

CLAIMS

1. Use of an agent that inhibits activity of a CARMA1-Bcl10-MALT1 signalosome complex in the preparation of a medicament for the treatment or prevention of cancer.
2. Use according to Claim 1, in which the cancer is selected from the group consisting of a carcinoma, a melanoma, a sarcoma, a myeloma, a leukemia or a lymphoma.
3. Use according to Claim 1, in which the cancer is melanoma, colon cancer, a solid tumor, head and neck cancer, non-small cell lung cancer, bladder cancer or kidney cancer.
4. Use according to Claim 1, in which a subject is diagnosed as having cancer, or the results of an assay that diagnoses a subject as having cancer are received, prior to administration of the agent to the subject.
5. Use according to Claim 1, in which the agent comprises a checkpoint inhibitor comprising a small molecule, an inhibitory nucleic acid, an inhibitory polypeptide, antibody or antigen-binding domain thereof or antibody reagent that binds an immune checkpoint polypeptide and inhibits its activity.
6. Use according to Claim 5, in which the immune checkpoint polypeptide is selected from the group consisting of PD-L1, PD-L2, PD-1, CTLA-4, TIM-3, LAG-3, VISTA and TIGIT.
7. Use according to Claim 5, in which the checkpoint inhibitor inhibits PD-1 and is selected from the group consisting of Pembrolizumab, Nivolumab, AUNP-12 and Pidilizumab, or wherein the checkpoint inhibitor inhibits PD-L1 and is selected from the group consisting of Atezolizumab, MPDL3280A, Avelumab and Durvalumab.
8. Use according to Claim 1, in which the activity inhibited by the agent is at least one of:
 - (a) the CARMA1-Bcl10-MALT1 signalosome complex function;
 - (b) the formation of the CARMA1-Bcl10-MALT1 signalosome complex;
 - (c) the function of at least one component of the CARMA1-Bcl10-MALT1 signalosome complex; and
 - (d) the expression level of at least one component of the CARMA1-Bcl10-MALT1 signalosome complex.

9. Use according to Claim 1, in which the activity of a CARMA1-Bcl10-MALT1 signalosome complex is inhibited in a regulatory T cell.
10. Use according to Claim 1, in which the agent is selected from the group consisting of a small molecule, an inhibitory nucleic acid, an antibody or antigen-binding fragment thereof or antibody reagent or an inhibitory polypeptide or a pharmaceutically acceptable salt thereof.
11. Use according to Claim 10, in which the small molecule is a small molecule inhibitor of MALT1 paracaspase activity.
12. Use according to Claim 11, in which the small molecule inhibitor of MALT1 paracaspase activity is selected from the group consisting of MI-2 or an analog thereof, MI-2A1, MI-2A2, MI-2A3, MI-2A4, MI-2A5, MI-2A6, MI-2A7, a pyrazolo pyrimidine derivative, a phenothiazine derivative, a thiazolo-pyridine derivative and tetrapeptide Z-VRPR-FMK (SEQ ID NO: 7) or a pharmaceutically acceptable salt thereof.
13. Use according to Claim 12, in which the phenothiazine derivative is mepazine, thioridazine or promazine or a pharmaceutically acceptable salt thereof.
14. Use according to Claim 1, in which the agent comprises (S)-mepazine or a pharmaceutically acceptable salt thereof.
15. Use according to Claim 10, in which at least one anti-cancer therapy is to be further administered to the subject.
16. A cell engineered to have reduced CARMA1-Bcl10-MALT1 signalosome activity.
17. A cell according to Claim 16, in which the cell has been engineered:
 - (a) to inhibit the function of at least one gene selected from the group consisting of: CARMA1, Bcl10 and MALT1;
 - (b) to inhibit the function of at least one gene product selected from the group consisting of: CARMA1, Bcl10 and MALT1;
 - (c) to reduce the expression level of at least one gene selected from the group consisting of: CARMA1, Bcl10 and MALT1; and/or
 - (d) to reduce the expression level of at least one gene product selected from the group consisting of: CARMA1, Bcl10 and MALT1.

18. A cell according to Claim 16, in which the cell is an immune cell.
19. Use of a cell according to Claim 16 in the preparation of a medicament for the treatment or prevention of cancer.
20. Use of an agent that inhibits activity of a CARMA1-Bcl10-MALT1 signalosome
5 complex and a second therapeutic in the preparation of a medicament for the treatment or prevention of a cancer that is resistant to a checkpoint inhibitor therapy.
21. Use according to Claim 20, in which the second therapeutic is a checkpoint inhibitor therapy or an anti-cancer therapy.
22. Use according to Claim 21, in which the checkpoint inhibitor therapy is selected from
10 the group consisting of an anti-PD-L1 therapy, an anti-PD-L2 therapy, an anti-PD-1 therapy, an anti-CTLA-4 therapy, an anti-TIM-3 therapy, an anti-LAG-3 therapy, an anti-VISTA therapy and an anti-TIGIT therapy.