

# Cancer Research

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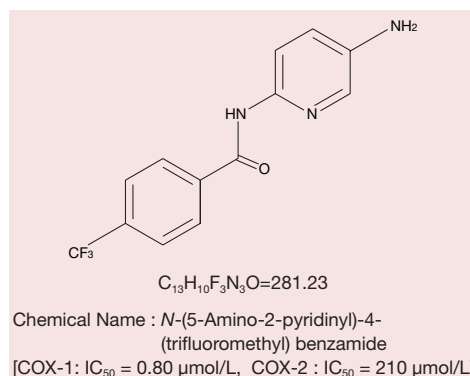
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**a COX-1-Selective Inhibitor**

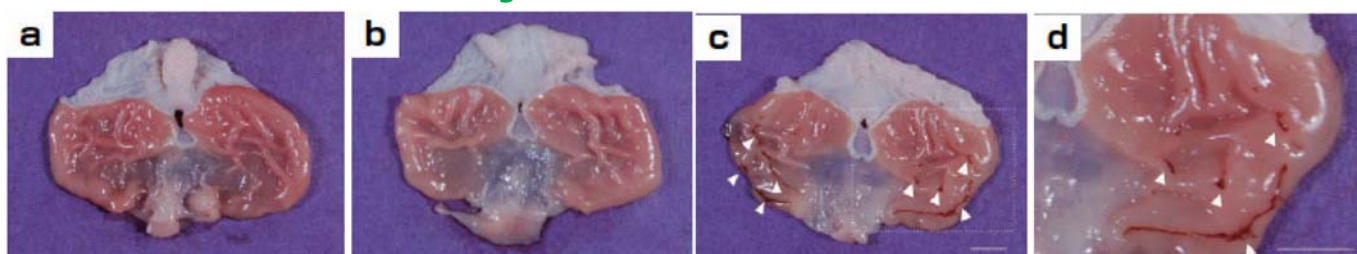
**TFAP**

Wako Catalog No. 205-17381 (10 mg) <for Cellbiology> Keep at -20°C

Cyclooxygenase 1(COX-1) inhibition has been thought to be a major mechanism of gastric damage by nonsteroidal anti-inflammatory drugs (NSAIDs). Dr. Kakuta reported that TFAP [ N-(5-Amino-2-pyridinyl)-4-(trifluoromethyl)benzamide], which has a structure clearly different from those of currently available COX-1-selective inhibitors, is a potent COX-1-selective inhibitor (COX-1: IC<sub>50</sub> = 0.80 ± 0.05 μM; COX-2: IC<sub>50</sub> = 210 ± 10 μM). TFAP causes little gastric damage in rats even at an oral dose of 300 mg/kg, though it has an analgesic effect at as low a dose as 10 mg/kg. The results show that COX-1-selective inhibitors can be analgesic agents without causing gastric damage. Wako has launched TFAP as a novel COX-1-selective inhibitor.

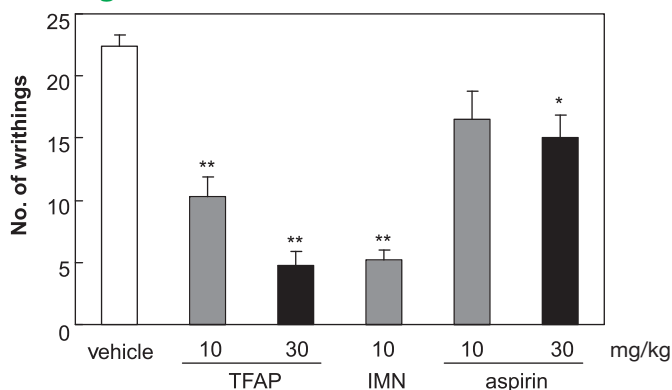


**Gastric Ulcer Formation Test using Rat Stomach**



Photographs of gastric damage of TFAP and Indomethacin Scale bars indicate 5 mm. White triangles indicate ulcers. a) Vehicle; b) treated with TFAP (300 mg/kg; p.o.); c) treated with indomethacin (10 mg/kg; p.o.); d) enlarged illustration of part c: While gastric damage was shown from the administration of indomethacin, no damage from TFAP administration.

**Analgesic Effect Test**

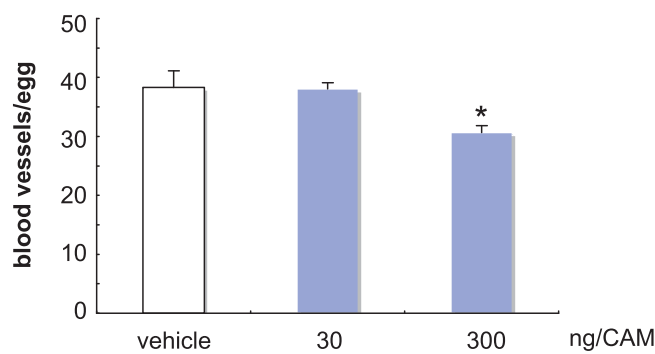


**Acetic acid-induced writhing test in mice**

Gray and black bars indicate number of writhes at 10 and 30 mg/kg; p.o., respectively. Each value is the average of the total number of writhes ± SEM ( n = 10-11/group). The followings indicate significant differences from the vehicle: (\*) p < 0.05; (\*\*) p < 0.01

( All data were provided by Dr. Hiroki Kakuta, Division of Pharmaceutical Sciences, Okayama Univ. Graduate School of Medicine, Dentistry and Pharmaceutical Sciences)

**Chorioallantoic Membrane (CAM) Assay**



The angiogenesis activity of TFAP was evaluated by the assay of chick chorioallantoic membrane (CAM). TFAP inhibited CAM angiogenesis at a 300 ng/CAM. TFAP was orally administered at 30 and 300 mg/kg. Data shown are the average of blood vessels/egg ± SEM ( n = 6/group). The following indicates significant difference from the vehicle: (\*) p < 0.05

**[References]**

Kakuta, H. et al. : Cyclooxygenase-1-selective inhibitors are attractive candidates for analgesics that do not cause gastric damage. Design and *in vitro/ in vivo* evaluation of a Benzamide-type Cyclooxygenase-1- selective inhibitor, *J. Med. Chem.*, **51**, 2400-2411 (2008).

Description	Wako Catalog No. (Pkg. Size)	Note
<b>TFAP</b> [N-(5-amino-2-pyridinyl)-4-(trifluoromethyl)benzamide] <for Cellbiology>	<b>205-17381 (10 mg)</b>	Novel Cyclooxygenase-1-Selective Inhibitor

### b Non-competitive PSA Inhibitor

#### PAQ-22 [3-(2,6-Diethylphenyl)-2,4-(1H, 3H)-quinazolinone]

**Wako Catalog No. 165-23581 (10 mg)** <for Cellbiology> Keep at RT\*

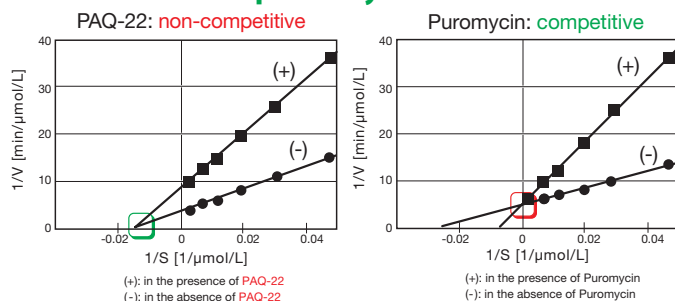
Puromycin-sensitive aminopeptidase (PSA), which is a neutral aminopeptidase with a substrate specificity similar to that of aminopeptidase N (APN), is distributed mainly in the brain and neurons. Although PSA regarded as an enkephalin-degrading enzyme, the physical roles/functions of PSA remain unclear. PSA is possibly related to cell division and Apoptosis. PSA was reported as a potent modifier of tau-induced pathology and was suggested as a possible tau-degrading enzyme in an unknown mechanism in Alzheimer's disease. PSA activity is inhibited by Puromycin but Puromycin also inhibits APN.

Wako has launched a non-peptide, small-molecular, non-competitive PSA Inhibitor, PAQ-22 and the structurally modified fluorescent bioprobe, DAMPAQ-22.

\*RT: room temperature



#### Line weaver-Burk plot analysis of PSA inhibition by PAQ-22 and Puromycin



Using living human monocytic cell MOLT-4, which is known to express PSA, PSA inhibitory activity of PAQ-22 and Puromycin was determined with an indicator, which is fluorescence generated from a fluorescent substrate Ala-MCA broken down by PSA. Lineweaver-Burk plot indicated that PAQ-22 acts as specific non-competitive inhibitor. On the other hand, Puromycin acts a competitive inhibitor. In addition, PAQ-22 and DAMPAQ-22 are easily incorporated into MOLT-4 under the general cell culture conditions.

#### APN-Inhibitory Activity of PAQ-22 and Puromycin

	PSA IC <sub>50</sub> (μmol/L)	APN IC <sub>50</sub> (μmol/L)
PAQ-22	3.8	>100
DAMPAQ-22	4.6	N/A
Puromycin	0.6	4.8

PSA- and APN-inhibitory activities were assayed by the use of L-Ala-MCA with MOLT-4. PAQ-22 is inactive toward APN, indicating that PAQ-22 is specific to PSA.

(These data were provided by Dr. Yuichi Hashimoto, Institute of Molecular and Cellular Biosciences, The University of Tokyo)

#### Fluorescent Bioprobe for Visualization of PSA in Living Cells

#### DAMPAQ-22 [3-(2,6-Diethyl-4-dansylaminophenyl)-1-methyl-2,4-(1H, 3H)-quinazolinone]

**Wako Catalog No. 049-30761 (2 mg)** <for Cellbiology> Keep at RT

C<sub>31</sub>H<sub>32</sub>O<sub>4</sub>N<sub>4</sub>S=556.68; CAS No. 519183-48-3; λ<sub>ex</sub>: 320 nm\*; λ<sub>em</sub>: 510 nm\*

DAMPAQ-22, which is structurally modified fluorescent bioprobe of PAQ-22 is also available. The cellular localization of PSA within the living body could be specifically visualized by the use of DAMPAQ-22<sup>2)</sup>.

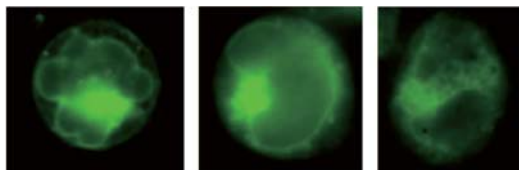
PSA IC<sub>50</sub>: 4.6 μmol/L (Please see the above mentioned table of PAQ-22)

No inhibitory activity toward APN and LAP.

\*: Excitation wavelength and fluorescence wavelength were not optimized. Please adjust them in accordance with the intended use or the experimental condition based on those wavelengths.



#### Visualization of PSA with DAMPAQ-22 in MOLT-4 cells



Fluorescent microscopic images of MOLT-4 cells treated with 10 μmol/L DAMPAQ-22 for 10 minutes.

(These data were provided by Dr. Yuichi Hashimoto, Institute of Molecular and Cellular Biosciences, The University of Tokyo)

#### [References]

- Kakuta, H., Tanatani, A., Nagasawa, K., Hashimoto, Y.: "(1H,3H)-quinazolinone skeleton", *Chem. Pharm. Bull.*, **51**, 1273-82 (2003).
- Kakuta, H., Koiso, Y., Nagasawa, K., Hashimoto, Y.: "Fluorescent Bioprobes for Visualization of Puromycin-Sensitive Aminopeptidase in Living Cells", *Bioorg. Med. Chem. Lett.*, **13**, 83-6 (2003)
- Bukowska, A., Tadge, J., Arndt, M., Wolke, C., Kähne, T., Bartsch, J., Faust, J., Neubert, K., Hashimoto, Y., Lendeckel, U.: "Transcriptional regulation of cytosol and membrane alanyl-aminopeptidase in human T cell subsets", *Biol Chem.*, **384**, 657-65 (2003).
- Sánchez-Morán, E., Jones, G.H., Franklin, F. C. and Santos, J. L.: *Plant Cell*, **16**, 2895 (2004).
- Thielitz, A., Bukowska, A., Wolke, C., Vetter, R., Lendeckel, U., Wrenger, S., Hashimoto, Y., Ansoerge, S., Gollnick, H. and Reinhold, D.: *Biochem. Biophys. Res. Commun.*, **321**, 795 (2004).

Wako commercialized new inhibitors which were discovered by Dr. Hiroyuki Osada, Antibiotics laboratory of Institute of Physical and Chemical Research (RIKEN) under license from RIKEN.

### c HSP60 Inhibitor

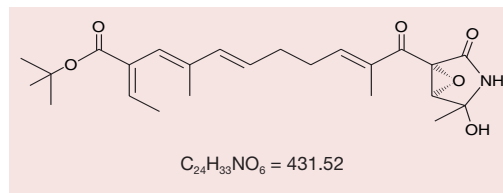
#### ETB (mixture of isomers) [Epolactaene Tertiary Butyl Ester]

Wako Catalog No. 051-07671 (200  $\mu$ L) <for Cellbiology> Keep at -20°C

This product is a derivative of epolactaene isolated from *Penicillium*. It has a more potent cytostatic effect on human neuroblastoma cells SH-SY 5Y than that of epolactaene, and induces apoptosis. Furthermore, it has been revealed that ETB induces apoptosis in human T-lymphoma cells Jurkat. Recently, HSP60 was identified as one of ETB binding proteins. ETB binds to HSP60 to inhibit chaperone activity.

#### [Reference]

Nagumo, Y., Kakeya, H., Shoji, M., Hayashi, Y., Dohmae, N. and Osada, H., "Epolactaene binds human Hsp60 Cys442 resulting in the inhibition of chaperone activity": *Biochem. J.*, **387**(3), 835-40 (2005)



### d Protein Synthesis Inhibitor

#### Reveromycin A Sodium Salt

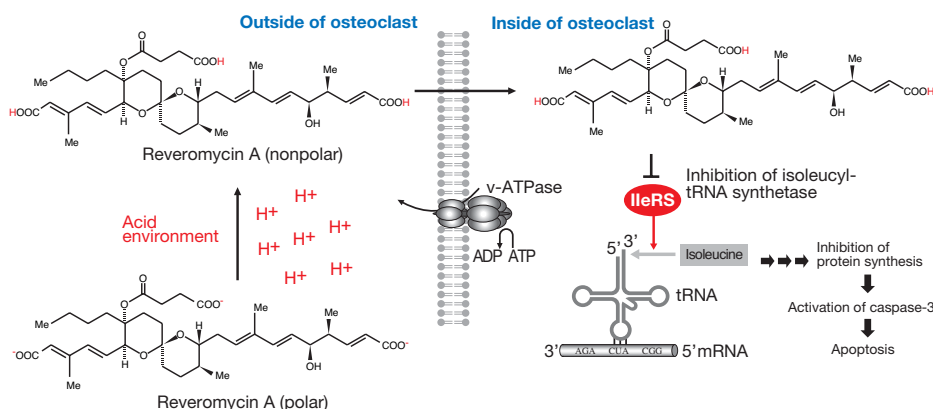
Wako Catalog No. 185-02181 (500  $\mu$ g)

<for Cellbiology>

Keep at -20°C

This product is an antibiotic isolated from *Streptomyces*. It targets isoleucyl-tRNA synthetase and inhibits protein synthesis in eukaryotes. It has been investigated for its antitumor and antifungal activities. However, recent studies have revealed that low-dose of reveromycin A induces cell death of activated osteoclasts, which leads to acidic environment. Thus it receives attention as a candidate for the treatment of osteoporosis/ multiple myeloma.

(This product is a sodium salt of the compound shown below.)



#### [Reference]

Woo, J.T., Kawatani, M., Kato, M., Shinki, T., Yonezawa, T., Kanoh, N., Nakagawa, H., Takami, M., Lee, K.H., Stern, P.H., Nagai, K. and Osada, H., "Reveromycin A, an agent for osteoporosis, inhibits bone resorption by inducing apoptosis specifically in osteoclasts": *Proc. Natl. Acad. Sci. USA*, **103** (12), 4729-34(2006).

### e Apoptosis Inhibitor

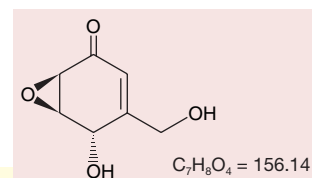
#### RKTS-33

Wako Catalog No. 182-02191 (200  $\mu$ g) <for Cellbiology> Keep at -20°C

This product is a derivative of epoxycyclohexenone isolated from *Paecilomyces*. It has lower toxicity than epoxycyclohexenone. Like epoxycyclohexenone, it inhibits apoptosis not by inhibition of perforin-dependent pathway by cytotoxic T lymphocytes but by selective inhibition of Fas ligand-dependent pathway alone.

#### [Reference]

Mitsui, T., Miyake, Y., Kakeya, H., Hayashi, Y., Osada, H. & Kataoka, T., "RKTS-33, an epoxycyclohexenone derivative that specifically inhibits Fas ligand-dependent apoptosis in CTL-mediated cytotoxicity": *Biosci. Biotechnol. Biochem.*, **69** (10), 1923-8 (2005).



### f Cell Cycle Inhibitor

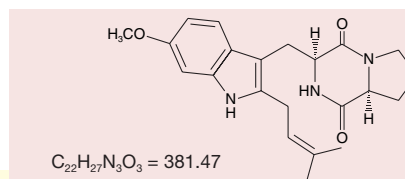
#### Tryprostatin A

Wako Catalog No. 203-16961 (500  $\mu$ g) <for Cellbiology> Keep at -20°C

This product is an alkaloid antibiotic isolated from *Aspergillus fumigatus*. It affects the microtubule-associated protein binding site and exhibits antitumor activity by inhibition of cell cycle progression in the M phase specifically.

#### [References]

- 1) Usui, T., Kondoh, M., Cui, C.B., Mayumi, T., Osada, H., "Tryprostatin A, a specific and novel inhibitor of microtubule assembly": *Biochem. J.*, **333**, 543-8 (1998).
- 2) Jain, H.D., Zhang, C., Zhou, S., Zhou, H., Ma, J., Liu, X., Liao, X., Deveau, A.M., Dieckhaus, C.M., Johnson, M.A., Smith, K.S., Macdonald, T.L., Kakeya, H., Osada, H. & Cook, J.M., "Synthesis and structure-activity relationship studies on tryprostatin A, an inhibitor of breast cancer resistance protein": *Bioorg. Med. Chem.*, **16**, 4626-51 (2008).



## g Histone Deacetylase (HDAC) Inhibitor

**Trichostatin A**, 99.0+ % (HPLC)

Wako Cat. No. 200-11993 (1 mg); 204-11991 (5 mg)

&lt;for Biochemistry &gt; Keep at -20°C

HDAC plays a central role in chromatin structure formation associated with the nuclear distribution of DNA. There are presently 17 known types of this enzyme in mammals, which are classified into 3 classes. Also, HDAC Class III has been reported to be associated with regulation of aging and life span.

HDAC inhibitors show connections with cell division cycles and

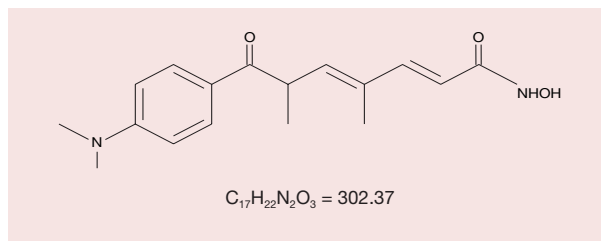
differentiation, as well as with antitumor activity and apoptosis-inducing activity through the inhibition of the deacetylating activity of HDAC. They can be used for studies on cellular functions involving histone deacetylase.

Trichostatin A (TSA), a *Streptomyces* product, specifically inhibits the cell cycle of normal rat fibroblasts in the G1 and G2 phases at very low concentrations as reported by Yoshida, *et al.* TSA-induced G2-arrest induces the formation of proliferative tetraploid cells. In addition, nanomolar concentration of TSA has been shown to cause an accumulation of highly acetylated histones *in vivo*, and markedly inhibit the activity of partially purified histone deacetylase *in vitro*.

TSA appears to be a useful product for researching the multiple functions of histone acetylation in regulatory mechanisms of eukaryotic cell proliferation and differentiation.

Source: *Streptomyces Hygroscopicus*

Solubility: Soluble in ethanol and acetone. 1 mg/10 mL (methanol)

**[References]**

- 1) Yoshida, M., Beppu, T.: "Reversible arrest of proliferation of rat 3Y1 fibroblasts in both the G1 and G2 phases by trichostatin A", *Exp. Cell. Res.*, **177**, 122-31 (1988)
- 2) Yoshida, M. *et al.*: "Potent and specific inhibition of mammalian histone deacetylase both in vivo and in vitro by trichostatin A", *J. Biol. Chem.*, **265**, 17174-9 (1990)
- 3) Dion, L.D. *et al.*: "Amplification of recombinant adenoviral transgene products occurs by inhibition of histone deacetylase", *VIROLOGY*, **231**, 201-9 (1997)

## h Metastasis Suppressing Agent

**MI-22 [Metastasis Inhibitor-22]**

Wako Catalog No. 132-15043 (5 mg); 136-15041 (200 mg)

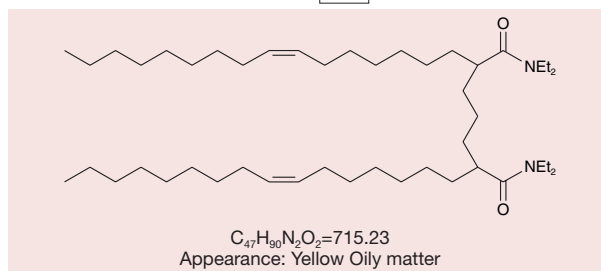
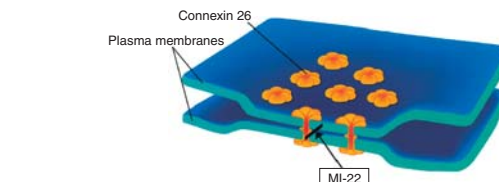
&lt;for Cellbiology &gt; Keep at 2~10°C

Recent studies have shown that the expression of connexin 26, a protein component of gap junction, is increased in cancer cell lines, and suggested that the protein is involved in the mechanism of metastasis in cancer cells.

It has been revealed that MI-22 (metastasis inhibitor-22), which is a derivative of oleamide, does not only inhibit the connexin 26-mediated formation of gap junction between cancer and other cells but inhibits the spontaneous metastasis *in vivo*.

**[Features]**

1. Oleamide Derivatives
2. Specific Inhibition of connexin 26
3. Inhibition of gap junction-mediated intercellular communications
4. Inhibition of spontaneous metastasis of mouse BL6 melanoma cells

**[References]**

- 1) Ito, A., Katoh, F., Kataoka, T. R., Okada, M., Tsubota, N., Asada, H., Yoshikawa, K., Maeda, S., Kitamura, Y., Yamasaki, H. and Nojima, H.: "A role for heterologous gap junctions between melanoma and endothelial cells in metastasis", *J. Clin. Invest.*, **105**, 1189-1197(2000).
- 2) Ito, A., Morita, N., Miura, D., Koma, Y., Kataoka, T. R., Yamasaki, H., Kitamura, Y., Kita, Y. and Nojima, H.: "A derivative of oleamide potently inhibits the spontaneous metastasis of mouse melanoma BL6 cells", *Carcinogenesis*, **25**, 2015-2022(2004).
- 3) Ohba Y., Kanao Y., Morita N., Fujii E., Hohrai M., Takatsuji M., Hirose H., Miura D., Watari A., Yutsudo M., Zhao H., Yabuta N., Ito A., Kita Y, Nojima H., "Oleamide derivatives suppress the spontaneous metastasis by inhibiting connexin 26", *Int. J. Cancer*, **121**, 2801-8 (2007)

Description	Wako Catalog No. (Pkg. Size)	Note
<b>MI-22</b> [ <i>N</i> <sup>1</sup> , <i>N</i> <sup>1</sup> , <i>N</i> <sup>2</sup> , <i>N</i> <sup>2</sup> -Tetraethyl-2,6-di[( <i>Z</i> )-7-hexadecenyl]-heptanediamide], 93% (HPLC)	<b>132-15043</b> ( 5 mg) <b>136-15041</b> (200 mg)	Filled with inert gas. Please arrange for immediate use after opening.

# A. Wako's Unique Products

## 2. Fluorescent Bioprobe of PSA

### Fluorescent Bioprobe for Visualization of PSA in Living Cells

#### DAMPAQ-22

[3-(2,6-Diethyl-4-dansylaminophenyl)-1-methyl-2,4-(1*H*, 3*H*)-quinazolinone]

Wako Catalog No. 049-30761 (2 mg) <for Cellbiology> Keep at RT  
C<sub>31</sub>H<sub>32</sub>O<sub>4</sub>N<sub>4</sub>S = 556.68; CAS No. 519183-48-3; λ<sub>ex</sub>: 320 nm\*; λ<sub>em</sub>: 510 nm\*

Puromycin-sensitive aminopeptidase (PSA), which is a neutral aminopeptidase with a substrate specificity similar to that of aminopeptidase N (APN), is distributed mainly in the brain and neurons. Although PSA regarded as an enkephalin-degrading enzyme, the physical roles/functions of PSA remain unclear. PSA is possibly related to cell division and Apoptosis. PSA was reported as a potent modifier of tau-induced pathology and was suggested as a possible tau-degrading enzyme in an unknown mechanism in Alzheimer's disease. PSA activity is inhibited by Puromycin but Puromycin also inhibits APN.

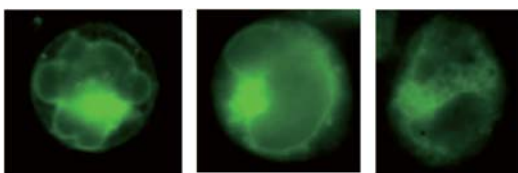
DAMPAQ-22, which is structurally modified fluorescent bioprobe of PAQ-22 (See the page 4) has been launched. The cellular localization of PSA within the living body could be specifically visualized by the use of DAMPAQ-22<sup>2)</sup>.



\*: Excitation wavelength and fluorescence wavelength were not optimized. Please adjust them in accordance with the intended use or the experimental condition based on those wavelengths.

PSA- inhibitory activity IC<sub>50</sub>: 4.6 μmol/L (Please see the page 4.)  
No inhibitory activity toward APN and LAP.

### ■ Visualization of PSA with DAMPAQ-22 in MOLT-4 cells



Fluorescent microscopic images of MOLT-4 cells treated with 10 μmol/L DAMPAQ-22 for 10 minutes.

(These data were provided by Dr. Yuichi Hashimoto, Institute of Molecular and Cellular Biosciences, The University of Tokyo)

#### [References]

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a Substrate for FDG-synthesis: Cancer Detection by PET\* using a tracer, <sup>18</sup>F-FDG \*: Positron emission tomography

**1,3,4,6-Tetra-O-acetyl-2-O-trifluoromethanesulfonyl-β-D-mannopyranose**

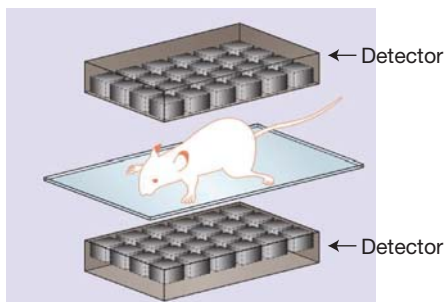
[Mannose Triflate], 98.0+% (HPLC)

Wako Catalog No. #209-16061 (5 × 20 mg); Keep at -20°C

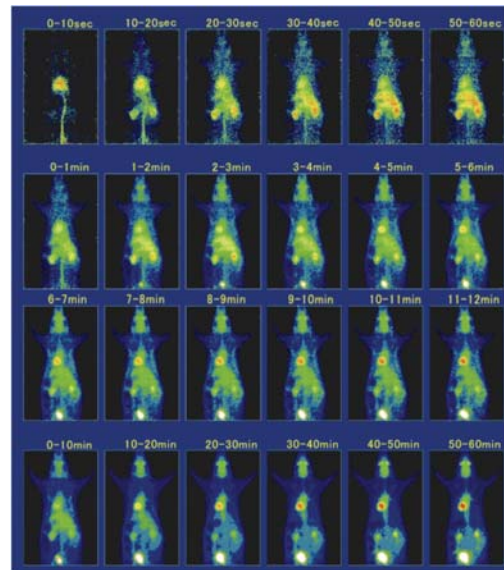
Mannose Triflate is used as a substrate for synthesis of PET reagent, <sup>18</sup>F-FDG. After nuclear transmutation of <sup>18</sup>O to <sup>18</sup>F in a cyclotron, <sup>18</sup>F-FDG (2-deoxy-2-<sup>18</sup>F-fluoro-D-glucose) is automatically synthesized from Mannose Triflate. Once purified, it is used for PET examination.

Since the half life of <sup>18</sup>F is 2 hours, it is synthesized just before use in each hospital. FDG is characterized by a tendency to accumulate more in tumor cells than in normal cells. Therefore, it is effective in early detection of recurrence and metastasis of various types of cancer such as lung cancer, colon cancer and breast cancer.

This product is packed in unit doses.



Example of imaging: It is observed that the tracer (<sup>18</sup>F-FDG) administered via the tail vein of rat is rapidly delivered to the heart, excreted via the liver → kidney → bladder, and accumulated in the cardiac muscle, retrobulbar area and brain.



[Features]

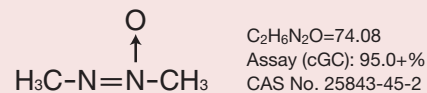
1. 20 mg of Mannose Triflate in unit doses.
2. Rubber stopper and aluminum cap are used.

Model rodent colon carcinogen

**Azoxymethane [AOM]**

AOM induces colon cancer in mice and rats effectively, and is widely used as a substance to cause colon tumors in laboratory animals in the research of cancer prevention substances and the mechanism of cancer formation. In addition, amidst growing concerns over rising cases of colon cancer, the search for cancer prevention substances is believed to be increasingly popular, and thus the importance of the role this product plays is growing.

The average dose of this product consists of a subcutaneous injection of 15 mg/kg (weight) in rats once a week, for a period of about 3 weeks. After a few weeks, precancerous lesions (ACF) are observed.



Description	Wako Catalog No. (Pkg. Size)	Induced Cancer, Storage condition
<b>Azoxymethane [AOM]</b> , 95.0+% (cGC) <for Cellbiology>	<b>011-20171</b> (100 mg)	Colon cancer, Keep at -20°C
<b>Related Products</b>		
<b>7,12-Dimethylbenz[α]anthracene</b> , 95.0+% (cGC) <Wako Special Grade>	<b>042-02801</b> ( 1 g)	Breast cancer, Keep at RT
<b>DMIP</b> [2-Amino-1,6-dimethylimidazo[4,5-b]pyridine], 98.0+% (HPLC) <for Biochemistry>	<b>049-24891</b> ( 20 mg)	Colon cancer, Keep at 2~10°C
<b>4-Nitroquinoline 1-oxide</b> , 98.0+% (HPLC) <Wako Special Grade>	<b>147-03421</b> ( 1 g)	Ovarian tumor, leukemia, Keep at 2~10°C
<b>PhIP Hydrochloride</b> , 99.0+% (HPLC) <for Biochemistry>	<b>163-15951</b> (100 mg)	Mouth cancer (tongue cancer), Keep at 2~10°C

Description	Note
<b>DNA or RNA Synthesis Inhibitors</b>	
<b>Actinomycin D</b> , 97.0+% (HPLC), Wako1st Grade Wako Cat. #018-21264 (1 mg); 014-21261 (5 mg); 010-21263 (25 mg)	<b>Antibiotic.</b> Selectively inhibit RNA synthesis (specially rRNA synthesis) by binding to the DNA.
<b>Bleomycin Hydrochloride</b> <for Biochemistry> Wako Cat. #028-07801 (10 mg) Potency: 1,400~2,000 µg/mg	<b>Antibiotics.</b> Exhibit an antitumor activity by inhibiting DNA synthesis and cleaving DNA strands.
<b>Bleomycin Sulfate</b> <for Pharmacology Research> Wako Cat. #027-15941 (10 mg); 023-15943 (50 mg)	
<b>1,4-Butanediol Dimethanesulfonate [Busulfan]</b> , 97.0+% (cGC) <Wako1st Grade> Wako Cat. #029-09352 (25 g)	<b>Alkylating compound:</b> Inhibit synthesis and duplication of DNA by alkylation of nucleic acids (mainly DNA) and other cell components to suppress cell division.
<b>Carboplatin</b> , 97.0+% (HPLC) <for Biochemistry> Wako Cat. #039-16041 (25 mg); 035-16043 (250 mg)	<b>Platinum complex:</b> Form crosslinks in double stranded DNA. Inhibit DNA synthesis followed by cell division.
<b>Cisplatin</b> , 98.0+% (HPLC) <for Pharmacology Research> Wako Cat. #033-20091 (200 mg); 039-20093 (2 g)	
<b>Cyclophosphamide Monohydrate</b> , 97.0+% (Titration) <for Biochemistry> Wako Cat. #030-12953 (1 g); 034-12951 (5 g)	<b>Alkylating compound:</b> Inhibit synthesis and duplication of DNA by alkylation of nucleic acids (mainly DNA) and other cell components to suppress cell division.
<b>Dacarbazine</b> , 98.0+% (Potentiometric titration) <for Pharmacology Research> Wako Cat. #047-29951 (200 mg); 043-29953 (1 g)	<b>Alkylating compound:</b> Cause DNA-damage by alkylation with diazomethane produced by metabolism.
<b>Daunorubicin Hydrochloride</b> <for Pharmacology Research> Wako Cat. #043-30041 (5 mg); 049-30043 (50 mg)	Anthracycline <b>antibiotic.</b> Inhibit DNA synthesis by binding the DNA. Induce apoptosis by Fas in Jurkat cells.
<b>Ifosfamide</b> , 98.0+% (HPLC) <for Pharmacology Research> Wako Cat. #090-05401 (50 mg); 096-05403 (500 mg)	<b>Alkylating compound:</b> Its active metabolites, 4-hydroxy ifosfamide and aldoifosfamide inhibit DNA synthesis of tumor cells.
<b>Melphalan</b> <for Pharmacology Research> Wako Cat. #135-15251 (100 mg); 131-15253 (1 g)	<b>Alkylating compound:</b> Considered to exhibit an antitumor effect by inhibiting nucleic acid synthesis caused by crosslinking formation between intra- or inter-DNA strands and between DNA and proteins.
<b>Mitomycin C</b> <for Biochemistry> Wako Cat. #134-07911 (10mg) Potency: 850+µg/mg	<b>Antibiotic</b> that causes crosslink breakage by binding to guanine residues of DNA and induces inhibition of DNA biosynthesis.
<b>Nimustine Hydrochloride</b> , 97.0+% (Titration) <for Pharmacology Research> Wako Cat. #142-08471 (250 mg); 148-08473 (1 g)	<b>Alkylating compound:</b> Water-soluble nitrosourea derivative. The main action mechanism is considered to be depolymerization of DNA and inhibition of DNA synthesis by DNA alkylation.
<b>Oxaliplatin</b> , 97.0+% (HPLC) <for Pharmacology Research> Wako Cat. #156-02691 (5 mg); 152-02693 (50 mg)	<b>Platinum complex,</b> form crosslinks in double stranded DNA. Inhibit DNA synthesis followed by cell division.
<b>Procarbazine Hydrochloride</b> , 98.0+% (Titration) <for Pharmacology Research> Wako Cat. #161-22581 (100 mg); 167-22583 (1 g)	<b>Alkylating compound:</b> Inhibit nucleic acid/protein synthesis by alkylating nucleic acids.
<b>Topoisomerase and Telomerase Inhibitors</b>	
<b>17-AAG</b> <for Cellbiology> Wako Cat. #012-20101 (1 mg)	Cause dephosphorylation of Akt by inhibition of HSP90 followed by inactivation of Akt and apoptosis.
<b>Camptothecin</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #038-18191 (100 mg); 034-18193 (500 mg)	Reversible Topoisomerase I inhibitor: Cause DNA-damage by binding to and stabilizing topoisomerase-DNA complex.
<b>Doxorubicin Hydrochloride [Adriamycin Hydrochloride]</b> <for Biochemistry> Wako Cat. #040-21521 (10 mg); 046-21523 (50 mg) Potency: 900+µg/mg	Anthracycline <b>antibiotic:</b> Cause DNA-damage by inhibiting Topoisomerase II.
<b>Ellagic Acid Dihydrate</b> , 99.0+% (HPLC) <for Biochemistry> Wako Cat. #056-05781 (5 g); 054-05782 (25 g)	Potent antioxidant that has antimutagenic and anticarcinogenic effects. Inhibits Topoisomerase I and II.
<b>(-)-Epigallocatechin Gallate</b> , 90.0+% (HPLC) <for Biochemistry> Wako Cat #059-05411 (100 mg)	Considered to act on a unit having reverse transcriptase activity, hTERT. Polyphenol: Catechin from green tea extracts
<b>Epirubicin Hydrochloride</b> <for Pharmacology Research> Wako Cat. #058-07561 (1 mg); 054-07563 (5 mg)	An anthracycline <b>antibiotic:</b> Stereoisomer of doxorubicin with an inverse stereochemistry of the OH group in the 4' position. Show less toxicity than doxorubicin hydrochloride.
<b>Etoposide Phosphate</b> , 85.0+% (HPLC) <for Biochemistry> Wako Cat. #058-06341 (5 mg)	Water-soluble derivative of etoposide. Cause DNA-damage by inhibiting Topoisomerase II.
<b>Geldanamycin, from <i>Streptomyces hygroscopicus</i></b> , 95.0+% (HPLC) <for Biochemistry> Wako Cat. #077-04571 (100 µg)	Inhibit chaperone activity of HSP90.
<b>Nalidixic Acid</b> , 98.5+% (Titration) <for Biochemistry> Wako Cat. #148-04791 (5 g); 146-04792 (25 g)	Causes DNA-damage by inhibiting DNA gyrase.

Description	Note
<b>Cytoskeletal Inhibitors and Cell-Division Inhibitors</b>	
<b>Colchicine</b> , 95.0+% (HPLC) <for Biochemistry> Wako Cat. #039-03851 (100 mg); 035-03853 (1 g)	Microtubule <b>depolymerizing agent</b> . Cell cycle synchronizing agent. Act as an ending factor of tubulin polymerization by binding to tubulin dimer, which induces inhibition of tubulin polymerization with very small concentration.
<b>Cytochalasin B</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #030-17551 (1 mg); 036-17553 (5 mg); 034-17554 (10 mg)	Bind to F-actin and induce <b>depolymerization</b> of F-actin by capping function that inhibits assembly of G-actin. Inhibit cytokinesis but not karyokinesis.
<b>Cytochalasin D</b> , 95.0+% (TLC) <for Biochemistry> Wako Cat. #037-17561 (1 mg); 033-17563 (10 mg)	Have nearly the same function as that of cytochalasin B, but do not show inhibitory activity in glucose transport unless stimulated by insulin.
<b>Demecolcine</b> , 90.0+% (Absorptiometry) <for Biochemistry> Wako Cat. #045-16963 (5 mg); 049-16961 (20 mg)	Microtubule <b>depolymerizing agent</b> . Cell cycle synchronizing agent. Have nearly the same function as and less toxicity than that of colchicine.
<b>Latrunculin A</b> , 93.0+% (HPLC) <for Biochemistry> Wako Cat. #125-04363 (1 mg); 129-04361 (5 mg)	Inhibit actin <b>polymerization</b> by binding with G-actin.
<b>Latrunculin B</b> <for Cellbiology> Wako Cat. #129-05101 (1 mg)	
<b>Mycalolide B</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #132-12081 (100 µg)	
<b>Paclitaxel</b> , 97.0+% (HPLC) <for Biochemistry> Wako Cat. #169-18616 (1 mg); 169-18611 (5 mg); 165-18613 (25mg); 163-18614 (100 mg)	Plant alkaloid: Bind to β-tubulin and stabilize microtubule, inducing inhibition of mitosis by inhibiting microtubule dynamics.
<b>Phalloidin</b> , 95.0+% (TLC) <for Biochemistry> Wako Cat. #165-15411 (1 mg)	Inhibit actin <b>depolymerization</b> by binding to and stabilizing F-actin.
<b>Podophyllotoxin</b> , 95.0+% (HPLC) <for Biochemistry> Wako Cat. #161-20901 (100 mg); 167-20903 (1 g)	Antimitotic agent. Bind in the vicinity of colchicine binding site of tubulin dimer and competitively inhibit microtubule formation by colchicine.
<b>Swinholide A</b> <for Biochemistry> Wako Cat. #197-11851 (10 µg)	Cleave actin filaments by binding to G-actin and stabilizing actin dimer.
<b>Vinblastine Sulfate</b> , 97.0+% (HPLC) <for Biochemistry> Wako Cat. #221-00751 (10 mg); 227-00753 (50 mg)	Plant alkaloid: <b>Inhibit polymerization</b> by exerting a selective action on tubulin, a structural protein of microtubule, during mitosis. Inhibit tubulin polymerization with low concentration and induce polymorphic assembly of tubulin with high concentration.
<b>Vindesine Sulfate</b> , 96.0+% (HPLC) <for Pharmacology Research> Wako Cat. #225-01631 (2 mg); 221-01633 (10 mg)	Plant alkaloid: Considered to exhibit an antitumor effect by acting on microtubule or tubulin, a structural protein of microtubule, during mitosis.
<b>Vinorelbine Ditartrate</b> , 98.0+% (HPLC) <for Pharmacology Research> Wako Cat. #222-01641 (10 mg); 228-01643 (50 mg)	Plant alkaloid: <b>Inhibit polymerization</b> by exerting a selective action on tubulin, a structural protein of microtubule, during mitosis.
<b>Antiangiogenic agents</b>	
<b>Angiostatin</b> , from Human <for Biochemistry> Wako Cat. #543-00941 (1 mg)	Considered to regulate induction of excessive vascularization by inhibiting migration of vascular endothelial cells.
<b>Fumagillin</b> , 95+% (TLC) <for Biochemistry> Wako Cat. #065-04071 (1 mg); 061-04073 (5 mg)	<b>Antibiotic</b> : Inhibit biosynthesis of sphingomyelin. Have a vascularization inhibitory activity.
<b>Irsogladine Maleate</b> , 97.0+% (Titration) <for Biochemistry> Wako Cat. #098-04581 (100 mg); 094-04583 (500 mg)	Antiulcer drug. Inhibit vascularization in HOME C and mouse CP assay.
<b>2-Methoxyestradiol</b> <for Cellbiology> Wako Cat. #138-15501 (10 mg); 134-15503 (50 mg)	Low molecular antiangiogenic agent without estrogenic activity. Inhibit microtubule assembly by binding to colchicine binding site of tubulin and arrest cell division in metaphase.
<b>Radicol</b> <for Cellbiology> Wako Cat. #183-01901 (1 mg)	Antibacterial macrocyclic lactone <b>antibiotic</b> with antimalarial activity. Have the ability to inhibit HSP90 and protein tyrosine kinase and show vascularization inhibitory activity.
<b>Suramin Sodium</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #199-10613 (100 mg); 193-10611 (200 mg)	Considered to have a vascularization inhibitory effect by preventing various growth factors from binding to the cell surface. Inhibit interaction between G protein and intracellular receptor site.
<b>(±)-Thalidomide</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #200-15131 (100 mg); 206-15133 (1 g); 204-15134 (10 g)	Inhibit biosynthesis of TNFα. Inhibit vascularization by bFGF in rabbit CP assay.
<b>Antimetabolite</b>	
<b>Carmofur</b> <for Pharmacology Research> Wako Cat. #035-20051 (1 g); 031-20053 (5 g)	Pyrimidine antimetabolite. Prodrug of 5-FU. Metabolized in vivo into 5-FU and inhibit DNA synthesis.
<b>Chlormadinone Acetate</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #035-15161 (1 g); 031-15163 (5 g)	Synthetic hormone agent: One of corpus luteum hormones. Inhibit effect of hormone relating to the prostate hyperplasia.
<b>Cytosine-1β-D(+)-arabinofuranoside [Cytarabine]</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #030-11951 (100 mg); 034-11954 (500 mg); 036-11953 (1 g)	Antimetabolic drug: Antiprimidine. Cytarabine triphosphate phosphorylated in cells strongly inhibits DNA polymerase I. In particular, strongly inhibit DNA synthesis.

Description	Note
<b>Antimetabolite</b> <span style="float: right;">-continued-</span>	
<b>Dexamethasone</b> , 98.0~102.0% (Titration) <for Biochemistry> Wako Cat. #047-18863 (100 mg); 041-18861 (1 g)	Synthetic hormone agent: Synthetic adrenal cortical hormone. Glucocorticoid. Inhibit phospholipase.
<b>Doxifluridine</b> <for Pharmacology Research> Wako Cat. #042-29901 (100 mg); 048-29903 (1 g)	Pyrimidine antimetabolite. Prodrug of 5-FU. Metabolized in vivo into 5-FU and inhibit DNA synthesis.
<b>5-Fluorouracil [5-FU]</b> , 98.5+% (HPLC) <Wako Special Grade> Wako Cat. #068-01401 (1 g); 064-01403 (5 g); 066-01402 (25 g)	Antipyrimidine. The metabolite inhibits DNA synthesis by inhibiting thymidylate synthase. It is incorporated into RNA instead of uracil and kills the cells.
<b>Flutamide</b> , 98.0+% (HPLC) <for Pharmacology Research> Wako Cat. #069-04851 (2 g); 065-04853 (10 g)	Synthetic hormone agent: Nonsteroidal antiandrogen. Inhibit androgen binding to androgen receptor.
<b>Hydroxyurea [Hydroxycarbamide]</b> , 90.0+% (Titration) <Practical Grade > Wako Cat. #085-06653 (5 g); 089-06651 (10 g)	Antimetabolic drug: Inhibit nucleoside diphosphate reductase in the DNA synthesis specific metabolic process and terminate DNA replication.
<b>Medroxyprogesterone Acetate</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #138-09991 (1 g); 134-09993 (5 g)	Synthetic hormone agent: Corpus luteum hormone agonist with antitumor activity. Inhibit vascularization.
<b>6-Mercaptopurine Monohydrate</b> , 98.0~102.0% <for Biochemistry> Wako Cat. #130-07991 (1 g); 136-07993 (5 g)	Antipurine. Inhibit nucleic acid (DNA) synthesis by binding to inosinic acid (IMP).
<b>Methotrexate</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #139-13571 (100 mg); 135-13573 (1 g)	Antifolic. Inhibit enzyme activity and purine synthesis by tightly binding to the active folate producing enzyme.
<b>Prednisolone</b> , 97.0~103.0% (Absorptiometry) <for Biochemistry> Wako Cat. #165-11491 (1 g); 161-11493 (5 g)	Synthetic hormone agent: Synthetic steroid hormone. Have action of adrenal cortical hormone and inhibit phospholipase.
<b>Tamoxifen Citrate</b> , 98.0+% (Titration) <for Biochemistry> Wako Cat. #209-14361 (250 mg); 205-14363 (1 g); 203-14364 (5 g); 207-14362 (25 g)	Synthetic hormone agent: Estrogen analog. Selectively bind to estrogen receptor. Exhibit estrogenic effect in the tissues such as bone and heart, and inhibit action of estrogen in the breasts and uterus.
<b>1-(2-Tetrahydrofuryl)-5-fluorouracil [Tegafur]</b> 98.0+% (Titration) <for Biochemistry> Wako Cat. #206-10351 (1 g); 202-10353 (5 g)	Antipyrimidine. Prodrug of 5-FU. Metabolized in vivo into 5-FU and inhibit DNA synthesis.
<b>Toremifene Citrate (mixture of isomers)</b> , 98.0+% (Titration) <for Pharmacology Research> Wako Cat. #200-16971 (500 mg); 206-16973 (2 g)	Inhibit binding of estradiol to the estrogen receptor. Considered to have cell-growth inhibitory activity by estradiol and by blocking of signaling pathway via IGF-1 receptor.
<b>Others</b>	
<b>AACOCF3 [Arachidonyltrifluoromethylketone]</b> <for Biochemistry> Wako Cat. #011-18461 (10mg)	Selective inhibitor of cPLA2 (Cytosolic phospholipase A2) and iPLA2 (Ca <sup>2+</sup> independent phospholipase A2) (IC <sub>50</sub> =15 μmol/L).
<b>AITRL, Human, recombinant</b> <for Cellbiology> Wako Cat. #014-19671 (20 μg)	One of the costimulatory molecules of TNF/TNF receptor family. AITRL-AITR interaction is important to control apoptosis via T cell proliferation or TCR.
<b>all-trans-Retinoic Acid [Tretinoin]</b> , 97.0+% (HPLC) <for Biochemistry> Wako Cat. #186-01114 ( 50 mg); 182-01116 (100 mg); 182-01111 (250 mg); 188-01113 ( 1 g)	Synthetic retinoids: Retinoic acids are considered to regulate proliferation and differentiation of cells by directly controlling gene expression in vivo.
<b>Am580</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #014-16631 (5 mg)	
<b>Am80</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #017-16621 (5 mg)	
<b>Ch 55</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #039-16781 (5 mg)	
<b>4-Amino-1,8-naphthalimide</b> <for Biochemistry> Wako Cat. #018-18611 (20 mg)	Strongly inhibit PARP. (IC <sub>50</sub> =0.18 μmol/L)
<b>Anisomycin</b> , 96.0+% (HPLC) <for Biochemistry> Wako Cat. #017-16861 (10 mg); 013-16863 (50 mg); 011-16864 (250 mg)	Activator of p54 and MAP kinase. Involved in activation of SAPKs. Induce apoptosis in human U937 cells.
<b>(+)-Brefeldin A</b> <for Cellbiology> Wako Cat. #022-15991 (5 mg); 028-15993 (25 mg)	Macrolide <b>Antibiotic</b> : Specifically and reversibly inhibit protein transport from endoplasmic reticulum to Golgi apparatus without affecting endocytosis or lysosome function.
<b>Calpain Inhibitor I</b> <for Cellbiology> Wako Cat. #031-19801 (10 mg)	Inhibit neutral cysteine proteases, such as calpain 1, calpain 2, cathepsin B and cathepsin L, and proteasome. Inhibit apoptosis in thymocytes and metamyelocytes.
<b>Caspase 6/caspase 8 inhibitor W-1 [Ac-IETD-CHO]</b> , 92.0+% (HPLC) <for Biochemistry> Wako Cat. #034-17331 (1 mg)	Specifically and reversibly inhibit Caspase 6 / Caspase 8 and related cysteine protease.
<b>Caspase3/CPP32 Inhibitor W-3 [Z-DEVD-FMK]</b> , 95.0+% (TLC) <for Biochemistry> Wako Cat. #034-16971 (1 mg)	Specifically inhibit cysteine protease activity of caspase 3. Have membrane permeability.

Description	Note
<b>Others</b> <span style="float: right;">-continued-</span>	
<b>CPP32/Apopain Inhibitor W-1</b> [AC-DEVD-CHO], 95.0+% (HPLC) <for Biochemistry> Wako Cat. #037-16961 (5 mg)	Caspase-3 inhibitor
<b>Cytotrienin A</b> <for Biochemistry> Wako Cat. #039-18241 (100 µg)	<b>Antibiotic</b> derived from actinomycetes. Low concentration treatment (10 ng/mL) induces apoptosis in HL-60.
<b>Deguelin</b> <for Cellbiology> Wako Cat. #047-29211 (5 mg)	Akt inhibitor. Inhibit cell proliferation in G2-M period. Induce apoptosis in precancerous and cancerous cell lines.
<b>Granzyme B Inhibitor W-2</b> [Z-AAD-CMK], 90.0+% (HPLC) <for Biochemistry> Wako Cat. #076-04301 (1 mg)	Inhibit human and mouse serine proteases, granzyme B.
<b>Herbimycin A</b> , 98.0+% (HPLC) <for Biochemistry> Wako Cat. #085-06491 (1 mg)	Inhibit tyrosine kinase of src by reacting with SH groups of cis residues in src.
<b>Leupeptin Hemisulfate Monohydrate</b> <for Biochemistry> Wako Cat. #122-03751 (5 mg); 126-03754 (10 mg); 128-03753 (25 mg); 122-03756 (100 mg)	Cysteine protease inhibitor: Show inhibitory effect of papain and cathepsin B.
<b>Pamidronate Disodium Salt Pentahydrate</b> , 98.0+% (HPLC) <for Pharmacology Research> Wako Cat. #165-23101 (10 mg); 161-23103 (100 mg)	Bone resorption inhibitor: Lower serum calcium level in patients with hypercalcemia caused by cancer.
<b>Staurosporine</b> , 95.0+% (HPLC) <for Biochemistry> Wako Cat. #197-10251 (100 µg); 193-10253 (500 µg)	Potent PKC inhibitor (IC <sub>50</sub> =2.7 nmol/L): Also inhibit PKA (IC <sub>50</sub> =8.2 nmol/L) and p60 <sup>v-src</sup> tyrosine kinase, the product of src, (IC <sub>50</sub> =6.4 nmol/L) to a similar extent.
<b>Tunicamycin</b> , 95.0+% (HPLC) <for Biochemistry> Wako Cat. #202-08241 (10 mg); 208-08243 (50 mg)	Inhibit N-linked glycosylation of glycoproteins by inhibiting the first reaction of glycoprotein synthesis system via the lipid intermediate pathway. Induce apoptosis mediated by endoplasmic reticulum stress.
<b>(+)-Wortmannin</b> [KY12420] <for Cellbiology> Wako Cat. #230-02341 (2 mg); 236-02343 (10 mg)	Have cell permeability and irreversibly inhibit PI3 kinase. Inhibit myosin light chain kinase at high concentration.
<b>Y-27632</b> , 98.0+% (HPLC) <for Cellbiology> Wako Cat. #257-00511 (1 mg); 253-00513 (5 mg)	Selective and potent ROCK inhibitor. Specifically suppress morphological changes in apoptosis.
<b>Immunostimulant</b>	
<b>Bestatin</b> , abt. 98.0+% (HPLC) Wako Cat. #027-14101 (100 mg)	Protease inhibitor: Specifically inhibit aminopeptidase B, leucine aminopeptidase, tripeptide aminopeptidase, and aminopeptidase on the membrane of mammalian cells.

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**Wako Pure Chemical Industries, Ltd.**<http://www.wako-chem.co.jp>

1-2, Doshomachi 3-Chome  
Chuo-Ku, Osaka 540-8605, Japan  
Tel: 81-6-6203-3741  
Fax: 81-6-6203-1999

**Wako Chemicals USA, Inc.**<http://www.wakousa.com>

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**Head Office** (Richmond, VA):  
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**European Office:**  
Fuggerstraße 12, D-41468  
Neuss, Germany  
Tel: 49-2131-311-0  
Fax: 49-2131-311100