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.

[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.

[0009a] In one aspect, the present disclosure provides 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 NO: 2 or SEQ ID NO: 26,

b) a VHCDR2 having a sequence set forth in SEQ ID NO: 47 or SEQ ID NO: 64, and

c) a VHCDR3 having a sequence set forth in SEQ ID NO: 83; and

the VL comprising,

a) a VLCDR1 having a sequence set forth in SEQ ID NO: 111,

b) a VLCDR2 having a sequence set forth in SEQ ID NO: 126, and

c) a VLCDR3 having a sequence set forth in SEQ ID NO: 142.

[0009b] In another aspect, the present disclosure provides an isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain and a light chain, the heavy chain comprising a molecule having a sequence consisting of SEQ ID NO: 255 and the light chain comprising a molecule having a sequence consisting of SEQ ID NO: 256.

[0009c] In another aspect, the present disclosure provides an isolated nucleic acid encoding the isolated antibody molecule as described herein.

[0009d] In another aspect, the present disclosure provides an expression vector comprising the nucleic acid as described herein.

[0009e] In another aspect, the present disclosure provides a prokaryotic or eukaryotic host cell comprising the vector as described herein.

[0009f] In another aspect, the present disclosure provides 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.

[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.

[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.

[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 (kon) and off-rate (koff) values. The equilibrium dissociation constants (K_D) were calculated from the kon and koff 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 $CaCl_2$, 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