

Claims

1. A pharmaceutical composition comprising:
 - (a) a recombinant nucleic acid, wherein the recombinant nucleic acid comprises a sequence encoding a chimeric fusion protein (CFP), the CFP comprising:
 - i. an extracellular domain comprising an anti-GPC3 binding domain,
 - ii. a transmembrane domain of FcR α or FcR β operatively linked to the extracellular domain;
 - iii. an intracellular domain comprising one or more intracellular signaling domains; and
 - (b) a pharmaceutically acceptable carrier;
 wherein the CFP forms a functional complex with FcR γ in myeloid cells.
2. The pharmaceutical composition of claim 1, wherein the anti-GPC3 binding domain comprises a functional antibody fragment, a single chain variable fragment (scFv), an Fab, a single-domain antibody (sdAb), a nanobody, a VH domain, a VL domain, a VNAR domain, a VHH domain, a bispecific antibody, a diabody, or a functional fragment or a combination thereof.
3. The pharmaceutical composition of claim 2, wherein the anti-GPC3 binding domain comprises a scFv.
4. The pharmaceutical composition of any one of claims 1-3, wherein the transmembrane domain comprises an FcR α transmembrane domain.
5. The pharmaceutical composition of any one of claims 1-4, wherein the one or more intracellular signaling domains comprise an intracellular domain derived from FcR α , FcR γ or FcR ϵ .
6. The pharmaceutical composition of claim 5, wherein the one or more intracellular signaling domains comprise an intracellular signaling domain derived from FcR α .
7. The pharmaceutical composition of any one of claims 1-6, wherein the anti-GPC3 binding domain binds to GPC3 with an affinity of <250nM.
8. The pharmaceutical composition of any one of claims 1-7, wherein the one or more intracellular signaling domains comprise a proinflammatory signaling domain.
9. The pharmaceutical composition of any one of claims 1-8, wherein the extracellular domain comprises an FcR α , FcR β , FcR ϵ or FcR γ extracellular domain.
10. The pharmaceutical composition of claim 9, wherein the extracellular domain comprises an FcR α extracellular domain.

11. The pharmaceutical composition of claim 1, wherein the extracellular domain comprises an FcR α extracellular domain, wherein the transmembrane domain comprises an FcR α transmembrane domain, and wherein the one or more intracellular signaling domains comprise an intracellular signaling domain derived from FcR α .
12. The pharmaceutical composition of any one of claims 1-11, wherein the CFP further comprises a signal peptide.
13. The pharmaceutical composition of claim ~~10~~12, wherein the signal peptide is a GMCSF signal peptide.
14. The pharmaceutical composition of any one of claims 1-13, wherein the transmembrane domain and the extracellular ~~antigen-binding~~ domain are operatively linked through a linker.
15. The pharmaceutical composition of any one of claims 1-14, wherein the pharmaceutical composition further comprises a pro-inflammatory polypeptide; optionally, wherein the pro-inflammatory polypeptide is a chemokine or a cytokine.
16. The pharmaceutical composition of any one of claims 1-15, wherein the recombinant nucleic acid is an mRNA or circRNA.
17. The pharmaceutical composition of any one of claims 1-16, wherein the recombinant nucleic acid is mRNA and is encapsulated by a lipid nanoparticle (LNP).
18. The pharmaceutical composition of claim 17, wherein the LNP comprises a polar lipid and a non polar lipid.
19. The pharmaceutical composition of any one of claims 1-18, wherein the pharmaceutical composition is formulated for systemic delivery, optionally wherein the pharmaceutical composition is formulated for delivery by intravenous route.