

Claims

1. A CD80 extracellular domain (ECD) fusion molecule comprising a human CD80 ECD polypeptide and a human IgG1 Fc domain, wherein the CD80 ECD fusion molecule comprises 15-60 molecules of sialic acid (SA), and wherein the CD80 ECD fusion molecule comprises the amino acid sequence of SEQ ID NO:20.
2. The fusion molecule of claim 1, wherein the CD80 ECD fusion molecule comprises 15-40 molecules of SA.
3. The fusion molecule of claim 1, wherein the CD80 ECD fusion molecule comprises 15-30 molecules of SA.
4. The fusion molecule of claim 1, wherein the CD80 ECD fusion molecule comprises 20-30 molecules of SA.
5. The fusion molecule of any one of claims 1-4, wherein the fusion molecule alone does not cause significant release of interferon gamma or TNF alpha from T-cells *in vitro*.
6. The fusion molecule of any one of claims 1-5, wherein the fusion molecule alone causes less release of interferon gamma or TNF alpha from T-cells *in vitro* than TGN1412 alone.

7. The fusion molecule of claim 6, wherein the fusion molecule alone is at least 1000-fold less potent at inducing interferon gamma or TNF alpha release compared to TGN1412 alone.
8. The fusion molecule of any one of claims 1-7, wherein the fusion molecule is capable of at least 90% tumor growth inhibition in at least one mouse syngeneic cancer model over a period of at least 1 week, 10 days, two weeks, or three weeks following administration of a single dose of the fusion molecule at 0.3 to 0.6 mg/kg.
9. The fusion molecule of claim 8, wherein the mouse syngeneic cancer model is a CT26 tumor model.

10. A composition comprising (i) CD80 ECD fusion molecules comprising human CD80 ECD polypeptide and a human IgG1 Fc domain, and (ii) at least one pharmaceutically acceptable carrier,

wherein the CD80 ECD fusion molecules comprise 15-60 moles of SA per mole of CD80 ECD fusion protein, and wherein the CD80 ECD fusion molecules comprise the amino acid sequence of SEQ ID NO:20.

11. The composition of claim 10, wherein the CD80 ECD fusion molecules comprise 15-40 moles of SA per mole of CD80 ECD fusion protein.

12. The composition of claim 10, wherein the CD80 ECD fusion molecules comprise 15-30 moles of SA per mole of CD80 ECD fusion protein.

13. The composition of claim 10, wherein the CD80 ECD fusion molecules comprise 20-30 moles of SA per mole of CD80 ECD fusion protein.

14. The composition of claim 10, wherein the CD80 ECD fusion molecules comprise at least 15 moles of SA per mole of CD80 ECD fusion protein.

15. The composition of claim 14, wherein the CD80 ECD fusion molecules comprise at least 20 moles of SA per mole of CD80 ECD fusion protein.
16. The composition of any one of claims 10-15, wherein the composition alone does not cause significant release of interferon gamma or TNF alpha from T-cells *in vitro*.
17. The composition of any one of claims 10-16, wherein the composition alone causes less release of interferon gamma or TNF alpha from T-cells *in vitro* than TGN1412 alone.
18. The composition of claim 17, wherein the composition alone is at least 1000-fold less potent at inducing interferon gamma or TNF alpha release compared to TGN1412 alone.
19. The composition of any one of claims 10-18, further comprising an additional therapeutic agent.
20. The composition of claim 19, wherein the additional therapeutic agent comprises a programmed cell death 1 (PD-1) /programmed cell death ligand 1 (PD-L1) inhibitor.
21. The composition of any one of claims 10-20, wherein the composition is capable of at least 90% tumor growth inhibition in at least one mouse syngeneic cancer

model over a period of at least one week, 10 days, two weeks, or three weeks following administration of a single dose of the composition at 0.3 to 0.6 mg/kg.

22. The composition of claim 21, wherein the mouse syngeneic cancer model is a CT26 tumor model.
23. A CD80 ECD fusion molecule comprising a human CD80 ECD polypeptide and a human IgG1 Fc domain with L234F, L235E, and P331S amino acid substitutions, wherein the CD80 ECD fusion molecule comprises the amino acid sequence of SEQ ID NO:21.
24. A composition comprising (i) CD80 ECD fusion molecules comprising the amino acid sequence of SEQ ID NO:20, and (ii) at least one pharmaceutically acceptable carrier, wherein the CD80 ECD fusion molecules comprise at least 15 moles of SA per mole of CD80 ECD fusion protein.
25. The composition of claim 24, wherein the CD80 ECD fusion molecules comprise at least 20 moles of SA per mole of CD80 ECD fusion protein.
26. Use of the CD80 extracellular domain (ECD) fusion molecule according to any one of claims 1-9 and 23 or the composition according to any one of claims 10-22, 24, and 25 in the manufacture of a medicament for treating cancer.
27. The use of claim 26, wherein the cancer is a solid tumor.
28. The use of claim 26, wherein the cancer is selected from colorectal cancer, breast cancer, gastric cancer, non-small cell lung cancer, melanoma, squamous cell carcinoma of the head and neck, ovarian cancer, pancreatic cancer, renal cell carcinoma, hepatocellular carcinoma, bladder cancer, and endometrial cancer.

29. The use of any one of claims 26-28, wherein the cancer is recurrent or progressive after a therapy selected from surgery, chemotherapy, radiation therapy, and a combination thereof.
30. A coding sequence that encodes the fusion molecule according to any one of claims 1-9 and 23.