

What is claimed is:

1. A polypeptide comprising an antibody that binds to MAdCAM and an IL-2 mutein polypeptide (IL-2 mutein), wherein the IL-2 mutein comprises an amino acid sequence of SEQ ID NO: 6 comprising one or more mutations of E15Q, H16N, Q22E, D84N, E95Q, Q126E, N29S, Y31S, Y31H, K35R, T37A, K48E, N71R, V69A, Q74P, N88D, N88R, C125A or C125S.
2. The polypeptide of claim 1, wherein the IL-2 mutein comprises a N88D or N88R mutation.
3. The polypeptide of claim 1, wherein the IL-2 mutein comprises a IL-2 sequence of SEQ ID NO: 6, wherein the polypeptide further comprises a mutation at a position that corresponds to position 53, 56, 80, or 118 of SEQ ID NO: 6.
4. The polypeptide of claim 3, wherein the mutation is a L to I mutation at position 53, 56, 80, or 118 of SEQ ID NO: 6.
5. The polypeptide of any one of claims 1 to 4, wherein the IL-2 mutein comprises one or more mutations of E15Q, H16N, Q22E, D84N, E95Q, Q126E, N29S, Y31S, Y31H, K35R, T37A, K48E, N71R, V69A, Q74P, C125A or C125S.
6. The polypeptide of any one of the preceding claims, wherein the IL-2 mutein comprises one or more mutations of E15Q, H16N, Q22E, D84N, E95Q, or Q126E.
7. The polypeptide of any one of the preceding claims, wherein the IL-2 mutein comprises one or more mutations of a V69A, Q74P, N88D, N88R, C125A, or C125S mutation in SEQ ID NO: 6.
8. The polypeptide of any of the preceding claims, wherein the IL-2 mutein is fused or linked to a Fc peptide.
9. The polypeptide of claim 8, wherein the Fc peptide comprises the sequence of SEQ ID NO: 21 or SEQ ID NO: 28.
10. The polypeptide of claim 9, wherein the Fc peptide comprises a mutation at one or more of positions of L234, L247, L235, L248, G237, and G250.

11. The polypeptide of claim 10, wherein the Fc peptide comprises a L234A mutation, a L235A mutation, and/or a G237A mutation.
12. The polypeptide of claim 1, wherein the polypeptide comprises a first chain and a second chain that form the polypeptide, wherein
the first chain comprises:
V_H-H_c-Linker-C₁, wherein V_H is a variable heavy domain that binds to MAdCAM with a V_L domain of the second chain; H_c is a heavy chain of antibody comprising CH1-CH2-CH3 domain, the Linker is a glycine/serine linker, and C₁ is the IL-2 mutein fused to a Fc protein in either the N-terminal or C-terminal orientation; and
the second chain comprises:
V_L-L_c, wherein V_L is a variable light chain domain that binds to MAdCAM with the V_H domain of the first chain, and the L_c domain is a light chain CK domain.
13. The polypeptide of claim 12, wherein the IL-2 mutein comprises a mutation at a position that corresponds to position 53, 56, 80, or 118 of SEQ ID NO: 6.
14. The polypeptide of claim 13, wherein the mutation is a L to I mutation at position 53, 56, 80, or 118 of SEQ ID NO: 6.
15. The polypeptide of claim 13, wherein the IL-2 mutein further comprises a mutation at a position that corresponds to position 69, 75, 88, or 125, or any combination thereof.
16. The polypeptide of claim 13, wherein the IL-2 mutein comprises:
 - (i) a mutation selected from the group consisting of: at one of L53I, L56I, L80I, and L118I; and
 - (ii) the mutations of V69A, Q74P, N88D or N88R, and
 - (iii) optionally a C125A or C125S mutation.
17. The polypeptide of claim 13, wherein the IL-2 mutein comprises a V69A, Q74P, N88D, L118I and a C125S mutation.
18. The polypeptide of claim 13, wherein the IL-2 mutein comprises a V69A, Q74P, N88D, L80I and a C125S mutation.

19. The polypeptide of any one of the preceding claims, wherein the IL-2 mutein comprises a sequence of SEQ ID NO: 40.
20. The polypeptide of any one of the preceding claims, wherein the IL-2 mutein comprises a sequence of SEQ ID NO: 41.
21. The polypeptide of any one of the preceding claims, wherein the IL-2 mutein comprises a sequence of SEQ ID NO: 55.
22. The polypeptide of any one of the preceding claims, wherein the IL-2 mutein comprises a sequence of SEQ ID NO: 56.
23. A pharmaceutical composition comprising the polypeptide of any one of claims 1-22.
24. Use of the polypeptide of any one of claims 1 to 22 in the manufacture of a medicament for treatment of inflammatory bowel disease in a subject.
25. Use of the polypeptide of polypeptide of any of claims 1 to 22 in the manufacture of a medicament for the treatment of auto-immune hepatitis, primary sclerosing cholangitis, Type 1 diabetes, a transplant, or GVHD.