Claims

1. A conjugate or its pharmaceutically acceptable salt, wherein said conjugate is water-insoluble and comprises a carrier moiety Z to which one or more moieties -L^2-L^1-D are conjugated, wherein

   each -L^2- is individually a chemical bond or a spacer moiety;

   each -L^1- is individually a linker moiety to which -D is reversibly and covalently conjugated; and

   each -D is individually a pattern recognition receptor agonist.

2. The conjugate of claim 1, wherein -D is selected from the group consisting of Toll-like receptor (TLR) agonists, NOD-like receptors (NLRs), RIG-I-like receptors, cytosolic DNA sensors, STING, and aryl hydrocarbon receptors (AhR).

3. The conjugate or its pharmaceutically acceptable salt of claim 1 or 2, wherein all moieties -D of the conjugate are identical.

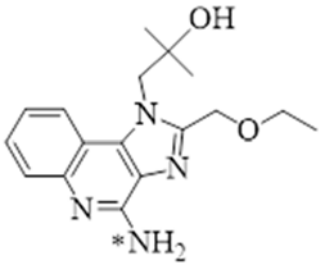
4. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 or 2, wherein the conjugate comprises more than one type of -D.

5. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 4, wherein -D is a Toll-like receptor agonist.

6. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 5, wherein -D is an agonist of TLR7/8.

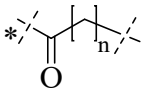
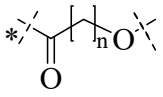
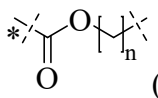
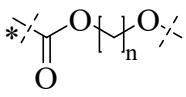
7. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 6, wherein -D is resiquimod.

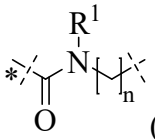
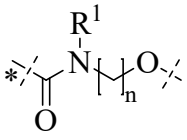
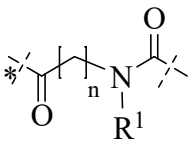
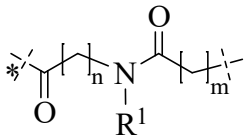
8. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 3 and 5 to 7, wherein -D is resiquimod and -L^1- is conjugated to -D via the aromatic amine functional group marked with the asterisk

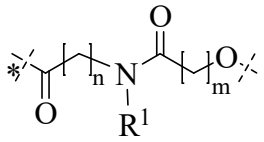
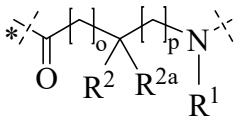
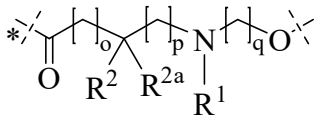


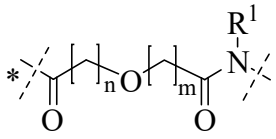
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9. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 8, wherein -L^1- is selected from the group consisting of formula (X-1), (X-2), (X-3), (X-4), (X-5), (X-6), (X-7), (X-8), (X-9), (X-10), (X-11) and (X-12);

 (X-1),  (X-2),  (X-3),  (X-4),

 (X-5),  (X-6),  (X-7), 

(X-8),  (X-9),  (X-10), 

(X-11) and  (X-12);

wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of an amine functional group of -D;

the unmarked dashed line indicates attachment to -L^2-;

-R^1 is selected from the group consisting of -H, C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl;

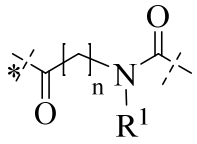
-R^2 and -R^{2a} are independently selected from the group consisting of -H, halogen, C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl;

n is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 and 25;

m is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 and 25;

o is an integer selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;
p is an integer selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10; and
q is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 and 25.

10. The conjugate or its pharmaceutically acceptable salt of claim 9, wherein -L^1- is of formula (X-7)

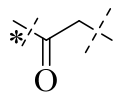
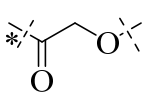
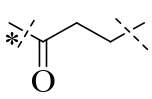
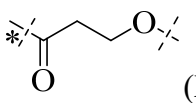
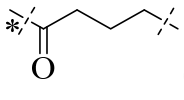
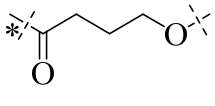
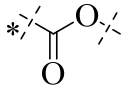
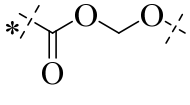
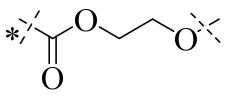
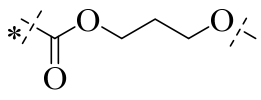
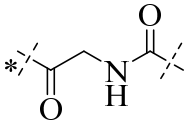

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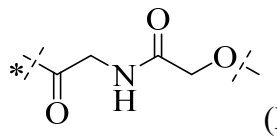
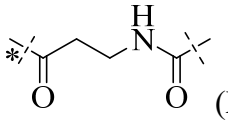
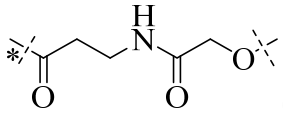
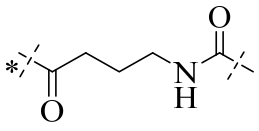
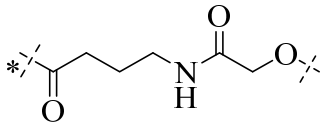
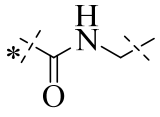
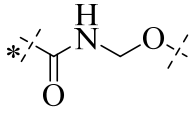
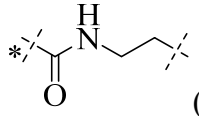
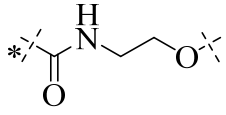
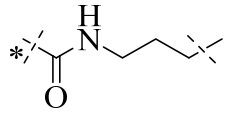
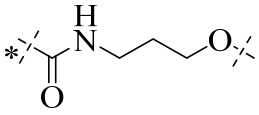
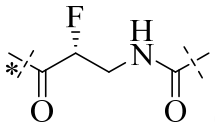
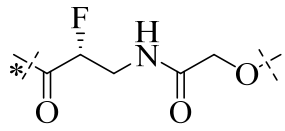
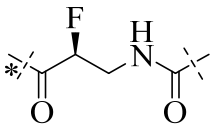
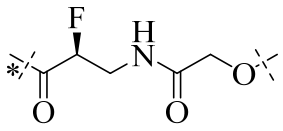
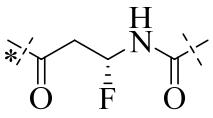
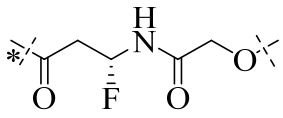
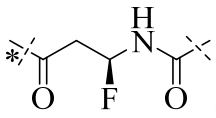
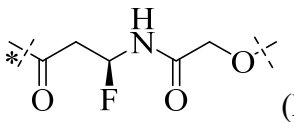
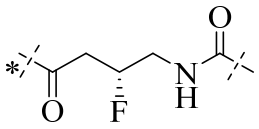
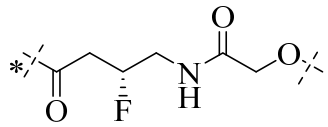
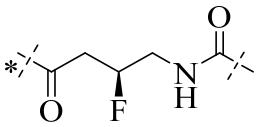
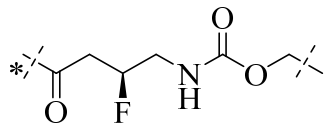
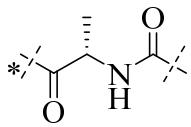
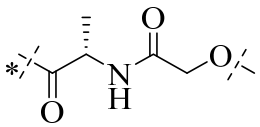
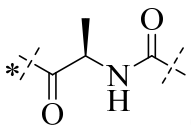
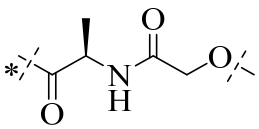
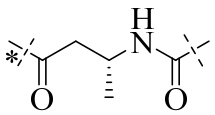
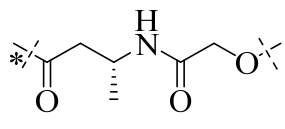
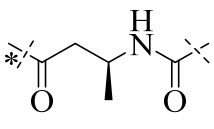
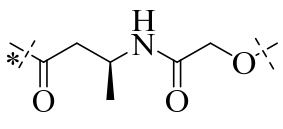
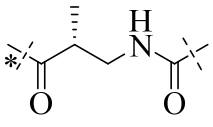
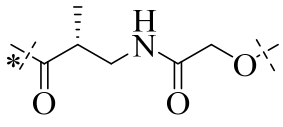
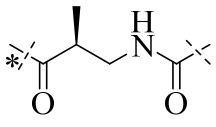
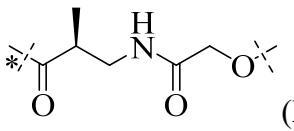
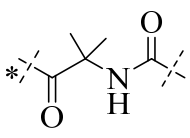
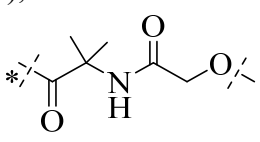
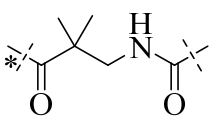
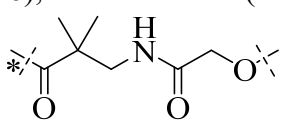
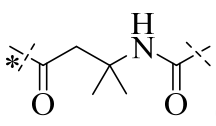
wherein
the dashed line marked with the asterisk indicates attachment to a nitrogen of an amine functional group of -D which nitrogen together with -(C=O)- forms an amide bond;
the unmarked dashed line indicates attachment to -L^2-;
-R^1 is selected from the group consisting of -H, C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl; and
n is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 and 25.

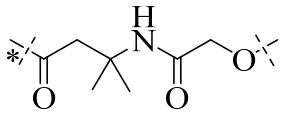
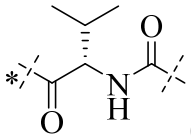
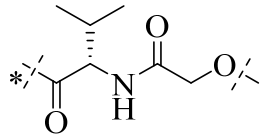
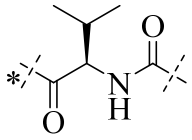
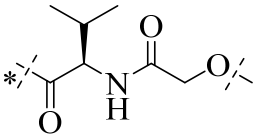
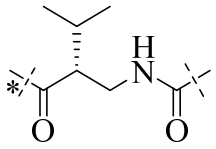
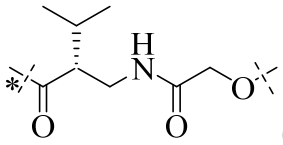
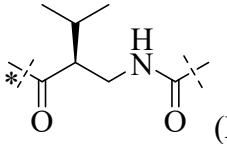
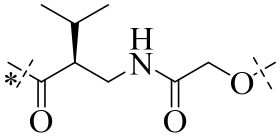
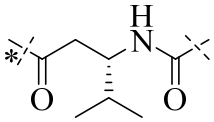
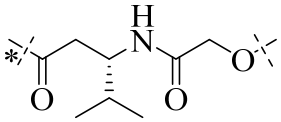
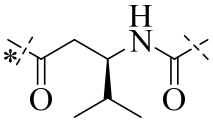
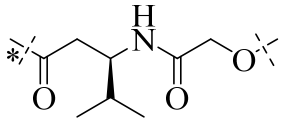
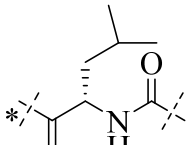
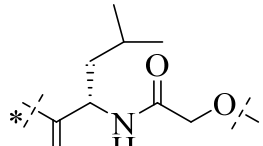
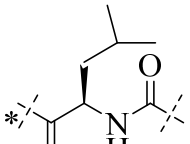
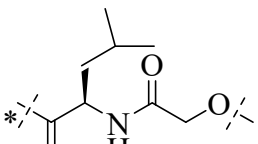
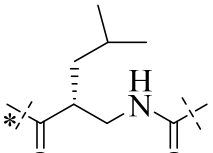
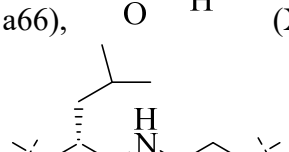
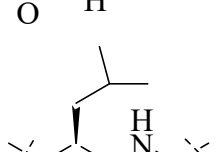
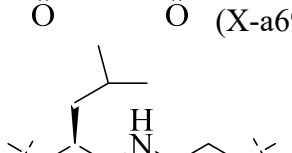
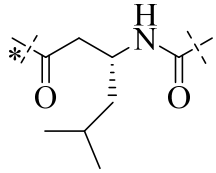
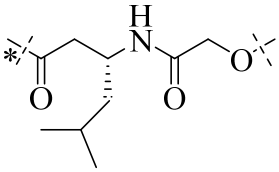
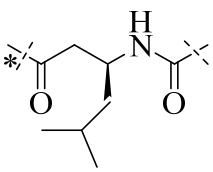
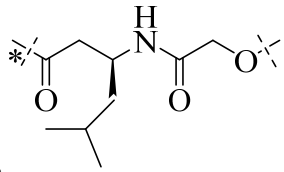
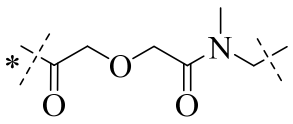
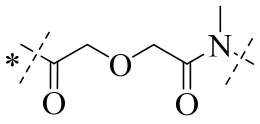
11. The conjugate or its pharmaceutically acceptable salt of claim 10, wherein n = 1.

12. The conjugate or its pharmaceutically acceptable salt of claims 10 or 11, wherein -R^1 is -H.

13. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 8, wherein -L^1- is selected from the group consisting of


(X-a1),

(X-a2),

(X-a3),

(X-a4),

(X-a5),

(X-a6),

(X-a7),

(X-a8),

(X-a9),

(X-a10),

(X-a11),

 (X-a12),  (X-a13),  (X-a14),  (X-a15),  (X-a16),  (X-a17),  (X-a18),  (X-a19),  (X-a20),  (X-a21),  (X-a22),  (X-a23),  (X-a24),  (X-a25),  (X-a26),  (X-a27),  (X-a28),  (X-a29),  (X-a30),  (X-a31),  (X-a32),  (X-a33),  (X-a34),  (X-a35),  (X-a36),  (X-a37),  (X-a38),  (X-a39),  (X-a40),  (X-a41),  (X-a42),  (X-a43),  (X-a44),  (X-a45),  (X-a46),  (X-a47),  (X-a48),  (X-a49),  (X-a50),  (X-


a51), 
(X-a52), 
(X-a53), 
(X-a54), 
(X-a55), 
(X-a56), 
(X-a57), 
(X-a58), 
(X-a59), 
(X-a60), 
(X-a61), 
(X-a62), 
(X-a63), 
(X-a64), 
(X-a65), 
(X-a66), 
(X-a67), 
(X-a68), 
(X-a69), 
(X-a70), 
(X-a71), 
(X-a72), 
(X-a73), 
(X-a74), 
(X-a75), 
(X-a76), 
(X-a77) and (X-a78);

wherein

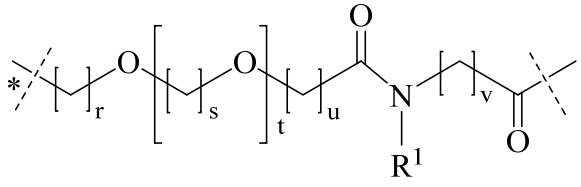
the dashed line marked with the asterisk indicates attachment to a nitrogen of an amine functional group of -D; and

the unmarked dashed line indicates attachment to -L^2-.

14. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 13, wherein -L^2- is a spacer moiety.

15. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 14, wherein -L^2- is a C_{1-20} alkyl chain, which is optionally interrupted by one or more groups independently selected from -O-, -T- and -C(O)N(R^{y1})-; and which C_{1-20} alkyl chain is optionally substituted with one or more groups independently selected from -OH, -T and -C(O)N($R^{y6}R^{y6a}$); wherein -R^{y1}, -R^{y6}, -R^{y6a} are independently selected from the group consisting of H and C_{1-4} alkyl and wherein T is selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl.

16. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 15, wherein -L^2- is of formula (A-1)



(A-1),

wherein

the dashed line marked with the asterisk indicates attachment to -L^1-,

the unmarked dashed line indicates attachment to Z,

r is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;

s is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;

t is selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;

u is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;

v is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10; and

-R^1 is selected from the group consisting of -H, C_{1-10} alkyl, C_{1-10} alkenyl and C_{1-10} alkynyl.

17. The conjugate or its pharmaceutically acceptable salt of claim 16, wherein r = 1, s = 2, t = 2, u = 1, v = 2 and -R^1 is -H.

18. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 17, wherein Z is a hydrogel.

19. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 18, wherein Z is a PEG-based or hyaluronic acid-based hydrogel.

20. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 19, wherein Z is a PEG-based hydrogel.

21. A pharmaceutical composition comprising one or more conjugates or their pharmaceutically acceptable salt of any one of claims 1 to 20 and at least one excipient.

22. The pharmaceutical composition of claim 21, wherein the pharmaceutical composition comprises one or more additional drug.

23. The pharmaceutical composition of claim 22, wherein the one or more additional drug is selected from the group consisting of cytotoxic/chemotherapeutic agents, immune checkpoint inhibitors or antagonists, immune checkpoint agonists, multi-specific drugs, antibody-drug conjugates (ADC), radionuclides or targeted radionuclide therapeutics, DNA damage repair inhibitors, tumor metabolism inhibitors, pattern recognition receptor agonists, protein kinase inhibitors, chemokine and chemoattractant receptor agonists, chemokine or chemokine receptor antagonists, cytokine receptor agonists, death receptor agonists, CD47 or SIRPα antagonists, oncolytic drugs, signal converter proteins, epigenetic modifiers, tumor peptides or tumor vaccines, heat shock protein (HSP) inhibitors, proteolytic enzymes, ubiquitin and proteasome inhibitors, adhesion molecule antagonists, and hormones including hormone peptides and synthetic hormones.

24. The conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 20 or the pharmaceutical composition of any one of claims 21 to 23 for use as a medicament.

25. Use of the conjugate or its pharmaceutically acceptable salt of any one of claims 1 to 20 for the manufacture of a medicament for the treatment of a cell-proliferation disorder.

26. The use of claim 25, wherein the cell-proliferation disorder is cancer.

27. The use of claim 26, wherein the cancer is selected from the group consisting of liquid tumors, solid tumors and lymphomas.

28. The use of claim 27, wherein the solid tumor or lymphoma is selected from the group consisting of lip and oral cavity cancer, oral cancer, liver cancer/hepatocellular cancer, primary liver cancer, lung cancer, lymphoma, malignant mesothelioma, malignant thymoma, skin cancer, intraocular melanoma, metastasic squamous neck cancer with occult primary, childhood multiple endocrine neoplasia syndrome, mycosis fungoides, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, oropharyngeal cancer, ovarian cancer, pancreatic cancer, parathyroid cancer, pheochromocytoma, pituitary tumor, adrenocortical carcinoma, AIDS-related malignancies, anal cancer, bile duct cancer, bladder cancer, brain and nervous system cancer, breast cancer, bronchial adenoma/carcinoid, gastrointestinal carcinoid tumor, carcinoma, colorectal cancer, endometrial cancer, esophageal cancer, extracranial germ cell tumor, extragonadal germ cell tumor, extrahepatic bile duct cancer, gallbladder cancer, gastric (stomach) cancer, gestational trophoblastic tumor, head and neck cancer, hypopharyngeal cancer, islet cell carcinoma (endocrine pancreas), kidney cancer/renal cell cancer, laryngeal cancer, pleuropulmonary blastoma, prostate cancer, transitional cell cancer of the renal pelvis and ureter, retinoblastoma, salivary gland cancer, sarcoma, Sezary syndrome, small intestine cancer, genitourinary cancer, malignant thymoma, thyroid cancer, Wilms' tumor and cholangiocarcinoma.

29. The use of claims 25 to 29, wherein said conjugate or its pharmaceutically acceptable salt or the pharmaceutical composition is administered intratumorally.

30. The use of claims 25 to 29, wherein the use includes in addition to the administration of the conjugate, its pharmacologically acceptable salt or the pharmaceutical composition the administration of at least one cancer therapeutic.

31. The use of claim 30, wherein the at least one cancer therapeutic is selected from the group consisting of cytotoxic/chemotherapeutic agents, immune checkpoint inhibitors or antagonists, immune checkpoint agonists, multi-specific drugs, antibody-drug conjugates (ADC), radionuclides or targeted radionuclide therapeutics, DNA damage repair inhibitors, tumor metabolism inhibitors, pattern recognition receptor agonists,

protein kinase inhibitors, chemokine and chemoattractant receptor agonists, chemokine or chemokine receptor antagonists, cytokine receptor agonists, death receptor agonists, CD47 or SIRPα antagonists, oncolytic drugs, signal converter proteins, epigenetic modifiers, tumor peptides or tumor vaccines, heat shock protein (HSP) inhibitors, proteolytic enzymes, ubiquitin and proteasome inhibitors, adhesion molecule antagonists, and hormones including hormone peptides and synthetic hormones.