SZABO SCANDIC

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# Produktinformation

- Forschungsprodukte & Biochemikalien
- Zellkultur & Verbrauchsmaterial
- Diagnostik & molekulare Diagnostik
- Laborgeräte & Service

Weitere Information auf den folgenden Seiten!
See the following pages for more information!

## Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

## Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand


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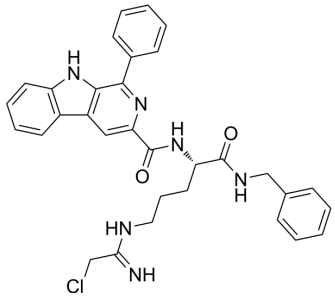
# PAD4-IN-4

| | |
|---|---|
| **Cat. No.:** | HY-162494 |
| **Molecular Formula:** | $C_{32}H_{31}ClN_6O_2$ |
| **Molecular Weight:** | 567.08 |
| **Target:** | Protein Arginine Deiminase |
| **Pathway:** | Epigenetics |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |



## BIOLOGICAL ACTIVITY

**Description**

PAD4-IN-4 (compound 28) is a potent PAD4 inhibitor ($IC_{50}$=0.79 ± 0.09 μM). PAD4-IN-4 improves the tumor immune microenvironment by reshaping neutrophil phenotype, upregulating the proportions of dendritic cells and M1 macrophages, and reducing the amount of myeloid-derived suppressor cells. PAD4-IN-4 can be used for Triple-negative breast cancer research[1].

**$IC_{50}$ & Target**

| PAD4 | PAD2 |
|---|---|
| 0.79 μM ($IC_{50}$) | 2.97 μM ($IC_{50}$) |

**In Vitro**

PAD4-IN-4 displays substantial inhibitory activity toward PAD2 and PAD4 ($IC_{50}$=2.97 ± 0.29 and 0.79 ± 0.09 μM), with the best PAD4 selectivity[1].

PAD4-IN-4 suppresses the proliferation of TNBC cells in vitro (4T1 $IC_{50}$: 2.39 ± 0.54 μM; MDA-MB468 $IC_{50}$: 2.34 ± 0.23 μM), with relatively low toxicity toward normal breast cells (MCF-10A $IC_{50}$: 8.39 ± 0.60 μM)[1].

PAD4-IN-4 (0.5, 1, 2 μM; 48 h) has enhanced antimetastasis activity for TNBC cells[1].

PAD4-IN-4 (0.5, 1, 2 μM; 48 h) is a potent PAD4 inhibitor for blocking histone citrullination and neutrophil extracellular trap (NET) formation[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

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|---|---|
| Cell Line: | TNBC cells |
| Concentration: | 0.5, 1, 2 μM |
| Incubation Time: | 48 h |
| Result: | Reduced the number of metastatic cells and wound closure rate less than that of 7 at the equivalent dose, indicating that compound 28 had enhanced antimetastasis activity. |

Immunofluorescence[1]

| | |
|---|---|
| Cell Line: | TNBC cells and neutrophils |
| Concentration: | 0.5, 1, 2 μM |
| Incubation Time: | 48 h |

| | |
|---|---|
| Result: | Inhibited histone citrullination and NET formation. |

**In Vivo**

PAD4-IN-4 (1, 5, 10 mg/kg; i.v.; every 2 days for a total of nine times) can dosedependently suppress the lung metastasis of TNBC. PAD4-IN-4 is a promising candidate against TNBC without obvious toxicity in orthotopic 4T1-luc xenograft model in BALB/c mice[1].

PAD4-IN-4 alters the tumor microenvironment from a suppressive condition to an antitumor milieu by modulating the proportion of immune cells and reshaping the neutrophil phenotype and function[1].

Pharmacokinetic Analysis in Male Sprague−Dawley rats[1]

| Compound | Route | Dose (mg/kg) | $AUC_{0\_t}$ (ng•h/mL) | $AUC_{0\_INF}$ (ng•h/mL) | $T_{1/2}$ (h) | $T_{max}$ (h) | $C_{max}$ (ng/mL) | Cl (L•h/kg) |
|---|---|---|---|---|---|---|---|---|
| 7 | i.v. | 3.5 | 14893.52 | 17214.17 | 0.13 | 0.08 | 251.2 | 571.87 |
| 28 | i.v. | 3.5 | 9525.86 | 17346.55 | 0.25 | 0.08 | 297.71 | 105.24 |

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|---|---|
| Animal Model: | orthotopic 4T1-luc xenograft model in BALB/c mice[1]. |
| Dosage: | 1, 5, 10 mg/kg |
| Administration: | Intravenous injection (i.v.) |
| Result: | The tumor growth inhibition of the high-dose 28-treated group was 61.8%, whereas the positive control doxorubicin hydrochloride group reached 54.6%.<br>Had no significant differences in viscero−somatic ratio and serum biochemical indices (ALT, AST, UREA, and CREA-S) were observed in the 28-treated group.<br>Increased the proportion of mature TANs MHC-II+ TANs whereas it suppressed the proportion of pro-tumor phenotypes PD-L1+ /MHC-II+ TANs and MHC-II− TANs. |

## REFERENCES

[1]. Zhu D, et al. A β-Carboline Derivate PAD4 Inhibitor Reshapes Neutrophil Phenotype and Improves the Tumor Immune Microenvironment against Triple-Negative Breast Cancer[J]. Journal of Medicinal Chemistry, 2024.



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