

associated carbohydrate antigens have contributed to various aspects of cancer development and progression, including proliferation, invasion, angiogenesis and metastasis (Fuster, Nat Rev Cancer, 5:526-42 (2005) and Dube, Nat Rev Drug Discovery, 4:477-88 (2005)).

[0006] One type of glycosylation are sialic acids and they are typically found to be terminating branches of N-glycans, O-glycans and glycosphingolipids. Within sialic acids, a variety of diversity are created through alpha linkages between the nine-carbon backbone and secondary diversity through modifications at these carbon positions. Examples of sialylated glycosylation found include sLeA, sLeC and sialyl Lewis X (glycan structure of each is found in Table 1).

[0007] These glycans are all examples of terminally sialylated glycans. While sLeC is the non-fucosylated precursor of sLeA, sLeX is a stereo isomer of sLeA. In general, sLeC is typically not found on normal human tissue, but found on murine tissues. Thus, antibodies that bind to both sLeA and sLeC would be useful for drug development especially for use in in vivo murine models of disease.

[0008] In general, antibodies that are suited for development as a pharmaceutical agent to treat disease and/or disorders have high specificity, selectivity and affinity. Thus, anti-glycan antibodies are typically not suited for development as pharmaceutical agents partially due to carbohydrate antigens have limited immunogenicity and the observed affinities of anti-carbohydrate antibodies are typically lower by factors of 10^3 - 10^5 than antibodies specific for protein or peptide antigens (Ghassemi, Glycobiology, 25(9): 920-952 (Sept 2015)). The overall low binding of carbohydrates is usually accompanied by relative fast k_{on} and k_{off} rates, which results in an overall lower K_D for anti-glycan antibodies.

[0009] The present invention addresses the need for an alternative antibody therapy that targets glycan epitopes for patients having disorders affecting the digestive system, including inflammatory bowel disease and cancers of the digestive system.

SUMMARY-OF-THE-INVENTION

[0010] The present ~~invention~~disclosure provides for antibodies or antigen binding portions thereof, comprising a variable region that bind to a carbohydrate antigen or a fragment thereof.

[0011] In one aspect, ~~provided herein is the present disclosure refers to~~ an antibody, or an antigen-binding portion thereof, that binds to sialyl Lewis A (sLeA) and sialyl Lewis C (sLeC), wherein the binding affinity of such antibody or antigen-binding portion to sLeA is of K_D of 60 μ M or less and the binding affinity to sLeC is of K_D 100 μ M or less. In some ~~embodiment~~examples, the antibody or

antigen-binding portion does not bind to sialyl Lewis X (sLeX). In some embodimentexamples, the antibody or antigen-binding portion is a humanized antibody or humanized antigen-binding portion.

[0012] In another aspectexample, provided herein is an antibody, or an antigen-binding portion thereof, that binds to sLeA and sLeC, comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a sequence having a 90-100% sequence identity to SEQ ID NO:1, SEQ ID NO: 2, or SEQ ID NO:3, and the light chain variable region comprises a sequence having a 90-100% sequence identity to SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO:7. In some embodimentexamples, the antibody or antigen-binding portion does not bind to sLeX. In some embodimentexamples, the heavy chain variable region comprises a CDR-H1 comprising the sequence of SEQ ID NO:12, a CDR-H2 comprising the sequence of SEQ ID NO:13, and a CDR-H3 comprising the sequence of SEQ ID NO:14; and the light chain variable region comprises a CDR-L1 comprising a sequence selected from the group consisting of SEQ ID NOS:15-17, a CDR-L2 comprising the sequence of SEQ ID NO:18, and a CDR-L3 comprising the sequence of SEQ ID NO:19. In some embodimentexamples, the heavy chain variable region comprises the sequence of SEQ ID NO:3, and the light chain variable region comprises a sequence selected from the group consisting of SEQ ID Nos:5-8. In some embodimentexamples, the heavy chain variable region comprises the sequence of SEQ ID NO:3, and the light chain variable region comprises the sequence of SEQ ID No:8. In some embodimentexamples, the heavy chain variable region comprises the sequence of SEQ ID NO:4, and the light chain variable region comprises the sequence of SEQ ID NO:9 or 10.

[0013] In another aspectexample, provided herein is an antibody, or an antigen binding portion thereof, that binds to sLeA and sLeC, comprising a heavy chain variable region, wherein the heavy chain variable region comprises a sequence having a 90-100% sequence identity to SEQ ID NO: 3. In some embodimentexamples, the antibody or antigen-binding portion comprises a light chain variable region, wherein the light chain variable region comprises a sequence having a 90-100% sequence identity to a sequence selected from the group consisting of SEQ ID Nos:5-11.

[0013a] In one aspect, the present disclosure refers to an antibody, or an antigen-binding portion thereof, that binds to sLeA and sLeC, comprising a heavy chain variable region and a light chain variable region, wherein: the heavy chain variable region comprises a sequence having a 90-100% sequence identity to SEQ ID NO:1, SEQ ID NO: 2, SEQ ID NO:3, or SEQ ID NO: 4; and the light chain variable region comprises a sequence having a 90-100% sequence identity to SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO:8, SEQ ID NO: 9, SEQ ID NO: 10, or SEQ ID NO: 11.

[0013b] In one aspect, the present disclosure refers to an antibody, or an antigen-binding portion thereof, that binds to sLeA and sLeC, comprising a heavy chain variable region, wherein the heavy chain variable region comprises a sequence having a 90-100% sequence identity to SEQ ID NO: 3.

[0014] In another aspectexample, provided herein is an antibody, or an antigen binding portion thereof, that binds to sLeA and sLeC, comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a CDR-H1 comprising the sequence of SEQ ID NO:12, a CDR-H2 comprising the sequence of SEQ ID NO:13, and a CDR-H3 comprising the sequence of SEQ ID NO:14; and wherein the light

chain variable region comprises a CDR-L1 comprising a sequence selected from the group consisting of SEQ ID NOs:15-17, a CDR-L2 comprising the sequence of SEQ ID NO:18, and a CDR-L3 comprising the sequence of SEQ ID NO:19. In some embodimentexamples, the antibody or antigen-binding portion comprises a heavy chain variable region and a light chain variable region of a single antibody shown in Table 6.

[0014a] In one aspect, the present disclosure refers to an antibody, or an antigen-binding portion thereof, that binds to sLeA and sLeC, comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a CDR-H1 comprising the sequence of SEQ ID NO:12, a CDR-H2 comprising the sequence of SEQ ID NO:13, and a CDR-H3 comprising the sequence of SEQ ID NO:14; and wherein the light chain variable region comprises a CDR-L1 comprising a sequence selected from the group consisting of SEQ ID NOs:15-17, a CDR-L2 comprising the sequence of SEQ ID NO:18, and a CDR-L3 comprising the sequence of SEQ ID NO:19.

[0015] In another aspectexample, provided herein is one or more polynucleotide(s) encoding the antibody or antigen-binding portion thereof according to any one of the above embodimentexamples. In another aspectexample, provided herein is a vector comprising the one or more polynucleotide(s) according to any one of the above embodimentexamples. In another aspectexample, provided herein is a host cell comprising the one or more polynucleotide(s) according to any one of the above embodimentexamples or the vector according to any one of the above embodimentexamples. In another aspectexample, provided herein is a method of producing an antibody, the method comprising culturing the host cell according to any one of the above embodimentexamples such that the antibody is produced. In some embodimentexamples, the method further comprises recovering the antibody from the host cell. In another aspectexample, provided herein is a pharmaceutical composition comprising the antibody or antigen-binding portion thereof according to any one of the above embodimentexamples and a pharmaceutically acceptable carrier.

[0015a] In one aspect, the present disclosure refers to a polynucleotide encoding the antibody or antigen-binding portion thereof disclosed herein.

[0015b] In one aspect, the present disclosure refers to a vector comprising the polynucleotide disclosed herein.

[0015c] In one aspect, the present disclosure refers to a host cell comprising the polynucleotide disclosed herein or the vector disclosed herein.

[0015d] In one aspect, the present disclosure refers to a method of producing an antibody, the method comprising culturing the host cell disclosed herein such that the antibody is produced, optionally wherein the method further comprises recovering the antibody from the host cell.

[0015e] In one aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody or antigen-binding portion thereof disclosed herein and a pharmaceutically acceptable carrier.

[0016] In another aspectexample, provided herein is a method of treating or ameliorating a symptom of a digestive disease or disorder wherein said method comprises administering to an individual with said digestive disease or disorder an effective amount of an antibody, antigen-binding portion, or pharmaceutical composition described herein. In some embodimentexamples, the digestive disease or disorder is selected from inflammatory bowel disease, irritable bowel syndrome, pancreatic cancer, or colon cancer. In some embodimentexamples, the digestive disease or disorder is inflammatory bowel disease. In some embodimentexamples, the inflammatory bowel disease is Crohn's Disease or ulcerative colitis. In some embodimentexamples, the individual is a human.

[0016a] In one aspect, the present disclosure refers to use of an effective amount of the antibody or antigen-binding portion disclosed herein or the pharmaceutical composition disclosed herein in the manufacture of a medicament for treating or ameliorating a symptom of a digestive disease or disorder in an individual with said digestive disease or disorder, optionally wherein the individual is a human.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] FIG. 1A are microscopic images from in vitro scratch wound assays using T84 cells at time 0 and 24 hour after treatment with either human IgG control or antibody clone 4772. **FIG. 1B** illustrates the difference in wound healing activity observed after 24 hours of treatment.

CLAIMS

What is claimed is:

1. An antibody, or an antigen-binding portion thereof, that binds to sialyl Lewis A (sLeA) and sialyl Lewis C (sLeC), wherein the binding affinity of such antibody or antigen-binding portion to sLeA is of K_D of 60 μ M or less and the binding affinity to sLeC is of K_D 100 μ M or less.
2. The antibody or antigen-binding portion of claim 1, wherein the antibody or antigen-binding portion does not bind to sialyl Lewis X (sLeX).
3. The antibody or antigen-binding portion of claim 1 or claim 2, wherein the antibody or antigen-binding portion is a humanized antibody or humanized antigen-binding portion.
4. An antibody, or an antigen-binding portion thereof, that binds to sLeA and sLeC, comprising a heavy chain variable region and a light chain variable region, wherein:
 - the heavy chain variable region comprises a sequence having a 90-100% sequence identity to SEQ ID NO:1, SEQ ID NO: 2, SEQ ID NO:3, or SEQ ID NO: 4; and
 - the light chain variable region comprises a sequence having a 90-100% sequence identity to SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO:8, SEQ ID NO: 9, SEQ ID NO: 10, or SEQ ID NO: 11.
5. The antibody or antigen-binding portion of claim 4, wherein the antibody or antigen-binding portion does not bind to sLeX.
6. The antibody or antigen-binding portion of claim 4 or claim 5, wherein the heavy chain variable region comprises a CDR-H1 comprising the sequence of SEQ ID NO:12, a CDR-H2 comprising the sequence of SEQ ID NO:13, and a CDR-H3 comprising the sequence of SEQ ID NO:14; and wherein the light chain variable region comprises a CDR-L1 comprising a sequence selected from the group consisting of SEQ ID NOs:15-17, a CDR-L2 comprising the sequence of SEQ ID NO:18, and a CDR-L3 comprising the sequence of SEQ ID NO:19.

7. The antibody or antigen-binding portion of claim 4, wherein the heavy chain variable region comprises the sequence of SEQ ID NO:3, and wherein the light chain variable region comprises a sequence selected from the group consisting of SEQ ID Nos:5-8.
8. The antibody or antigen-binding portion of claim 7, wherein the light chain variable region comprises the sequence of SEQ ID NO:8.
9. The antibody or antigen-binding portion of claim 4, wherein the heavy chain variable region comprises the sequence of SEQ ID NO:4, and wherein the light chain variable region comprises a sequence selected from the group consisting of SEQ ID Nos:9-10.
10. An antibody, or an antigen-binding portion thereof, that binds to sLeA and sLeC, comprising a heavy chain variable region, wherein the heavy chain variable region comprises a sequence having a 90-100% sequence identity to SEQ ID NO: 3.
11. The antibody or antigen-binding portion of claim 10, wherein the antibody or antigen-binding portion comprises a light chain variable region, wherein the light chain variable region comprises a sequence having a 90-100% sequence identity to a sequence selected from the group consisting of SEQ ID Nos:5-11.
12. An antibody, or an antigen-binding portion thereof, that binds to sLeA and sLeC, comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a CDR-H1 comprising the sequence of SEQ ID NO:12, a CDR-H2 comprising the sequence of SEQ ID NO:13, and a CDR-H3 comprising the sequence of SEQ ID NO:14; and wherein the light chain variable region comprises a CDR-L1 comprising a sequence selected from the group consisting of SEQ ID NOs:15-17, a CDR-L2 comprising the sequence of SEQ ID NO:18, and a CDR-L3 comprising the sequence of SEQ ID NO:19.
13. A polynucleotide encoding the antibody or antigen-binding portion thereof of any one of claims 1-12.
14. A vector comprising the polynucleotide of claim 13.

15. A host cell comprising the polynucleotide of claim 13 or the vector of claim 14.

16. A method of producing an antibody, the method comprising culturing the host cell of claim 15 such that the antibody is produced, optionally wherein the method further comprises recovering the antibody from the host cell.

~~17. The method of claim 16, further comprising recovering the antibody from the host cell.~~

~~178.~~ A pharmaceutical composition comprising the antibody or antigen-binding portion thereof of any one of claims 1-12 and a pharmaceutically acceptable carrier.

~~189. Use of an effective amount of the antibody or antigen-binding portion of any one of claims 1-12 or the pharmaceutical composition of claim 17 in the manufacture of a medicament for~~ A method of treating or ameliorating a symptom of a digestive disease or disorder in an individual with said digestive disease or disorder, optionally wherein the individual is a human ~~wherein said method comprises administering to an individual with said digestive disease or disorder an effective amount of the antibody or antigen-binding portion of any one of claims 1-12 or the pharmaceutical composition of claim 18.~~

1920. The method-use of claim 189, wherein the digestive disease or disorder is selected from the group consisting of inflammatory bowel disease, irritable bowel syndrome, pancreatic cancer and colon cancer.

~~201.~~ The method-use of claim 1920, wherein the digestive disease or disorder is inflammatory bowel disease, optionally wherein the inflammatory bowel disease is Crohn's Disease or ulcerative colitis.

~~22. The method of claim 21, wherein the inflammatory bowel disease is Crohn's Disease or ulcerative colitis.~~

~~23. The method of any one of claims 19-22, wherein the individual is a human.~~