

[0005] As such, there is a serious and long-felt need for the development of cancer treatments with increased efficacy.

SUMMARY

[0006] In one aspect, the present disclosure refers to the use of an antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating or preventing cancer in a subject in need thereof, wherein the antibody or antigen-binding fragment thereof comprises: (a) a heavy chain variable region comprising: GYTFTSYDIN (SEQ ID NO: 24), WIYPGDGSTNYNEKFKG (SEQ ID NO: 25), and/or ARRGLRYYFDY (SEQ ID NO: 26); and a light chain variable region comprising: RASQDIRNYLN (SEQ ID NO: 32), YTSRLHS (SEQ ID NO: 33), and QQVNTLPWT (SEQ ID NO: 34); or (b) a heavy chain variable region comprising: GYSITSDYAWN (SEQ ID NO: 56), YITYSGSTSYNPSLKS (SEQ ID NO: 57), and/or ARSGYRYDDAMDY (SEQ ID NO: 58); and a light chain variable region comprising: KSSQSLLSSNNQKNYLA (SEQ ID NO: 64), FASTRES (SEQ ID NO: 65), and QQHYRTPLT (SEQ ID NO: 66). In another example, there is described use of an agent that inhibits TMIGD2 expression, activity, or both in the manufacture of a medicament for treating or preventing cancer in a subject in need thereof. Examples of the present disclosure describe methods of treating or preventing cancer in a subject in need thereof, the methods comprising administering to the subject an effective amount of an agent that inhibits TMIGD2 expression, activity, or both.

[0007] In some examples, the agent is selected from the group consisting of an antibody agent, a mRNA targeting agent, a small molecule agent, and a gene editing agent.

[0008] In some examples, the mRNA targeting agent is an antisense agent or an RNAi agent. In some examples, the antisense agent comprises or consists of a nucleic acid sequence complementary to an mRNA encoded by SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6, or the antisense agent comprises or consists of a nucleic acid sequence with about 80%, 90%, 95%, 96%, 97%, 98%, 99%, 99.5%, or higher identity to an mRNA encoded by SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6.

[0009] In some examples, the RNAi agent is selected from the group consisting of a short interfering RNA (siRNA), a double-stranded RNA (dsRNA), a micro-RNA (miRNA), a piwi-RNA (piRNA), a small nucleolar RNA (snoRNA), a tRNA-derived small RNAs (tsRNAs), a small regulatory RNA (srRNA), and a short hairpin RNA (shRNA) molecule. In some examples, the RNAi agent comprises or consists of a nucleic acid sequence complementary to an mRNA encoded by SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6, or the RNAi agent comprises or consists of a nucleic acid sequence with about 80%, 90%, 95%, 96%, 97%, 98%, 99%, 99.5% or higher identity to an mRNA encoded by SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6.

[0010] In some examples, the gene editing agent is selected from the group consisting of a TALEN-based agent, ZFN-based agent, and a CRISPR-based agent. In some examples, the gene editing agent knocks out or knocks down expression of TMIGD2.

CLAIMS

1. Use of an antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating or preventing cancer in a subject in need thereof, wherein the antibody or antigen-binding fragment thereof comprises:

- (a) a heavy chain variable region comprising:
GYTFTSYDIN (SEQ ID NO: 24),
WIYPGDGSTNYNEKFKG (SEQ ID NO: 25), and/or
ARRGLRYYFDY (SEQ ID NO: 26); and
a light chain variable region comprising:
RASQDIRNYLN (SEQ ID NO: 32),
YTSRLHS (SEQ ID NO: 33), and
QQVNTLPWT (SEQ ID NO: 34); or
- (b) a heavy chain variable region comprising:
GYSITSDYAWN (SEQ ID NO: 56),
YITYSGSTSYNPSLKS (SEQ ID NO: 57), and/or
ARSGYRYDDAMDY (SEQ ID NO: 58); and
a light chain variable region comprising:
KSSQSLLSSNNQKNYLA (SEQ ID NO: 64),
FASTRES (SEQ ID NO: 65), and
QQHYRTPLT (SEQ ID NO: 66).

2. The use of claim 1, wherein the antibody or antigen-binding fragment thereof specifically binds an epitope in the extracellular domain of TMIGD2.

3. The use of claim 2, wherein the extracellular domain of TMIGD2 comprises residues 1-150 of SEQ ID NO:1 or SEQ ID NO:2, or residues 1-30 of SEQ ID NO:3.

4. The use of any one of claims 1-3, wherein the antibody or antigen-binding fragment thereof comprises:

(a) a heavy chain variable region comprising SEQ ID NO: 23, or an amino acid sequence with at least 85% or higher identity to SEQ ID NO: 23; and/or a light chain variable region comprising SEQ ID NO: 31, or an amino acid sequence with at least 85% or higher identity to SEQ ID NO: 31; or

(b) a heavy chain variable region comprising SEQ ID NO: 55, or an amino acid sequence with at least 85% or higher identity to SEQ ID NO: 55; and/or a light chain variable region comprising SEQ ID NO: 63, or an amino acid sequence with at least 85% or higher identity to SEQ ID NO: 63.

5. The use of any one of claims 1-4, wherein the cancer is a human hematologic malignancy.

6. The use of claim 5, wherein the human hematologic malignancy is selected from myeloid neoplasm, acute myeloid leukemia (AML), AML with recurrent genetic abnormalities, AML with myelodysplasia-related changes, therapy-related AML, acute leukemias of ambiguous lineage, myeloproliferative neoplasm, essential thrombocythemia, polycythemia vera, myelofibrosis (MF), primary myelofibrosis, systemic mastocytosis, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, chronic myeloid leukemia, chronic neutrophilic leukemia, chronic eosinophilic leukemia, myelodysplastic syndromes (MDS), refractory anemia with ringed sideroblasts, refractory cytopenia with multilineage dysplasia, refractory anemia with excess blasts (type 1), refractory anemia with excess blasts (type 2), MDS with isolated del (5q), unclassifiable MDS, myeloproliferative/myelodysplastic syndromes, chronic myelomonocytic leukemia, atypical chronic myeloid leukemia, juvenile myelomonocytic leukemia, unclassifiable myeloproliferative/myelodysplastic syndromes, lymphoid neoplasms, precursor lymphoid neoplasms, B lymphoblastic leukemia, B lymphoblastic lymphoma, T lymphoblastic leukemia, T lymphoblastic lymphoma, mature B-cell neoplasms, diffuse large B-cell lymphoma, primary central nervous system lymphoma, primary mediastinal B-cell lymphoma, Burkitt lymphoma/leukemia, follicular lymphoma, chronic lymphocytic leukemia, small lymphocytic lymphoma, B-cell prolymphocytic leukemia, lymphoplasmacytic

lymphoma, Waldenström macroglobulinemia, mantle cell lymphoma, marginal zone lymphomas, post-transplant lymphoproliferative disorders, HIV-associated lymphomas, primary effusion lymphoma, intravascular large B-cell lymphoma, primary cutaneous B-cell lymphoma, hairy cell leukemia, multiple myeloma, monoclonal gammopathy of unknown significance (MGUS), smoldering multiple myeloma, or solitary plasmacytomas (solitary bone and extramedullary).

7. The use of claim 1, wherein the antibody or antigen-binding fragment thereof is a chimeric antibody, humanized antibody, or murine antibody.