

CLAIMS:

1. A method of determining response to PD-1/PD-L1 based immunotherapy in a subject suffering from cancer, the method comprising measuring sCD28 levels in said subject at at least two time points wherein at least one of those time points is after initiation of said PD-1/PD-L1 based immunotherapy, wherein an increase in sCD28 levels from a first time point to a second time point after initiation of said PD-1/PD-L1 based immunotherapy indicates said subject is not a responder to said immunotherapy and a decrease or no change in sCD28 levels from said first time point to said second time point after initiation of said PD-1/PD-L1 based immunotherapy indicates said subject is a responder to said immunotherapy, thereby determining response to PD-1/PD-L1 based immunotherapy in a subject.
2. The method of claim 1, wherein said first time point is before or at the time of initiation of said immunotherapy.
3. The method of claim 1, wherein said first time point is after initiation of said immunotherapy.
4. The method of any one of claims 1 to 3, wherein said second time point is at least 6 weeks after said first time point.
5. The method of any one of claims 1 to 4, wherein said second time point is at most 7 weeks after said first time point.
6. The method of any one of claims 1 to 5, wherein
 - a. said first time point is at or before initiation of said immunotherapy and said second time point is 7 weeks or 13 weeks after initiation of said immunotherapy; or
 - b. said first time point is at 7 weeks after initiation of said immunotherapy and said second time point is 13 weeks after initiation of said immunotherapy.
7. The method of any one of claims 1 to 6, wherein a decrease in sCD28 levels from said first time point to said second time point after initiation of said PD-1/PD-L1 based immunotherapy indicates said subject is a responder to said immunotherapy.
8. The method of any one of claims 1 to 7, wherein a decrease is a decrease of at least 1 ng/ml sCD28.
9. The method of any one of claims 1 to 8, further comprising at least one of:
 - a. discontinuing said immunotherapy to a subject that is not a responder;

- b. administering a different immunotherapy to a subject that is a non-responder;
 - c. continuing to administer said PD-1/PD-L1 based immunotherapy to a subject that is a responder; and
 - d. increasing a dose of said PD-1/PD-L1 based immunotherapy administered to a subject that is a responder.
10. A method of diagnosing cancer relapse in a subject in need thereof, the method comprising measuring soluble CD28 (sCD28) levels in said subject, wherein an increase in sCD28 levels in said subject indicates cancer relapse, thereby diagnosing cancer relapse in said subject.
11. A method of predicting cancer relapse in a subject in need thereof, the method comprising measuring soluble CD28 (sCD28) levels in said subject, wherein an increase in sCD28 levels in said subject indicates an imminent cancer relapse, thereby predicting cancer relapse in said subject.
12. The method of claim 10 or 11, wherein said subject suffers from cancer and said cancer is in remission.
13. The method of claim 10 or 11, wherein said subject previously had cancer and is currently cancer free.
14. The method of any one of claims 10 to 13, wherein said subject has undergone or is undergoing immunotherapy.
15. The method of claim 14, wherein said immunotherapy is PD-1, PD-L1 and/or CD80 based immunotherapy.
16. The method of any one of claims 10 to 15, wherein said increase is as compared to sCD28 levels in said subject before relapse.
17. The method of any one of claims 1 to 16, wherein said increase is as compared to a predetermined threshold.
18. The method of any one of claims 1 to 17, wherein said increase is an increase of at least 50%.
19. The method of any one of claims 1 to 18, wherein said increase is an increase to at least 6 ng/mL sCD28.
20. The method of any one of claims 1 to 19, wherein said increase is an increase of at least 1 ng/ml sCD28.

21. The method of any one of claims 1 to 20, wherein said measuring comprises obtaining a sample from said subject and measuring sCD28 levels in said sample.
22. The method of claim 21, wherein said sample is a blood sample.
23. The method of any one of claims 10 to 22, wherein said measuring comprises measuring at a plurality of time points, wherein at least one time point is at a time when said subject is known to be in remission or cancer free, and wherein at least one time point is at a time when the subject is at risk of relapse.
24. The method of claim 23, wherein remission comprises a partial response and a complete response to a therapy.
25. The method of claim 23 or 24, wherein at said time point when said subject is known to be in remission or cancer free sCD28 levels are below 5 ng/mL.
26. The method of any one of claims 10 to 25, wherein said subject before performance of said method has blood sCD28 levels below 6 ng/mL.
27. The method of any one of claims 1 to 26, wherein said cancer is selected from skin cancer, urothelial cancer, lung cancer, and renal cancer.
28. The method of claim 27, wherein said cancer is selected from melanoma, and urothelial cancer.
29. The method of any one of claims 10 to 28, wherein imminent is within the next 20 weeks.
30. The method of any one of claims 1 to 29, further comprising administering another immunotherapy to a subject diagnosed with or predicted for cancer relapse or determined to be a non-responder to said immunotherapy.
31. The method of claim 30, wherein said immunotherapy is selected from:
 - a. a checkpoint inhibitor;
 - b. a chimeric antigen receptor (CAR) based therapy; and
 - c. a cancer vaccine.
32. The method of claims 31, wherein said checkpoint inhibitor is a PD-1 and/or PD-L1 based immunotherapy.