

example, colorectal cancer, head and neck cancer, pancreatic cancer (Kunzli et al., *Am J Physiol*, 2006, 292: 223-230), bladder cancer, brain cancer, breast cancer, gastric cancer, hepatocellular carcinoma, lung cancer, non-small cell lung cancer (Li et al., *Oncoimmunology*, 2017, 6: 6), chronic lymphocytic leukemia (Pulte et al., *Clin Lymphoma Myeloma Leuk*, 2011, 11(4): 367-372) and lymphoma, melanoma (Dzhandzhugazyan et al., *FEBS Letters*, 1998, 430: 227-230), ovarian cancer, and prostate cancer, among others) suggesting this enzyme is involved in the development and progression of malignancies. Modulators of CD39 may provide potential therapies for these types of cancers.

[0006] Interactions between tumor cells and their microenvironment are important for tumorigenesis. CD39 can participate in tumor immunoescape by inhibiting the activation, clonal expansion, and homing of tumor-specific T cells, impairing tumor cell killing by effector T lymphocytes. In addition to these immunoregulatory roles, CD39 can contribute directly to the modulation of cancer cell growth, differentiation, invasion, migration, metastasis, and angiogenesis. CD39 is important for both the initiation of angiogenesis and the progression of neovascularization. CD39 on vasculature mediates the angiogenic process in mouse models of melanoma, lung, and liver malignancy.

[0007] Modulators of CD39 activity may also provide potential therapeutics for the treatment of CD39 conditions including, but not limited to, autoimmune diseases and infections. In particular, modulators of CD39 activity may provide potential therapeutics for diseases such as, for example, without limitation, Celiac disease (Cook et al., *American Academy of Allergy, Asthma & Immunology*, 2017, Article in Press), colitis (Longhi et al., *JCI Insight*. 2017, 2(9)), thrombotic disease (Marcus et al., *Journal of Pharmacology and Experimental Therapeutics*, 2003, 305, 1: 9-16), HIV infection (zur Wiesch et al., *Journal of Virology*, 2011, Feb: 1287-1297), HBV infection, HCV infection, and inflammatory bowel disease (Friedman et al. *PNAS*, 2009, 106, 39: 16788-16793) and Crohn's disease (Bai et al., *J Immunol*, 2014, 3366-3377).

SUMMARY

[0008] Provided herein are antibodies that selectively bind CD39. In some examples, the antibodies bind human CD39. In some examples, the antibodies also bind homologs of human CD39.

[0008a] In one aspect, there is provided an antigen binding protein that binds specifically to a human CD39 (hCD39) and is capable of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18 of the following:

- a) inhibiting binding of CD39 to ATP;
- b) inhibiting conversion by CD39 of ATP to ADP and/or ADP to AMP;
- c) decreasing affinity of CD39 for ATP or ADP;
- d) inhibiting or impeding release of ADP or AMP from CD39;
- e) impeding or inhibiting CD39 processivity;
- f) inhibiting platelet aggregation;
- g) decreasing levels of phosphate, ADP, AMP, and/or adenosine and/or increasing levels of ATP;
- h) increasing T effector cell function;
- i) decreasing the number of regulatory T cells in tissues or in circulation;
- j) suppressing regulatory T cells or regulatory T cell activity;
- k) increasing B cell function;
- l) increasing antigen presenting cell function;
- m) inhibiting CD39 function on tumor cells;
- n) inhibiting processing of at least one of phospho-antigen from phosphorylated isoprenoid, phosphorylated vitamin B metabolite, and/or phosphorylated riboflavin;
- o) decreasing or preventing activation of phospho antigen specific T cells selected from MAIT cells and $\gamma\delta$ T cells;
- p) inhibiting angiogenesis;
- q) increasing proliferation of stimulated CD4⁺ and CD8⁺ T cells;
- r) increasing stimulated PBMC Secretion of INF- γ , TNF- α , IL-2 and/or IL-1 β .

[0009] In some examples, the antibodies comprise at least one CDR sequence defined by a consensus sequence provided in this disclosure. In some examples, the

antibodies comprise an illustrative CDR, V_H, or V_L sequence provided in this disclosure, heavy chain or light chain provided in the disclosure, or a variant thereof. In some examples, the variant is a variant with one or more conservative amino acid substitutions.

[0010] Also provided are compositions and kits comprising the antibodies. In some examples, the compositions are pharmaceutical compositions. Any suitable pharmaceutical composition may be used. In some examples, the pharmaceutical composition is a composition for parenteral administration.

[0010a] In another aspect, there is provided a pharmaceutical composition comprising an effective amount of an antibody which binds to hCD39 and has 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 of the following of characteristics:

- a) blocks or decreases hydrolysis of ATP to ADP and/or ADP to AMP as determined by at least one of: (i) a decreased phosphate release (Pi), (ii) an increase in ATP levels, and (iii) a decrease of ADP, AMP, and/or adenosine levels,
- b) increases T effector cell activity;
- c) suppresses regulatory T cell or decreases a regulatory T cell activity;
- d) decreases number of regulatory T cells in tissues or in circulation;
- e) increases B cell function;
- f) increases antigen presenting cell function;
- g) inhibits CD39 function on tumor cells;
- h) blocks or inhibits processing of at least one of phospho-antigen from a phosphorylated isoprenoid, phosphorylated vitamin B metabolite, and phosphorylated riboflavin;
- i) decreases or prevents activation of phospho antigen specific T cells selected from MAIT cells and $\gamma\delta$ T cells;
- k) inhibits angiogenesis;
- l) decreases affinity for ATP and/or ADP;
- m) inhibits release of ADP or AMP from CD39;
- n) impedes or inhibits CD39 processivity;
- o) inhibits platelet aggregation;
- p) increases proliferation of stimulated CD4⁺ and CD8⁺ T cells;
- r) increases stimulated PBMC Secretion of INF- γ , TNF- α , IL-2, and/or IL-1 β .

[0010b] In another aspect, there is provided a pharmaceutical composition comprising the antigen-binding protein as described herein.

[0010c] In another aspect, there is provided an antigen binding protein that competes or is capable of competing for binding to human CD39 with a reference antigen binding protein, wherein the reference antigen binding protein is the antigen binding protein as described herein.

[0010d] In another aspect, there is provided an antigen binding protein that binds to or is capable of competing for binding to human CD39 with a reference antigen binding protein, wherein the reference antigen binding protein binds to an epitope at positions 143-158 or 274-277 of SEQ ID NO: 249 on a human CD39 polypeptide, including, but not limited to, D150, E153, R154 or N99 alone or in combination with D150, E153, R154 or any combination thereof.

[0010e] In another aspect, there is provided an isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL), VH and/or VL comprising 1, 2, 3, 4, 5, or 6 of:

- a) a VHCDR1 having the sequence set forth in SEQ ID NOs: 1-45,
- b) a VHCDR2 having the sequence set forth in SEQ ID NOs: 46-81,
- c) a VHCDR3 having the sequence set forth in SEQ ID NOs: 82-109,
- d) a VLCDR1 having the sequence set forth in SEQ ID NOs: 110-124,
- e) a VLCDR2 having the sequence set forth in SEQ ID NOs: 125-140, and
- f) a VLCDR3 having the sequence set forth in SEQ ID NOs: 141-166.

[0010f] In another aspect, there is provided an isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL),

the VH comprising,

- a) a VHCDR1 having a sequence set forth in SEQ ID NOs: 1-45,
- b) a VHCDR2 having a sequence set forth in SEQ ID NOs: 46-81, and

- c) a VHCDR3 having a sequence set forth in SEQ ID NOs: 82-109; and
the VL comprising,
 - a) a VLCDR1 having a sequence set forth in SEQ ID NO: 110-124,
 - b) a VLCDR2 having a sequence set forth in SEQ ID NO: 125-140, and
 - c) a VLCDR3 having a sequence set forth in SEQ ID NO: 141-166.

[0010g] In another aspect, there is provided an isolated nucleic acid encoding an antigen binding protein as described herein.

[0010h] In another aspect, there is provided an expression vector comprising the nucleic acid as described herein.

[0010i] In another aspect, there is provided a prokaryotic or eukaryotic host cell comprising the vector as described herein.

[0010j] In another aspect, there is provided an oncolytic virus encoding the nucleic acid as described herein.

[0010k] In another aspect, there is provided a method for the production of a recombinant protein comprising the steps of expressing a nucleic acid as described herein in a prokaryotic or eukaryotic host cell and recovering the protein from the cell or the cell culture supernatant.

[0011] This disclosure also provides methods of using the anti-CD39 antibodies provided herein. In some examples, the method is a method of treatment. In some examples, the method is a diagnostic method. In some examples, the method is an analytical method. In some examples, the method is a method of purifying and/or quantifying CD39.

[0011a] In another aspect, there is provided use of a pharmaceutical composition comprising the antigen binding protein as described herein or the pharmaceutical composition as described herein in the manufacture of a medicament for the treatment of a subject suffering from cancer, a chronic infection, or from an inflammatory disease.

[0011b] In another aspect, there is provided use of a pharmaceutical composition comprising the antigen binding protein as described herein in the manufacture of a medicament for modulating immune system function in a subject in need thereof, wherein a population of immune cells of the subject is to be contacted with the pharmaceutical

composition, under conditions such that the immune system is modulated.

[0011c] In another aspect, there is provided use of a pharmaceutical composition comprising an antigen binding protein in the manufacture of a medicament for inducing or enhancing an immune response in a subject in need thereof, wherein the immune response is generated against a tumor antigen.

[0011d] In another aspect, there is provided a method of screening for a test compound comprising an antigen binding protein as described herein capable of inhibiting an activity of CD39, comprising the steps of:

contacting a test sample containing CD39 with a test compound;

comparing the activity of the test sample to a control sample;

whereby a decrease in the activity of CD39 in the test sample compared to the control sample identifies the compound as one that inhibits the activity of CD39.

[0011e] In another aspect, there is provided an isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL),

VH comprising at least one of:

a) a VHCDR1 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 1-45,

b) a VHCDR2 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 46-81, and

c) a VHCDR3 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 82-109; and

VL comprising at least one of:

a) a VLCDR1 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 110-124,

b) a VLCDR2 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 125-140, and

c) a VLCDR3 having an amino acid sequence that is at least 90% identical to the

sequence set forth in SEQ ID NOs 141-166.

[0011f] In another aspect, there is provided an isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL),

VH comprising at least one of:

- a) a VHCDR1 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 1-45,
- b) a VHCDR2 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 46-81, and
- c) a VHCDR3 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 82-109; and

VL comprising at least one of:

- a) a VLCDR1 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 110-124,
- b) a VLCDR2 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 125-140, and
- c) a VLCDR3 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 141-166.

[0011g] In another aspect, there is provided an isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain and a light chain, the heavy chain comprising one or more molecules having a sequence consisting of one of SEQ ID NO: 255, SEQ ID NO: 257, SEQ ID NO: 259, SEQ ID NO: 261, SEQ ID NO: 263, SEQ ID NO: 265, SEQ ID NO: 267, SEQ ID NO: 269, SEQ ID NO: 271, SEQ ID NO: 273, SEQ ID NO: 275, SEQ ID NO: 277, SEQ ID NO: 279, SEQ ID NO: 281, SEQ ID NO: 283, SEQ ID NO: 285, SEQ ID NO: 287, SEQ ID NO: 289, SEQ ID NO: 291, SEQ ID NO: 293, or SEQ ID NO: 295 and the light chain comprising one or more molecules having a sequence consisting of one of SEQ ID NO: 256, SEQ ID NO: 258, SEQ ID NO: 260, SEQ ID NO: 262, SEQ ID NO: 264, SEQ ID NO: 266, SEQ ID NO: 268, SEQ ID NO: 270, SEQ ID NO: 272, SEQ ID NO: 274, SEQ ID NO: 276, SEQ ID NO: 278, SEQ ID NO: 280, SEQ ID NO: 282, SEQ ID NO: 284, SEQ ID NO: 286, SEQ ID NO: 288, SEQ ID NO: 290, SEQ ID NO: 292, SEQ ID

NO: 294, or SEQ ID NO: 296.

[0011h] In another aspect, there is provided an isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain and a light chain,

a) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 255 and the light chain comprising one or more, each molecule having a sequence consisting of SEQ ID NO: 256;

b) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 257 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 258;

c) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 259 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 260;

d) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 261 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 262;

e) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 263 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 264;

f) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 265 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 266;

g) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 267 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 268;

h) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 269 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 270;

i) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 271 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 272;

j) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 273 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 274;

k) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 275 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 276;

l) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 277 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 278

m) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 279 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 280;

n) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 281 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 282;

o) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 283 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 284;

p) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 285 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 286;

q) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 287 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 288;

r) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 289 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 290;

s) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 291 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 292;

t) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 293 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 294; or

u) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 295 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 296.

[0011i] In another aspect, there is provided an isolated nucleic acid encoding an antigen binding protein as described herein.

[0011j] In another aspect, there is provided an isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL), VH and/or VL comprising 1, 2, 3, 4, 5, or 6 of:

a) a VHCDR1 sequence comprising:

(i) a Kabat CDRH1 sequence defined by the consensus sequence S-Y- Δ_3 -M- Δ_5 (SEQ ID NOS: 25-29 and 44-45), where Δ_3 is E, F, Q, or Y and Δ_5 is H or Y;

(ii) a Kabat CDR-H1 sequence defined by the consensus sequence θ_1 - θ_2 - θ_3 -I-S (SEQ ID NOS: 30-37), where θ_1 is A, H, K, L, S, or W; θ_2 is L, M, N, or T; and θ_3 is A or P;

(iii) a Kabat CDR-H1 sequence defined by the consensus sequence η_1 -Y- η_3 -I-S (SEQ ID NOS: 38-41), where η_1 is S, K, N, or R and η_3 is A or G;

(iv) a Chothia CDR-H1 sequence defined by the consensus sequence G-Y-T-F- Ω_5 -S-Y (SEQ ID NOS: 1-2 and 4-6), where Ω_5 is T, K, Q, F, or V;

- (v) a Chothia CDR-H1 sequence defined by the consensus sequence G-G-T-F- v_5 - v_6 -Y (SEQ ID NOS: 17-22 and 24), where v_5 is S, G, or E and v_6 is S, K, R, or S; or
- (vi) a Chothia CDR-H1 consensus sequence defined by the consensus sequence G-G-T-F- κ_5 - κ_6 - κ_7 (SEQ ID NOS: 7-16), where κ_5 is S, Q, P, or A; κ_6 is S, K, H, L, A, or W; and κ_7 is Y, L, T, N, or M,
- b) a VHCDR2 sequence comprising:
- (i) a Kabat CDR-H2 sequence defined by the consensus sequence ϵ_1 -I-N-P- ϵ_5 - ϵ_6 -G-S-T- ϵ_{10} -Y-A-Q-K-F-Q-G (SEQ ID NOS: 63-66 and 68), where ϵ_1 is K, S, R, or V; ϵ_5 is L, R, or S; ϵ_6 is G or V; and ϵ_{10} is S or W;
- (ii) a Kabat CDR-H2 sequence defined by the consensus sequence G-I- α_3 - α_4 - α_5 - α_6 -G-T-A-N-Y-A-Q-K-F-Q-G (SEQ ID NOS: 69-72), where α_3 is I or L or is absent; α_4 is P or is absent; and α_5 is I, G, or R; and α_6 is A, F, or G;
- (iii) a Kabat CDR-H2 sequence defined by the consensus sequence β_1 -I-I-P- β_5 - β_6 -G- β_8 -A-N-Y-A-Q-K-F-G-Q (SEQ ID NOS: 74 and 76-79), where β_1 is S or G; β_5 is I, E, S, or T; β_6 is F, I, or S; and β_8 is I or T;
- (iv) a Chothia CDR-H2 sequence defined by the consensus sequence N-P- ϵ_5 - ϵ_6 -G-S-T (SEQ ID NOS: 46-48), where ϵ_5 is L, R, or S and ϵ_6 is G or V;
- (v) a Chothia CDR-H2 sequence defined by the consensus sequence α_3 - α_4 - α_5 - α_6 -G-T-A (SEQ ID NOS: 51-54), where α_3 is I or L or is absent; α_4 is P or is absent; and α_5 is I, G, or R; and α_6 is A, F, or G; or
- (vi) a Chothia CDR-H2 sequence defined by the consensus sequence I-P- β_5 - β_6 -G- β_8 -A (SEQ ID NOS: 56-60), where β_5 is I, E, S, or T; β_6 is F, I, or S; and β_8 is I or T,
- c) a VHCDR3 sequence comprising:
- (i) a CDR-H3 sequence defined by the consensus sequence G-K-R-E-G-G-T-E-Y-L-R-Y₁₂ (SEQ ID NOS: 82-86), where Y₁₂ is H, K, S, N, or V;

- (ii) a CDR-H3 sequence defined by the consensus sequence E-S-G- Φ_4 -Y-R-D-H-R-L- Φ_{11} -V (SEQ ID NOS: 94-96), where Φ_4 is G or T and Φ_{11} is D or G; or
- (iii) a CDR-H3 sequence defined by the consensus sequence G-G-A-K-Y-A- Θ_7 - Θ_8 - Θ_9 -G-M-D-V (SEQ ID NOS: 87-93), where Θ_7 is S, V, G, or R; Θ_8 is T, Q, K, G, or R; and Θ_9 is Y, H, L, or W,
- d) a VLCDR1 sequence comprising:
- (i) a CDR-L1 sequence defined by the consensus sequence ϕ_1 -A-S- ϕ_4 - ϕ_5 -V- ϕ_7 - ϕ_8 - ϕ_9 -Y-L-A (SEQ ID NOS: 1101-114), where ϕ_1 is E, K, or R; ϕ_4 is Q or E; ϕ_5 is S or Y; ϕ_7 is S or A; ϕ_8 is S or Y; and ϕ_9 is D or S;
- (ii) a CDR-L1 sequence defined by the consensus sequence $\bar{\phi}_1$ -A-S-Q- $\bar{\phi}_5$ - $\bar{\phi}_6$ - $\bar{\phi}_7$ - $\bar{\phi}_8$ - $\bar{\phi}_9$ -L- $\bar{\phi}_{11}$ (SEQ ID NOS: 118 and 120-123), where $\bar{\phi}_1$ is Q or R; $\bar{\phi}_5$ is D or S; $\bar{\phi}_6$ is I or V; $\bar{\phi}_7$ is G or S; $\bar{\phi}_8$ is N, R, or S; $\bar{\phi}_9$ is N, Y, or W; and $\bar{\phi}_{11}$ is A or N; or
- (iii) a CDR-L1 sequence defined by the consensus sequence K-S-S- Γ_4 -S-V-L- Γ_8 -S- Γ_{10} -N-N-K-N-Y-L-A (SEQ ID NOS: 115-117), where Γ_4 is Q, R or K; Γ_8 is F or Y; and Γ_{10} is S or N,
- e) a VLCDR2 sequence comprising:
- (i) a CDR-L2 sequence defined by the consensus sequence ψ_1 -A-S- ψ_4 -R- ψ_6 - ψ_7 (SEQ ID NOS: 125-136), where ψ_1 is G or Y, ψ_4 is S or N; ψ_6 is A or H; and ψ_7 is T, Y, or N;
- (ii) a CDR-L2 sequence defined by the consensus sequence D-A-S- χ_4 -R-A-T (SEQ ID NOS: 138 and 139), where χ_4 is N or K; or
- (iii) a CDR-L2 sequence defined by the consensus sequence W-A-S-T-R- σ_6 -S (SEQ ID NOS: 131 and 133-134), where σ_6 is A, E, or Q, and
- f) a VLCDR3 sequence comprising:
- (i) a CDR-L3 sequence defined by the consensus sequence Q-Q-Y- π_4 - π_5 - π_6 - π_7 -T (SEQ ID NOS: 141-147), where π_4 is G, H, or Y; π_5 is S, N, F, G, or R; π_6 is S, Y, A, G, or R; and π_7 is P, I, or L;

(ii) a CDR-L3 sequence defined by consensus sequence Q-Q- λ_3 - λ_4 - λ_5 - λ_6 -P-T (SEQ ID NOS: 148-150), where λ_3 is R, F, H, S, L, D, Y, or V; λ_4 is S, V, T, G, L, Y, or N; λ_5 is N, L, F, K, or V; and λ_6 is W, F, Y, or L;

(iii) a CDR-L3 sequence defined by the consensus sequence Q-Q-Y- ρ_3 - ρ_4 -W-P-L-T (SEQ ID NOS: 151 and 152), where ρ_3 is N or L and ρ_4 is N or L; or

(iv) a CDR-L3 sequence defined by the consensus sequence Q-Q- ω_3 - ω_4 - ω_5 - ω_6 -P- ω_8 -T (SEQ ID NOS: 153-156), where ω_3 is Y or F; ω_4 is Y or W; ω_5 is S, L, T, or F; ω_6 is T, Y, or F; and ω_8 is L or P.

[0012] In some examples, the antibodies are used to treat a disease or condition. In some examples, the disease or condition is selected from a cancer, autoimmune disease, and infection.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] **FIG. 1** provides a table showing monovalent affinity of anti-huCD39 antibodies to recombinant human CD39 extracellular domain. The table provides binding kinetics of anti-CD39 antibodies interacting with soluble recombinant human CD39 (ENTDP1) extracellular domain (ECD) by biolayer interferometry (ForteBio Octet). Anti-CD39 antibodies were captured on an anti-human Fc sensor and exposed to recombinant human CD39 ECD at concentration ranging from 10-300 nanomolar. The kinetic data was globally fit with a simple 1:1 Langmuir binding model to yield on-rate (k_{on}) and off-rate (k_{off}) values. The equilibrium dissociation constants (K_D) were calculated from the k_{on} and k_{off} values.

[0014] **FIGS. 2 A-E** show inhibition of enzymatic catabolism of ATP and ADP to Pi by human CD39 extracellular domain (ECD). Recombinant human CD39 at a final concentration of either 10 nanomolar (A-D) or 5 nanomolar (E) was incubated with anti-CD39 IgGs at a final concentration of either 1 micromolar (A-D) or 0.25 micromolar (E) in 25 mM Tris, 5 mM CaCl₂, pH 7.5 at room temperature for 2 hours. ATP (500 micromolar) was added to the reaction and incubated at 37°C for 60 minutes. Residual ATP levels in the reaction were measured using the CellTiter-Glo assay. Data values are the average of two replicates.

[0015] **FIG. 2 F** shows antibodies that bind to CHO cells expressing human or cyno

WHAT IS CLAIMED IS:

1. An antigen binding protein that binds specifically to a human CD39 (hCD39) and is capable of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18 of the following:
 - a) inhibiting binding of CD39 to ATP;
 - b) inhibiting conversion by CD39 of ATP to ADP and/or ADP to AMP;
 - c) decreasing affinity of CD39 for ATP or ADP;
 - d) inhibiting or impeding release of ADP or AMP from CD39;
 - e) impeding or inhibiting CD39 processivity;
 - f) inhibiting platelet aggregation;
 - g) decreasing levels of phosphate, ADP, AMP, and/or adenosine and/or increasing levels of ATP;
 - h) increasing T effector cell function;
 - i) decreasing the number of regulatory T cells in tissues or in circulation;
 - j) suppressing regulatory T cells or regulatory T cell activity;
 - k) increasing B cell function;
 - l) increasing antigen presenting cell function;
 - m) inhibiting CD39 function on tumor cells;
 - n) inhibiting processing of at least one of phospho-antigen from phosphorylated isoprenoid, phosphorylated vitamin B metabolite, and/or phosphorylated riboflavin;
 - o) decreasing or preventing activation of phospho antigen specific T cells selected from MAIT cells and $\gamma\delta$ T cells;
 - p) inhibiting angiogenesis;
 - q) increasing proliferation of stimulated $CD4^+$ and $CD8^+$ T cells;
 - r) increasing stimulated PBMC Secretion of $INF-\gamma$, $TNF-\alpha$, IL-2 and/or IL-1 β .
2. The antigen binding protein of claim 1, wherein the antigen binding protein has 1, 2, 3, 4, 5, 6, or 7 of the following characteristics:
 - a) is a monoclonal antibody;
 - b) is a human antibody, a humanized antibody, or a chimeric antibody;

- c) is a bispecific antibody, a multi-specific antibody, a diabody, or a multivalent antibody;
 - d) is of the IgG1, IgG2, IgG3, IgG4, or IgM type;
 - e) is an antigen-binding antibody fragment;
 - f) is a Fab fragment, a Fab' fragment, a F(ab')₂ fragment, or an Fv fragment; and/or
 - g) is a single chain antibody, a single domain antibody, or a nanobody.
3. A pharmaceutical composition comprising an effective amount of an antibody which binds to hCD39 and has 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 of the following of characteristics:
- a) blocks or decreases hydrolysis of ATP to ADP and/or ADP to AMP as determined by at least one of: (i) a decreased phosphate release (Pi) , (ii) an increase in ATP levels, and (iii) a decrease of ADP, AMP, and/or adenosine levels,
 - b) increases T effector cell activity;
 - c) suppresses regulatory T cell or decreases a regulatory T cell activity;
 - d) decreases number of regulatory T cells in tissues or in circulation;
 - e) increases B cell function;
 - f) increases antigen presenting cell function;
 - g) inhibits CD39 function on tumor cells;
 - h) blocks or inhibits processing of at least one of phospho-antigen from a phosphorylated isoprenoid, phosphorylated vitamin B metabolite, and phosphorylated riboflavin;
 - i) decreases or prevents activation of phospho antigen specific T cells selected from MAIT cells and $\gamma\delta$ T cells;
 - k) inhibits angiogenesis;
 - l) decreases affinity for ATP and/or ADP;
 - m) inhibits release of ADP or AMP from CD39;
 - n) impedes or inhibits CD39 processivity;
 - o) inhibits platelet aggregation;
 - p) increases proliferation of stimulated CD4⁺ and CD8⁺ T cells;

r) increases stimulated PBMC Secretion of INF- γ , TNF- α , IL-2, and/or IL-1 β .

4. A pharmaceutical composition comprising the antigen-binding protein of claim 1 or claim 2.

5. The pharmaceutical composition of claim 4, further comprising an effective amount of at least one of the following

- a) an anti-PD-1 antibody,
- b) an anti-PD-L1 antibody,
- c) an anti-CD73 antibody,
- d) an anti-CD38 antibody,
- e) an anti-A2A receptor antibody,
- f) an anti-A2B receptor antibody,
- g) an anti-A2A/A2B dual receptor antibody, or any combination thereof,
or
- h) a small molecule inhibitor,

or a combination thereof.

6. The pharmaceutical composition of claim 4 or claim 5, further comprising one or both of

- a) an antibody to an inhibitory receptor or ligand and/or
- b) an antibody to a costimulatory receptor or ligand,

or a combination thereof.

7. The pharmaceutical composition of claim 6, wherein

(i) the inhibitory receptor or ligand is at least one of CTLA-4, PD-L2, LAG-3, Tim3, neuritin, BTLA, CECAM-1, CECAM-5, VISTA, LAIR1, CD160, 2B4, TGF-R, HHLA2, ILT2, ILT3, ILT4, HLA-G, HLA-C, and/or a Killer-cell immunoglobulin-like receptor (KIR) and/or

(ii) the costimulatory receptor or ligand is at least one of OX40, CD2, CD27, CDS, ICAM-1, LFA-1, ICOS (CD278), 4-1BB (CD137), GITR, CD28, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, Nkp80, CD160, B7-H3, and/or CD83.

8. The pharmaceutical composition of Claim 7, wherein the costimulatory receptor or ligand LFA-1 further comprises an LFA-1 β -chain CD18 and/or an LFA-1 α -chain CD11a.

9. The antigen binding protein of Claim 1, wherein the antigen binding protein has one or more of the following characteristics:

a) binds to a human CD39 polypeptide or a variant thereof with a KD of less than about 20 nM;

b) binds to a cyno CD39 polypeptide or a variant thereof with a KD of less than about 200 nM;

c) binds to a murine CD39 polypeptide or a variant thereof with a KD of less than about 200 nM; or

d) a combination of at least 2 of a), b), and c).

10. An antigen binding protein that competes or is capable of competing for binding to human CD39 with a reference antigen binding protein, wherein the reference antigen binding protein is the antigen binding protein of claim 1.

11. An antigen binding protein that binds to or is capable of competing for binding to human CD39 with a reference antigen binding protein, wherein the reference antigen binding protein binds to an epitope at positions 143-158 or 274-277 of SEQ ID NO: 249 on a human CD39 polypeptide, including, but not limited to, D150, E153, R154 or N99 alone or in combination with D150, E153, R154 or any combination thereof.
12. The antigen binding protein of claim 10 or claim 11, wherein the antigen binding protein and the reference antibody cross-compete or are capable of cross-competing for binding to a human CD39.
13. The antigen binding protein of claim 1, comprising a human heavy chain constant region or fragment or a variant thereof, wherein the constant region variant comprises up to 20 conservatively modified amino acid substitutions from any sequence set forth SEQ ID NOs: 179-218.
14. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL), VH and/or VL comprising 1, 2, 3, 4, 5, or 6 of:
- a) a VHCDR1 having the sequence set forth in SEQ ID NOs: 1-45,
 - b) a VHCDR2 having the sequence set forth in SEQ ID NOs: 46-81,
 - c) a VHCDR3 having the sequence set forth in SEQ ID NOs: 82-109,
 - d) a VLCDR1 having the sequence set forth in SEQ ID NOs: 110-124,
 - e) a VLCDR2 having the sequence set forth in SEQ ID NOs: 125-140, and
 - f) a VLCDR3 having the sequence set forth in SEQ ID NOs: 141-166.
15. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL),

the VH comprising,

- a) a VHCDR1 having a sequence set forth in SEQ ID NOs: 1-45,
- b) a VHCDR2 having a sequence set forth in SEQ ID NOs: 46-81, and
- c) a VHCDR3 having a sequence set forth in SEQ ID NOs: 82-109; and

the VL comprising,

- a) a VLCDR1 having a sequence set forth in SEQ ID NO: 110-124,
- b) a VLCDR2 having a sequence set forth in SEQ ID NO: 125-140, and
- c) a VLCDR3 having a sequence set forth in SEQ ID NO: 141-166.

- 16. An isolated nucleic acid encoding an antigen binding protein according to claim 1, claim 14, or claim 15.
- 17. An expression vector comprising the nucleic acid according to claim 16.
- 18. A prokaryotic or eukaryotic host cell comprising the vector of claim 17.
- 19. An oncolytic virus encoding the nucleic acid of either of claims 16 or 17.
- 20. A method for the production of a recombinant protein comprising the steps of expressing a nucleic acid according to claim 16 in a prokaryotic or eukaryotic host cell and recovering the protein from the cell or the cell culture supernatant.
- 21. Use of a pharmaceutical composition comprising the antigen binding protein of claim 1 or the pharmaceutical composition of claim 3 in the manufacture of a medicament for the treatment of a subject suffering from cancer, a chronic infection, or from an inflammatory disease.

22. The use of claim 21, wherein the cancer is a solid cancer.
23. The use of claim 21, wherein the cancer is a hematological cancer.
24. Use of a pharmaceutical composition comprising the antigen binding protein of claim 1 in the manufacture of a medicament for modulating immune system function in a subject in need thereof, wherein a population of immune cells of the subject is to be contacted with the pharmaceutical composition, under conditions such that the immune system is modulated.
25. Use of a pharmaceutical composition comprising an antigen binding protein in the manufacture of a medicament for inducing or enhancing an immune response in a subject in need thereof, wherein the immune response is generated against a tumor antigen.
26. The use of Claim 24 or Claim 25, wherein the subject is a human subject.
27. The use of claim 25, wherein the antigen binding protein comprises a bispecific antibody or a complexing antigen binding protein.
28. The use of claim 27, wherein the antigen binding protein, the bispecific antibody, or the complexing antigen binding protein is to be administered in an amount sufficient to achieve 1, 2, 3, 4, 5, 6, or 7 of the following in the subject:
- a) reduction of CD39 ATPase activity in a target cell population;

- b) reduction of regulatory T cells suppression of activity of effector T cells;
- c) reduction of levels of regulatory T cells;
- d) activation of effector T cells;
- e) induction or enhancement of effector T cell proliferation;
- f) inhibition of tumor growth; and/or
- g) induction of tumor regression.

29. The use of claim 28, wherein the target cell population comprises T cells, B cells, monocytes, macrophages, dendritic cells, myeloid-derived suppressor cells, and/or tumor cells.

30. The use of claim 25, wherein the use further comprises one or more of the following

- a) chemotherapy to be administered;
- b) radiation therapy to be administered; and/or
- c) one or more additional therapeutic agents to be administered.

31. The use of claim 30, wherein the one or more additional therapeutic agents comprise one or more immunostimulatory agents.

32. The use of claim 31, wherein the one or more immunostimulatory agents comprise an antagonist to an inhibitory receptor of an immune cell.

33. The use of claim 32, wherein the inhibitory receptor is at least one of CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, Tim3, neuritin, BTLA, CECAM-1, CECAM-5,

VISTA, LAIR1, CD160, 2B4, TGF-R, and/or a Killer-cell immunoglobulin-like receptor (KIR).

34. The use of claim 31, wherein the one or more immunostimulatory agents comprise an agonist of a co-stimulatory receptor of an immune cell.

35. The use of claim 34, wherein the co-stimulatory receptor is OX40, CD2, CD27, CDS, ICAM-1, LFA-1, ICOS (CD278), 4-1BB (CD137), GITR, CD28, CD30, CD40, BAFRR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, or a CD83 ligand.

36. The use of claim 35, wherein the costimulatory receptor or ligand LFA-1 further comprises an LFA-1 β -chains CD18 and/or an LFA-1 α -chain CD11a.

37. The use of claim 31, wherein the one or more immunostimulatory agents comprise a cytokine.

38. The use of claim 37, wherein the cytokine is at least one of IL-2, IL-5, IL-7, IL-12, IL-15, and/or IL-21.

39. The use of claim 31, wherein the one or more immunostimulatory agents comprise an oncolytic virus.

40. The use of claim 39, wherein the oncolytic virus is a Herpes simplex virus, a Vesicular stomatitis virus, an adenovirus, a Newcastle disease virus, a vaccinia virus, or a maraba virus.

41. The use of claim 31, wherein the one or more immunostimulatory agents comprise a chimeric antigen engineered T cell.

42. The use of claim 31, wherein the one or more immunostimulatory agents comprise a bi- or multispecific T cell directed antibody.

43. The use of claim 25, wherein the one or more additional therapeutic agents comprise at least one trap for an immune suppressive agent.

44. The use of Claim 43, wherein the at least one trap for an immune suppressive agent comprises at least one of an anti-TGF-beta antibody, a TGFb receptor trap, an anti-IL-10 antibody and/or anti-IL-10 receptor trap, and/or an anti-IL-35 antibody trap and/or an anti-IL-35 receptor trap.

45. The use of any one of any of claims 3-44, wherein administration of the pharmaceutical composition results in induction or enhancement of proliferation of a T-effector cell, or modulation of I-kappaB and/or NF- κB in the T cell, or modulation of CD39 activity in the T cell, or T cell receptor induced signaling in a T-effector cell, or a combination thereof.

46. A method of screening for a test compound comprising an antigen binding protein of claim 1 capable of inhibiting an activity of CD39, comprising the steps of:

contacting a test sample containing CD39 with a test compound;

comparing the activity of the test sample to a control sample;

whereby a decrease in the activity of CD39 in the test sample compared to the control sample identifies the compound as one that inhibits the activity of CD39.

47. The method of Claim 46, wherein the control sample comprises a sample not contacted with a test compound.

48. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL),

VH comprising at least one of:

a) a VHCDR1 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 1-45,

b) a VHCDR2 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 46-81, and

c) a VHCDR3 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 82-109; and

VL comprising at least one of:

a) a VLCDR1 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 110-124,

b) a VLCDR2 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 125-140, and

c) a VLCDR3 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs 141-166.

49. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL),

VH comprising at least one of:

a) a VHCDR1 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 1-45,

b) a VHCDR2 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 46-81, and

c) a VHCDR3 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 82-109; and

VL comprising at least one of:

a) a VLCDR1 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 110-124,

b) a VLCDR2 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 125-140, and

c) a VLCDR3 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 141-166.

50. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain and a light chain, the heavy chain comprising one or more molecules having a sequence consisting of one of SEQ ID NO: 255, SEQ ID NO: 257, SEQ ID NO: 259, SEQ ID NO: 261, SEQ ID NO: 263, SEQ ID NO: 265, SEQ ID NO: 267, SEQ ID NO: 269, SEQ ID NO: 271, SEQ ID NO: 273, SEQ ID NO: 275, SEQ ID NO: 277, SEQ ID NO: 279, SEQ ID NO: 281, SEQ ID NO: 283, SEQ ID NO: 285, SEQ ID NO: 287, SEQ ID NO: 289, SEQ ID NO: 291, SEQ ID NO: 293, or SEQ ID NO: 295 and the light chain comprising one or more molecules having a sequence consisting of one of SEQ ID NO: 256, SEQ ID NO: 258, SEQ ID NO: 260, SEQ ID NO: 262, SEQ ID NO: 264, SEQ ID NO: 266, SEQ ID NO: 268, SEQ ID NO: 270, SEQ ID NO: 272, SEQ ID NO: 274, SEQ ID NO: 276, SEQ ID NO: 278, SEQ ID NO: 280, SEQ ID NO: 282, SEQ ID NO: 284, SEQ ID NO: 286, SEQ ID NO: 288, SEQ ID NO: 290, SEQ ID NO: 292, SEQ ID NO: 294, or SEQ ID NO: 296.

51. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain and a light chain,

- a) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 255 and the light chain comprising one or more, each molecule having a sequence consisting of SEQ ID NO: 256;
- b) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 257 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 258;
- c) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 259 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 260;
- d) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 261 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 262;
- e) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 263 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 264;
- f) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 265 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 266;
- g) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 267 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 268;
- h) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 269 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 270;
- i) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 271 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 272;

j) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 273 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 274;

k) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 275 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 276;

l) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 277 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 278

m) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 279 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 280;

n) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 281 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 282;

o) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 283 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 284;

p) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 285 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 286;

q) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 287 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 288;

r) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 289 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 290;

s) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 291 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 292;

t) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 293 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 294; or

u) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 295 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 296.

52. An isolated nucleic acid encoding an antigen binding protein according to any one of claims 48-51.

53. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL), VH and/or VL comprising 1, 2, 3, 4, 5, or 6 of:

a) a VHCDR1 sequence comprising:

(i) a Kabat CDRH1 sequence defined by the consensus sequence S-Y- Δ_3 -M- Δ_5 (SEQ ID NOS: 25-29 and 44-45), where Δ_3 is E, F, Q, or Y and Δ_5 is H or Y;

(ii) a Kabat CDR-H1 sequence defined by the consensus sequence θ_1 - θ_2 - θ_3 -I-S (SEQ ID NOS: 30-37), where θ_1 is A, H, K, L, S, or W; θ_2 is L, M, N, or T; and θ_3 is A or P;

(iii) a Kabat CDR-H1 sequence defined by the consensus sequence η_1 -Y- η_3 -I-S (SEQ ID NOS: 38-41), where η_1 is S, K, N, or R and η_3 is A or G;

(iv) a Chothia CDR-H1 sequence defined by the consensus sequence G-Y-T-F- Ω_5 -S-Y (SEQ ID NOS: 1-2 and 4-6), where Ω_5 is T, K, Q, F, or V;

- (v) a Chothia CDR-H1 sequence defined by the consensus sequence G-G-T-F- v_5 - v_6 -Y (SEQ ID NOS: 17-22 and 24), where v_5 is S, G, or E and v_6 is S, K, R, or S; or
 - (vi) a Chothia CDR-H1 consensus sequence defined by the consensus sequence G-G-T-F- κ_5 - κ_6 - κ_7 (SEQ ID NOS: 7-16), where κ_5 is S, Q, P, or A; κ_6 is S, K, H, L, A, or W; and κ_7 is Y, L, T, N, or M,
- b) a VHCDR2 sequence comprising:
- (i) a Kabat CDR-H2 sequence defined by the consensus sequence ϵ_1 -I-N-P- ϵ_5 - ϵ_6 -G-S-T- ϵ_{10} -Y-A-Q-K-F-Q-G (SEQ ID NOS: 63-66 and 68), where ϵ_1 is K, S, R, or V; ϵ_5 is L, R, or S; ϵ_6 is G or V; and ϵ_{10} is S or W;
 - (ii) a Kabat CDR-H2 sequence defined by the consensus sequence G-I- α_3 - α_4 - α_5 - α_6 -G-T-A-N-Y-A-Q-K-F-Q-G (SEQ ID NOS: 69-72), where α_3 is I or L or is absent; α_4 is P or is absent; and α_5 is I, G, or R; and α_6 is A, F, or G;
 - (iii) a Kabat CDR-H2 sequence defined by the consensus sequence β_1 -I-I-P- β_5 - β_6 -G- β_8 -A-N-Y-A-Q-K-F-G-Q (SEQ ID NOS: 74 and 76-79), where β_1 is S or G; β_5 is I, E, S, or T; β_6 is F, I, or S; and β_8 is I or T;
 - (iv) a Chothia CDR-H2 sequence defined by the consensus sequence N-P- ϵ_5 - ϵ_6 -G-S-T (SEQ ID NOS: 46-48), where ϵ_5 is L, R, or S and ϵ_6 is G or V;
 - (v) a Chothia CDR-H2 sequence defined by the consensus sequence α_3 - α_4 - α_5 - α_6 -G-T-A (SEQ ID NOS: 51-54), where α_3 is I or L or is absent; α_4 is P or is absent; and α_5 is I, G, or R; and α_6 is A, F, or G; or
 - (vi) a Chothia CDR-H2 sequence defined by the consensus sequence I-P- β_5 - β_6 -G- β_8 -A (SEQ ID NOS: 56-60), where β_5 is I, E, S, or T; β_6 is F, I, or S; and β_8 is I or T,
- c) a VHCDR3 sequence comprising:
- (i) a CDR-H3 sequence defined by the consensus sequence G-K-R-E-G-G-T-E-Y-L-R- Y_{12} (SEQ ID NOS: 82-86), where Y_{12} is H, K, S, N, or V;
 - (ii) a CDR-H3 sequence defined by the consensus sequence E-S-G- Φ_4 -Y-R-D-H-R-L- Φ_{11} -V (SEQ ID NOS: 94-96), where Φ_4 is G or T and Φ_{11} is D or

G; or

(iii) a CDR-H3 sequence defined by the consensus sequence G-G-A-K-Y-A- $\mathfrak{D}_7$ - $\mathfrak{D}_8$ - $\mathfrak{D}_9$ -G-M-D-V (SEQ ID NOS: 87-93), where $\mathfrak{D}_7$ is S, V, G, or R; $\mathfrak{D}_8$ is T, Q, K, G, or R; and $\mathfrak{D}_9$ is Y, H, L, or W,

d) a VLCDR1 sequence comprising:

(i) a CDR-L1 sequence defined by the consensus sequence ϕ_1 -A-S- ϕ_4 - ϕ_5 -V- ϕ_7 - ϕ_8 - ϕ_9 -Y-L-A (SEQ ID NOS: 1101-114), where ϕ_1 is E, K, or R; ϕ_4 is Q or E; ϕ_5 is S or Y; ϕ_7 is S or A; ϕ_8 is S or Y; and ϕ_9 is D or S;

(ii) a CDR-L1 sequence defined by the consensus sequence $\mathfrak{O}_1$ -A-S-Q- $\mathfrak{O}_5$ - $\mathfrak{O}_6$ - $\mathfrak{O}_7$ - $\mathfrak{O}_8$ - $\mathfrak{O}_9$ -L- $\mathfrak{O}_{11}$ (SEQ ID NOS: 118 and 120-123), where $\mathfrak{O}_1$ is Q or R; $\mathfrak{O}_5$ is D or S; $\mathfrak{O}_6$ is I or V; $\mathfrak{O}_7$ is G or S; $\mathfrak{O}_8$ is N, R, or S; $\mathfrak{O}_9$ is N, Y, or W; and $\mathfrak{O}_{11}$ is A or N; or

(iii) a CDR-L1 sequence defined by the consensus sequence K-S-S- Γ_4 -S-V-L- Γ_8 -S- Γ_{10} -N-N-K-N-Y-L-A (SEQ ID NOS: 115-117), where Γ_4 is Q, R or K; Γ_8 is F or Y; and Γ_{10} is S or N,

e) a VLCDR2 sequence comprising:

(i) a CDR-L2 sequence defined by the consensus sequence ψ_1 -A-S- ψ_4 -R- ψ_6 - ψ_7 (SEQ ID NOS: 125-136), where ψ_1 is G or Y, ψ_4 is S or N; ψ_6 is A or H; and ψ_7 is T, Y, or N;

(ii) a CDR-L2 sequence defined by the consensus sequence D-A-S- χ_4 -R-A-T (SEQ ID NOS: 138 and 139), where χ_4 is N or K; or

(iii) a CDR-L2 sequence defined by the consensus sequence W-A-S-T-R- σ_6 -S (SEQ ID NOS: 131 and 133-134), where σ_6 is A, E, or Q, and

f) a VLCDR3 sequence comprising:

(i) a CDR-L3 sequence defined by the consensus sequence Q-Q-Y- π_4 - π_5 - π_6 - π_7 -T (SEQ ID NOS: 141-147), where π_4 is G, H, or Y; π_5 is S, N, F, G, or R; π_6 is S, Y, A, G, or R; and π_7 is P, I, or L;

(ii) a CDR-L3 sequence defined by consensus sequence Q-Q- λ_3 - λ_4 - λ_5 - λ_6 -P-T (SEQ ID NOS: 148-150), where λ_3 is R, F, H, S, L, D, Y, or V; λ_4 is S, V, T,

G, L, Y, or N; λ_5 is N, L, F, K, or V; and λ_6 is W, F, Y, or L;

(iii) a CDR-L3 sequence defined by the consensus sequence Q-Q-Y- ρ_3 - ρ_4 -W-P-L-T (SEQ ID NOS: 151 and 152), where ρ_3 is N or L and ρ_4 is N or L; or

(iv) a CDR-L3 sequence defined by the consensus sequence Q-Q- ω_3 - ω_4 - ω_5 - ω_6 -P- ω_8 -T (SEQ ID NOS: 153-156), where ω_3 is Y or F; ω_4 is Y or W; ω_5 is S, L, T, or F; ω_6 is T, Y, or F; and ω_8 is L or P.