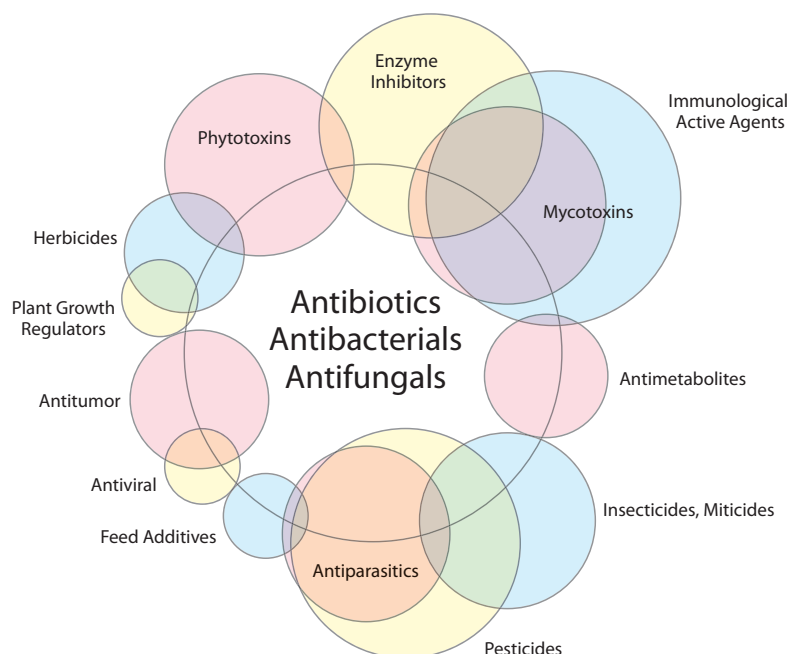


# Rare Antibiotics & Unique Natural Products

## Introduction

The definition of the term “**antibiotics**” has evolved and is much broader compared to the past, when an antibiotic had to be produced by a microorganism and had to be directed to bacteria or other microorganisms. Today antibiotics include next to secondary metabolites isolated from microorganisms, semisynthetic derivatives and chemically synthesized compounds (e.g. sulfonamides), which have antibacterial, anti-microbial, antifungal and antiprotozoal or similar effects and are potentially useful as antitumor agents, chemotherapeutic agents, enzyme inhibitors, hypocholesterolemic agents, immunosuppressive agents, antimetabolites, plant growth modulators, feed additives, or inhibitors (insecticides, miticides, antiparasitics, phytotoxins, herbicides, etc.).

Antibiotics can be classified based on their mechanism of action (MoA), chemical structures, mode of production (fermentation, synthetic or semisynthetic), producing organisms (actinobacteria, fungi (incl. **mycotoxins**), filamentous bacteria) or spectrum of activity. Some antibiotics inhibit cell wall biosynthesis, protein synthesis, nucleic acid synthesis, metabolic pathways or interfere with cell membrane integrity. They also can be classified by their molecular biological activities (anti-infective, anticancer and other activities).



**FIGURE:** Bioactive metabolites.

Adapted from *Antibiotics: Current innovations and future trends*: S. Sanchez & A.L. Demain (2015)

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The majority of the antibiotic drug class in use today was discovered in the "golden era" of antibiotic research from the 1930s to the 1970s. Meanwhile, pathogenic bacteria developed rapidly **antibiotic/antimicrobial resistance (AMR)** and **multidrug-resistance (MDR)** causing an urgent threat to public health. New families of antibiotics are continuously required to combat new diseases caused by evolving pathogens. The need for development of novel antibiotics is currently very high.

In addition, recent studies on gut microbiota have shown its immense impact on human health. It plays a key role in digestion, metabolism and immune function and has widespread impact beyond the gastrointestinal tract. Changes in the biodiversity of the gut microbiota are associated with pathologies such as inflammatory diseases, metabolic syndrome or cancer and have far reaching consequences on host health and development. Further understanding of the importance of developing and maintaining gut microbiota diversity may lead to targeted interventions.

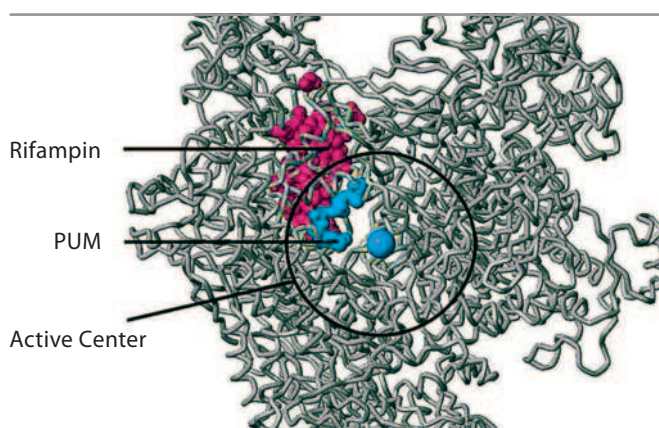
AdipoGen Life Sciences provides next to key standard research antibiotics, rare metabolites/antibiotics with new chemical structures (often only described once in literature and afterwards lost to research) or old already forgotten substances for lead drug research, seeking new "antibiotics" with new mode of actions and new molecular targets. In addition, these substances can be used for *in vitro* or *in vivo* studies based on their biological activities or as standard secondary metabolites, important as chemo-taxonomic markers of microbial species.

**For simplification this brochure uses a classification of antibiotics focusing into research areas. All compounds are listed into one class only. From plants only selected isolates are included.**

**For a complete list of compounds and activity information, please visit our website [www.adipogen.com](http://www.adipogen.com).**

## Rifamycins versus NEW Pseudouridimycin Bacterial DNA-dependent RNA Polymerase Inhibitors

The rifamycins are a group of antibiotics which are a subclass of the larger family of ansamycins. They are particularly effective against mycobacteria, and are therefore used to treat tuberculosis, leprosy and mycobacterium avium complex (MAC) infections. The rifamycins have a unique mechanism of action, selectively inhibiting bacterial DNA-dependent RNA polymerase (RNAP), due to the high affinity of rifamycins for the prokaryotic RNA polymerase and a very poor affinity for the analogous mammalian enzyme. Crystal structure data of the antibiotic bound to RNA polymerase indicates that rifamycin blocks synthesis by causing strong steric clashes with the growing oligonucleotide ("steric-occlusion" mechanism). Rifamycins show no cross-resistance with other antibiotics in clinical use. However, despite their activity against bacteria resistant to other antibiotics, the rifamycins themselves suffer from a rather high frequency of resistance. Single step high level resistance to the rifamycins occurs as the result of a single amino acid change in the bacterial DNA-dependent RNA polymerase.



**FIGURE:** Different binding sites of the bacterial DNA-dependent RNAP Inhibitors Rifampin (Rifamycin) and Pseudouridimycin

AdipoGen Life Sciences offers a broad panel of uniquely available rifamycins, which were isolated from actinobacteria and semi-synthetically derived. All of these derivatives are bacterial RNA polymerase inhibitors.

PRODUCT NAME	PID
Rifamycin AF-K43033	AG-CN2-0320
Rifamycin AF	AG-CN2-0321
Rifamycin AF-K55517	AG-CN2-0322
Rifamycin AF-K56035	AG-CN2-0323
Rifamycin AF-K28259	AG-CN2-0324
Rifamycin AF-API	AG-CN2-0325
Rifamycin AF-EPTAPI	AG-CN2-0326
Rifamycin AF-K91725	AG-CN2-0327
Rifamycin AF-DA	AG-CN2-0328
Rifamycin AF-O13	AG-CN2-0336

PRODUCT NAME	PID
Rifamycin AF-pNFI	AG-CN2-0338
Rifamycin AG	AG-CN2-0329
Rifamycin AMI-DA	AG-CN2-0330
Rifamycin AMP-DA	AG-CN2-0331
Rifamycin M14	AG-CN2-0332
Rifamycin O	AG-CN2-0333
Rifamycin PR-14	AG-CN2-0334
Rifamycin PR-3	AG-CN2-0335
Rifamycin S, 8-Methyl-	AG-CN2-0337

UNIQUE

## Antibiotic Pseudouridimycin

The newly discovered antibiotic Pseudouridimycin [PUM] is the first nucleoside-analog inhibitor that selectively inhibits bacterial RNA polymerase but not human RNA polymerases. It mimics nucleoside-triphosphate (NTP), the chemical "building block" that bacterial RNA polymerase uses to synthesize RNA. PUM binds tightly to the NTP binding site on bacterial RNA polymerase and, by occupying the NTP binding site, prevents NTPs from binding. Because PUM inhibits through a different binding site (see Figure, blue) and mechanism than rifampin, PUM exhibits no cross-resistance with rifampin. In addition it has a much lower spontaneous resistance rate than rifampin and kills a broad spectrum of drug-sensitive and drug-resistant bacteria *in vitro* and *in vivo*.

### Pseudouridimycin

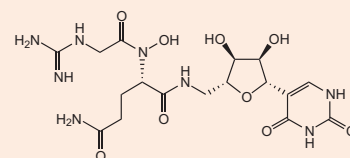
AG-CN2-0316

1 mg | 5 mg

Formula:  $C_{17}H_{26}N_8O_9$ 

MW: 486.4

CAS: 1566586-52-4

Source: *Streptomyces* sp. (Actinobacteria)

LIT: Pseudouridimycin: The First Nucleoside Analogue That Selectively Inhibits Bacterial RNA Polymerase: M.F. Chellat & R. Riedl; Angew. Chem. Int. Ed. Engl. **56**, 13184 (2017)

## Other Selected Antibiotics isolated from Bacteria Species

### Nargenicin A1

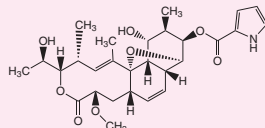
BVT-0204

1 mg | 5 mg

Formula:  $C_{28}H_{37}NO_8$ 

MW: 515.6

CAS: 70695-02-2

Source: *Actinomyces* sp. Gö301 (Actinobacteria)

Antibiotic against Gram-positive bacteria.

Effective against multi-resistant strains (MRSA).

### Thaxtomin A

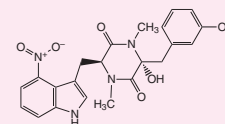
BVT-0206

1 mg | 5 mg

Formula:  $C_{22}H_{22}N_4O_6$ 

MW: 438.4

CAS: 122380-18-1

Source: *Streptomyces bottropensis* Gö-Dra 17 (Actinobacteria)

Phytotoxin. Plant cell necrosis inducer.  
Natural cellulose synthesis inhibitor.

PRODUCT NAME	BIOLOGICAL ACTIVITY	PID
<b>Aureothricin</b>	Potent bacterial and yeast RNA polymerases inhibitor.	BVT-0345
<b>Aurodox</b>	Protein biosynthesis (EF-Tu) inhibitor.	AG-CN2-0133
<b>Enterocin</b>	Broad spectrum activity against Gram-positive and Gram-negative bacteria.	AG-CN2-0116
<b>Josamycin</b>	Broad spectrum antimicrobial.	CDX-J0001
<b>Kirromycin</b>	Protein biosynthesis (EF-Tu) inhibitor.	BVT-0157
<b>Lysolipin I</b>	Antibacterial, antifungal and anticoccidial. Cell wall synthesis inhibitor.	BVT-0037
<b>Nocardamine</b>	Siderophore (iron (Fe) chelating compound).	AG-CN2-0150
<b>Orthoformimycin</b>	Protein synthesis inhibitor. Bacterial translation elongation inhibitor.	AG-CN2-0314
<b>Paramagnetoquinone A/B</b>	Potent antibacterial agent.	AG-CN2-0315
<b>Purpuromycin</b>	Protein synthesis inhibitor.	AG-CN2-0317
<b>Ramoplanin A2</b>	Antibacterial. Cell wall synthesis inhibitor by forming a complex with Lipid II.	AG-CN2-0318
<b>Simocyclinone D8</b>	Bacterial DNA gyrase inhibitor.	BVT-0290
<b>Thermorubin</b>	Antibacterial. Inhibits the initiation stage of bacterial protein synthesis.	AG-CN2-0339
<b>Valinomycin</b>	K <sup>+</sup> -selective ionophore.	CDX-P0163
<b>Zelkovamycin</b>	Antibacterial.	AG-CN2-0128

# Lantibiotics & Thiazolypeptides (RiPPs)

## Ribosomally Synthesized and Post-translationally Modified Peptides

Lantibiotics (a subset of lanthipeptides with antimicrobial activity) are ribosomally synthesized peptides that undergo posttranslational modifications to yield the active structures containing the typical thioether-linked lanthionines (Lans) or methyllanthionines (Melans). Lantibiotics with antibacterial activity are divided into different classes according to their biogenesis and into two groups type A and type B, according to their different modes of action. The target molecule for both type A and B lantibiotics has been shown to be lipid II, the basic peptidoglycan precursor. In general, type B lantibiotics (e.g. actagardine) bind to lipid II and inhibit cell wall synthesis whereas binding of type A lantibiotics (e.g. nisin) to lipid II seems to facilitate pore formation and more rapid cell death. As lantibiotics bind lipid II (a highly conserved structure) at a site different from that affected by vancomycin and related glycopeptides, they represent important leads in the ongoing fight against the rise of antibiotic-resistant strains of bacteria and are active against multidrug-resistant (MDR) Gram-positive pathogens.

Thiazolypeptides are highly modified, ribosomally synthesized peptides that inhibit bacterial protein synthesis by affecting either elongation factor Tu or the loops defined by 23S rRNA and the L11 protein. Most thiazolypeptides show potent activity against Gram-positive pathogens.

Collaborating with



UNIQUE

### NAI-107 [Microbisporicin A1/A2 Mixture]

AG-CN2-0307

1 mg | 5 mg

**Formula:**  $C_{94}H_{127}ClN_{26}O_{27}S_5$  (A1)  
 $C_{94}H_{127}ClN_{26}O_{26}S_5$  (A2)

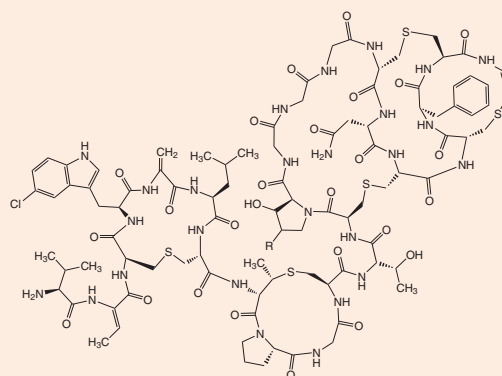
**MW:** 2249.0 (A1; R=OH)  
 2233.0 (A2; R=H)

**CAS:** 845293-74-5 [A1/A2 Mixture]

**Source:** *Microbispora* sp. (Actinobacteria)

Antibacterial class I lantibiotic. Inhibits cell wall synthesis and consequently bacterial growth by forming a complex with lipid intermediate II (Lipid II), a key intermediate in peptidoglycan biosynthesis. Active against aerobic and anaerobic Gram-positive pathogens, including all antibiotic-resistant strains (e.g. MRSA and VRE) in whole cell and *in vitro* assays as well as *in vivo*. Rapidly bactericidal and highly efficacious in experimental models of infection (septicemia, endocarditis, granuloma pouch) and developed for **treatment of serious infections by multiresistant Gram-positive bacteria**.

**LIT:** Advancing cell wall inhibitors towards clinical applications: S.I. Maffioli, et al.; J. Ind. Microbiol. Biotechnol. **43**, 177 (2016) (Review) • The Lantibiotic NAI-107 Efficiently Rescues *Drosophila melanogaster* from Infection with Methicillin-Resistant *Staphylococcus aureus* USA300: T.T. Thomsen, et al.; Antimicrob. Agents Chemother. **60**, 5427 (2016) • Microbisporicin (NAI-107) protects *Galleria mellonella* from infection with *Neisseria gonorrhoeae*: N. Hofkens, et al.; Microbiol. Spectr. **11**, e0282523 (2023)



PRODUCT NAME	BIOLOGICAL ACTIVITY	SOURCE	PID
<b>Actagardine</b>	Tetracyclic class II lantibiotic. Specifically inhibits peptidoglycan synthesis.	Actinobacteria	AG-CN2-0300
<b>BE-31405</b>	Broad spectrum antifungal agent. Inhibits the protein synthesis.	Fungi	AG-CN2-0302
<b>GE2270A</b>	Thiopeptide antibiotic. Inhibitor of domain II of elongation factor Tu (EF-Tu).	Actinobacteria	AG-CN2-0303
<b>GE2270 D2</b>	Thiopeptide antibiotic. Inhibitor of elongation factor Tu (EF-Tu).	Actinobacteria	AG-CN2-0304
<b>GE23077 A1/B1</b>	Cyclic heptapeptide antibiotic. Potent and selective bacterial RNAP inhibitor.	Actinobacteria	AG-CN2-0305
<b>GE81112 A/B</b>	Tetrapeptide antibiotic. Potent and selective inhibitor of bacterial protein synthesis.	Actinobacteria	AG-CN2-0306
<b>NAI-108</b>	Antibacterial class I lantibiotic. Brominated variant of NAI-107. Cell wall synthesis inhibitor.	Actinobacteria	AG-CN2-0308
<b>NAI-112</b>	Labionin-containing class III lanthipeptide. Antinociceptive agent.	Actinobacteria	AG-CN2-0309
<b>NAI-802</b>	Actagardine-related class II lantibiotic. Cell wall synthesis inhibitor.	Actinobacteria	AG-CN2-0310
<b>NAI-857</b>	Antibacterial class I lantibiotic. Cell wall synthesis inhibitor.	Actinobacteria	AG-CN2-0311
<b>NAI-97 [Planosporicin]</b>	Antibacterial class I lantibiotic. Cell wall synthesis inhibitor.	Actinobacteria	AG-CN2-0312



## Quorum Sensing – Targeting the Bacterial Biofilm

Quorum sensing is a signaling system used by bacteria to coordinate gene expression, biofilm formation, virulence and antibiotic resistance based upon their population density. The system involves the exchange of signaling molecules among bacteria via cell receptors. Next to the potential antimicrobial functionality, quorum-sensing molecules are recently investigated for their use in immunology and oncology, based on findings that they can modulate prokaryote-eukaryote signaling and due to the similarities between the bacterial quorum-sensing mechanisms and the metastatic process initiated by tumor cells.

### Tropodithietic acid [TDA] **UNIQUE**

BVT-0152

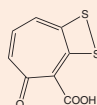
Formula:  $C_8H_4O_3S_2$ 

MW: 212.3

CAS: 750590-18-2

Source: *Roseobacter gallaeciensis* (Proteobacteria)

1 mg | 5 mg

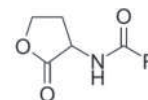


Quorum sensing bacterial signal substance. Active against Gram-positive and Gram-negative bacteria. Antifungal and anti-nematodical. Shows antitumor activity.

**LIT:** Dual function of tropodithietic acid as antibiotic and signaling molecule in global gene regulation of the probiotic bacterium *Phaeobacter inhibens*: P.G. Beyersmann, et al.; Sci. Rep. 7, 730 (2017)

### N-Acylhomoserine Lactones (AHLs)

FIGURE: General chemical structure of a N-Acylhomoserine Lactone.



N-Acylhomoserine Lactones (AHL) are involved in quorum sensing, controlling gene expression and cellular metabolism. The diverse applications of this kind of molecule include regulation of virulence in general, infection prevention and formation of biofilms.

Visit [www.adipogen.com](http://www.adipogen.com) for a broad Panel of DL-Homoserine Lactones and Quorum Sensing Agents!

## Exosome Biogenesis Modulators

RAS signaling directly regulates the sorting of a variety of cargos into exosomes. RAS proteins are small GTPases that play a critical role in cell signaling pathways. Farnesyltransferase (FTase) is responsible for the addition of a farnesyl group to RAS proteins, which is an essential step in their proper function and localization within the cell. Targeting exosome biogenesis might be crucial for RAS signaling inhibitors to exert their anticancer effects.

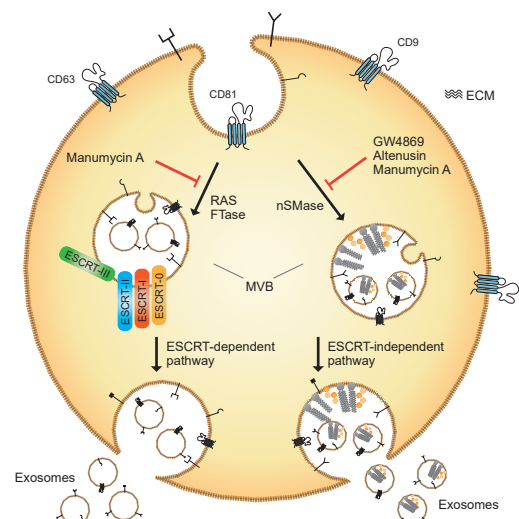


FIGURE: Schematic of exosome biogenesis and inhibition.

THE **SOURCE** **BULK**

### Manumycin A

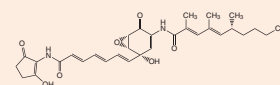
AG-CN2-2000

1 mg | 5 mg | 10 mg

Formula:  $C_{31}H_{38}N_2O_7$ 

MW: 550.6

CAS: 52665-74-4

Source: *Streptomyces parvulus* (Actinobacteria)

Manumycin A is a selective inhibitor of FTase, suppressing thereby RAS/RAF/ERK1/2 signaling and inhibiting exosome biogenesis and secretion.

#### Rasfarnesyltransferase Inhibitors

<b>Andrastin A</b>	Fungi	AG-CN2-0144
<b>Deoxymanumycin A</b>	Actinobacteria	BVT-0158
<b>Dihydromanumycin A</b>	Actinobacteria	BVT-0414
<b>Manumycin A</b>	Actinobacteria	BVT-0091
<b>Manumycin B</b>	Actinobacteria	BVT-0264
<b>Palmarumycin C3</b>	Fungi	BVT-0078
<b>Saquayamycin B1</b>	Actinobacteria	BVT-0382

# Antibiotics for Cancer Research

Antibiotics comprise many chemical structures and act by different mechanisms to reveal their antineoplastic and immune regulating properties. Their different mode of actions, including DNA and RNA synthesis inhibitors, DNA crosslinkers, DNA strand break inducers, DNA-cleaving agents, microtubule stabilizing agents, P-glycoprotein efflux pump inhibitors, metabolic modulators or other kinase/enzyme inhibitors, make antibiotics important research tools, targeting processes such as apoptosis, angiogenesis, autophagy, proteasomal degradation, cell cycle, proliferation or immunometabolism. The structural diversity make them also attractive scaffolds for potential future therapeutics.

## DNA/RNA Synthesis & Replication Modulators

### THE STANDARDS

#### Actinomycin D

BVT-0089

5 mg | 25 mg

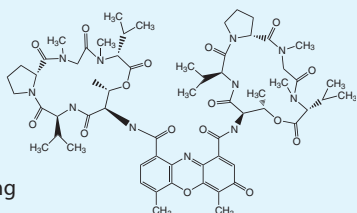
Formula:  $C_{62}H_{86}N_{12}O_{16}$

MW: 1255.4

CAS: 50-76-0

Source: *Streptomyces parvulus* (Actinobacteria)

Potent RNA synthesis inhibitor. DNA intercalating agent.



#### (+)-Aphidicolin

BVT-0307

1 mg | 5 mg | 25 mg

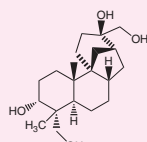
Formula:  $C_{20}H_{34}O_4$

MW: 338.5

CAS: 38966-21-1

Source: *Phoma* sp. BS 7210. (Fungi)

Reversible inhibitor of eukaryotic nuclear DNA replication. Specific DNA polymerase  $\alpha$  and  $\delta$  inhibitor in eukaryotic cells. Useful for cell synchronization.



PRODUCT NAME	TARGET	PID
<b>Alternariol</b>	Topoisomerase II $\alpha$	BVT-0465
<b>Antibiotic UK-1</b>	Topoisomerase II	BVT-0013
<b>Becatecarin</b>	Topoisomerase II	BVT-0258
<b>Borrelidin</b>	Threonyl-tRNA Synthetase	BVT-0098
<b>Chartreusin</b>	Topoisomerase II	BVT-0005
<b>Chrysomycin A</b>	Topoisomerase II	BVT-0099
<b>Chrysomycin B</b>	Topoisomerase II	BVT-0100
<b>Cordycepin</b>	DNA/RNA Synthesis	CDX-C0339
<b>Daptomycin</b>	DNA/RNA Synthesis	AG-CN2-0542
<b>3-Deoxyaphidicolin</b>	DNA Polymerase $\alpha$	BVT-0451
<b>Doxorubicin HCl</b>	DNA/RNA Synthesis	CDX-D0257
<b>Heliquinomycin</b>	DNA Helicase	AG-CN2-0091
<b>Gilvocarcin V</b>	Cross-linking between DNA/Histone H3	BVT-0256
<b>5-Methylmellein</b>	DNA Polymerase I	BVT-0413
<b>Mitomycin C</b>	DNA Synthesis	CDX-M0161
<b>OM173-<math>\alpha</math>A</b>	DNMT3B	AG-CN2-0158
<b>Rebeccamycin</b>	Topoisomerase I	BVT-0139
<b>Reticulol</b>	Topoisomerase I	BVT-0011
<b>Rubrofusarin</b>	RNA Polymerase	BVT-0395
<b><math>\beta</math>-Rubromycin</b>	Telomerase	BVT-0251
<b><math>\gamma</math>-Rubromycin</b>	Telomerase	BVT-0007

## Specific Vacuolar-type H<sup>+</sup>-ATPase Inhibitors

### THE SOURCE BULK

#### Concanamycin A (high purity)

BVT-0237

25  $\mu$ g | 100  $\mu$ g | 1 mg | 5 mg

Formula:  $C_{46}H_{75}NO_{14}$

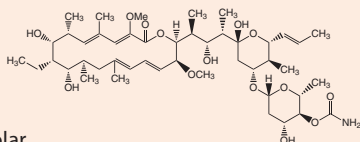
MW: 866.1

CAS: 80890-47-7

Source: *Streptomyces* sp. (Actinobacteria)

Potent and specific vacuolar H<sup>+</sup>-ATPase inhibitor.

Also Available: **Concanamycin B & C**



### THE SOURCE BULK

#### Bafilomycin A<sub>1</sub> (high purity)

AG-CN2-2001

100  $\mu$ g | 1 mg | 5 mg

Formula:  $C_{35}H_{58}O_9$

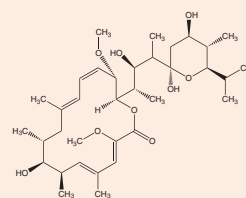
MW: 622.8

CAS: 88899-55-2

Source: *Streptomyces griseus* (Actinobacteria)

Specific vacuolar-type H<sup>+</sup>-ATPase inhibitor. Distinguishes among different types of ATPases.

Also Available: **Bafilomycin B<sub>1</sub>, C<sub>1</sub> & D**



# Immunosuppressive Antibiotics

The common immunosuppressive antibiotics are involved in cell proliferation pathways and include calcineurin (FK-506, cyclosporin A, ascomycin), mTOR (everolimus, rapamycin) and purine synthesis (mycophenolic acid) inhibitors. Inhibition of calcineurin leads to inhibition of NFAT activation, reduced IL-2 production and consequently to reduced T cell proliferation. Inhibition of mTOR leads to inhibition of IL-2 mediated cell cycle, which consequently blocks T cell activation and B cell differentiation. Blockade of purine synthesis by inhibiting inosine monophosphate dehydrogenase (IMPDH) leads to a selective inhibition of lymphocyte proliferation.

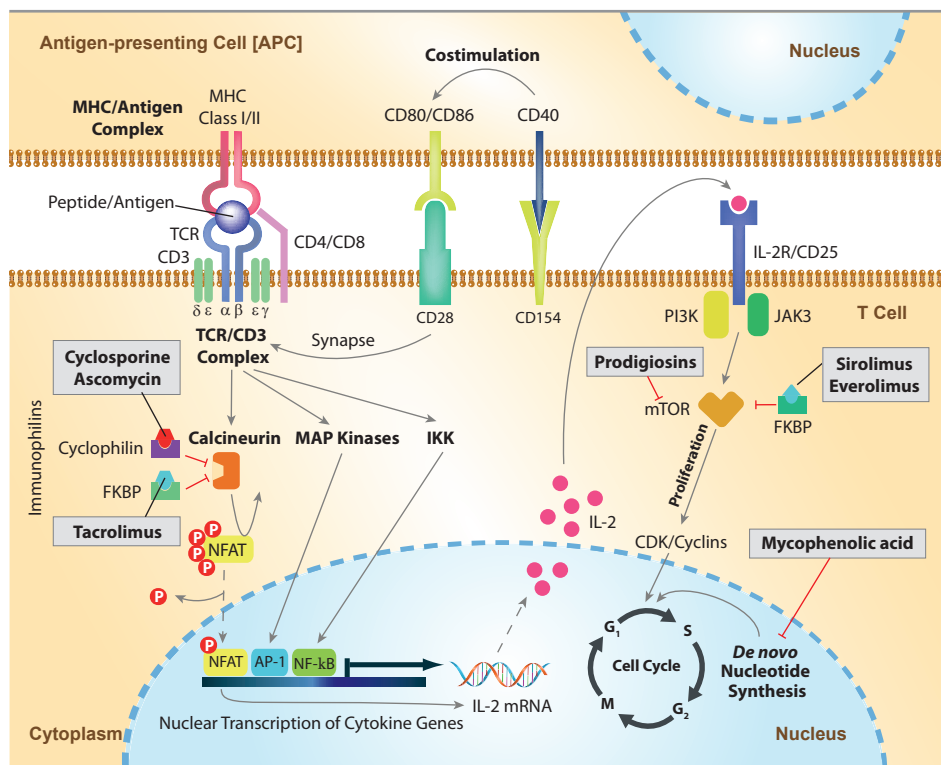


FIGURE: Mechanisms of T Cell Immunosuppression.

## Everolimus

AG-CN2-0520

CDX-E0074

Formula:  $C_{53}H_{83}NO_{14}$

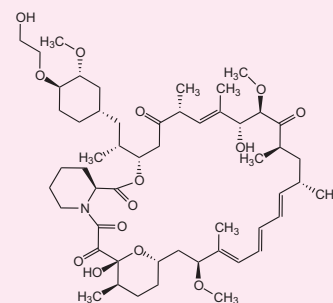
MW: 958.2

CAS: 159351-69-6

Source: *Streptomyces hygroscopicus* (Actinobacteria) / Semi-synthetic

Potent immunosuppressive agent. Binds with high affinity to the FK-506 binding protein-12 (FKBP12) to generate an immunosuppressive complex that inhibits the activation of the mammalian target of rapamycin (mTOR). Shows also anticancer and antibacterial activities.

1 mg | 5 mg | 25 mg  
100 mg | 250 mg



PRODUCT NAME	TARGET	SOURCE	PID
Rapamycin [Sirolimus]	mTOR	Actinobacteria	AG-CN2-0025
FK-506 [Tacrolimus]	Calcineurin	Actinobacteria	AG-CN2-0047
Ascomycin (high purity) [Immunomycin]	Calcineurin	Actinobacteria	AG-CN2-0420
Cyclosporin A	Calcineurin	Fungi	AG-CN2-0079
Cyclosporin C	Calcineurin	Fungi	AG-CN2-0443
Pimecrolimus	Calcineurin	Synthetic	CDX-P0598
Also Available: Cyclosporin D, Cyclosporin H			
Mycophenolic acid [MPA]	Purine Synthesis	Fungi	AG-CN2-0419
Prodigiosin	mTOR	Proteobacteria	AG-CN2-0105
Undecylprodigiosin . HCl	mTOR	Actinobacteria	BVT-0422
Butylcycloheptylprodigiosin	mTOR	Actinobacteria	BVT-0423

# Cell Metabolism / Immunometabolism Modulators

## **m** Atpenin A5 (synthetic)

AG-CN2-0100

250 µg | 1 mg

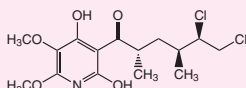
Formula:  $C_{15}H_{21}Cl_2NO_5$

MW: 366.2

CAS: 119509-24-9

Source: Originally isolated from *Penicillium* sp. FO-125 (Fungi)

Potent and specific mitochondrial complex II (succinate-ubiquinone oxidoreductase) inhibitor.



## **m** Heptelidic acid

AG-CN2-0118

250 µg | 1 mg

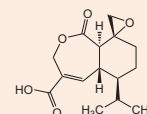
Formula:  $C_{15}H_{20}O_5$

MW: 280.3

CAS: 74310-84-2

Source: *Trichoderma* sp. (Fungi)

Potent selective GAPDH inhibitor. Selectively kills high-glycolytic cancer cells through glucose-dependent active ATP deprivation.



PRODUCT NAME	TARGET	SOURCE	PID
<b>Aureothin</b>	NADH dehydrogenase (Complex I) inhibitor / OXPHOS.	Actinobacteria	BVT-0303
<b>m Fusicin</b>	NADH dehydrogenase (Complex I) inhibitor / OXPHOS.	Fungi	AG-CN2-0138
<b>m Harzianopyridone</b>	Succinate-Q Oxidoreductase (Complex II) inhibitor / OXPHOS.	Fungi	AG-CN2-0149
<b>Iromycin A</b>	NADH dehydrogenase (Complex I) inhibitor / OXPHOS.	Actinobacteria	BVT-0262
<b>Itaconate</b>	Succinate dehydrogenase (SDH) inhibitor.	Synthetic	AG-CN2-0426
<b>4-Octyl itaconate</b>	Succinate dehydrogenase (SDH) inhibitor.	Synthetic	AG-CR1-3700
<b>Oligomycin A</b>	ATPases (F0F1) inhibitor / OXPHOS.	Actinobacteria	AG-CN2-0517
<b>m Phomoxanthone A</b>	Disrupts inner mitochondrial membrane.	Fungi	BVT-0453
<b>Propionyl-L-carnitine . HCl</b>	Stimulates pyruvate dehydrogenase activity.	Synthetic	AG-CR1-3595
<b>Venturicidin A</b>	ATPases (F0F1) inhibitor / OXPHOS.	Actinobacteria	BVT-0454

# Microtubule & F-actin Modulators

## THE SOURCE BULK

### Latrunculin B

AG-CN2-0031

500 µg | 1 mg

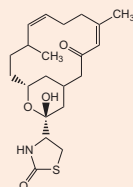
Formula:  $C_{20}H_{29}NO_5S$

MW: 395.5

CAS: 76343-94-7

Source: *Latrunculia magnifica* (Marine)

Actin polymerization inhibitor. Potent phagocytosis inhibitor. Anticancer compound. Inhibits tumor cell invasion.



## THE SOURCE

### Jasplakinolide

AG-CN2-0037

50 µg | 100 µg

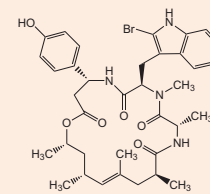
Formula:  $C_{36}H_{45}BrN_4O_6$

MW: 709.7

CAS: 102396-24-7

Source: *Jaspis splendens* (Marine)

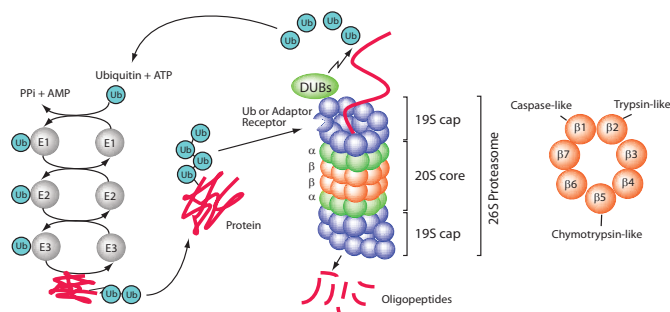
Cell permeable, non-fluorescent F-actin probe. Potent inducer of actin polymerization and stabilization. Tool used for autophagy/phagocytosis research.



PRODUCT NAME	TARGET	SOURCE	PID
<b>m Citrinin</b>	Tubulin polymerization and mitotic spindle assembly inhibitor.	Fungi	AG-CN2-0101
<b>m Curvulin</b>	Microtubule assembly inhibitor.	Fungi	BVT-0097
<b>m Cytochalasin B</b>	Actin polymerization inhibitor.	Fungi	AG-CN2-0504
<b>m Cytochalasin H</b>	Actin polymerization inhibitor.	Fungi	BVT-0447
<b>m Cytochalasin J</b>	Actin and myosin inhibitor.	Fungi	BVT-0450
<b>Ilimaquinone</b>	Cytoplasmic microtubule inhibitor.	Marine	AG-CN2-0038
<b>Latrunculin A</b>	Actin polymerization inhibitor.	Marine	AG-CN2-0027
<b>16-epi-Latrunculin B</b>	Actin polymerization inhibitor.	Marine	AG-CN2-0034
<b>m Phomopsin A</b>	Microtubule assembly inhibitor.	Fungi	AG-CN2-0515
<b>Sceptrin . 2HCl</b>	Actin polymerization inhibitor.	Marine	AG-CN2-0440
<b>Swinholide A</b>	Actin filament (F-actin) inhibitor.	Marine	AG-CN2-0035



# The Ubiquitin-Proteasome System (UPS)



The **ubiquitin-proteasome system (UPS)** and the autophagic-lysosomal pathway are the two major **degradation systems** for both native and misfolded proteins in eukaryotic cells. The regulated proteolysis of bulk and misfolded proteins is strictly controlled by the 26S proteasome complex, which consists of the 19S regulatory cap and the 20S proteasome core. Although eukaryotic 20S proteasomes harbor seven different  $\beta$ -subunits in their two-fold symmetrical  $\alpha$ 7 $\beta$ 7 $\beta$ 7 $\alpha$ 7 stacked complexes, only three  $\beta$ -subunits per  $\beta$ -ring [**subunits  $\beta$ 1 (caspase-like),  $\beta$ 2 (trypsin-like) and  $\beta$ 5 (chymotrypsin-like)**] are proteolytically active. These three  $\beta$ -subunits are major targets for small molecule proteasome inhibitors. **Proteasome inhibition** has implications in a number of human diseases such as cancer, inflammation and ischemic stroke and is an important therapeutic target.

## BULK UNIQUE

### Potent 20S Proteasome Inhibitor

#### Salinosporamide A

AG-CN2-0444

100  $\mu$ g | 1 mg | 5 mg | 50 mg

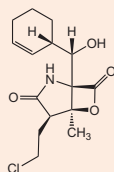
Formula:  $C_{15}H_{20}ClNO_4$

MW: 313.8

CAS: 437742-34-2

Source: *Salinospora tropica* (Marine)

Inhibits all three catalytic activities: chymotrypsin-like ( $EC_{50} = 3.5nM$ ); trypsin-like ( $EC_{50} = 28nM$ ); caspase-like ( $EC_{50} = 430nM$ ).



PRODUCT NAME	TARGET	PID
<b>Epoxomicin</b>	Predominant chymotrypsin-like activity inhibitor.	AG-CN2-0422
<b>Kendomycin</b>	Chymotrypsin-like inhibitor.	BVT-0001
<b>Lactacystin</b>	Chymotrypsin-like, trypsin-like and caspase-like activity inhibitor.	AG-CN2-0104
<b>clasto-Lactacystin <math>\beta</math>-lactone</b>	Chymotrypsin-like, trypsin-like and caspase-like activity inhibitor.	AG-CN2-0442

## Protein Phosphatase 2A (PP2A) Inhibitors

### THE SOURCE

Protein Phosphatase 2A (PP2A) is an important and ubiquitously expressed serine/threonine phosphatase and regulates the function by dephosphorylating many critical cellular molecules like Akt, p53, c-Myc and  $\beta$ -catenin. It plays a critical role in cellular processes, such as cell proliferation, signal transduction and apoptosis.

PRODUCT NAME	SOURCE	PID
<b>Cantharidin</b>	Blister Beetle	CDX-C0643
<b>Cytostatin</b>	Actinobacteria	AG-CN2-0093
<b>Fostriecin</b>	Actinobacteria	AG-CN2-0057
<b>Okadaic acid (high purity)</b>	Marine	AG-CN2-0056
<b>Okadaic acid . ammonium salt (high purity)</b>	Marine	AG-CN2-0058
<b>Okadaic acid . sodium salt (high purity)</b>	Marine	AG-CN2-0062
<b>Rubratoxin A</b>	Fungi	AG-CN2-0092

# Protein Kinase & Enzyme Modulation

A protein kinase is an enzyme that modifies other proteins by chemically adding phosphate groups to them (phosphorylation). Phosphorylation usually results in a functional change of the target protein (substrate) by changing enzyme activity, cellular location or association with other proteins. Therefore, protein kinase (or in general enzyme such as synthase, transferase, etc.) inhibitors can be used to treat diseases due to hyperactive protein kinases/enzymes or to modulate cell functions to overcome other disease drivers and are used in the treatment of cancer and inflammatory disorders.

	PRODUCT NAME	TARGET	SOURCE	PID
	<b>PKC, CDK and GSK Inhibitors</b>			
m	Butyrolactone I	CDK-1, -2 and -5	Fungi	BVT-0448
m	Calphostin C	PKC, PKA, PKG, DAG, Phospholipase D1 and D2, MLCK, c-Src	Fungi	AG-CN2-0430
m	Cercosporin	PKC	Fungi	AG-CN2-0111
	Debromohymenialdisine	PKC & MEK-1	Marine	AG-CN2-0068
	Hymenidin	CDK5/p25, GSK-3β	Marine	AG-CN2-0503
	K-252a	PKC, PKA, PKG	Actinobacteria	AG-CN2-0019
	K-252c	PKC	Actinobacteria	AG-CN2-0097
	Phenylmethylene hydantoin	GSK-3β	Marine	AG-CN2-0041
	Staurosporine	PKA, PKC, PKG, CaM kinase, MLCK, CDK-1, -2, -4, -5, GSK-3β, Pim-1, (Topo II)	Actinobacteria	AG-CN2-0022
	<b>HDAC Inhibitors</b>			
m	Apicidin	HDAC	Fungi	AG-CN2-0087
m	Dihydrochlamydocin	HDAC	Fungi	AG-CN2-0115
	Psammaplin A	Class I HDAC	Marine	AG-CN2-0088
	<b>PI3K Inhibitors</b>			
m	Bostrycin	PI3K/Akt	Fungi	AG-CN2-0175
m	Viridol	PI3K	Fungi	AG-CN2-0126
m	Wortmannin	PI3K	Fungi	AG-CN2-0023
	<b>Other Enzyme Inhibitors</b>			
	Actinonin	PDF, MMP and Mepain A	Actinobacteria	AG-CN2-0161
	Ageladine A . trifluoroacetate	MMP-1, -2, -8, -9, -12, -13, TYK2, DYRK2, Dyrk1A, YSK4, RPS6KA1/2	Marine	AG-CMA-1001
m	Altenusin	pp60c-Src, cFMS receptor tyrosine kinase, MLCK	Fungi	AG-CN2-0143
m	Anomalin A	Non-specific protein kinases	Fungi	AG-CN2-0006
	Benadrostin	PARP	Actinobacteria	BVT-0079
m	Cephalochromin	PDE	Fungi	BVT-0440
m	Curvularin	iNOS (NOSII)	Fungi	AG-CN2-0147
	Decoyinine	GMP synthetase	Actinobacteria	BVT-0030
m	Fumagillin	MetAP2	Fungi	AG-CN2-0529
m	Hypothemycin	Threonine/tyrosine-specific kinase	Fungi	BVT-0067
m	Penicillide	Calpain	Fungi	AG-CN2-0122
	Psicofuranine	Antimetabolite of the purine biosynthesis	Actinobacteria	BVT-0284
m	Pyridoxatin	MMP-2	Fungi	AG-CN2-0123
	Streptochlorin	Tyrosinase	Actinobacteria	AG-CN2-0141
	Terreic acid	MurA, BTK	Fungi	BVT-0477
m	Xanthomegnin	iNOS (NOSII)	Fungi	BVT-0365

## HSP90 Inhibitors

THE SOURCE

HSP90 (heat shock protein 90) is a chaperone protein that assists other proteins to fold properly, stabilizes proteins against heat stress and aids in protein degradation. It also stabilizes a number of proteins required for tumor growth, which is why HSP90 inhibitors are investigated as anti-cancer drugs.

	PRODUCT NAME	SOURCE	PID
	Geldanamycin	Actinobacteria	BVT-0196
	17-AAG	Semi-synthetic	BVT-0244
	17-DMAG	Semi-synthetic	AG-CN2-0540
	Herbimycin A	Actinobacteria	AG-CN2-0429
m	Radicalol	Fungi	AG-CN2-0021

## Hypoxia-inducible Factor (HIF)-1 Inhibitors

Hypoxia-inducible factor (HIF)-1 is a transcription factor for dozens of target genes and plays an integral role in the body's response to low oxygen concentrations or hypoxia. HIF-1 is among the primary genes involved in the homeostatic process, which can increase vascularization in hypoxic areas such as localized ischemia and tumors. As HIF-1 allows for survival and proliferation of cancerous cells due to its angiogenic properties, inhibition potentially could prevent the spread of cancer.

### THE SOURCE

	PRODUCT NAME	SOURCE	PID
m	<b>Chetomin</b>	Fungi	BVT-0161
	<b>Echinosporin</b>	Actinobacteria	BVT-0006
	<b>Echinomycin</b>	Actinobacteria	BVT-0267

## Selected Anticancer Compounds

### THE SOURCE

#### m Fumitremorgin C

BVT-0189

250 µg | 1 mg

Formula:  $C_{22}H_{25}N_3O_3$ 

MW: 379.5

CAS: 118974-02-0

Source: *Aspergillus fumigatus* (Fungi)

Mycotoxin. Potent and specific inhibitor of the breast cancer resistance protein (BCRP; ABCG2).

#### Mensacarcin

BVT-0028

1 mg | 5 mg

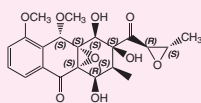
Formula:  $C_{21}H_{24}O_9$ 

MW: 420.4

CAS: 808750-39-2

Source: *Streptomyces bottropensis* (Actinobacteria)

Anti-melanoma drug lead compound. Effective in BRAF V600E mutation cell lines.



#### m Beauvericin

AG-CN2-0043

1 mg | 5 mg

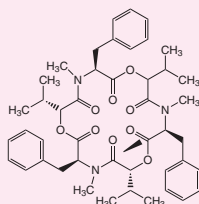
Formula:  $C_{45}H_{57}N_3O_9$ 

MW: 784.0

CAS: 26048-05-5

Source: *Beauveria* sp. (Fungi)

Anti-melanoma drug lead compound. Effective in BRAF V600E mutation

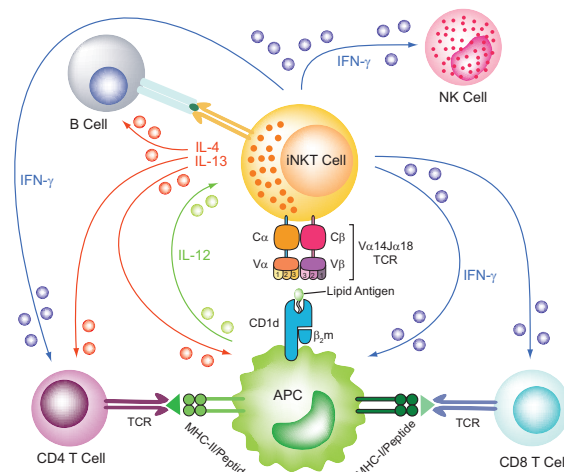


	PRODUCT NAME	SOURCE	PID
	<b>Acetomycin</b>	Actinobacteria	BVT-0150
	<b>Actinomycin X2</b>	Actinobacteria	BVT-0375
	<b>Ansatrienin A</b>	Actinobacteria	BVT-0246
m	<b>Aranorosin</b>	Fungi	AG-CN2-0114
m	<b>Asperphenamate</b>	Fungi	AG-CN2-0171
	<b>Avarol</b>	Marine	AG-CN2-0044
m	<b>Averantin</b>	Fungi	BVT-0169
m	<b>Bikaverin</b>	Fungi	AG-CN2-0130
m	<b>Chaetoglobosin A</b>	Fungi	BVT-0092
m	<b>Cladosporone bisepoxide</b>	Fungi	BVT-0065
m	<b>10,11-Dehydrocurvularin</b>	Fungi	AG-CN2-0165
	<b>Elaiophylin</b>	Actinobacteria	BVT-0185
m	<b>Globosuxanthone A</b>	Fungi	AG-CN2-0174
m	<b>Harzianum A</b>	Fungi	AG-CN2-0117
	<b>Hexacyclinic acid</b>	Actinobacteria	BVT-0261
m	<b>Macrosphelide A</b>	Fungi	AG-CN2-0152
m	<b>Malformin A1</b>	Fungi	AG-CN2-0169
m	<b>Malformin C</b>	Fungi	AG-CN2-0107
m	<b>5-Methoxysterigmatocystin</b>	Fungi	BVT-0416
m	<b>Neoxaline</b>	Fungi	AG-CN2-0154
m	<b>Ophiobolin A</b>	Fungi	AG-CN2-0431
m	<b>Phomoxanthone A</b>	Fungi	AG-CN2-0017
	<b>Polyketomycin</b>	Actinobacteria	BVT-0033
	<b>Rasfonin</b>	Helminth	AG-CN2-0173
m	<b>Roridin E</b>	Fungi	AG-CN2-0176
	<b>Reductiomycin</b>	Actinobacteria	BVT-0292
	<b>Rubiginone A2</b>	Actinobacteria	BVT-0023
	<b>Rubiginone B2</b>	Actinobacteria	BVT-0026
	<b>Rubiginone D2</b>	Actinobacteria	BVT-0024
	<b>Sarcophine</b>	Marine	BVT-0305
	<b>Sipholenol A</b>	Marine	AG-CN2-0506
	<b>Siphenone A</b>	Marine	AG-CN2-0507
m	<b>Terrein</b>	Fungi	BVT-0193
	<b>Violacein</b>	Proteobacteria	BVT-0473
m	<b>(-)-Viriditoxin</b>	Fungi	AG-CN2-0471

## CD1d Ligands – Potent iNKT Stimulators

Invariant natural killer T (iNKT) cells are a subset of innate-like lymphocytes that express a characteristic antigen receptor that includes an invariant TCR- $\alpha$  chain and recognize glycolipid antigens bound by the major histocompatibility complex (MHC)-class-I-related protein CD1d. iNKT cells are activated early during a variety of infections and inflammatory diseases and contribute to the subsequent development of adaptive immune responses. Consequently, iNKT cells play a critical role in the development and resolution of inflammatory diseases and represent attractive targets for the development of immunotherapies. In cancer, iNKT cells were attributed a role in immunosurveillance and act as potent activators of antitumor immunity when stimulated with a synthetic agonist.

FIGURE: iNKT Cell Activation by APC-presented Lipid Antigens.



### THE SOURCE BULK

#### $\alpha$ -Galactosylceramide [KRN7000]

AG-CN2-0013

250  $\mu$ g | 1 mg | 5 mg

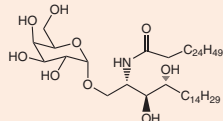
Formula:  $C_{50}H_{99}NO_9$

MW: 858.3

CAS: 158021-47-7

Source: Synthetic.

Derivative of Agelasphins isolated from marine sponge *Agelas mauritanus*.



PRODUCT NAME	PID
$\alpha$ -Galactosylceramide (Dansylated)	AG-CN2-0514
4-Fluorophenylundecanoyl- $\alpha$ -galactosylceramide [7DW8-5]	AG-CN2-0519
$\alpha$ -Galactosylceramide Analog I (water soluble) [KBC-007]	AG-CR1-3608
$\alpha$ -GalCer Analog 8	AG-CR1-3622
OCH (Truncated Analog of $\alpha$ -GalCer)	AG-CR1-3593
$\alpha$ -Mannosylceramide	AG-CR1-3594
$\beta$ -Mannosylceramide	AG-CR1-3621

## Selected Compounds from Marine Sources

PRODUCT NAME	BIOLOGICAL ACTIVITY	PID
<b>Aerothionin</b>	Anti-mycobacterial.	AG-CN2-0453
<b>Agelasine D</b>	Antifouling compound. Antimycobacterial and antibacterial agent. Inhibits the enzyme BCG 3185c, disrupting bacterial homeostasis. Antineoplastic against several cancer cell lines, including the drug resistant renal cancer cell line (ACHN).	AG-CN2-0492
<b>(-)-Ageloxime D</b>	Antifouling compound. Inhibits biofilm formation but not bacterial growth of <i>Staphylococcus epidermidis</i> . Cytotoxic against L5178Y mouse lymphoma cells.	AG-CN2-0016

## Selected Synthetic Antibiotics

PRODUCT NAME	BIOLOGICAL ACTIVITY	PID
<b>Amikacin disulfate salt</b>	Protein synthesis inhibitor.	CDX-A0286
<b>Amikacin hydrate</b>	Protein synthesis inhibitor.	CDX-A0287
<b>Ampicilline sodium salt</b>	Bacterial cell-wall synthesis inhibitor.	CDX-A0313
<b>Balofloxacin</b>	DNA gyrase inhibitor.	CDX-B0302
<b>Cordycepin</b>	DNA/RNA synthesis inhibitor.	CDX-C0339
<b>D-Cycloserine</b>	Bacterial cell-wall synthesis inhibitor.	CDX-D0356
<b>Ethionamide</b>	InHA enzyme inhibitor.	CDX-E0237
<b>Flumequine</b>	DNA synthesis inhibitor.	CDX-F0079
<b>Linezolid</b>	Protein synthesis inhibitor.	CDX-L0031
<b>Moxifloxacin hydrochloride</b>	DNA gyrase inhibitor.	CDX-M0189
<b>Sancycline</b>	Protein synthesis inhibitor.	CDX-S0344

# Antibiotics for Metabolic Syndrome Research

## THE STANDARDS

### Streptozotocin

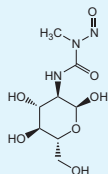
AG-CN2-0046

50 mg | 250 mg | 1 g

Formula:  $C_8H_{15}N_3O_7$ 

MW: 265.2

CAS: 18883-66-4

Source: Synthetic. Originally isolated from *Streptomyces achromogenes* (Actinobacteria)Diabetes inducer. Induces diabetes mellitus in animal models through its toxic effects on pancreatic  $\beta$ -cells.

## UNIQUE

### Pyripyropene A

AG-CN2-0106

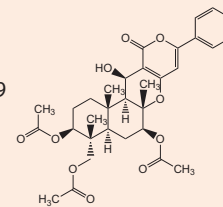
250  $\mu$ g | 1 mgFormula:  $C_{31}H_{37}NO_{10}$ 

MW: 583.6

CAS: 7147444-03-9

Source: *Aspergillus fumigatus* FO-1289 (Fungi)

Highly specific inhibitor of acyl-coenzyme A:cholesterol acetyltransferase 2 (ACAT2).



	PRODUCT NAME	TARGET	SOURCE	PID
	Agistatin B	Cholesterol biosynthesis	Fungi	BVT-0223
	Agistatin D	Cholesterol biosynthesis	Fungi	BVT-0286
	Agistatin E	Cholesterol biosynthesis	Fungi	BVT-0231
	Amidepsine A	Diacylglycerol acyltransferase (DGAT)	Fungi	AG-CN2-0109
	Amidepsine D	Diacylglycerol acyltransferase (DGAT)	Fungi	AG-CN2-0110
	Cerulenin	Fatty acid synthase (FASN) / Palmitoylation	Fungi	AG-CN2-0513
	Chaetoviridin A	Cholesteryl ester transfer protein (CETP)	Fungi	BVT-0419
	Convulxin	Glycoprotein GPVI receptor	Snake venom	AG-CN2-0465
	Decarestrictine D	Cholesterol biosynthesis	Fungi	BVT-0283
	Deoxynojirimycin	$\alpha$ -Glucosidase I and II	Actinobacteria	BVT-0112
	EM574	Motilin receptor	Actinobacteria	AG-CN2-0102
	Geodin	Glucose uptake	Fungi	AG-CN2-0139
	(R,R)-Hymeglusin	HMG-CoA synthase	Fungi	AG-CN2-0103
	(3S,6R)-Lateritin	Acyl-CoA:cholesterol acyltransferase (ACAT)	Fungi	AG-CN2-0042
	Lovastatin	HMG-CoA reductase	Fungi	AG-CN2-0051
	N-Methyl-1-deoxynojirimycin	$\alpha$ -Glucosidase	Actinobacteria	BVT-0130
	Orlistat	DAGL $\alpha$	Actinobacteria	AG-CN2-0050
	Sclerotiorin	Cholesteryl ester transfer protein (CETP)	Fungi	AG-CN2-0054
	Skyrin	Receptor-selective glucagon antagonist	Fungi	AG-CN2-0001
	Sterigmatocystin	Acyl-CoA:cholesterol acyltransferase 2 (ACAT2)	Fungi	BVT-0171
	Terpendole C	Acyl-CoA:cholesterol acyltransferase (ACAT1 & 2)	Fungi	AG-CN2-0125
	Terpendole E	Acyl-CoA:cholesterol acyltransferase (ACAT)	Fungi	AG-CN2-0127

## UNIQUE

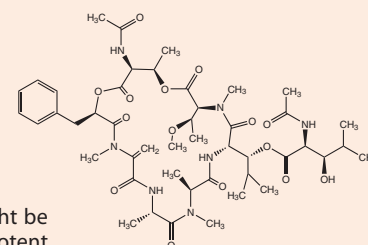
### YM-254890

AG-CN2-0509

500  $\mu$ g | 1 mgFormula:  $C_{46}H_{69}N_7O_{15}$ 

MW: 960.1

CAS: 568580-02-9

Source: *Chromobacterium* sp. QS3666 (Proteobacteria)Cyclic depsipeptide composed of unique amino acids differing from normal amino acids. Might be used as a starting point for new approaches in cancer drug discovery. Membrane permeable, potent and selective  $G\alpha_q$  family inhibitor.  $G\alpha_q$  signaling has been shown to regulate brown/beige adipocytes.LIT: The  $G_q$  signalling pathway inhibits brown and beige adipose tissue: K. Klepac, et al.; Nat. Commun. 7, 10895 (2016)



# Antibiotics for Inflammation & Neuroscience Research

## Inflammatory & Viral Target Modulators

THE STANDARDS

### Nigericin . sodium salt

AG-CN2-0020

5 mg | 25 mg

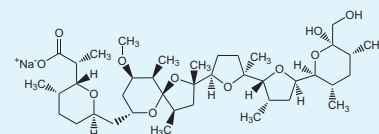
Formula:  $C_{40}H_{67}O_{11} \cdot Na$

MW: 724.0 . 23.0

CAS: 28643-80-3

Source: *Streptomyces hygroscopicus* (Actinobacteria)

High affinity ionophore for monovalent cations such as  $H^+$ ,  $K^+$ ,  $Na^+$ ,  $Pb^{2+}$ . Used as a standard NLRP3/NALP3 activator. In addition, shows antibacterial (Gram-positive), antifungal, antitumor and antiviral activity.



	PRODUCT NAME	TARGET	SOURCES	PID
m	Alternariol monomethyl ether	Hepatitis C NS3-4A protease	Fungi	BVT-0323
m	Antibiotic L-696,474	HIV-1 protease	Fungi	BVT-0331
m	Asperloxine A	Anti-inflammatory	Fungi	BVT-0266
m	Auranofin	5-Lipoxygenase (5-LOX)	Synthetic	AG-CR1-3611
	Aurantimycin A	C5a antagonist	Actinobacteria	BVT-0398
	Boromycin	HIV-1 integrase	Actinobacteria	AG-CN2-0166
m	Butyrolactone II	5-Lipoxygenase (5-LOX)	Fungi	AG-CN2-0423
m	Corynesidone A	ROS and RNS scavenger	Fungi	AG-CN2-0496
	Elasnin	Leukocyte elastase	Actinobacteria	BVT-0342
m	Funalenone	HIV-1 integrase	Fungi	AG-CN2-0137
	10Z-Hymenialdisine	MEK-1, NF- $\kappa$ B, MARK	Marine	AG-CN2-0067
m	Mutolide	NF- $\kappa$ B	Fungi	BVT-0070
	Myxochelin A	5-Lipoxygenase (5-LOX)	Proteobacteria	AG-CN2-0470
	Nebularine (high purity)	Adenosine deaminase	Actinobacteria	BVT-0304
m	Petasol	HIV-1 Tat transduction	Fungi	BVT-0439
m	Pyranonigrin A	DPPH and superoxide scavenger	Fungi	AG-CN2-0156
m	Rugulosin	HIV-1 integrase	Fungi	BVT-0444
m	(R)-Semiovioxanthin	I $\kappa$ B (Inhibitor of NF- $\kappa$ B), TNF- $\alpha$ , MAPK	Fungi	BVT-0360
	Siamycin I	HIV envelope glycoprotein gp41	Actinobacteria	AG-CN2-0146

## Neuroscience Target Modulators

	PRODUCT NAME	TARGET	SOURCES	PID
m	Amauromine	CB1 receptor	Fungi	AG-CN2-0113
m	epi-Aszonalenin A	Substance P	Fungi	AG-CN2-0163
	NEW Collinolactone	A $\beta$ Aggregates, Tau Tangles	Actinobacteria	BVT-0480
m	Cyclophenin	Acetylcholinesterase (AChE)	Fungi	AG-CN2-0134
m	Fulvic Acid	Tau and Ab aggregation	Fungi	AG-CN2-0135
m	NG 012	Nerve growth factor (NGF)	Fungi	AG-CN2-0155
m	Paxilline	Calcium-activated potassium (BKCa) channels Sarco/endoplasmic reticulum $Ca^{2+}$ -ATPase (SERCA)	Fungi	AG-CN2-0167
	Pimprinine	Monoamine oxidase (MAO)	Actinobacteria	BVT-0297
	Pikromycin	Prolyl endopeptidase (PREP)	Actinobacteria	BVT-0400
m	Pseurotin D	Apomorphine	Fungi	BVT-0426
m	Quinolactacin A	Acetylcholinesterase (AChE)	Fungi	AG-CN2-0164
m	Roquefortine C	Cytochrome p450	Fungi	BVT-0425
m	Territrem B	Acetylcholinesterase (AChE)	Fungi	AG-CN2-0142
m	Verruculogen	KCa1.1 channels	Fungi	BVT-0443

## Potent TRPV1 Agonist for Pain Relief

### THE SOURCE

#### Resiniferatoxin (RTX)

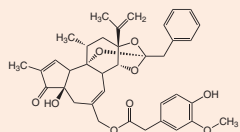
AG-CN2-0534

0.1 mg | 0.5 mg

Formula:  $C_{37}H_{40}O_9$ 

MW: 628.7

CAS: 57444-62-9

Source: *Euphorbia resinifera*  
(Plant)

The plant *Euphorbia resinifera* (Resin spurge) contains a milky latex. It is the most potent irritant known so far and was used in ancient traditional medicine for its analgesic properties. The irritant principle of the cactus-like plant was isolated and identified as resiniferatoxin (RTX).

Resiniferatoxin (RTX), an analog of capsaicin, is a highly potent transient receptor potential vanilloid 1 (TRPV1) agonist ( $K_i=43\text{pM}$ ) and acts as a selective modulator of primary afferent neurons. **The primary action of RTX is to activate sensory neurons responsible for the perception of pain.**

## Standard Reagent for THP-1 Cell Differentiation

The human monocytic cell line THP-1 is the most widely used cell line for *in vitro* studies investigating primary human macrophage function. The reason is that following the differentiation of THP-1 cells using PMA, they acquire a macrophage-like phenotype, which mimics in many respects, primary human macrophages (M0 macrophages). PMA is a potent activator of protein kinase C (PKC), which is a key regulator of macrophage differentiation. When PMA is added to THP-1 cells, it causes them to express the surface markers CD14, CD16 and CD68, which are characteristic for M0 macrophages. PMA also induces the production of pro-inflammatory cytokines by M0 macrophages. Further treatment with PMA can activate M0 macrophages and differentiate them into M1 or M2 macrophages. The differentiation of THP-1 cells into

M0 macrophages is a complex process, important for the immune response to infection and injury.

PMA is commonly used to activate protein kinase C (PKC), a family of enzymes involved in various cellular processes such as cell growth, differentiation, proliferation and apoptosis (programmed cell death). PMA can activate all isoforms of PKC, but it has a particularly strong affinity for PKC $\alpha$ , PKC $\epsilon$  and PKC $\delta$ .

### THP1 Differentiation using PMA

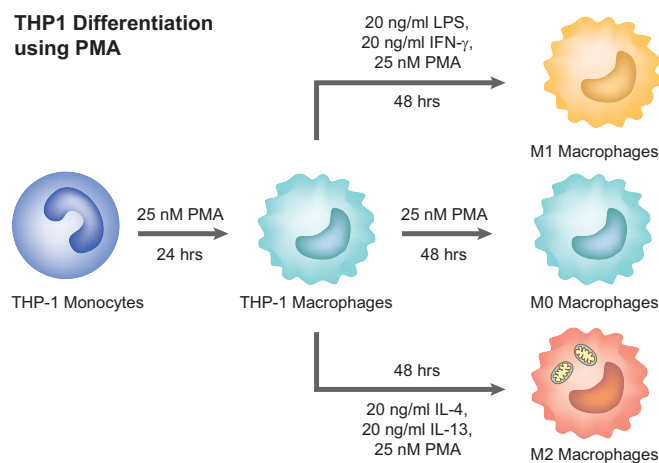


FIGURE: THP1 cell differentiation into macrophages using PMA.

### THE SOURCE BULK

#### Phorbol 12-myristate 13-acetate [PMA]

AG-CN2-0010

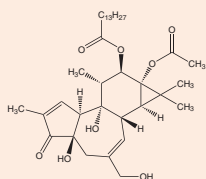
1 mg | 5 mg | 10 mg | 25 mg

Formula:  $C_{36}H_{56}O_8$ 

MW: 616.8

CAS: 16561-29-8

Source: Semi-synthetic from plant.



## Newly Introduced High Purity Natural Products

### THE SOURCE

#### Spilanthol

AG-CN2-0543

5 mg

Excellent stable model compound for sensory/chemoreception studies. Shown to have a broad range of biological properties.

### THE SOURCE

#### Taspine

AG-CN2-0544

1 mg | 5 mg | 10 mg

Potent acetylcholinesterase (AChE) inhibitor, dual topoisomerase inhibitor, VEGFR-2 inhibitor and P2X4 receptor inhibitor.

# Key Research Natural Products / Antibiotics for Your Lab

**BULK from the Original Source**

## Cell Selection, Gene Expression and Membrane Traffic

PRODUCT NAME	PRODUCT DESCRIPTION	SOURCE	PID
Anhydrotetracycline . HCl	Used with tetracycline-controlled gene expression systems in bacteria. No antibiotic activity.	Actinobacteria	CDX-A0197
(+)-Brefeldin A	Protein transport inhibitor. Tool to study membrane traffic and vesicle transport dynamics.	Fungi	AG-CN2-0018
G418 . sulfate	Cell selective agent.	Actinobacteria	AG-CN2-0030
Gentamicin sulfate (USP Grade)	Cell selective agent.	Actinobacteria	AG-CN2-0066
Puromycin . 2HCl	Cell selective agent.	Actinobacteria	AG-CN2-0078
Tetracycline . HCl	Cell selective agent.	Actinobacteria	CDX-T0096

## Ionophore Antibiotics

PRODUCT NAME	SOURCE	PID
Enniatin A	Fungi	AG-CN2-0477
Enniatin A1	Fungi	AG-CN2-0478
Enniatin B	Fungi	AG-CN2-0479
Enniatin B1	Fungi	AG-CN2-0480

PRODUCT NAME	SOURCE	PID
Ionomycin (free acid)	Actinobacteria	AG-CN2-0416
Ionomycin . Ca	Actinobacteria	AG-CN2-0418
Lasalocid A . Na	Actinobacteria	CDX-L0015
Lasalocid A . Na Solution	Actinobacteria	CDX-L0515

**Also Available:**

**Colistin sulfate (USP & Ph.Eur. Grade) – Potent Bacterial Membrane Disruptor!**

THE SOURCE

## Potent Tumor Promoters

PRODUCT NAME	SOURCE	PID
Phorbol 12-myristate 13-acetate [PMA; TPA]	Plant	AG-CN2-0010
Thapsigargin (high purity)	Plant	AG-CN2-0003

PMA is the most commonly-used phorbol ester. It binds to and activates protein kinase C (PKC) at nM concentrations.

Thapsigargin is a potent non-TPA/PMA tumor promoter.

THE SOURCE

## Gene Expression Inducers

PRODUCT NAME	SOURCE	PID
Ecdysone	Plant	AG-CN2-0071
20-Hydroxyecdysone	Plant	AG-CN2-0072
Makisterone A	Plant	AG-CN2-0073
Muristerone A	Plant	AG-CN2-0070
Ponasterone A	Plant	AG-CN2-0053

Ecdysone receptor (EcR) agonists. Inducers of ecdysone-inducible gene expression systems in mammalian cells and transgenic animals.