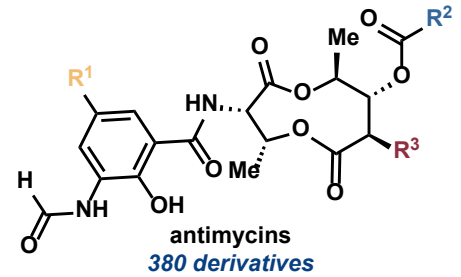
- Fungi



(-)-PF-1018

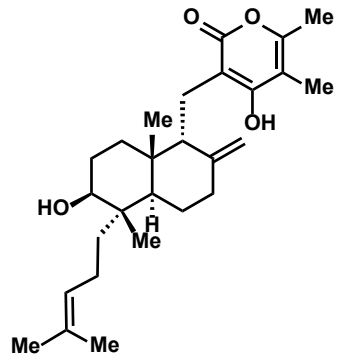
Structural Diversification of Natural Products

- Redirecting Biosynthesis



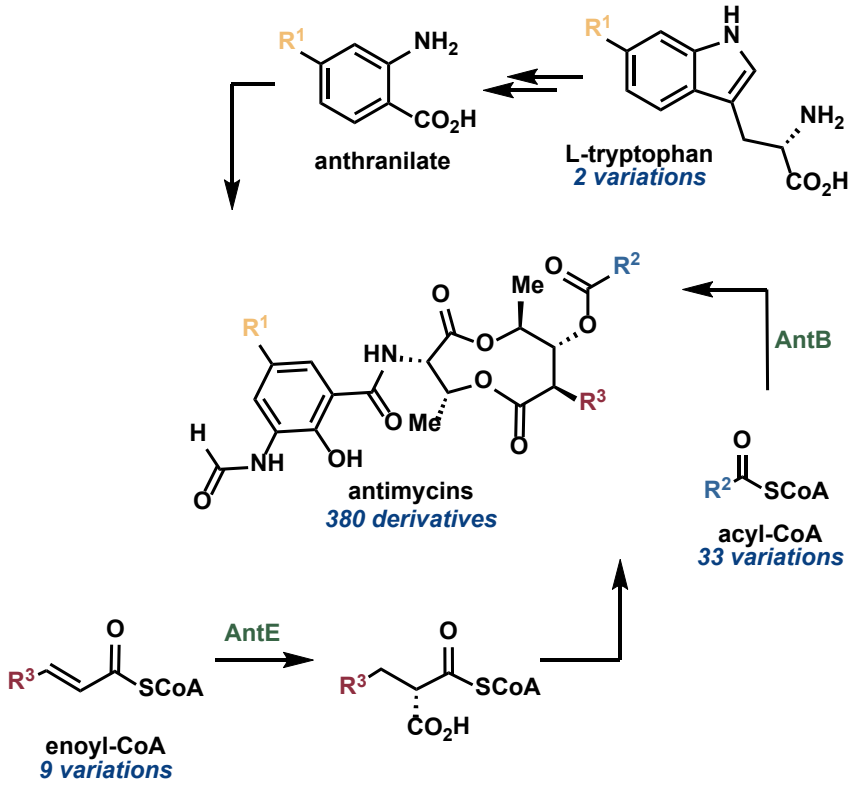
antimycins
380 derivatives

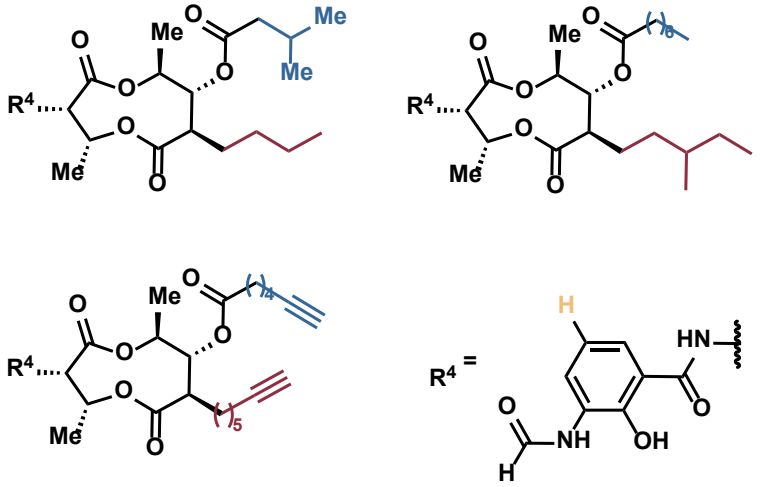
- Combinatorial Biosynthesis



Structural Diversification of Natural Products:

Precursor Directed Biosynthesis

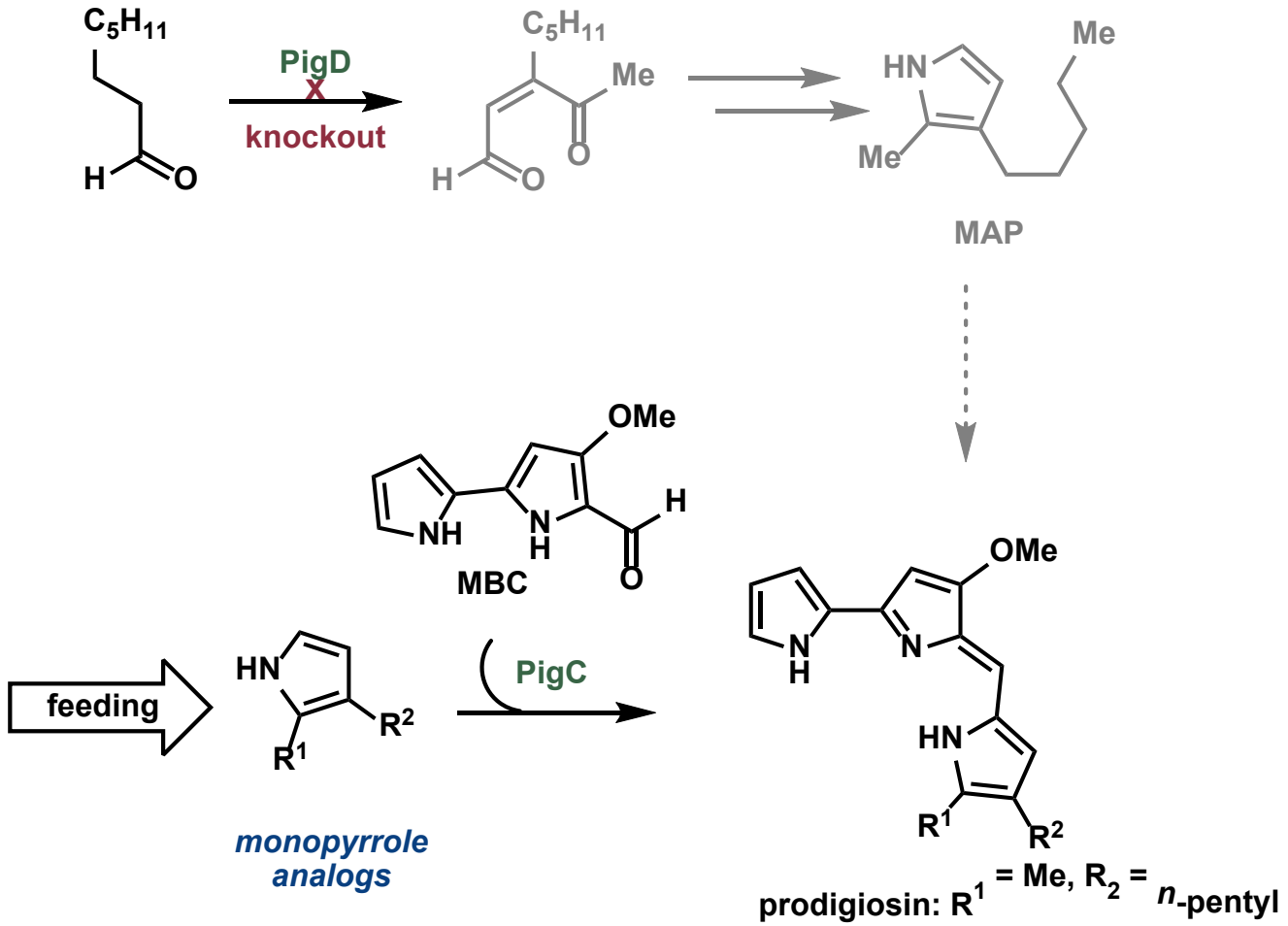




Angew. Chem., Int. Ed., **2013**, *52* (47), 12308– 12312

Structural Diversification of Natural Products:

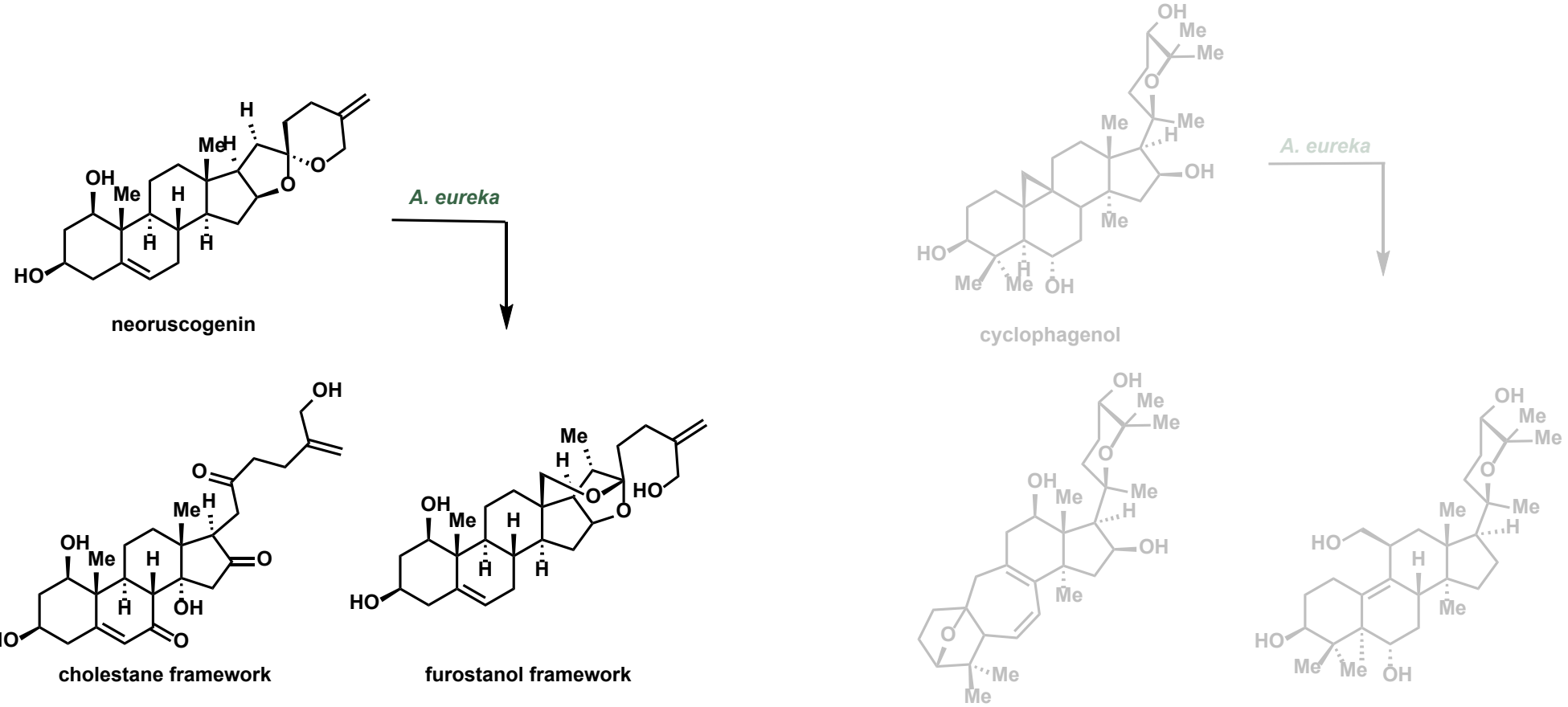
Mutational Biosynthesis



ACS Synth. Biol., **2017**, *6* (9), 1757– 1765: *Org. Lett.*, **2021**, *23* (16), 6563– 6567

Structural Diversification of Natural Products:

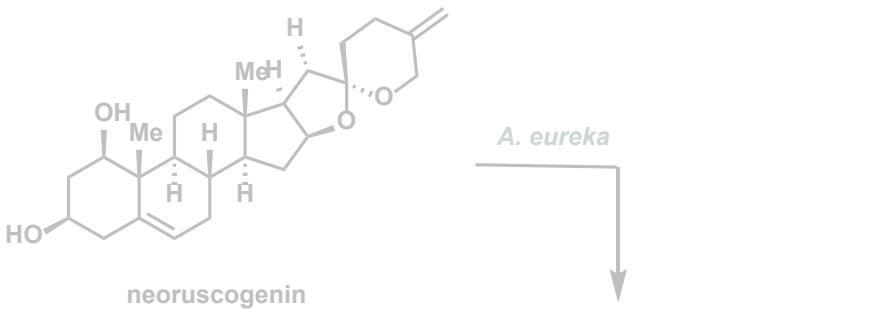
Redirecting Biosynthesis with Biotransformation

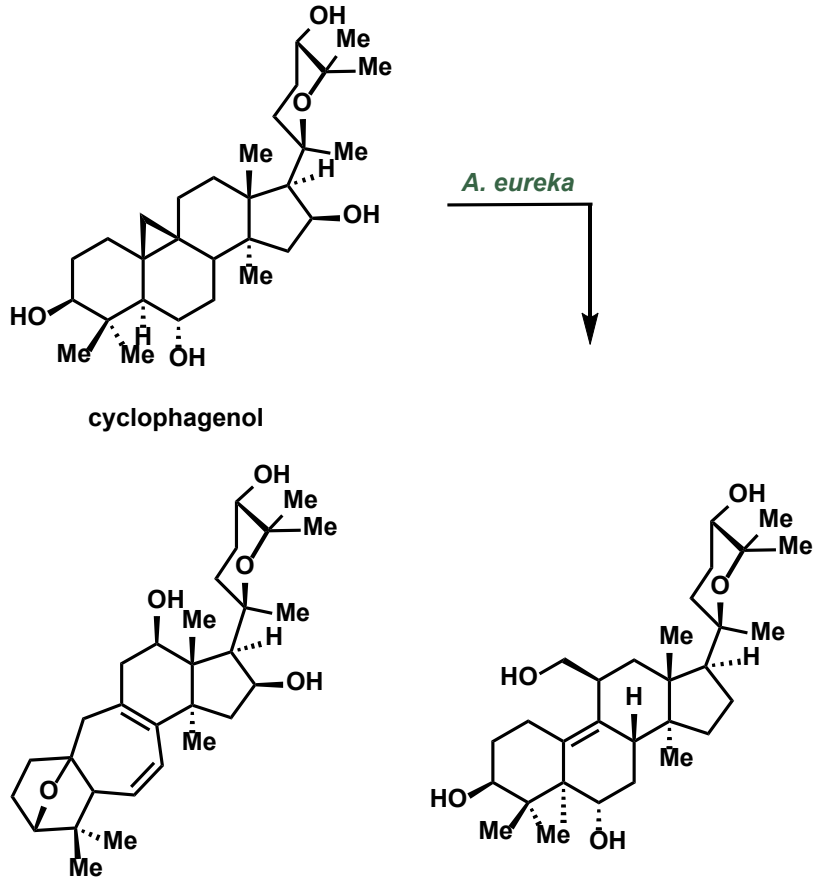


J. Nat. Prod., **2018**, *81* (6), 1357– 1367: *Sci. Rep.*, **2022**, *12* (1), 1848

Structural Diversification of Natural Products:

Redirecting Biosynthesis with Biotransformation

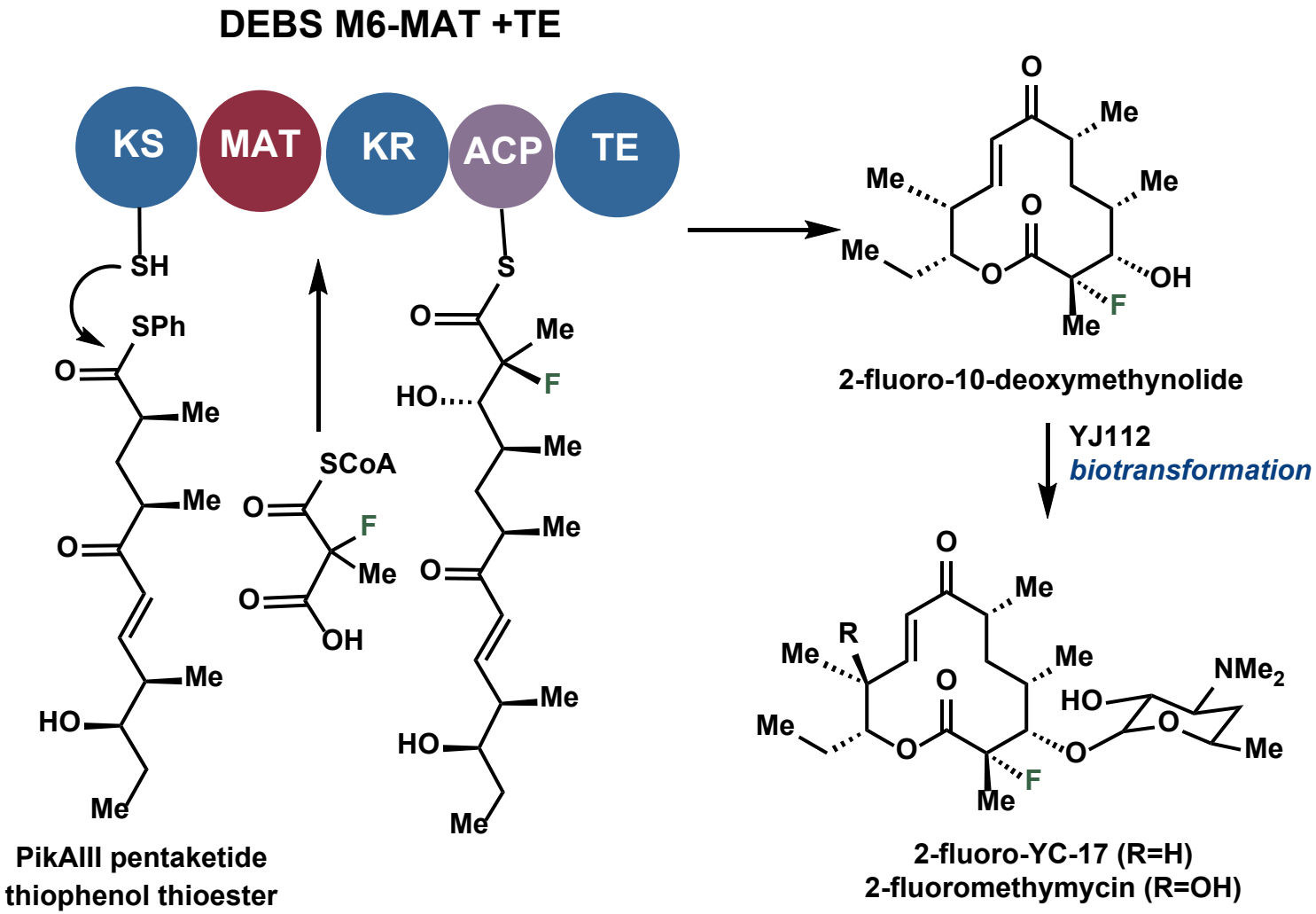




J. Nat. Prod., **2018**, *81* (6), 1357– 1367: *Sci. Rep.*, **2022**, *12* (1), 1848

Structural Diversification of Natural Products:

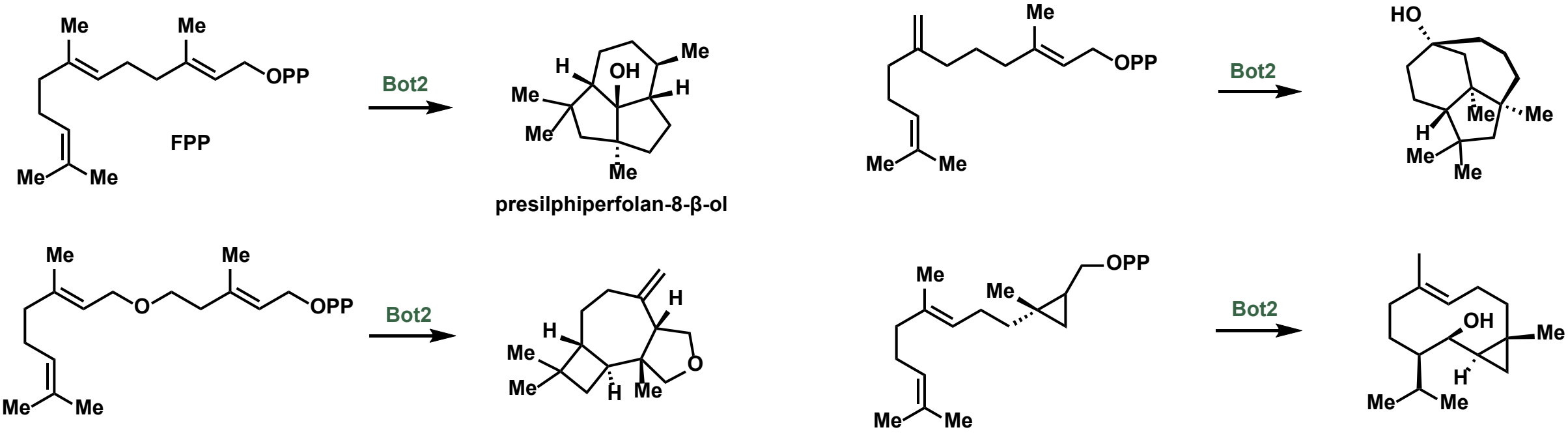
Redirecting Polyketide Biosynthesis



Nat. Chem. Biol. **2022**, *18* (8), 886– 893

Structural Diversification of Natural Products:

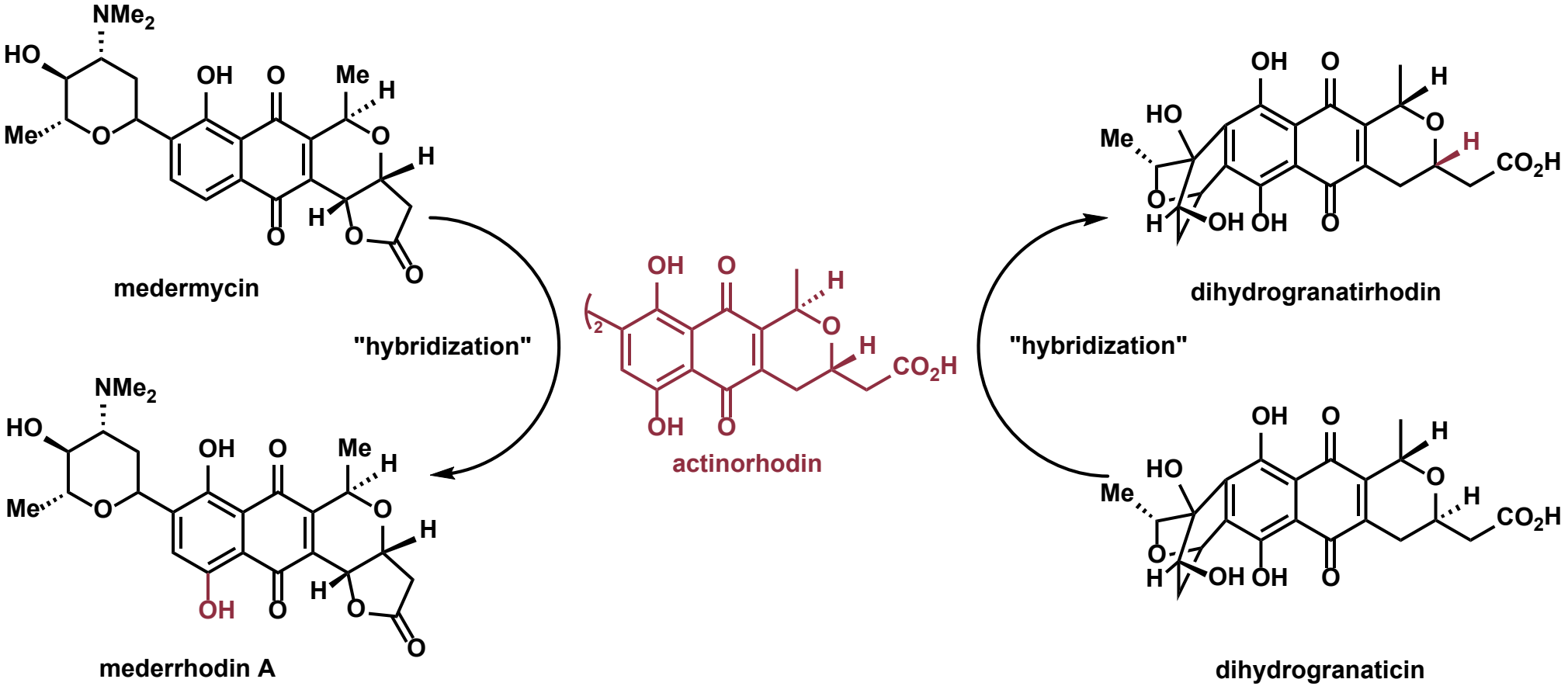
Redirecting Terpene Biosynthesis with Precursors



Org. Lett., **2023**, *25* (48), 8575–8579: *Org. Biomol. Chem.*, **2022**, *20*, 7833-7839: *Org. Lett.* **2024**, *26* (28), 5888–5892: *Org. Lett.* **2020**, *22* (11), 4360–4365

Structural Diversification of Natural Products:

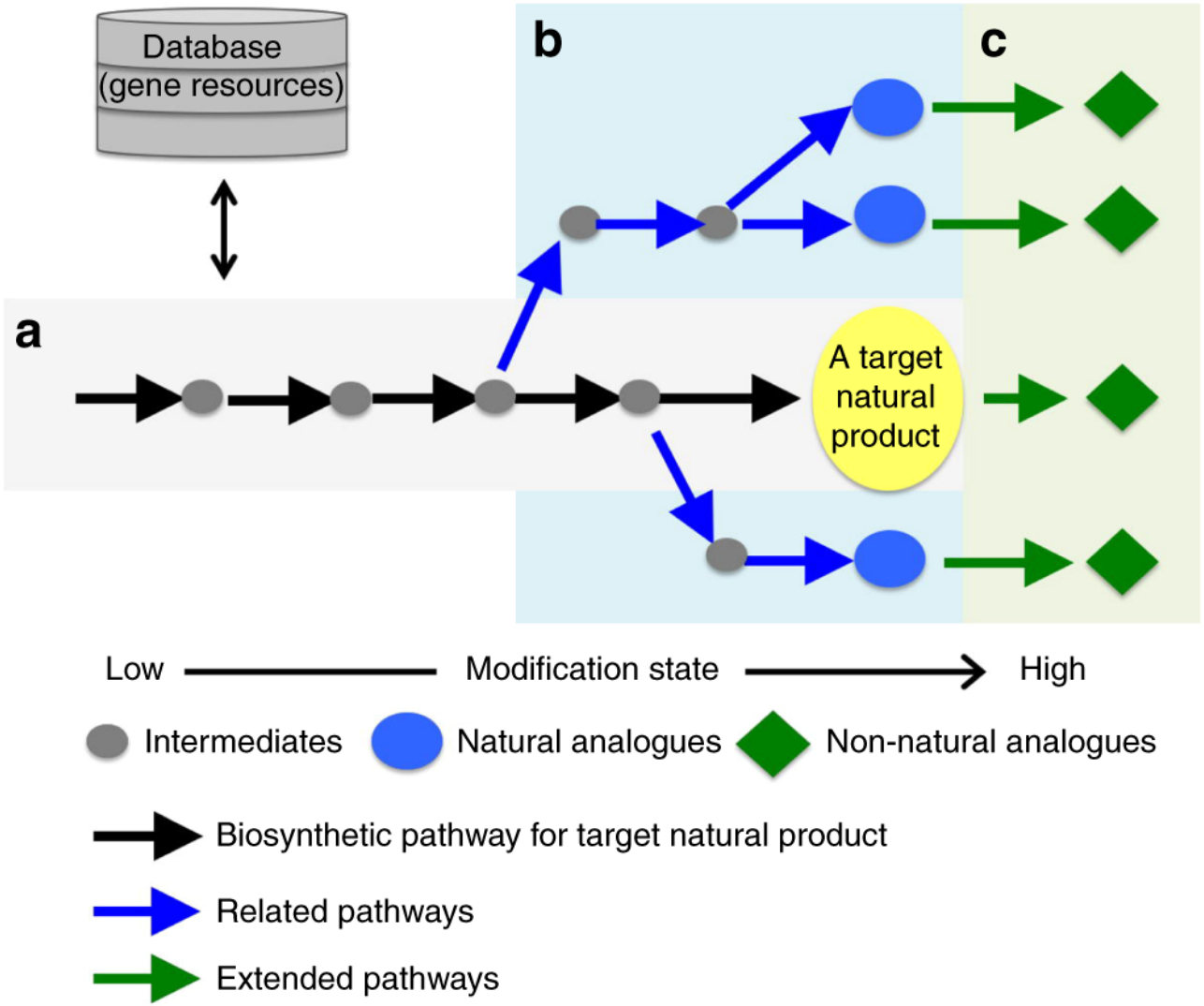
Combinatorial Biosynthesis of Hybrid Antibiotics



Nature, **1985**, *314*, 642-644

Structural Diversification of Natural Products:

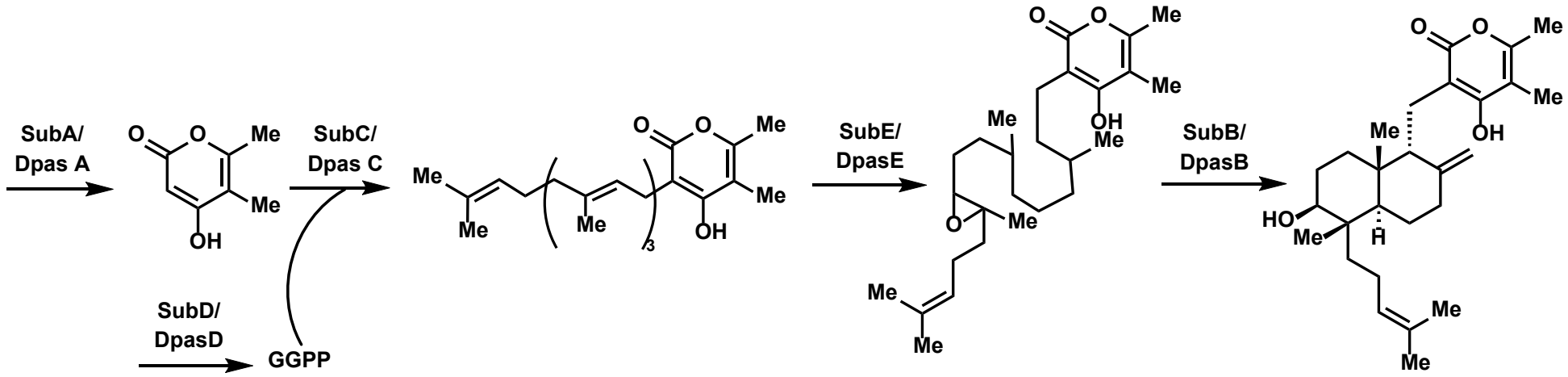
Combinatorial Biosynthesis of Decalin-Containing Diterpenoid Pyrones

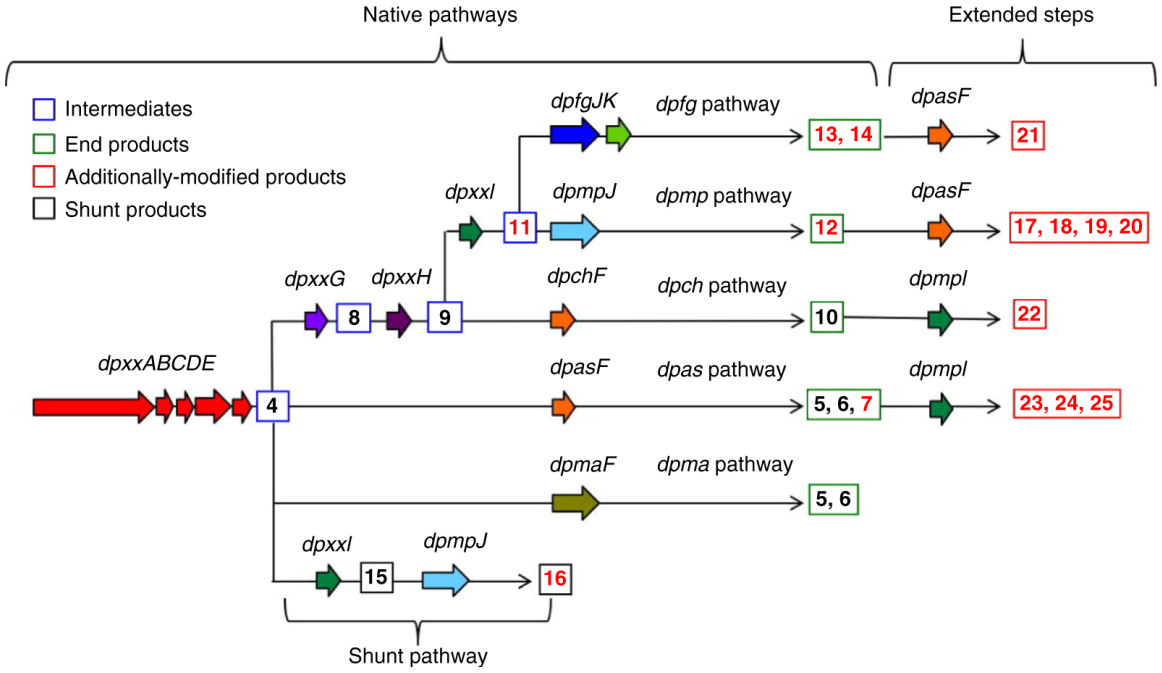


Nature Commun., **2020**, *11*, 1830

Structural Diversification of Natural Products:

Combinatorial Biosynthesis of Decalin-Containing Diterpenoid Pyrones

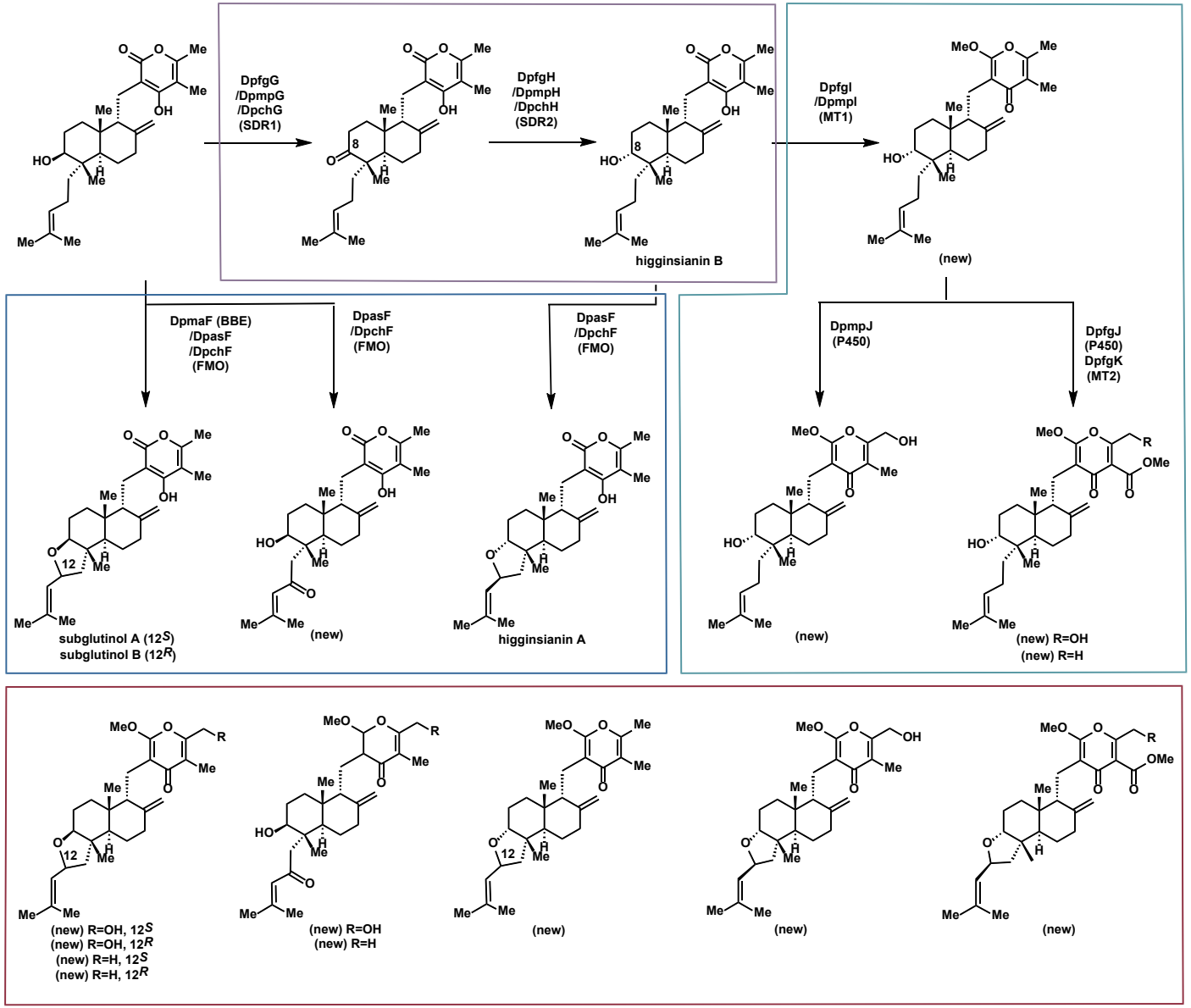




Nature Commun., **2020**, *11*, 1830

Structural Diversification of Natural Products:

Combinatorial Biosynthesis of Decalin-Containing Diterpenoid Pyrones



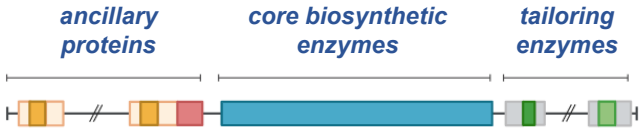
C-8 stereochemistry inversions
C-5 modifications
pyrone ring modifications
extended pathway products

Nature Commun., **2020**, *11*, 1830

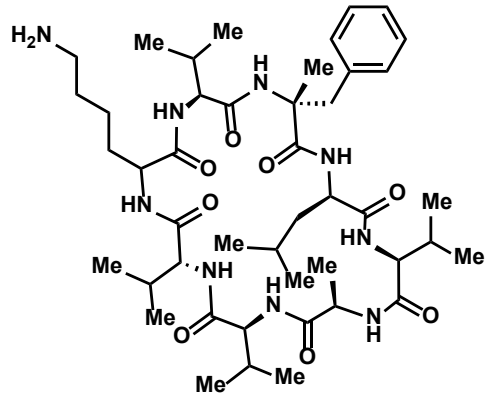
Synthetic Biology in Natural Product Biosynthesis

Advances in Tools for Natural Product Discovery

- **Bioinformatics and Machine Learning**



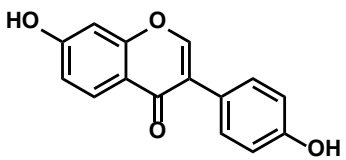
- **Synthetic Biology Tools for Mining Silent BGCs**



surugamide I

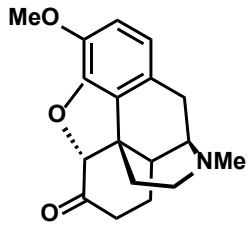
Heterologous Expression Natural Product Pathways

- **Bacteria**



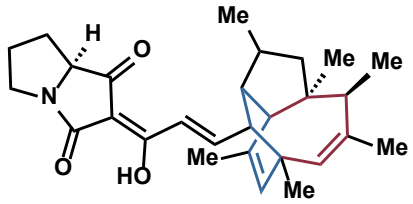
Daidzein

- **Yeast**



hydrocodone

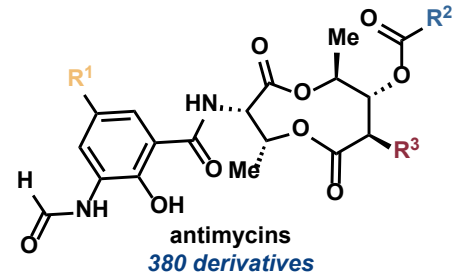
- **Fungi**



(-)-PF-1018

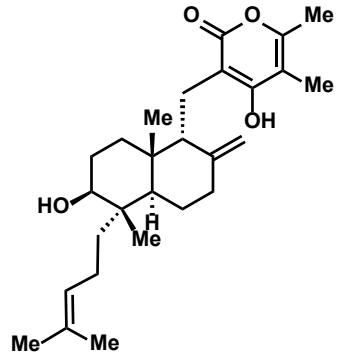
Structural Diversification of Natural Products

- **Redirecting Biosynthesis**

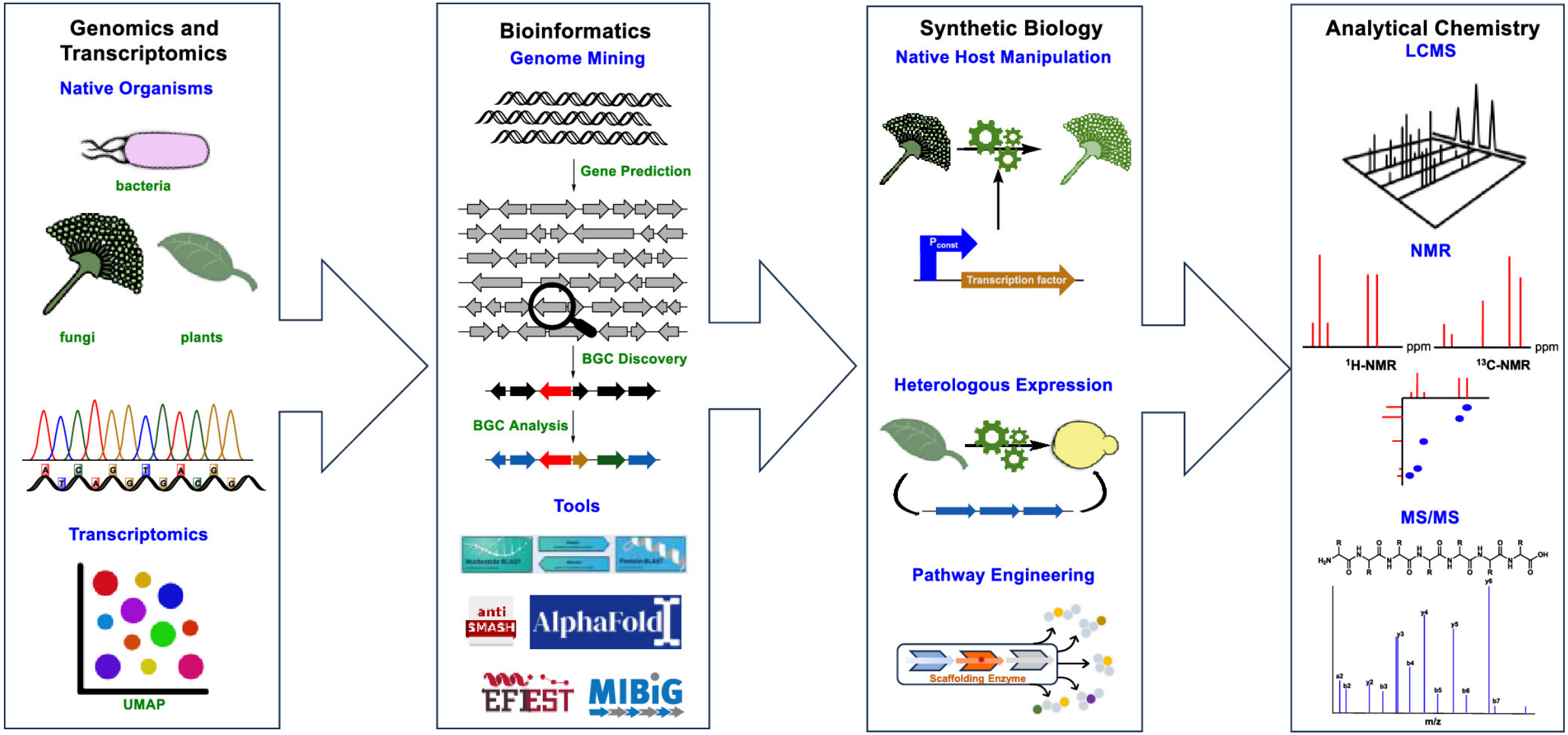


antimycins
380 derivatives

- **Combinatorial Biosynthesis**



Synthetic Biology Workflow Overview:



Chem. Rev., **2025**, *125* (7), 3814–3931