CLAIMS

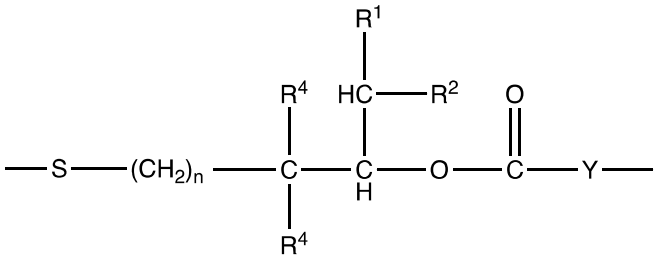
1. A hydrogel comprising crosslinked conjugates of formula (III)

$$M\text{-}[Z^*\text{-}L\text{-}D]_q \quad (III)$$

wherein M is a polyethylene glycol of average molecular weight between 10,000 and 60,000 daltons;

Z* is a connecting functionality;

L has the formula below,



wherein

n is an integer from 0 to 6;

R^1 is -CN, $-NO_2$, $-COR^5$, $-SOR^5$, or $-SO_2R^5$, wherein R^5 is C_1-C_6 alkyl, aryl, heteroaryl, or NR^6_2, wherein each R^6 is independently C_1-C_6 alkyl, aryl, or heteroaryl, or both R^6 groups are taken together with the nitrogen to which they are attached to form a heterocyclic ring, and wherein each of R^5 and R^6 is independently optionally substituted;

R^2 is H or alkyl;

each R^4 is independently C_1-C_3 alkyl or the two R^4 are taken together with the carbon atom to which they attach to form a 3-6 member ring;

S is absent or $(CH_2CH_2O)_h(CH_2)_gCONH$ wherein g = 1-6 and h = 0-1000;

Y is $NH(CH_2CH_2O)_p(CH_2)_m$ wherein m = 2-6 and p = 0-1000;

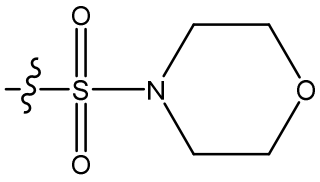
D is an IL-15 or an IL-15•IL-15RαSu fusion protein; and

q is an integer from 1 to 10.

2. The hydrogel of claim 1, wherein Z* comprises a carboxamide, amide, oxime, triazole, thioether, thiosuccinimide, or ether.

3. The hydrogel of claim 2, wherein Z* comprises a carboxamide, oxime, thioether, or triazole.

4. The hydrogel of claim 1, wherein R^1 is -CN or $-SO_2R^5$, wherein R^5 is C_1-C_6 alkyl, aryl, heteroaryl, or NR^6_2, wherein each R^6 is independently C_1-C_6 alkyl, aryl, or heteroaryl, and R^2 is H, and wherein each of R^5 and R^6 is independently optionally substituted.

5. The hydrogel of claim 4, wherein R^1 is -CN, $SO_2N(CH_3)_2$, $-SO_2CH_3$, $-SO_2Ph$, $-SO_2PhCl$, , $-SO_2CH(CH_3)_2$, $-SO_2N(CH_3)(CH_2CH_3)$, or $-SO_2N(CH_2CH_2OCH_3)_2$.

6. The hydrogel of any one of claims 1-5, wherein R^2 is H.

7. The hydrogel of any one of claims 1-6, wherein M is a multi-armed chain.

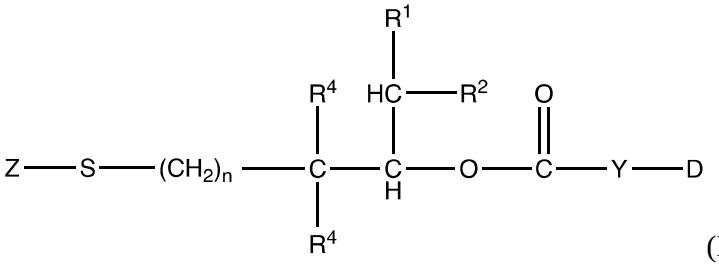
8. The hydrogel of any one of claims 1-7, wherein each crosslink of the crosslinked conjugates of the hydrogel comprises a cleavable linker.

9. The hydrogel of any one of claims 1-8, wherein p is 0.

10. The hydrogel of any one of claims 1-9, wherein D is an IL-15 of SEQ ID No:12, SEQ ID No:13, SEQ ID No: 14, or SEQ ID No. 15.

11. The hydrogel of any one of claims 1-9, wherein D is an IL-15•IL-15RαSu fusion protein of SEQ ID No:16 or SEQ ID No:17.

12. A linker-drug of formula (Ia)



(Ia),

wherein:

n is an integer from 0 to 6;

R^1 is -CN, $-NO_2$, $-COR^5$, $-SOR^5$, or $-SO_2R^5$, wherein R^5 is C_1-C_6 alkyl, aryl, heteroaryl, or NR^6_2, wherein each R^6 is independently C_1-C_6 alkyl, aryl, or heteroaryl, or both R^6 groups are taken together with the nitrogen to which they are attached to form a heterocyclic ring, and wherein each of R^5 and R^6 is independently optionally substituted;

R^2 is H or alkyl;

each R^4 is independently C_1-C_3 alkyl or the two R^4 are taken together with the carbon atom to which they attach to form a 3-6 member ring;

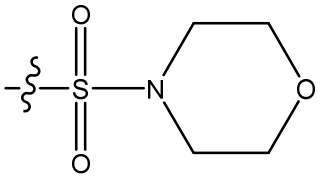
Z is a group for connecting the linker to a macromolecular carrier;

S is absent or is $(CH_2CH_2O)_h(CH_2)_gCONH$, wherein g is an integer from 1 to 6 and h is an integer from 0 to 1000;

Y is $NH(CH_2CH_2O)_p(CH_2)_m$, wherein m is an integer from 2 to 6 and p is an integer from 0 to 1000; and

D is an IL-15 or an IL-15•IL-15RαSu fusion protein.

13. The linker-drug of claim 12, wherein R^1 is -CN or $-SO_2R^5$, wherein R^5 is C_1-C_6 alkyl, aryl, heteroaryl, or NR^6_2, wherein each R^6 is independently C_1-C_6 alkyl, aryl, or heteroaryl, and R^2 is H, and wherein each of R^5 and R^6 is independently optionally substituted.

14. The linker-drug of claim 13, wherein R^1 is -CN, $SO_2N(CH_3)_2$, $-SO_2CH_3$, $-SO_2Ph$, $-SO_2PhCl$, -  , $-SO_2CH(CH_3)_2$, $-SO_2N(CH_3)(CH_2CH_3)$, or $-SO_2N(CH_2CH_2OCH_3)_2$.

15. The linker-drug of any one of claims 12-14, wherein R^2 is H.

16. The linker-drug of any one of claims 12-15, wherein p is 0.

17. The linker-drug of any one of claims 12-16, wherein D is an IL-15 of SEQ ID No:12, SEQ ID No:13, SEQ ID No: 14, or SEQ ID No. 15.

18. The linker-drug of any one of claims 12-16, wherein D is an IL-15•IL-15RαSu fusion protein of SEQ ID No:16 or SEQ ID No:17.

19. The hydrogel of any one of claims 1-11 for use in a method of treating a disease or a condition in a subject in need thereof, wherein the disease or condition is an autoimmune disease; chronic graft-vs-host disease (cGVHD) associated with inadequate reconstitution of tolerogenic $CD4^+$ $CD25^+$ $FOXP3^+$ regulatory T cells; systemic lupus erythrematosis; sarcoidosis; Hepatitis C-induced vasculitis; alopecia; rheumatoid arthritis; inflammatory bowel disease; multiple sclerosis; or type-1 diabetes.

20. The linker-drug of any one of claims 12-18 for use in a method of treating a disease or a condition in a subject in need thereof, wherein the disease or condition is an autoimmune disease; chronic graft-vs-host disease (cGVHD) associated with inadequate reconstitution of tolerogenic $CD4^+$ $CD25^+$ $FOXP3^+$ regulatory T cells; systemic lupus erythrematosis; sarcoidosis; Hepatitis C-induced vasculitis; alopecia; rheumatoid arthritis; inflammatory bowel disease; multiple sclerosis; or type-1 diabetes.