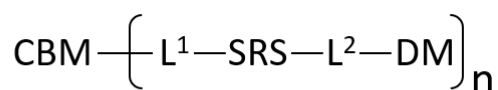
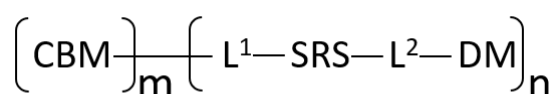


We claim:

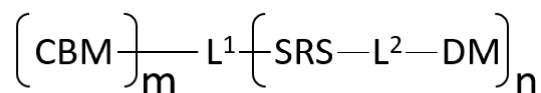
1. A binder-drug conjugate represented by any one of the formula:



or



or

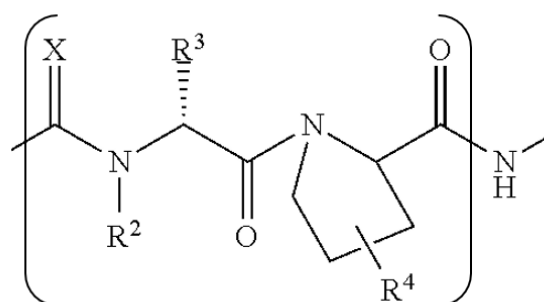


wherein

CBM represents is a bispecific antibody which binds to CTLA-4 and PD-L1;

L^1 represents a spacer or a bond;

SRS represents a substrate recognition sequence cleaved by fibroblast activating protein alpha ($\text{FAP}\alpha$) and represented by



wherein

R^2 represents H or a ($\text{C}_1\text{-C}_6$) alkyl, and preferably is H;

R^3 represents H or a ($\text{C}_1\text{-C}_6$) 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;

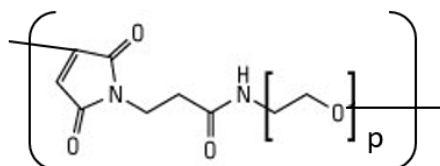
L^2 represents a self immolative linker that is cleavable by an enzyme present extracellularly in the disease tissue;

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

m represents an integer from 1 to 6; and

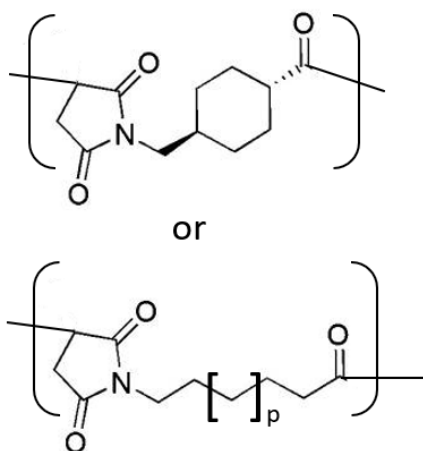
n represents an integer from 1 to 500, more preferably 1 to 100, 1 to 10 or 1 to 5.

2. The binder-drug conjugate of claim 1, wherein the disease tissue is a tumor.
3. The binder-drug conjugate of claim 1 or 2, wherein the target cell is a tumor cell.
4. The binder-drug conjugate of any one of claims 1-3, wherein L^1 is a hydrocarbon (straight chain or cyclic) such as 6-maleimidocaproyl, maleimidopropanoyl and maleimidomethyl cyclohexane-1-carboxylate, or L^1 is N-Succinimidyl 4-(2-pyridylthio) pentanoate, N- Succinimidyl 4-(N-maleimidomethyl) cyclohexane-1 carboxylate, N-Succinimidyl (4-iodo-acetyl) aminobenzoate, or L^1 is a polyether such as a poly(ethylene glycol).
5. The binder-drug conjugate of any one of claims 1-3, wherein CBM comprises a thiol, and L^1 is a poly(ethylene glycol) coupled to the thiol group through a maleimide moiety, L^1 being represented in the formula



wherein, p represents an integer from 1 to 100, preferably 6 to 50, more preferably 6 to 12.

6. The binder-drug conjugate of any one of claims 1-3, wherein CBM includes a thiol, and L^1 is a hydrocarbon moiety coupled to the thiol group through a maleimide moiety, L^1 being represented in the formula



wherein p represents an integer from 1 to 20, preferably 1 to 4.

7. The binder-drug conjugate of any one of claims 1-6, wherein L^2 is a self immolative linker selected from the group consisting of $-\text{NH}-(\text{CH}_2)_4-\text{C}(=\text{O})-$, $-\text{NH}-(\text{CH}_2)_3-\text{C}(=\text{O})-$, p -aminobenzyloxycarbonyl (PABC) and 2,4-bis(hydroxymethyl)aniline.

8. The binder-drug conjugate of any one of claims 1-7, wherein DM induces macrophage pyroptosis.

9. The binder-drug conjugate of any claims 1-8, wherein DM is cytotoxic to cancer associated fibroblasts (CAFs).

10. The binder-drug conjugate of any claims 1-9, wherein DM polarizes tumor associated macrophage towards M1 macrophage or inhibits M2 macrophage immunosuppressive activity.

11. The binder-drug conjugate of any claims 1-10, wherein DM accelerates T-cell priming and/or dendritic cell trafficking.

12. The binder-drug conjugate of any claims 1-11, wherein DM inhibits or depletes Treg cells, such as by blocking immunosuppressive function or migration to lymph nodes and/or the tumor microenvironment.
13. The binder-drug conjugate of any one of claims 1-12, wherein DM has a molecular weight less than 5000 amu, preferably less than 2500 amu.
14. The binder-drug conjugate of any one of claims 1-13, wherein DM is Val-boroPro.
15. A pharmaceutical composition comprising the binder-drug conjugate of any one of claims 1-14; and a pharmaceutically acceptable excipient.
16. Use of the binder-drug conjugate of any one of claims 1-14 in the manufacture of a medicament for treating cancer.
17. The use of claim 16, wherein the cancer is acute myeloid leukemia (AML).
18. The use of claim 16 or 17, wherein the medicament is to be conjointly administered with a PGE2 inhibitor.