effective amount of a therapeutic agent that specifically binds the cell surface antigen to treat the subject for cancer. The subject methods may include selectively enhancing cell surface presentation of target antigens or neoantigens, and selectively decreasing cell surface presentation of other antigens or neoantigens. Examples of the subject methods also include use of the bryostatin agents to sensitize target cells to clearance by the subject's immune system.

In one aspect, the present disclosure relates to a use of a bryostatin agent and a therapeutic agent in the manufacture of a medicament for treating a subject for cancer, wherein the bryostatin agent and the therapeutic agent are to be administered to the subject,

wherein the bryostatin agent enhances cell surface antigen or neoantigen presentation and persistence on target cells of the subject; and

wherein the therapeutic agent specifically binds the cell surface antigen to treat the subject for cancer.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1, panels A-D, illustrate the synthetic strategy for preparation of bryostatin and analogs and binding structures with Protein Kinase C (PKC). Panel A: Retrosynthetic analysis of the bryostatin scaffold with pharmacophoric elements of the C-ring subunit identified as the C1 carbonyl, C19 hemiketal, and C26 alcohol. C13 (indicted with the sphere) is highlighted as an area of interest for analog synthesis. Panel B: Rendering of the PKC-bryostatin-membrane ternary complex. Bryostatin 1 shown inside the rectangular box. Pharmacophoric elements of the C-ring subunit of the bryostatin scaffold (see FIG. 1, panel A) interact directly with PKC (dark gray) while the A and B rings are imbedded in the plasma membrane (light gray). Panel C: Representative conformers of the bryostatin scaffold bound to PKC that fit experimentally determined intramolecular distances determined by REDOR NMR. Panel D: Convergent construction of the bryostatin scaffold from acid 1 and enal 2. C13 functionality provides a versatile starting point for late-stage diversification, avoiding interference with the pharmacophoric elements of the C ring (as identified in FIG. 1, panel A).

WHAT IS CLAIMED IS:

1. Use of a bryostatin agent and a therapeutic agent in the manufacture of a medicament for treating a subject for cancer, wherein the bryostatin agent and the therapeutic agent are to be administered to the subject,

wherein the bryostatin agent enhances cell surface antigen or neoantigen presentation and persistence on target cells of the subject; and

wherein the therapeutic agent specifically binds the cell surface antigen to treat the subject for cancer.

2. The use of claim 1, wherein the subject is relapsed or refractory to targeted anticancer therapy.

3. The use of claim 1, wherein the target cancer cells present cell surface antigen on the target cell surface is at a therapeutically ineffective level before the bryostatin agent is to be administered.

4. The use of claim 1, wherein the bryostatin agent to be administered enhances one or more of a) expression of cell surface antigens, b) translocation of expressed cell surface antigens to the target cell surface, and c) persistence of cell surface antigens on the target cell surface.

5. The use of any one of claims 1-4, wherein the therapeutic agent is selected from chimeric antigen receptor expressing T cells (CAR T-cells), CAR-natural killer cells (CAR-NK cells), antibody agent, antibody drug conjugate (ADC) and bispecific antibody agent.

6. The use of any one of claims 1-5, wherein the cancer is leukemia or B cell lymphoma.

7. The use of any one of claims 1-5, wherein the cancer is melanoma, prostate cancer, breast cancer, ovarian cancer, esophageal cancer, or kidney cancer.

8. The use of any one of claims 1-7, wherein the level or expression or presentation of the cell surface antigen in target cancer cells of a sample that had been obtained from the subject is to be determined.

9. The use of any one of claims 1-8, wherein at least one additional anti-cancer therapy is to be administered the patient, wherein the additional anti-cancer therapy is selected from radiation therapy, chemotherapy, immunotherapy, checkpoint inhibitors, surgery and vasculature-targeting therapy.

10. The use of any one of claims 1-9, wherein one or more biomarkers in a sample that had been obtained from the subject is to be assessed to assay the status of the cancer.