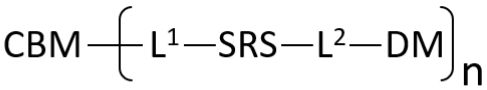
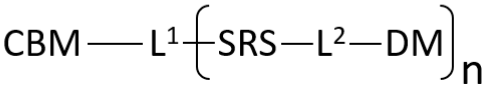
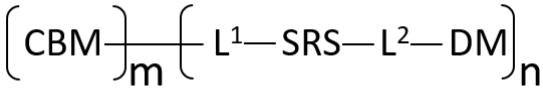
We claim:

1. A binder-drug conjugate represented by any one of the formula:



or





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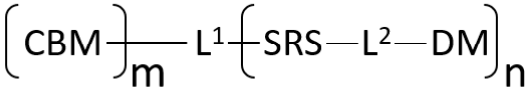


wherein

CBM represents a PD-L1 binding affimer polypeptide having an amino acid sequence represented in general formula (I)

MIPRGLSEAKPATPEIQEIVDKVKPQLEEKTNETYGKLEAVQYKT
QVLA-$(Xaa1)_{n1}$-STNYYIKVRAGDNKYMHLKVFNGP-$(Xaa2)_{m1}$-
ADRVLTGYQVDKNKDDELTGF **(SEQ ID No. 5)**.

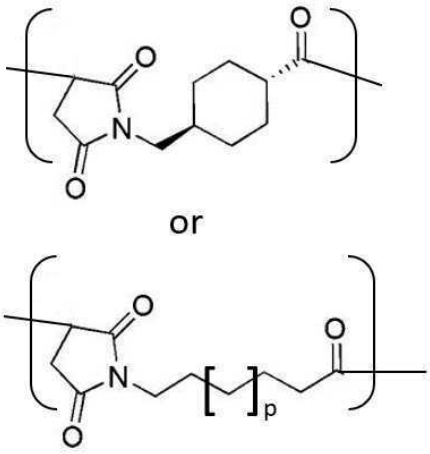
(I)

(Xaa1) is an amino acid sequence having at least 95% homology to any one of SEQ ID Nos. 6 to 40;

(Xaa2) is an amino acid sequence having at least 95% homology to any one of SEQ ID Nos. 41 to 75;

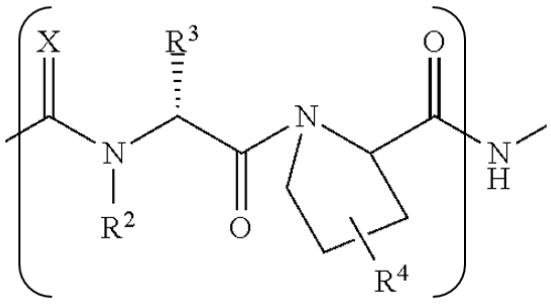
n1 and m1 are each, independently, an integer from 3 to 20;

each L^1 is represented by the formula:



wherein independently for each occurrence p represents an integer from 1 to 20;

SRS represents a substrate recognition sequence cleaved by fibroblast activating protein alpha (FAPα) and represented by



wherein

R^2 represents H or a (C_1-C_6) alkyl, and preferably is H;

R^3 represents H or a (C_1-C_6) alkyl, preferably is methyl, ethyl, propyl, or isopropyl, and more preferably methyl;

R^4 is absent or represents a (C_1-C_6) alkyl, —OH, —NH_2, or halogen;

X represents O or S;

—NH— represents an amine that is part of L^2 if L^2 is a self immolative linker or part of DM if L^2 is a bond;

L^2 represents a self immolative linker that is cleavable by an enzyme present extracellularly in the disease tissue;

DM represents an immuno-DASH inhibitor that inhibits the enzymatic activity of DPP8 and DPP9;

m represents an integer from 1 to 6; and
n represents an integer from 1 to 500, more preferably 1 to 100, 1 to 10 or 1 to 5.

2. The binder-drug conjugate of claim 1, wherein n is an integer from 1 to 100.

3. The binder-drug conjugate of claim 1 or 2, wherein n is an integer from 1 to 5.

4. The binder-drug conjugate of any one of claims 1-3, wherein L^2 is a self immolative linker selected from the group consisting of —NH—$(CH_2)_4$—C(=O)—, —NH—$(CH_2)_3$—C(=O)—, p-aminobenzyloxycarbonyl (PABC) and 2,4-bis(hydroxymethyl)aniline.

5. The binder-drug conjugate of any one of claims 1-4, wherein DM induces macrophage pyroptosis.

6. The binder-drug conjugate of any claims 1-5, wherein DM is cytotoxic to cancer associated fibroblasts (CAFs).

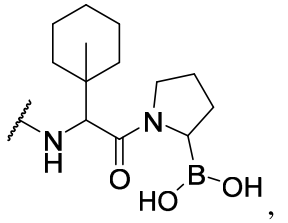
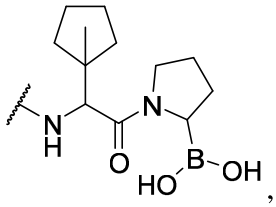
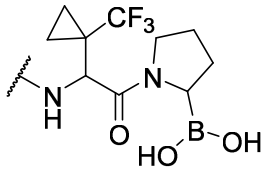
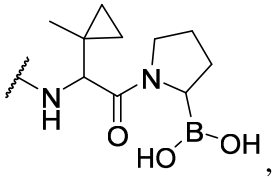
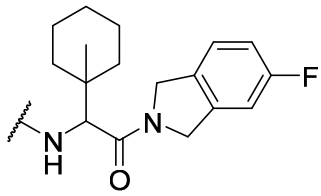
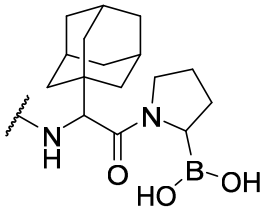
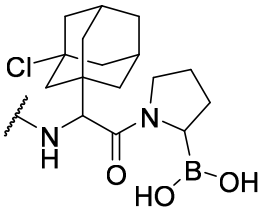
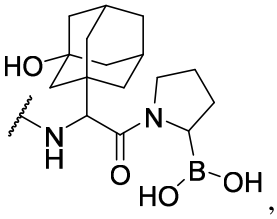
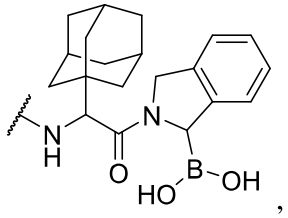
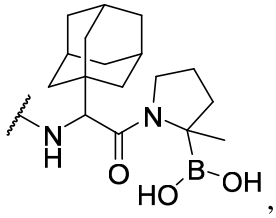
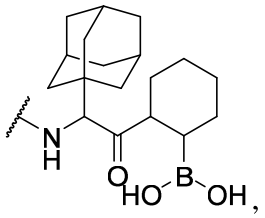
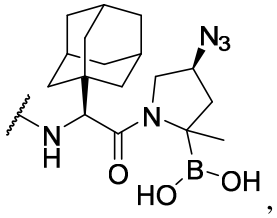
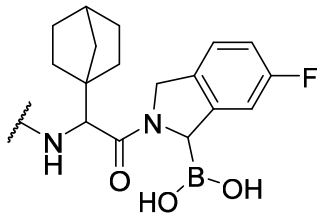
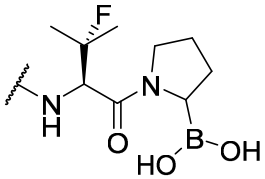
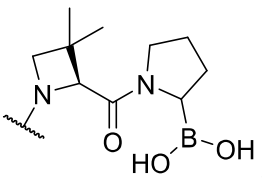
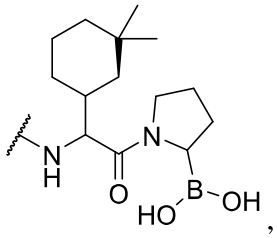
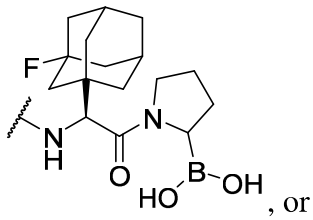
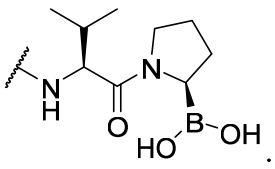
7. The binder-drug conjugate of any claims 1-6, wherein DM polarizes tumor associated macrophage towards M1 macrophage or inhibits M2 macrophage immunosuppressive activity.

8. The binder-drug conjugate of any claims 1-7, wherein DM accelerates T-cell priming and/or dendritic cell trafficking.

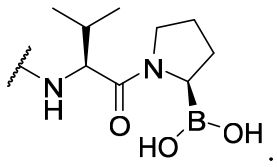
9. The binder-drug conjugate of any claims 1-8, wherein DM inhibits or depletes Treg cells, such as by blocking immunosuppressive function or migration to lymph nodes and/or the tumor microenvironment.

10. The binder-drug conjugate of any one of claims 1-9, wherein DM has a molecular weight less than 5000 amu, preferably less than 2500 amu.

11. The binder-drug conjugate of any one of claims 1-10, wherein DM is

,
,
,
,
,
,
,
,
,
,
,
,
,
,
,
,
, or
.

12. The binder-drug conjugate of any one of claims 1-10, wherein DM is

.

13. A pharmaceutical composition comprising the binder-drug conjugate of any one of claims 1-12; and a pharmaceutically acceptable excipient.

14. Use of the binder-drug conjugate of any one of claims 1-12 in the manufacture of a medicament for treating cancer.

15. The use of claim 14, wherein the cancer is acute myeloid leukemima (AML).

16. The use of claim 14 or 15, wherein the medicament is to be conjointly administered with a PGE2 inhibitor.