

Claims:

[Claim 1]. An antigen-binding molecule, optionally isolated, which is capable of binding to VISTA and inhibiting VISTA-mediated signalling, wherein the antigen-binding molecule comprises:

(i) a heavy chain variable (VH) region incorporating the following CDRs:

HC-CDR1 having the amino acid sequence of SEQ ID NO:290

HC-CDR2 having the amino acid sequence of SEQ ID NO:291

HC-CDR3 having the amino acid sequence of SEQ ID NO:278; and

(ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid sequence of SEQ ID NO:41

LC-CDR2 having the amino acid sequence of SEQ ID NO:295

LC-CDR3 having the amino acid sequence of SEQ ID NO:43.

[Claim 2]. The antigen-binding molecule according to claim 1, wherein the antigen-binding molecule comprises:

a VH region comprising an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO:289; and

a VL region comprising an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO:297.

[Claim 3]. The antigen-binding molecule according to claim 1 or claim 2, wherein the antigen-binding molecule comprises:

a VH region incorporating the following framework regions (FRs):

HC-FR1 having the amino acid sequence of SEQ ID NO:63

HC-FR2 having the amino acid sequence of SEQ ID NO:292

HC-FR3 having the amino acid sequence of SEQ ID NO:293

HC-FR4 having the amino acid sequence of SEQ ID NO:281.

[Claim 4]. The antigen-binding molecule according to any one of claims 1 to 3, wherein the antigen-binding molecule comprises:

a VL region incorporating the following framework regions (FRs):

LC-FR1 having the amino acid sequence of SEQ ID NO:288

LC-FR2 having the amino acid sequence of SEQ ID NO:298

LC-FR3 having the amino acid sequence of SEQ ID NO:284

LC-FR4 having the amino acid sequence of SEQ ID NO:47.

[Claim 5]. The antigen-binding molecule according to any one of claims 1 to 4, wherein the antigen-binding molecule comprises the heavy chain constant sequence of IgG4.

[Claim 6]. The antigen-binding molecule according to any one of claims 1 to 5, wherein the antigen-binding molecule comprises the light chain constant sequence of SEQ ID NO:211.

[Claim 7]. An antigen-binding molecule, optionally isolated, comprising (i) an antigen-binding molecule according to any one of claims 1 to 6, and (ii) an antigen-binding molecule capable of binding to an antigen other than VISTA.

5 [Claim 8]. A chimeric antigen receptor (CAR) comprising an antigen-binding molecule according to any one of claims 1 to 7.

[Claim 9]. A nucleic acid, or a plurality of nucleic acids, optionally isolated, encoding an antigen-binding molecule according to any one of claims 1 to 7, or a CAR according to claim 8.

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[Claim 10]. An expression vector, or a plurality of expression vectors, comprising a nucleic acid or a plurality of nucleic acids according to claim 9.

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[Claim 11]. A cell comprising an antigen-binding molecule according to any one of claims 1 to 7, a CAR according to claim 8, a nucleic acid or a plurality of nucleic acids according to claim 9, or an expression vector or a plurality of expression vectors according to claim 10.

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[Claim 12]. A method comprising culturing a cell comprising a nucleic acid or a plurality of nucleic acids according to claim 9, or an expression vector or a plurality of expression vectors according to claim 10, under conditions suitable for expression of the antigen-binding molecule or CAR from the nucleic acid(s) or expression vector(s).

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[Claim 13]. A composition comprising an antigen-binding molecule according to any one of claims 1 to 7, a CAR according to claim 8, a nucleic acid or a plurality of nucleic acids according to claim 9, an expression vector or a plurality of expression vectors according to claim 10, or a cell according to claim 11.

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[Claim 14]. The composition according to claim 13, additionally comprising an agent capable of inhibiting signalling mediated by an immune checkpoint molecule other than VISTA, optionally wherein the immune checkpoint molecule other than VISTA is selected from PD-1, CTLA-4, LAG-3, TIM-3, TIGIT and BTLA.

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[Claim 15]. Use of an antigen-binding molecule according to any one of claims 1 to 7, a CAR according to claim 8, a nucleic acid or a plurality of nucleic acids according to claim 9, an expression vector or a plurality of expression vectors according to claim 10, a cell according to claim 11, or a composition according to claim 13 or claim 14, in the manufacture of a medicament for use in a method of treating a cancer comprising cells expressing VISTA, or a cancer comprising infiltration of cells expressing VISTA.

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[Claim 16]. The use according to claim 15, wherein the cancer is selected from: a cancer comprising cancer cells expressing VISTA, a hematological cancer, leukemia, acute myeloid leukemia, lymphoma, B cell lymphoma, T cell lymphoma, multiple myeloma, mesothelioma, a solid tumor, lung cancer, non-small cell lung carcinoma, gastric cancer, gastric carcinoma, colorectal cancer, colorectal carcinoma, colorectal adenocarcinoma, uterine cancer, uterine corpus endometrial carcinoma, breast cancer, triple negative

breast invasive carcinoma, liver cancer, hepatocellular carcinoma, pancreatic cancer, pancreatic ductal adenocarcinoma, thyroid cancer, thymoma, skin cancer, melanoma, cutaneous melanoma, kidney cancer, renal cell carcinoma, renal papillary cell carcinoma, head and neck cancer, squamous cell carcinoma of the head and neck (SCCHN), ovarian cancer, ovarian carcinoma, ovarian serous cystadenocarcinoma, prostate cancer and/or prostate adenocarcinoma.

[Claim 17]. The use according to claim 15 or claim 16, wherein the method additionally comprises administration of an agent capable of inhibiting signalling mediated by an immune checkpoint inhibitor other than VISTA, optionally wherein the immune checkpoint inhibitor other than VISTA is selected from PD-1, CTLA-4, LAG-3, TIM-3, TIGIT or BTLA.

[Claim 18]. An *in vitro* complex, optionally isolated, comprising an antigen-binding molecule according to any one of claims 1 to 7 bound to VISTA.

[Claim 19]. A method for detecting VISTA, comprising contacting a sample containing, or suspected to contain, VISTA with an antigen-binding molecule according to any one of claims 1 to 7 *in vitro*, and detecting the formation of a complex of the antigen-binding molecule with VISTA.

[Claim 20]. A method of selecting or stratifying a subject for treatment with a VISTA-targeted agent, the method comprising contacting, *in vitro*, a sample from the subject with an antigen-binding molecule according to any one of claims 1 to 7 and detecting the formation of a complex of the antigen-binding molecule with VISTA.

[Claim 21]. Use of an antigen-binding molecule according to any one of claims 1 to 7 as an *in vitro* diagnostic or prognostic agent.