

Product Data Sheet

Product Name: ML-T7
Cat. No.: GC26676

Chemical Properties

Cas. No. 459789-75-4

SMILES O=C1C2=C(C(C13OC(C4C(N(C5=CC=C(C=C5Cl)Cl)C(C43)=O)=O)C6=CC=C(C)C=C6)=O)C=CC=C2

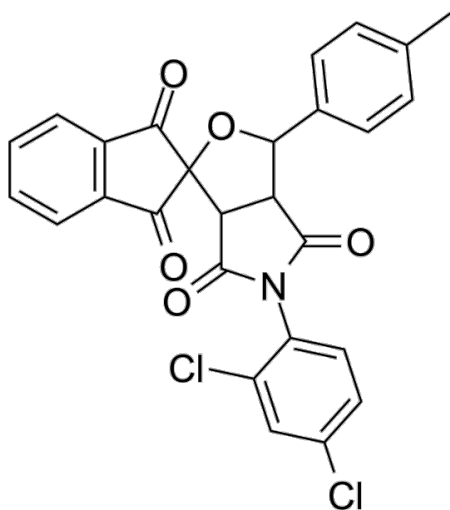
Formula $C_{27}H_{17}Cl_2NO_5$ M.Wt 506.33

Solubility DMSO : 66.67 mg/mL (131.67 mM; Storage -20°C
Need ultrasonic)

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Bone marrow cells

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method For generation of dendritic cells (DCs), bone marrow cells were isolated by flushing femurs, tibias and humeri and plated in RPMI1640 medium supplemented with 10% FBS, 1% penicillin-streptomycin, 50 μ M 2-Mercaptoethanol, 10ng/mL GM-CSF and 5ng/ml IL-4. After 6 days, 10 μ g/mL LPS was used to induce DC maturation in the presence of DMSO or ML-T7. DC maturation markers were detected using flow cytometric analysis 24h later.

Reaction Conditions 10 μ M; 24h

Applications ML-T7 enhanced maturation marker expression and antigen-presenting capacity in LPS (1 μ g/mL)-stimulated DC.

Animal experiment [2]:

Animal models Akt/cMyc-induced HCC C57BL/6 mice models

Preparation Method Mice were treated with ML-T7 at different doses (DMSO as control, every 2 days) from day 13 to day 32.

Dosage form 20 and 50mg/kg; i.p.; every 2 days for 20days

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Applications

Mouse body weight showed no significant difference during treatment with ML-T7 at different doses. Compared with control treatment with DMSO, treatment with ML-T7 at doses of 20 and 50mg/kg markedly inhibited tumor growth as measured by in vivo bioluminescence imaging and prolonged survival. Liver-to-body weight ratios, as well as serum concentrations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), were suppressed by ML-T7 at doses of 20 and 50mg/kg. Systemic administration of ML-T7 at doses of 20 and 50mg/kg caused significantly increased CD8⁺ T cells and increased the Ki67-positive CD8⁺ T cells in both tumor and spleen. ML-T7 enhanced the polyfunctionality (coproduction of IFN- γ , TNF- α , and IL-2) of tumor-infiltrating and splenic CD8⁺ T cells and reduced the expression of PD-1 in CD8⁺ T cells, implying an inhibition of T cell exhaustion.

References:

[1] Ma, Shuaiya et al. "Identification of a small-molecule Tim-3 inhibitor to potentiate T cell-mediated antitumor immunotherapy in preclinical mouse models." Science translational medicine vol. 15,722 (2023): eadg6752.

Background

ML-T7 is a potent T cell immunoglobulin and mucin domain-containing protein 3 (Tim-3) inhibitor, which targets the FG-CC' loop and binds to Tim-3 to disrupt the interaction between Tim-3 and phosphatidylserine/carcinoembryonic antigen-related cell adhesion molecule 1 (PtdSer/CEACAM1). The K_d values of ML-T7 binds to hTim-3 and mTim-3 are 6.98 and 7.40 μ M, respectively. Tim-3 is highly expressed on exhausted T cells in tumors and mediates T-cell terminal differentiation and exhaustion during chronic viral infection and tumor progression. ML-T7 promoted T cell survival and suppressed T cell exhaustion to enhance the antitumor activity of CD8⁺ cytotoxic T lymphocytes (CTLs) and chimeric antigen receptor (CAR) T cells in vitro and in vivo^[1].

In vitro, ML-T7 (1-20 μ M; 4h) dose-dependently promoted cell proliferation, cytokine production, and cytotoxicity of C57BL/6-Tg(TcraTcrb)1100Mjb/J (OT-I) mice CD8⁺ CTLs^[1]. ML-T7 (10 μ M; 48h) significantly enhanced the production of IFN- γ , TNF- α , CD107a, and granzyme B in the human NK92

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

and increased its cytotoxic activity against K562-Fluc cells at different effector-to-target (E:T) ratios^[1]. ML-T7 (10 μ M; 24h) enhanced maturation marker expression and antigen-presenting capacity in LPS (1 μ g/mL)-stimulated dendritic cells (DC)^[1].

In vivo, ML-T7 (20 and 50mg/kg; i.p.; every 2 days for 20 days) enhanced dendritic cell maturation, increased the infiltration and multifunctionality of CD8⁺ T cells, and reduced PD-1 expression and T-cell exhaustion, thereby significantly inhibiting tumor growth and prolonging survival in Akt/c-Myc-induced HCC C57BL/6 mice models^[1]. ML-T7 (50mg/kg; i.p.; every 2 days for 20 days) increased the number and activity of CD8⁺ T cells in tumors and spleens, alleviated T-cell exhaustion, enhanced NK-cell function and dendritic cell maturation, and significantly suppressed tumor progression and prolonged survival in Akt/N-Ras-induced HCC mouse model^[1].

References:

[1] Ma, Shuaiya et al. "Identification of a small-molecule Tim-3 inhibitor to potentiate T cell-mediated antitumor immunotherapy in preclinical mouse models." Science translational medicine vol. 15,722 (2023): eadg6752.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA