

## Manumycin A – Exosome Biogenesis Inhibitor

Manumycin A, a natural antibiotic, was identified as an inhibitor of exosome biogenesis and secretion. **Manumycin A is a selective inhibitor of FTase. By inhibiting the farnesylation of RAS, Manumycin A suppresses RAS/RAF/ERK1/2 signaling and reduces exosome generation.**

**Exosomes** are small vesicles that are released by cells into the extracellular space. They play an important role in intercellular communication and are involved in a wide range of physiological and pathological processes. They can act as a means of transporting molecules between cells, help to modulate the immune system and regulate cell proliferation, differentiation and apoptosis. Some recent studies have found exosomes to be a potential diagnostic marker for cancer and other diseases, while others have investigated the use of exosomes as a way to deliver therapeutic molecules to specific cells or tissues.

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 anti-cancer effects.**

**LITERATURE REFERENCES:** Manumycin A suppresses exosome biogenesis and secretion via targeted inhibition of Ras/Raf/ERK1/2 signaling and hnRNP H1 in castration-resistant prostate cancer cells: A. Datta, et al.; *Cancer Lett.* **408**, 73 (2017) • Inhibiting extracellular vesicles formation and release: a review of EV inhibitors: M. Catalano & L. O'Driscoll; *J. Extracell. Vesicles* **9**, 1703244 (2019) (Review) • Exosome biogenesis: machinery, regulation, and therapeutic implications in cancer: Q.-F. Han, et al.; *Mol. Cancer* **21**, 207 (2022) (Review) • Dissecting exosome inhibitors: therapeutic insights into small-molecule chemicals against cancer: J.H. Kim, et al.; *Exp. Mol. Med.* **54**, 1833 (2022)

### Manumycin A

AG-CN2-2000

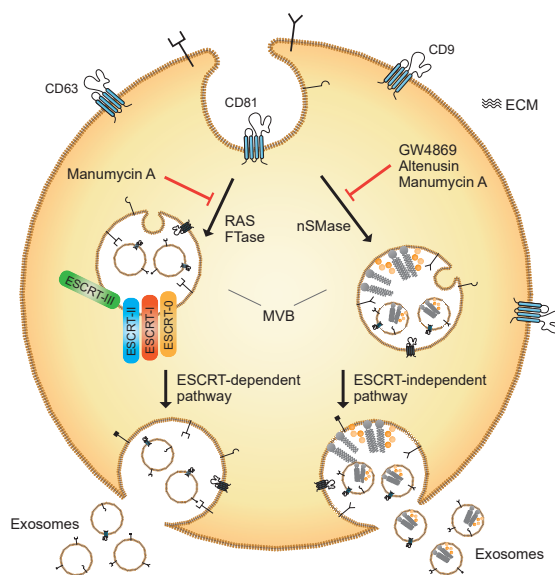
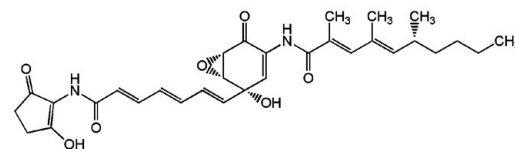
1 mg | 5 mg | 10 mg

**BULK from Stock!**

CAS: 52665-74-4

Source: Isolated from *Streptomyces parvulus*

Purity: >98% HPLC



**FIGURE:** Schematic of exosome biogenesis and inhibition (adapted from M. Catalano & L. O'Driscoll; *J. Extracell. Vesicles* **9**, 1703244 (2019).

## Other Small Molecule Modulators of Exosome Biogenesis and Derivatives

| PRODUCT NAME              | PID         | PRODUCT DESCRIPTION  |
|---------------------------|-------------|--|
| <b>Palmarumycin C3</b>    | BVT-0078    | RAS-farnesyltransferase inhibitor.   |
| <b>Altenusin</b>          | AG-CN2-0143 | Non-competitive nSMase inhibitor.  |
| <b>Arglabin</b>           | AG-CN2-0458 | RAS-farnesyltransferase inhibitor.   |
| <b>OM173-αA</b>           | AG-CN2-0158 | RAS-competitive non-CAAX mimetic type farnesyltransferase (FTase) inhibitor. |
| <b>Andrastin A</b>        | AG-CN2-0144 | Protein farnesyltransferase (PFTase) inhibitor.                              |
| <b>Manumycin B</b>        | BVT-0264    | RAS-farnesyltransferase (FTase) inhibitor.                                   |
| <b>Dihydromanumycin A</b> | BVT-0414    | Manumycin A derivative not yet tested for its biological activity.           |
| <b>Deoxymanumycin A</b>   | BVT-0158    | Manumycin A derivative not yet tested for its biological activity.           |

## STANDARD Exosomes Markers

Sensitive and specific antibodies are an essential tool for the detection of extracellular vesicles (EVs), including exosomes, which express antigens with 3D conformations and/or post-translational modifications that often differ from the cellular counterpart. The group of tetraspanin proteins CD9, CD63 and CD81 are the most common EV-associated markers reported in the literature and have been used for EV capture in many studies, including ELISA, flow cytometry and lab-on-a-chip assays. Each of these tetraspanins has been demonstrated to play an active role in EV biogenesis or cargo sorting, suggesting their essential role in the EV secretory pathway. Ansell Corporation offers specific and sensitive antibodies for tetraspanin detection and exosome capture and a plethora of additional antigen-specific antibodies which consequently allow to phenotype EV populations based on the antigen profile.

### Specific Tetraspanin [TSPAN] Antibodies: Exosomal Membrane Biomarkers

| PRODUCT NAME                             | PID      | PRODUCT DESCRIPTION  |
|--|----------|--|
| <b>anti-CD9 (human), mAb (SN4)</b>       | ANC-156- | Recognizes human CD9 [TSPAN-29]. Works in Flow Cytometry.                  |
| <b>anti-CD37 (human), mAb (IPO-24)</b>   | ANC-186- | Recognizes human CD37 [TSPAN26]. Works in Flow Cytometry.                  |
| <b>anti-CD53 (human), mAb (63.5A3)</b>   | ANC-204- | Recognizes human CD53 [TSPAN25]. Works in Flow Cytometry.                  |
| <b>anti-CD63 (human), mAb (AHN16.1)</b>  | ANC-215- | Recognizes human CD63 [TSPAN30]. Works in Flow Cytometry, IHC.             |
| <b>anti-CD81 (human), mAb (1.3.3.22)</b> | ANC-302- | Recognizes human CD81 [TSPAN28]. Works in Flow Cytometry and Western blot. |

For a List of human CD Antibodies available through AdipoGen Life Sciences, please download the Ansell Corporation Brochure.

## Tim-4: Exosomal Capturing/Sorting Biomarkers

EV membranes are rich in phosphatidylserine (PS) and Tim-4 binds to PS on the surface of EVs. A recent protocol describes an affinity-based method for isolating EVs using streptavidin magnetic beads conjugated with Tim-4-biotin to capture EVs in a calcium-dependent manner. This protocol could replace ultracentrifugation, which is the most commonly used method for purifying EVs. This Tim-4-dependent method gives a good yield and high purity and allows isolation of all populations of EVs compared to other approaches (ultracentrifugation, PEG precipitation or selected antibodies immunoprecipitation).

**LITERATURE REFERENCES:** High purity isolation and sensitive quantification of extracellular vesicles using affinity to Tim-4: T. Yoshida, et al.; Curr. Prot. Cell Biol. 77, 3.45.1-3.45.18 (2017)

| PRODUCT NAME                                    | PID          | PRODUCT DESCRIPTION   |
|---|--------------|---|
| <b>Tim-4 (mouse):Fc (human) (rec.) (Biotin)</b> | AG-40B-0180B | Used to isolate extracellular vesicles. Works in human and mouse. |
| <b>Tim-4 (mouse):Fc (human) (rec.)</b>          | AG-40B-0180  | Used to isolate extracellular vesicles. Works in human and mouse. |
| <b>Tim-4 (mouse):Fc (mouse) (rec.)</b>          | CHI-MF-110T4 | Used to isolate extracellular vesicles. Works in mouse.           |
| <b>Tim-4 (human):Fc (mouse) (rec.)</b>          | CHI-HF-211T4 | Used to isolate extracellular vesicles. Works in human.           |
| <b>Tim-4 (human):Fc (human) (rec.)</b>          | CHI-HF-210T4 | Used to isolate extracellular vesicles. Works in human.           |