conventional antigen-binding molecules that bind to molecules expressed on the surfaces of regulatory T cells and exhausted T cells and also have ADCC activity. Furthermore, the present inventors discovered pharmaceutical compositions that can treat various carcinomas by having the antigen-binding molecule as an active ingredient.

More specifically, the present invention provides the following:

[1] an antigen-binding molecule that inhibits immune response-suppressing activity of a cell having an immune response-suppressing function, comprising:

(i) a domain that binds to a molecule expressed on the surface of a cell having an immune response-suppressing function; and

(ii) a T cell receptor complex-binding domain;

[2] the antigen-binding molecule of [1], wherein the cell having immune response-suppressing function is a regulatory T cell or an exhausted T cell;

[3] the antigen-binding molecule of [1], wherein the molecule expressed on the surface of a cell having an immune response-suppressing function is any molecule selected from among CTLA4, PD1, TIM3, LAG3, CD244 (2B4), CD160, GARP, OX40, CD137 (4-1BB), CD25, VISTA, BTLA, TNFR25, CD57, KLRG1, CCR2, CCR5, CCR6, CD39, CD73, CD4, CD18, CD49b, CD1d, CD5, CD21, TIM1, CD19, CD20, CD23, CD24, CD38, CD93, IgM, B220(CD45R), CD317, PD-L1, CD11b, Ly6G, ICAM-1, FAP, PDGFR, Podoplanin, and TIGIT;

[4] the antigen-binding molecule of [3], wherein the molecule expressed on the surface of a cell having an immune response-suppressing function is any molecule selected from among CTLA4, TIM3, LAG3, CD137 (4-1BB), CD25, CCR5, CCR6, CD38, TIGIT, and OX40;

[5] the antigen-binding molecule of any one of [1] to [4], wherein the T cell receptor complex-binding domain is a T cell receptor-binding domain;

[6] the antigen-binding molecule of any one of [1] to [4], wherein the T cell receptor complex-binding domain is a CD3-binding domain;

[7] the antigen-binding molecule of any one of [1] to [6], which further comprises an FcRn-binding domain;

[8] the antigen-binding molecule of [7], wherein the FcRn-binding domain is an Fc region of an antibody;

[9] the antigen-binding molecule of [8], wherein the FcRn-binding domain is an Fc region of an antibody having reduced Fcγ receptor-binding activity;

[10] the antigen-binding molecule of any one of [1] to [9], which is a multispecific antibody;

[11] a pharmaceutical composition comprising the antigen-binding molecule of any one of [1] to [10] as an active ingredient;

[12] a pharmaceutical composition for use in inhibiting an immune response-suppressing activity, comprising the antigen-binding molecule of any one of [1] to [10] as an active ingredient;

[13] the pharmaceutical composition of [12], wherein the inhibition of an immune response-suppressing activity is inhibition caused by a T cell;
[14] the pharmaceutical composition of [13], wherein the inhibition caused by a T cell is inhibition resulting from cytotoxic activity of the T cell;
[15] the pharmaceutical composition of any one of [12] to [14], wherein the immune response-suppressing activity is an activity by a regulatory T cell or an exhausted T cell;
[16] the pharmaceutical composition of any one of [12] to [14], wherein the immune response-suppressing activity is an activity of a cell expressing any molecule selected from among CTLA4, PD1, TIM3, LAG3, CD244 (2B4), CD160, GARP, OX40, CD137 (4-1BB), CD25, VISTA, BTLA, TNFR25, CD57, KLRG1, CCR2, CCR5, CCR6, CD39, CD73, CD4, CD18, CD49b, CD1d, CD5, CD21, TIM1, CD19, CD20, CD23, CD24, CD38, CD93, IgM, B220(CD45R), CD317, PD-L1, CD11b, Ly6G, ICAM-1, FAP, PDGFR, Podoplanin, and TIGIT;
[17] the pharmaceutical composition of any one of [11] to [16], for use in treating cancer;
[18] the pharmaceutical composition of claim 17, wherein the cancer is selected from the group consisting of ovarian cancer, gastric cancer, esophageal cancer, pancreatic cancer, renal cell carcinoma, hepatocellular carcinoma, breast cancer, malignant melanoma, non-small-cell lung cancer, cervical cancer, glioblastoma, prostate cancer, neuroblastoma, chronic lymphocytic leukemia, papillary thyroid cancer, colorectal cancer, Hodgkin's lymphoma, and endometriosis;
[19] Also disclosed herein is a method for inducing cytotoxicity, suppressing cell proliferation, activating immunity against a cancer cell or a cancer cell-comprising tumor tissue , or treating or preventing cancer, which comprises the step of administering the antigen-binding molecule of any one of [1] to [10] or the pharmaceutical composition of any one of [11] to [18];
[20] the antigen-binding molecule of any one of [1] to [10] or the pharmaceutical composition of any one of [11] to [18] for use in inducing cytotoxicity, suppressing cell proliferation, activating immunity against a cancer cell or a cancer cell-comprising tumor tissue, or treating or preventing cancer;
[21] use of the antigen-binding molecule of any one of [1] to [10] in the production of the pharmaceutical composition of any one of [11] to [18]; and
[22] a method for producing the pharmaceutical composition of any one of [11] to [18], which comprises the step of using the antigen-binding molecule of any one of [1] to [10].

Furthermore, the present disclosure relates to methods for treating or preventing cancer, or for inhibiting suppression of an immune response, which comprise administering an antigen-binding molecule of the present invention or a pharmaceutical composition of the present invention to patients in need of treatment. The present disclosure also relates to a kit for use in the methods of the present invention, which comprises an antigen-binding molecule of the

present invention. The present disclosure also relates to the use of an antigen-binding molecule of the present invention in producing a pharmaceutical composition for inhibiting immune response-suppression. Furthermore, the present disclosure relates to antigen-binding molecules of the present invention or pharmaceutical compositions of the present invention for use in the methods of the present disclosure.

Brief Description of the Drawings

Fig. 1 presents a schematic diagram showing cytotoxic activity against cancer cells by bispecific antibodies that target a cancer antigen expressed on cancer cells and CD3 expressed on T cells.

Fig. 2-1 presents a schematic diagram showing crosslinking between T cells caused by crosslinking between CD3s on different T cells *via* an anti-CD3 antibody.

Fig. 2-2 presents a schematic diagram showing crosslinking between CD3s on the same T cell *via* an anti-CD3 antibody.

Fig. 3 presents a schematic diagram showing that an anti-CTLA4/CD3 bispecific antibody causes crosslinking between CTLA4 and CD3 on the same regulatory T cell, and therefore, does not cause intercellular crosslinking between an effector T cell and a regulatory T cell. This schematic diagram shows a regulatory T cell as the target cell and CTLA4 as the antigen, but the target cell and antigen are not limited thereto.

Fig. 4 presents a schematic diagram showing intercellular crosslinking caused by crosslinking between CD3 on an effector T cell and CTLA4 on a regulatory T cell *via* an anti-CTLA4/CD3 bispecific antibody. This schematic diagram shows a regulatory T cell as the target cell and CTLA4 as the antigen, but the target cell and antigen are not limited thereto.

Fig. 5 presents a graph showing the ADCC activity of the anti-mouse CTLA4 antibody hUH02hUL01-mFa55 on mouse CTLA4-expressing cells.

Fig. 6 presents a graph showing the cytotoxic activity of the anti-mouse CTLA4/anti-mouse CD3 bispecific antibody (hUH02UL01/2C11-F760) on mouse CTLA4-expressing cells.

Fig. 7-1 presents a schematic diagram showing crosslinking between a mouse CTLA4-bound bead and a mouse CD3-bound bead by an anti-mouse CTLA4/anti-mouse CD3 bispecific antibody.

Fig. 7-2 presents a graph showing the experiment results of crosslinking between mouse CTLA4-bound beads and mouse CD3-bound beads *via* anti-mouse CTLA4/anti-mouse CD3 bispecific antibodies (N = 3). The graph shows the mean values and standard deviations for each of the measurement results.

Fig. 7-3 presents a graph showing the experiment results of crosslinking between mouse

10. The antigen-binding molecule of any one of claims 1 to 9, which is a multispecific antibody.

11. A pharmaceutical composition comprising the antigen-binding molecule of any one of claims 1 to 10 as an active ingredient.

12. A pharmaceutical composition for use in inhibiting an immune response-suppressing activity, comprising the antigen-binding molecule of any one of claims 1 to 10 as an active ingredient.

13. The pharmaceutical composition of claim 12, wherein the inhibition of an immune response-suppressing activity is inhibition caused by a T cell.

14. The pharmaceutical composition of claim 13, wherein the inhibition caused by a T cell is inhibition resulting from cytotoxic activity of the T cell.

15. The pharmaceutical composition of any one of claims 12 to 14, wherein the immune response-suppressing activity is an activity by a regulatory T cell or an exhausted T cell.

16. The pharmaceutical composition of any one of claims 12 to 14, wherein the immune response-suppressing activity is an activity of a cell expressing any molecule selected from among CTLA4, PD1, TIM3, LAG3, CD244 (2B4), CD160, GARP, OX40, CD137 (4-1BB), CD25, VISTA, BTLA, TNFR25, CD57, KLRG1, CCR2, CCR5, CCR6, CD39, CD73, CD4, CD18, CD49b, CD1d, CD5, CD21, TIM1, CD19, CD20, CD23, CD24, CD38, CD93, IgM, B220(CD45R), CD317, PD-L1, CD11b, Ly6G, ICAM-1, FAP, PDGFR, Podoplanin, and TIGIT.

17. The pharmaceutical composition of any one of claims 11 to 16 for use in treating cancer.

18. The pharmaceutical composition of claim 17, wherein the cancer is selected from the group consisting of ovarian cancer, gastric cancer, esophageal cancer, pancreatic cancer, renal cell carcinoma, hepatocellular carcinoma, breast cancer, malignant melanoma, non-small-cell lung cancer, cervical cancer, glioblastoma, prostate cancer, neuroblastoma, chronic lymphocytic leukemia, papillary thyroid cancer, colorectal cancer, Hodgkin's lymphoma, and endometriosis.