

CLAIMS

I claim:

1. A method for treating a patient with a tumor comprising administering to said patient a therapeutically effective amount of a Zn(II) agent.
2. A method for treating a patient with a tumor comprising administering to said patient a therapeutically effective amount of a Zn(II) agent in combination with an immune-oncology agent.
3. The method according to claim 2, wherein said immune-oncology agent is an immune checkpoint inhibitor.
4. The method according to claim 3, wherein said immune checkpoint inhibitor is an anti-cytotoxic T-lymphocyte antigen-4 (CTLA-4) antibody or an antigen-binding portion thereof that binds specifically to CTLA-4 and inhibits CTLA-4 activity; or a programmed cell death-1 (PD-1) antibody or an antigen-binding portion thereof that binds specifically to a PD-1 receptor and inhibits PD-1 activity.
5. The method according to any one of claims 1 to 4, wherein said tumor includes tumor cells that have genetic instability mutations and/or genetic instability due to gene overexpression.
6. The method according to claim 5, wherein said genetic instability mutations are dysfunctional mutations in one or more genes selected from

ATM; ATR; PAXIP1; BRCA1; BRCA2; WRN; RFC1; RPA1; ERCC1; ERCC4; ERCC6; MGMT; PARP1; PARP2; NEIL3; XRCC1; MLH1; PMS2; TP53; CREBBP; JAK1; NFKB1; MSH2; MSH3; MSH6; and MLH3.

7. A method for increasing the tumor infiltrating leukocyte population of CD4+T cells and CD8+T cells in a tumor in a patient comprising administering to said patient having said tumor a therapeutically effective amount of a Zn(II) agent.

8. A method for increasing the tumor infiltrating leukocyte population of CD4+T cells and CD8+T cells in a tumor in a patient comprising administering to said patient having said tumor a therapeutically effective amount of a Zn(II) agent in combination with an immune-oncology agent.

9. The method according to claim 8, wherein said immune-oncology agent is an immune checkpoint inhibitor.

10. The method according to claim 8, wherein said immune checkpoint inhibitor is an anti-cytotoxic T-lymphocyte antigen-4 (CTLA-4) antibody or an antigen-binding portion thereof that binds specifically to CTLA-4 and inhibits CTLA-4 activity; or a programmed cell death-1 (PD-1) antibody or an antigen-binding portion thereof that binds specifically to a PD-1 receptor and inhibits PD-1 activity.

11. The method according to any one of claims 1-10, wherein said Zn(II) agent comprises Zn(II)/ γ -polyglutamic acid and/or Zn(II)/ α -polyglutamic acid.
12. A method for treating a tumor in a patient, comprising administering a therapeutically effective amount of (i) a Zn(II)/polyglutamic acid agent in combination with (ii) an immune-oncology agent that targets a T-lymphocyte marker, a macrophage marker, or a natural killer cell marker.
13. The method of claim 12, wherein the T-lymphocyte marker is lymphocyte activation gene 3 (LAG-3).
14. The method of claim 12, wherein the T-lymphocyte marker is T-cell immunoglobulin- and mucin-domain-containing molecule 3 (TIM-3).
15. The method of claim 12, wherein the T-lymphocyte marker is T-cell immunoglobulin and ITIM domain (TIGIT).
16. The method of claim 12, wherein the T-lymphocyte marker is B7-H3 (CD276).
17. The method of claim 12, wherein the T-lymphocyte marker is V-domain containing Ig suppressor of T-cell activation (VISTA).
18. The method of claim 12, wherein the T-lymphocyte marker is inducible T-cell costimulator (ICOS).

19. The method of claim 12, wherein the T-lymphocyte marker is CD27.
20. The method of claim 12, wherein the T-lymphocyte marker is glucocorticoid-induced TNF receptor (GITR).
21. The method of claim 12, wherein the macrophage marker is CD47.
22. The method of claim 12, wherein the macrophage marker is indoleamine-2,3-dioxygenase (IDO).
23. The method of claim 12, wherein the natural killer cell marker is killer immunoglobulin-like receptor (KIR).
24. The method of claim 12, wherein the natural killer cell marker is CD94/NKG2A.
25. The method of any one of claims 12 to 24, wherein said Zn(II)/polyglutamic acid agent comprises polyglutamic acid conjugated to a tumor-targeting moiety and/or a charge-carrying moiety.
26. The method of claim 25, wherein said polyglutamic acid conjugated to a tumor-targeting moiety and/or a charge-carrying moiety is γ -polyglutamic acid.

27. The method of claim 25, wherein the molecular weight of said polyglutamic acid is in the range of about 2.5 kDa to about 60 kDa.

28. The method according to claim 5, wherein said genetic instability due to overexpression is caused by overexpression of APOBEC3B.