

such associations could be utilized as an integral component in efforts to identify specific subsets of UC or CD patients, such as TNF-IR patients, who would be expected to significantly benefit from treatment with anti-beta7 integrin subunit antibodies, for example where the therapeutic agent is or has been shown in clinical studies to be of therapeutic benefit in such specific UC or CD patient subpopulation.

[0017] The invention described herein meets certain of the above-described needs and provides other benefits.

[0018] All references cited herein, including patent applications and publications, are incorporated by reference in their entirety for any purpose.

SUMMARY

[0019] The methods of the disclosure are based, at least in part, on the discovery that mRNA expression levels of certain genes in intestinal biopsies and in peripheral whole blood, as well as cellular protein expression levels of certain genes in intestinal biopsies are predictive of responsiveness of patients suffering from a gastrointestinal inflammatory disorder to treatment with integrin beta7 antagonists.

[0020] In one aspect, the present invention refers to a method of predicting the response of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising an anti-beta7 antibody or a fragment thereof~~integrin beta7 antagonist~~, the method comprising: (a) measuring the baseline level of mRNA expression of at least one gene in a biological sample obtained from the patient prior to the therapy, wherein the gene is selected from integrin beta7, integrin alphaE, and CD3epsilon, (b) comparing the baseline mRNA expression level detected in the sample to a reference level that is obtained from a population of human subjects, and (c) predicting that the patient will respond to the therapy when the baseline level of mRNA expression has been measured as elevated compared to the reference level and predicting that the patient will not respond to the therapy when the baseline level of mRNA expression has been measured as low compared to the reference level. Accordingly, in one example, methods of predicting the response of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising an integrin beta7 antagonist are disclosed. In certain examples, a biological sample is obtained from the patient and levels of mRNA expression are measured. In one example, expression of integrin beta7 mRNA is measured. In one example, expression of integrin alphaE mRNA is measured. In one example, expression of CD3epsilon is measured. In one example, expression of a combination of two or three mRNAs selected from integrin beta7, integrin alphaE, and CD3epsilon is measured. In one example, the biological sample is a tissue biopsy sample. In one example, the biopsy is obtained from intestinal tissue.

expression level of one or more of integrin beta7, integrin alphaE, or CD3epsilon is low compared to a reference value, which in certain examples, is a median value. In one example, the response is clinical remission. In one example, the response is mucosal healing. In one example, the response is clinical response. In certain examples, remission in the patient is determined to be induced when the absolute Mayo Clinic Score ≤ 2 and no individual subscore >1 , which is also referred to as clinical remission. In certain examples, mucosal healing is determined to have occurred when the patient is determined to have an endoscopy subscore of 0 or 1 as assessed by flexible sigmoidoscopy. In certain such examples, patients who experience mucosal healing are determined to have an endoscopy subscore of 0.

[0021] In another aspect, the present invention refers to a method of predicting responsiveness of a gastrointestinal inflammatory disorder patient to an anti-beta7 antibody or a fragment thereof ~~integrin beta7-antagonist~~ treatment, the method comprising determining the baseline mRNA expression level of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon in a biological sample obtained from the patient prior to the treatment, wherein elevated baseline mRNA expression level compared to a reference level identifies the patient as one who is likely to respond to the anti-beta7 antibody or fragment thereof ~~integrin beta7-antagonist treatment~~, wherein the reference level is obtained from a population of human subjects. In another example, methods of predicting responsiveness of a gastrointestinal inflammatory disorder patient to an integrin beta7 antagonist treatment are disclosed. In one example, the mRNA expression level of integrin beta7 in a biological sample from the patient is determined. In one example, the mRNA expression level of integrin alphaE in a biological sample from the patient is determined. In one example, the mRNA expression level of CD3epsilon in a biological sample from the patient is determined. In one example, the mRNA expression level of two or three mRNAs selected from integrin beta7, integrin alphaE, and CD3epsilon in a biological sample from the patient is determined. In certain example, elevated integrin beta7 mRNA expression compared to a reference value, for example, a median value, or elevated integrin alphaE mRNA expression compared to a reference value, for example, a median value, or elevated CD3epsilon mRNA expression compared to a reference value, for example, a median value, detected in the biological sample identifies the patient as one who is likely to respond to integrin beta7 antagonist treatment.

[0022] In yet another example, a biological sample is obtained from the patient and the number of cells expressing one or a combination of certain proteins are measured and compared to the total number of cells or the number of protein-expressing cells is determined in a high power field under a light microscope. In one example, the number of integrin beta7-expressing cells is measured. In one example, the number of integrin alphaE-

number of cells expressing one or a combination of integrin beta7, integrin alphaE, or CD3epsilon is measured by an immunohistochemical method. In certain examples, the number of cells expressing one or a combination of integrin beta7, integrin alphaE, or CD3epsilon is compared to the total number of cells in a given area. In one example, the patient is predicted to respond to therapy comprising the integrin beta7 antagonist if the number of cells expressing one or more of integrin beta7, integrin alphaE, or CD3epsilon is elevated (or high) compared to a reference value, for example, a median value. In one example, the patient is predicted to not respond to therapy comprising the integrin beta7 antagonist if the number of cells expressing one or more of integrin beta7, integrin alphaE, or CD3epsilon is low compared to a reference value, for example, a median value. In one example, the response is clinical remission. In one example, the response is mucosal healing. In one example, the response is clinical response. In certain examples, remission in the patient is determined to be induced when the absolute Mayo Clinic Score ≤ 2 and no individual subscore >1 , which is also referred to as clinical remission. In certain examples, mucosal healing is determined to have occurred when the patient is determined to have an endoscopy subscore of 0 or 1 as assessed by flexible sigmoidoscopy. In certain such examples, patients who experience mucosal healing are determined to have an endoscopy subscore of 0.

[0023] In still another aspect, the present invention refers to a method of identifying a patient suffering from a gastrointestinal inflammatory disorder as likely to respond to a therapy comprising an anti-beta7 antibody or a fragment thereof ~~integrin-beta7 antagonist~~, the method comprising (a) measuring the baseline level of mRNA expression of at least one gene in a biological sample obtained from the patient prior to the therapy, wherein the at least one gene is selected from integrin beta7, integrin alphaE, and CD3epsilon; (b) comparing the baseline level of mRNA expression measured in (a) to a reference level that is obtained from a population of human subjects; and (c) identifying the patient as more likely to respond to the therapy comprising an anti-beta7 antibody or fragment thereof ~~integrin-beta7 antagonist~~ when the baseline level of mRNA expression measured in (a) is above the reference level. In another example, methods of identifying a patient suffering from a gastrointestinal inflammatory disorder as likely to respond to a therapy comprising an integrin beta7 antagonist are disclosed. In certain examples, the methods comprise: (a) measuring the level of mRNA expression of at least one gene in a biological sample from the patient, wherein the at least one gene is selected from integrin beta7, integrin alphaE, and CD3epsilon; (b) comparing the level of mRNA expression measured in (a) to a reference level; and (c) identifying the patient as more likely to respond to the therapy comprising an integrin beta7 antagonist when the level of mRNA expression measured in (a) is above the reference level. In

one example, the patient is a human. In one example, the patient is a TNF inadequate responder (TNF-IR). In one example, the gastrointestinal inflammatory disorder is an inflammatory bowel disease. In one example, the inflammatory bowel disease is ulcerative colitis or Crohn's disease. In one example, the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission.

[0024] In a further aspect, the present invention refers to use of an anti-beta7 antibody or a fragment thereof ~~integrin beta7 antagonist~~ in the manufacture of a medicament for treating a patient having a gastrointestinal inflammatory disorder, the use comprising (a) measuring the baseline level of mRNA expression of at least one gene in a biological sample obtained from the patient prior to administration of a medicament comprising an anti-beta7 antibody or a fragment thereof, wherein the at least one gene is selected from integrin beta7, integrin alphaE, and CD3epsilon; (b) comparing the baseline level of mRNA expression measured in (a) to a reference level that is obtained from a population of human subjects; (c) identifying the patient as more likely to respond ~~a therapy comprising an integrin beta7 antagonist to the medicament~~ when the baseline level of mRNA expression measured in (a) is above the reference level; and (d) ~~the use of the medicament is to be administered to the patient identified in (c) as more likely to respond to the medicament when the level of mRNA expression measured in (a) is above the reference level~~. In another example, methods of treating a patient having a gastrointestinal inflammatory disorder are disclosed. In certain examples, the methods comprise: (a)

measuring the level of mRNA expression of at least one gene in a biological sample from the patient, wherein the at least one gene is selected from integrin beta7, integrin alphaE, and CD3epsilon; (b) comparing the level of mRNA expression measured in (a) to a reference level; (c) identifying the patient as more likely to respond a therapy comprising an integrin beta7 antagonist when the level of mRNA expression measured in (a) is above the reference level; and (d) administering the therapy when the level of mRNA expression measured in (a) is above the reference level, thereby treating the gastrointestinal inflammatory disorder. In one example, 100 mg of the integrin beta7 antagonist is administered subcutaneously once every four weeks. In one example, a flat loading dose of 420 mg of the integrin beta7 antagonist is administered subcutaneously, followed two weeks after administration of the loading dose by a second subcutaneous administration of 300 mg of the integrin beta7 antagonist, followed two weeks after the second administration by a third subcutaneous administration of 300 mg of the integrin beta7 antagonist, followed four weeks after the third administration by subcutaneous administration of 300 mg of the integrin beta7 antagonist and thereafter subcutaneous administration of 300 mg of the integrin beta7 antagonist once every four weeks. In one example, the patient is a human. In one example, the patient is a TNF inadequate responder (TNF-IR). In one example, the gastrointestinal inflammatory disorder is an inflammatory bowel disease. In one example, the inflammatory bowel disease is ulcerative colitis or Crohn's disease. In one example, the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission. In one example, administration of the integrin beta7 antagonist results in one or more of the following: (1) a 3-point decrease and 30% reduction from baseline in MCS and ≥ 1 -point decrease in rectal bleeding subscore or absolute rectal bleeding score of 0 or 1, (2) an endoscopic subscore of 0 or 1, (3) MCS ≤ 2 with no individual subscore > 1 .

[0025] In still yet another aspect, the present invention refers to a method of predicting the response of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising an anti-beta7 antibody or a fragment thereof ~~integrin beta7 antagonist~~, the method comprising: (a) measuring the baseline number of cells expressing ~~at least one protein selected from integrin beta7, integrin alphaE, and CD3epsilon~~ in a biological sample obtained from the patient prior to the therapy, (b) comparing the baseline number of integrin alphaE-expressing cells measured in the sample to a reference number of integrin alphaE-expressing cells that is obtained from a population of human subjects ~~level~~, and (c) predicting that the patient will respond to the therapy when the baseline number of integrin alphaE ~~protein~~-expressing cells has been measured as elevated compared to the reference number of integrin alphaE-expressing cells ~~level~~ and predicting that the patient will not respond to the therapy when the baseline number of integrin alphaE ~~protein~~-expressing cells has been measured as low compared to the reference number of integrin alphaE-expressing cells ~~level~~. In another example, methods of predicting the response of a patient suffering from a gastrointestinal

the patient is a human. In one example, the patient is a TNF inadequate responder (TNF-IR). In one example, the gastrointestinal inflammatory disorder is an inflammatory bowel disease. In one example, the inflammatory bowel disease is ulcerative colitis or Crohn's disease. In one example, the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission. In one example, the biological sample is intestinal tissue. In one example, the methods comprise measuring the number of expressing cells by an immunohistochemical method. In one example, the measuring comprises contacting the sample with an agent that specifically binds to integrin beta7 protein, integrin alphaE protein, or CD3epsilon protein and detecting the amount of complex formed, and thereby measuring the number of expressing cells. In one example, the number of expressing cells in the sample is divided by the total number of cells in the sample. In one example, the number of expressing cells in a high power field under a light microscope is determined. In one example, the reference level is a median value.

[0026] In another aspect, the present invention refers to a method of predicting responsiveness of a gastrointestinal inflammatory disorder patient to an anti-beta7 antibody or a fragment thereof ~~integrin beta7 antagonist treatment~~, the method comprising determining the baseline number of cells expressing ~~at least one protein selected from integrin beta7, integrin alphaE, and~~ CD3epsilon in a biological sample obtained from the patient prior to the treatment, wherein elevated baseline numbers of integrin alphaE-expressing cells compared to a reference number of integrin alphaE-expressing cells ~~level~~ identifies the patient as one who is likely to respond to the anti-beta7 antibody or a fragment thereof ~~integrin beta7 antagonist treatment~~, wherein the reference number of integrin alphaE-expressing cells is obtained from a population of human subjects. In one example, methods of predicting responsiveness of a gastrointestinal inflammatory disorder patient to an integrin beta7 antagonist treatment are disclosed. In certain examples, the methods comprise determining the number of cells expressing at least one protein selected from integrin beta7, integrin alphaE, and CD3epsilon in a biological sample from the patient, wherein elevated numbers of expressing cells compared to a reference level identifies the patient as one who is likely to respond to the integrin beta7 antagonist treatment. In one example, the patient is a human. In one example, the patient is a TNF inadequate responder (TNF-IR). In one example, the gastrointestinal inflammatory disorder is an inflammatory bowel disease. In one example, the inflammatory bowel disease is ulcerative colitis or Crohn's disease. In one example, the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission. In one example, the biological sample is intestinal tissue. In one example, the methods comprise measuring the number of expressing cells by an immunohistochemical method. In one example, the measuring comprises contacting

[0027] In yet another aspect, the present invention refers to a method of identifying a patient suffering from a gastrointestinal inflammatory disorder as likely to respond to a therapy comprising an anti-beta7 antibody or a fragment thereof~~integrin beta7 antagonist~~, the method comprising (a) measuring the baseline number of cells expressing integrin alphaE ~~at least one protein~~ in a biological sample obtained from the patient prior to the treatment, wherein the ~~at least one protein is selected from integrin beta7, integrin alphaE, and CD3epsilon~~; (b) comparing the baseline number of integrin alphaE-expressing cells measured in (a) to a reference number of integrin alphaE-expressing cells that is obtained from a population of human subjects~~level~~; and (c) identifying the patient as more likely to respond to the therapy comprising an anti-beta7 antibody or a fragment thereof~~integrin beta7 antagonist~~ when the baseline number of integrin alphaE-expressing cells measured in (a) is above the reference number of integrin alphaE-expressing cells~~level~~. In another example, methods of identifying a patient suffering from a gastrointestinal inflammatory disorder as likely to respond to a therapy comprising an integrin beta7 antagonist are disclosed. In certain examples, the methods comprise: (a) measuring the number of cells expressing at least one protein in a biological sample from the patient, wherein the at least one protein is selected from integrin beta7, integrin alphaE, and CD3epsilon; (b) comparing the number of cells measured in (a) to a reference level; and (c) identifying the patient as more likely to respond to the therapy comprising an integrin beta7 antagonist when the number of cells measured in (a) is above the reference level. In one example, the patient is a human. In one example, the patient is a TNF inadequate responder (TNF-IR). In one example, the gastrointestinal inflammatory disorder is an inflammatory bowel disease. In one example, the inflammatory bowel disease is ulcerative colitis or Crohn's disease. In one example, the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission. In one example, the biological sample is intestinal tissue. In one example, the methods comprise measuring the number of expressing cells by an immunohistochemical method. In one example, the measuring comprises contacting the sample with an agent that specifically binds to integrin beta7 protein, integrin alphaE protein, or CD3epsilon protein and detecting the amount of complex formed, and thereby measuring the number of expressing cells. In one example, the number of expressing cells in the sample is divided by the total number of cells in the sample. In one example, the number of expressing cells in a high power field under a light microscope is determined. In one example, the reference level is a median value.

[0028] In yet still another aspect, the present invention refers to use of an anti-beta7 antibody or a fragment thereof~~integrin beta7 antagonist~~ in the manufacture of a medicament for treating a patient having a gastrointestinal inflammatory disorder, the use comprising (a) measuring the baseline number of cells expressing integrin alphaE ~~at least one protein~~ in a biological sample obtained from the patient prior to administration of a medicament comprising an anti-beta7 antibody or a fragment thereof~~;~~, wherein the ~~at least one protein is~~

selected from integrin beta7, integrin alphaE, and CD3epsilon; (b) comparing the baseline number of integrin alphaE-expressing cells measured in (a) to a reference number of integrin alphaE-expressing cells that is obtained from a population of human subjects level; (c) ~~identifying the patient as more likely to respond to the medicament therapy comprising an integrin beta7 antagonist when the baseline number of integrin alphaE protein-expressing cells measured in (a) is above the reference number level~~; and (d) ~~the use of the medicament is to be administered to the patient identified in (c) as more likely to respond to the medicament when the number of protein-expressing cells measured in (a) is above the reference level~~. In another example, methods of treating a patient having a gastrointestinal inflammatory disorder are disclosed. In certain examples, the method comprise: (a) measuring the number of cells expressing at least one protein in a biological sample from the patient, wherein the at least one protein is selected from integrin beta7, integrin alphaE, and CD3epsilon; (b) comparing the number of expressing cells measured in (a) to a reference level; (c) identifying the patient as more likely to respond a therapy comprising an integrin beta7 antagonist when the number of expressing cells measured in (a) is above the reference level; and (d) administering the therapy when the number of expressing cells measured in (a) is above the reference level, thereby treating the gastrointestinal inflammatory disorder. In one example, 100 mg of the integrin beta7 antagonist is administered subcutaneously once every four weeks. In one example, a flat loading dose of 420 mg of the integrin beta7 antagonist is administered subcutaneously, followed two weeks after administration of

the loading dose by a second subcutaneous administration of 300 mg of the integrin beta7 antagonist, followed two weeks after the second administration by a third subcutaneous administration of 300 mg of the integrin beta7 antagonist, followed four weeks after the third administration by subcutaneous administration of 300 mg of the integrin beta7 antagonist and thereafter subcutaneous administration of 300 mg of the integrin beta7 antagonist once every four weeks. In one example, the patient is a human. In one example, the patient is a TNF inadequate responder (TNF-IR). In one example, the gastrointestinal inflammatory disorder is an inflammatory bowel disease. In one example, the inflammatory bowel disease is ulcerative colitis or Crohn's disease. In one example, the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission. In one example, administration of the integrin beta7 antagonist results in one or more of the following: (1) a 3-point decrease and 30% reduction from baseline in MCS and ≥ 1 -point decrease in rectal bleeding subscore or absolute rectal bleeding score of 0 or 1, (2) an endoscopic subscore of 0 or 1, (3) MCS ≤ 2 with no individual subscore > 1 . In one example, the biological sample is intestinal tissue. In one example, the methods comprise measuring the number of expressing cells by an immunohistochemical method. In one example, the measuring comprises contacting the sample with an agent that specifically binds to integrin beta7 protein, integrin alphaE protein, or CD3epsilon protein and detecting the amount of complex formed, and thereby measuring the number of expressing cells. In one example, the number of expressing cells in the sample is divided by the total number of cells in the sample. In one example, the number of expressing cells in a high power field under a light microscope is determined. In one example, the reference level is a median value.

[0028a] In another aspect, the present invention refers to use of an anti-beta7 antibody or a fragment thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder in a patient, the use comprising a medicament comprising an anti-beta7 antibody or a fragment thereof is to be administered to the patient, wherein a biological sample obtained from the patient prior to administration of the medicament has been determined to express elevated mRNA expression levels of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon compared to a reference level that is obtained from a population of human subjects; or wherein the patient has been selected for treatment based on elevated mRNA expression levels of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon in a biological sample obtained from the patient prior to administration of the medicament compared to a reference level that is obtained from a population of human subjects.

[0029] In still yet another example, an integrin beta7 antagonist for use in treating a patient having a gastrointestinal inflammatory disorder is disclosed. In certain examples, the patient is treated or selected for treatment when the level of mRNA expression of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon is above a reference level. In certain examples, the patient is treated or selected for treatment when the number of cells expressing at least on protein selected from integrin beta7, integrin alphaE, and CD3epsilon is elevated or high compared to a reference level. In one example, the reference level is a median value. In one example, the integrin beta7 antagonist is for use in treating the patient wherein 100 mg is administered subcutaneously once every four weeks. In one example, the integrin beta7 antagonist is for use in treating the patient wherein a flat loading dose of 420 mg of the integrin beta7 antagonist is administered subcutaneously,

WHAT IS CLAIMED IS:

1. A method of predicting the response of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising an anti-beta7 antibody or a fragment thereof, the method comprising:

- (a) measuring the baseline level of mRNA expression of at least one gene in a biological sample obtained from the patient prior to the therapy, wherein the gene is selected from integrin beta7, integrin alphaE, and CD3epsilon,
- (b) comparing the baseline mRNA expression level detected in the sample to a reference level that is obtained from a population of human subjects, and
- (c) predicting that the patient will respond to the therapy when the baseline level of mRNA expression has been measured as elevated compared to the reference level and predicting that the patient will not respond to the therapy when the baseline level of mRNA expression has been measured as low compared to the reference level.

2. A method of predicting responsiveness of a gastrointestinal inflammatory disorder patient to an anti-beta7 antibody or a fragment thereof treatment, the method comprising determining the baseline mRNA expression level of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon in a biological sample obtained from the patient prior to the treatment, wherein elevated baseline mRNA expression level compared to a reference level identifies the patient as one who is likely to respond to the anti-beta7 antibody or fragment thereof treatment, wherein the reference level is obtained from a population of human subjects.

3. A method of identifying a patient suffering from a gastrointestinal inflammatory disorder as likely to respond to a therapy comprising an anti-beta7 antibody or a fragment thereof, the method comprising:

- (a) measuring the baseline level of mRNA expression of at least one gene in a biological sample obtained from the patient prior to the therapy, wherein the at least one gene is selected from integrin beta7, integrin alphaE, and CD3epsilon;
- (b) comparing the baseline level of mRNA expression measured in (a) to a reference level that is obtained from a population of human subjects; and
- (c) identifying the patient as more likely to respond to the therapy comprising an anti-beta7 antibody or fragment thereof when the baseline level of mRNA expression measured in (a) is above the reference level.

4. Use of an anti-beta7 antibody or a fragment thereof in the manufacture of a medicament for treating a patient having a gastrointestinal inflammatory disorder, the use comprising:

- (a) measuring the baseline level of mRNA expression of at least one gene in a biological sample obtained from the patient prior to administration of a medicament comprising an anti-beta7 antibody or a fragment thereof, wherein the at least one gene is selected from integrin beta7, integrin alphaE, and CD3epsilon;
 - (b) comparing the baseline level of mRNA expression measured in (a) to a reference level that is obtained from a population of human subjects;
 - (c) identifying the patient as more likely to respond to the medicament when the baseline level of mRNA expression measured in (a) is above the reference level; and
 - (d) the medicament is to be administered to the patient identified in (c) as more likely to respond to the medicament.
5. The method of any one of claims 1-3 or use of claim 4, wherein between about 50 mg and 450 mg of the anti-beta7 antibody or a fragment thereof is to be administered subcutaneously to the patient.
6. The method of any one of claims 1-3 and 5 or use of claim 4 or 5, wherein about 50 mg, about 100 mg, about 150 mg, about 200 mg, about 300 mg, about 400 mg, about 420 mg, or 450 mg of the anti-beta7 antibody or a fragment thereof is to be administered subcutaneously to the patient.
7. The method of any one of claims 1-3 and 5-6 or use of any one of claims 4-6, wherein about 100 mg of the anti-beta7 antibody or a fragment thereof is to be administered subcutaneously once every four weeks to the patient.
8. The method of any one of claims 1-3 and 5-7 or use of any one of claims 4-7, wherein the patient is a human.
9. The method or use of claim 8, wherein the patient is a TNF inadequate responder (TNF-IR).
10. The method of any one of claims 1-3 and 5-9 or use of any one of claims 4-9, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease.
11. The method or use of claim 10, wherein the inflammatory bowel disease is ulcerative colitis or Crohn's disease.
12. The method or use of claim 11, wherein the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission.
13. The method of any one of claims 1-3 and 5-12 or use of any one of claims 4-12, wherein the biological sample is selected from intestinal tissue and peripheral whole blood.

14. The method of any one of claims 1-3 and 5-13 or use of any one of claims 4-13, wherein the baseline mRNA expression level is measured by a PCR method.
15. The method or use of claim 14, wherein the PCR method comprises qPCR.
16. The method of any one of claims 1-3 and 5-15 or use of any one of claims 4-15, wherein the measuring comprises amplifying one or more of integrin beta7 mRNA, integrin alphaE mRNA, or CD3epsilon mRNA and detecting the amplified mRNA, thereby measuring the baseline level of amplified mRNA.
17. The method of any one of claims 1-3 and 5-16 or use of any one of claims 4-16, wherein the reference level is a median value.
18. Use of an anti-beta7 antibody or a fragment thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder in a patient, the use comprising a medicament comprising an anti-beta7 antibody or a fragment thereof is to be administered to the patient, wherein
 - a biological sample obtained from the patient prior to administration of the medicament has been determined to express elevated mRNA expression levels of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon compared to a reference level that is obtained from a population of human subjects;
 - or
 - wherein the patient has been selected for treatment based on elevated mRNA expression levels of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon in a biological sample obtained from the patient prior to administration of the medicament compared to a reference level that is obtained from a population of human subjects.
19. The use of claim 18, wherein about 100 mg of the anti-beta7 antibody or fragment thereof is administered subcutaneously once every four weeks to the patient.
20. The use of claim 18 or claim 19, wherein the patient is a human.
21. The use of claim 20, wherein the patient is a TNF inadequate responder (TNF-IR).
22. The use of any one of claims 18-21, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease.
23. The use of claim 22, wherein the inflammatory bowel disease is ulcerative colitis or Crohn's disease.
24. The use of any one of claims 18-23, wherein the biological sample is selected from biopsy and peripheral whole blood.
25. The use of any one of claims 18-24, wherein the baseline mRNA expression level is measured by a PCR method.

26. The use of claim 25, wherein the PCR method comprises qPCR.
27. A method of predicting the response of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising an anti-beta7 antibody or a fragment thereof, the method comprising:
- (a) measuring the baseline number of cells expressing integrin alphaE in a biological sample obtained from the patient prior to the therapy,
 - (b) comparing the baseline number of integrin alphaE-expressing cells measured in the sample to a reference number of integrin alphaE-expressing cells that is obtained from a population of human subjects, and
 - (c) predicting that the patient will respond to the therapy when the baseline number of integrin alphaE-expressing cells has been measured as elevated compared to the reference number of integrin alphaE-expressing cells and predicting that the patient will not respond to the therapy when the baseline number of integrin alphaE-expressing cells has been measured as low compared to the reference number of integrin alphaE-expressing cells.
28. A method of predicting responsiveness of a gastrointestinal inflammatory disorder patient to an anti-beta7 antibody or a fragment thereof treatment, the method comprising determining the baseline number of cells expressing integrin alphaE in a biological sample obtained from the patient prior to the treatment, wherein elevated baseline number of integrin alphaE-expressing cells compared to a reference number of integrin alphaE-expressing cells identifies the patient as one who is likely to respond to the anti-beta7 antibody or a fragment thereof treatment, wherein the reference number of integrin alphaE-expressing cells is obtained from a population of human subjects.
29. A method of identifying a patient suffering from a gastrointestinal inflammatory disorder as likely to respond to a therapy comprising an anti-beta7 antibody or a fragment thereof, the method comprising:
- (a) measuring the baseline number of cells expressing integrin alphaE in a biological sample obtained from the patient prior to the treatment;
 - (b) comparing the baseline number of integrin alphaE-expressing cells measured in
 - (a) to a reference number of integrin alphaE-expressing cells that is obtained from a population of human subjects; and
 - (c) identifying the patient as more likely to respond to the therapy comprising an anti-beta7 antibody or a fragment thereof when the baseline number of integrin alphaE-expressing cells measured in (a) is above the reference number of integrin alphaE-expressing cells.

30. Use of an anti-beta7 antibody or a fragment thereof in the manufacture of a medicament for treating a patient having a gastrointestinal inflammatory disorder, the use comprising:

- (a) measuring the baseline number of cells expressing integrin alphaE in a biological sample obtained from the patient prior to administration of a medicament comprising an anti-beta7 antibody or a fragment thereof;
- (b) comparing the baseline number of integrin alphaE-expressing cells measured in (a) to a reference number of integrin alphaE-expressing cells that is obtained from a population of human subjects;
- (c) identifying the patient as more likely to respond to the medicament when the baseline number of integrin alphaE-expressing cells measured in (a) is above the reference number; and
- (d) the medicament is to be administered to the patient identified in (c) as more likely to respond to the medicament.

31. The method of any one of claims 27-29 or use of claim 30, wherein between about 50 mg and 450 mg of the anti-beta7 antibody or a fragment thereof is to be administered subcutaneously to the patient.

32. The method of any one of claims 27-29 and 31 or use of claim 30 or 31, wherein about 50 mg, about 100 mg, about 150 mg, about 200 mg, about 300 mg, about 400 mg, about 420 mg, or 450 mg of the anti-beta7 antibody or a fragment thereof is to be administered subcutaneously to the patient.

33. The method of any one of claims 27-29 and 31-32 or use of any one of claims 30-32, wherein about 100 mg of the anti-beta7 antibody or fragment thereof is to be administered subcutaneously once every four weeks to the patient.

34. The method of any one of claims 27-29 and 31-33 or use of any one of claims 30-33, wherein the patient is a human.

35. The method or use of claim 34, wherein the patient is a TNF inadequate responder (TNF-IR).

36. The method of any one of claims 27-29 and 31-35 or use of any one of claims 30-35, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease.

37. The method or use of claim 36, wherein the inflammatory bowel disease is ulcerative colitis or Crohn's disease.

38. The method or use of claim 37, wherein the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission.

39. The method of any one of claims 27-29 and 31-38 or use of any one of claims 30-38, wherein the biological sample is intestinal tissue.
40. The method of any one of claims 27-29 and 31-39 or use of any one of claims 30-39, comprising measuring the baseline number of integrin alphaE-expressing cells by an immunohistochemical method.
41. The method of any one of claims 27-29 and 31-40 or use of any one of claims 30-40, wherein the measuring comprises contacting the sample with an agent that specifically binds to integrin alphaE protein and detecting the amount of complex formed, and thereby measuring the baseline number of integrin alphaE-expressing cells.
42. The method of any one of claims 27-29 and 31-41 or use of any one of claims 30-41, wherein the baseline number of integrin alphaE-expressing cells in the sample is divided by the total number of cells in the sample.
43. The method of any one of claims 27-29 and 31-42 or use of any one of claims 30-42, wherein the baseline number of integrin alphaE-expressing cells in a high power field under a light microscope is determined.
44. The method of any one of claims 27-29 and 31-43 or use of any one of claims 30-43, wherein the reference number is a median value.
45. The method or use of claim 7 or claim 33, wherein the anti-beta7 antibody or fragment thereof is to be administered results in one or more of the following: (1) a 3-point decrease and 30% reduction from baseline in Mayo Clinic Score (MCS) and > 1-point decrease in rectal bleeding subscore or absolute rectal bleeding score of 0 or 1, (2) an endoscopic subscore of 0 or 1, (3) MCS < 2 with no individual subscore > 1.
46. The method of any one of claims 1-3, 5-17, 27-29 and 31-45, or the use of any one of claims 4-26 and 30-45, wherein the anti-beta7 antibody is a monoclonal anti-beta7 antibody.
47. The method of any one of claims 1-3, 5-17, 27-29 and 31-46 or use of any one of claims 4-26 and 30-46, wherein the anti-beta7 antibody is selected from a chimeric antibody, a human antibody, and a humanized antibody.
48. The method of any one of claims 1-3, 5-17, 27-29 and 31-47 or use of any one of claims 4-26 and 30-47, wherein the anti-beta7 antibody or fragment thereof comprises six hypervariable regions (HVRs), wherein:
- (i) HVR-L1 comprises amino acid sequence A1-A11, wherein A1-A11 is RASESVDTYLH (SEQ ID NO:1); RASESVDSLH (SEQ ID NO:7), RASESVDTLLH (SEQ ID NO:8), or RASESVDDLH (SEQ ID NO:9) or a variant of SEQ ID NOs:1, 7, 8 or 9 (SEQ ID NO:26) wherein amino acid A2 is selected from the group consisting of A, G, S, T, and V and/or amino acid A3 is selected from the group consisting of S, G, I, K, N, P, Q, R, and T,

and/or A4 is selected from the group consisting of E, V, Q, A, D, G, H, I, K, L, N, and R, and/or amino acid A5 is selected from the group consisting of S, Y, A, D, G, H, I, K, N, P, R, T, and V, and/or amino acid A6 is selected from the group consisting of V, R, I, A, G, K, L, M, and Q, and/or amino acid A7 is selected from the group consisting of D, V, S, A, E, G, H, I, K, L, N, P, S, and T, and/or amino acid A8 is selected from the group consisting of D, G, N, E, T, P and S, and/or amino acid A9 is selected from the group consisting of L, Y, I and M, and/or amino acid A10 is selected from the group consisting of L, A, I, M, and V and/or amino acid A11 is selected from the group consisting of H, Y, F, and S;

(ii) HVR-L2 comprises amino acid sequence B1-B8, wherein B1-B8 is KYASQSSIS (SEQ ID NO:2), RYASQSSIS (SEQ ID NO:20), or XaaYASQSSIS (SEQ ID NO:21, where Xaa represents any amino acid) or a variant of SEQ ID NOs:2, 20 or 21 (SEQ ID NO:27) wherein amino acid B1 is selected from the group consisting of K, R, N, V, A, F, Q, H, P, I, L, Y and Xaa (where Xaa represents any amino acid), and/or amino acid B4 is selected from the group consisting of S and D, and/or amino acid B5 is selected from the group consisting of Q and S, and/or amino acid B6 is selected from the group consisting of S, D, L, and R, and/or amino acid B7 is selected from the group consisting of I, V, E, and K;

(iii) HVR-L3 comprises amino acid sequence C1-C9, wherein C1-C9 is QQGNLSPNT (SEQ ID NO:3) or a variant of SEQ ID NO:3 (SEQ ID NO:28) wherein amino acid C8 is selected from the group consisting of N, V, W, Y, R, S, T, A, F, H, I L, and M;

(iv) HVR-H1 comprises amino acid sequence D1-D10 wherein D1-D10 is GFFITNNYWG (SEQ ID NO:4);

(v) HVR-H2 comprises amino acid sequence E1-E17 wherein E1-E17 is GYISYSGSTSYNPSLKS (SEQ ID NO:5), or a variant of SEQ ID NO:5 (SEQ ID NO:29) wherein amino acid E2 is selected from the group consisting of Y, F, V, and D, and/or amino acid E6 is selected from the group consisting of S and G, and/or amino acid E10 is selected from the group consisting of S and Y, and/or amino acid E12 is selected from the group consisting of N, T, A, and D, and/or amino acid 13 is selected from the group consisting of P, H, D, and A, and/or amino acid E15 is selected from the group consisting of L and V, and/or amino acid E17 is selected from the group consisting of S and G; and

(vi) HVR-H3 comprises amino acid sequence F2-F11 wherein F2 -F11 is MTGSSGYFDF (SEQ ID NO:6) or RTGSSGYFDF (SEQ ID NO:19); or comprises amino acid sequence F1-F11, wherein F1-F11 is AMTGSSGYFDF (SEQ ID NO:16), ARTGSSGYFDF (SEQ ID NO:17), or AQTGSSGYFDF (SEQ ID NO:18), or a variant of SEQ ID NOs:6, 16, 17, 18, or 19 (SEQ ID NO:30) wherein amino acid F2 is R, M, A, E, G, Q, S, and/or amino acid F11 is selected from the group consisting of F and Y.

49. The method or use of claim 48, wherein the anti-beta7 antibody or fragment thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:9;

(ii) HVR-L2 comprises SEQ ID NO:2;

(iii) HVR-L3 comprises SEQ ID NO:3;

(iv) HVR-H1 comprises SEQ ID NO:4;

(v) HVR-H2 comprises SEQ ID NO:5; and

(vi) HVR-H3 comprises SEQ ID NO:6 or SEQ ID NO:16 or SEQ ID NO:17 or SEQ ID NO:19.

50. The method or use of claim 49, wherein the anti-beta7 antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO:24 and a variable heavy chain comprising the amino acid sequence of SEQ ID NO:31.

51. The method or use of claim 50, wherein the anti-beta7 antibody is etrolizumab.

52. The method of any one of claims 1-3, 5-17, and 46-47, or the use of any one of claims 4-26 and 46-47, wherein the anti-beta7 antibody is a monoclonal anti-alpha4/beta7 antibody.

53. The method or use of claim 52, wherein the anti-alpha4/beta7 antibody is selected from vedolizumab and AMG 181.

WHAT IS CLAIMED IS:

1. A method of predicting the response of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising an integrin beta7 antagonist, the method comprising:

measuring the level of mRNA expression of at least one gene in a biological sample obtained from the patient, wherein the gene is selected from integrin beta7, integrin alphaE, and CD3epsilon,
comparing the mRNA expression level detected in the sample to a reference level,
and

predicting that the patient will respond to the therapy when the level of mRNA expression has been measured as elevated compared to the reference level and predicting that the patient will not respond to the therapy when the level of mRNA expression has been measured as low compared to the reference level.

2. A method of predicting responsiveness of a gastrointestinal inflammatory disorder patient to an integrin beta7 antagonist treatment, the method comprising determining the mRNA expression level of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon in a biological sample obtained from the patient, wherein elevated mRNA expression level compared to a reference level identifies the patient as one who is likely to respond to the integrin beta7 antagonist treatment.

3. A method of identifying a patient suffering from a gastrointestinal inflammatory disorder as likely to respond to a therapy comprising an integrin beta7 antagonist, the method comprising:

- (a) measuring the level of mRNA expression of at least one gene in a biological sample obtained from the patient, wherein the at least one gene is selected from integrin beta7, integrin alphaE, and CD3epsilon;
- (b) comparing the level of mRNA expression measured in (a) to a reference level; and
- (c) identifying the patient as more likely to respond to the therapy comprising an integrin beta7 antagonist when the level of mRNA expression measured in (a) is above the reference level.

4. Use of an integrin beta7 antagonist in the manufacture of a medicament for treating a patient having a gastrointestinal inflammatory disorder, the use comprising:

- (a) measuring the level of mRNA expression of at least one gene in a biological sample obtained from the patient, wherein the at least one gene is selected from integrin beta7, integrin alphaE, and CD3epsilon;
 - (b) comparing the level of mRNA expression measured in (a) to a reference level;
 - (c) identifying the patient as more likely to respond a therapy comprising an integrin beta7 antagonist when the level of mRNA expression measured in (a) is above the reference level; and
 - (d) the use of the medicament when the level of mRNA expression measured in (a) is above the reference level.
5. The use of claim 4, wherein 100 mg of the integrin beta7 antagonist is to be administered subcutaneously once every four weeks.
6. The method of any one of claims 1-3 or the use of any one of claims 4-5, wherein the patient is a human.
7. The method or use of claim 6, wherein the patient is a TNF inadequate responder (TNF-IR).
8. The use of claim 4, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease.
9. The use of claim 8, wherein the inflammatory bowel disease is ulcerative colitis or Crohn's disease.
10. The use of claim 9, wherein the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission.
11. The use of claim 4, wherein the biological sample is selected from intestinal tissue and peripheral whole blood.
12. The use of claim 4, wherein the mRNA expression level is measured by a PCR method.
13. The use of claim 12, wherein the PCR method comprises qPCR.
14. The use of claim 4, wherein the measuring comprises amplifying one or more of integrin beta7 mRNA, integrin alphaE mRNA, or CD3epsilon mRNA and detecting the amplified mRNA, thereby measuring the level of amplified mRNA.
15. The use of claim 4, wherein the reference level is a median value.
16. Use of an integrin beta7 antagonist in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder in a patient, the use comprising the patient is to be administered a therapeutically effective amount of an integrin beta7 antagonist, wherein

a biological sample obtained from the patient has been determined to express elevated mRNA expression levels of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon

or

wherein the patient has been selected for treatment based on elevated mRNA expression levels in the biological sample obtained from the patient of at least one gene selected from integrin beta7, integrin alphaE, and CD3epsilon.

17. The use of claim 16, wherein 100 mg of the integrin beta7 antagonist is administered subcutaneously once every four weeks.

18. The use of claim 17, wherein the patient is a human.

19. The use of claim 18, wherein the patient is a TNF inadequate responder (TNF-IR).

20. The use of claim 16, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease.

21. The use of claim 20, wherein the inflammatory bowel disease is ulcerative colitis or Crohn's disease.

22. The use of claim 16, wherein the biological sample is selected from biopsy and peripheral whole blood.

23. The use of claim 22, wherein the mRNA expression level is measured by a PCR method.

24. The use of claim 23, wherein the PCR method comprises qPCR.

25. A method of predicting the response of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising an integrin beta7 antagonist, the method comprising:

measuring the number of cells expressing at least one protein selected from integrin beta7, integrin alphaE, and CD3epsilon in a biological sample obtained from the patient, comparing the number of expressing cells measured in the sample to a reference level, and

predicting that the patient will respond to the therapy when the number of protein-expressing cells has been measured as elevated compared to the reference level and predicting that the patient will not respond to the therapy when the number of protein-expressing cells has been measured as low compared to the reference level.

26. A method of predicting responsiveness of a gastrointestinal inflammatory disorder patient to an integrin beta7 antagonist treatment, the method comprising determining the number of cells expressing at least one protein selected from integrin beta7, integrin alphaE, and CD3epsilon in a biological sample obtained from the patient, wherein elevated numbers of expressing cells compared to a reference level identifies the patient as one who is likely to respond to the integrin beta7 antagonist treatment.

27. A method of identifying a patient suffering from a gastrointestinal inflammatory disorder as likely to respond to a therapy comprising an integrin beta7 antagonist, the method comprising:

- (a) measuring the number of cells expressing at least one protein in a biological sample obtained from the patient, wherein the at least one protein is selected from integrin beta7, integrin alphaE, and CD3epsilon;
- (b) comparing the number of cells measured in (a) to a reference level; and
- (c) identifying the patient as more likely to respond to the therapy comprising an integrin beta7 antagonist when the number of cells measured in (a) is above the reference level.

28. Use of an integrin beta7 antagonist in the manufacture of a medicament for treating a patient having a gastrointestinal inflammatory disorder, the use comprising:

- (a) measuring the number of cells expressing at least one protein in a biological sample obtained from the patient, wherein the at least one protein is selected from integrin beta7, integrin alphaE, and CD3epsilon;
- (b) comparing the number of expressing cells measured in (a) to a reference level;
- (c) identifying the patient as more likely to respond a therapy comprising an integrin beta7 antagonist when the number of protein-expressing cells measured in (a) is above the reference level; and
- (d) the use of the medicament when the number of protein-expressing cells measured in (a) is above the reference level.

29. The use of claim 28, wherein 100 mg of the integrin beta7 antagonist is to be administered subcutaneously once every four weeks.

30. The method of any one of claims 25-27 or the use of any one of claims 28-29, wherein the patient is a human.

31. The method or use of claim 30, wherein the patient is a TNF inadequate responder (TNF-IR).

32. The method or use of claim 30, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease.
33. The method or use of claim 32, wherein the inflammatory bowel disease is ulcerative colitis or Crohn's disease.
34. The method or use of claim 33, wherein the inflammatory bowel disease is ulcerative colitis and the response is selected from clinical response, mucosal healing and remission.
35. The use of claim 28, wherein the biological sample is intestinal tissue.
36. The use of claim 28, comprising measuring the number of expressing cells by an immunohistochemical method.
37. The use of claim 28, wherein the measuring comprises contacting the sample with an agent that specifically binds to integrin beta7 protein, integrin alphaE protein, or CD3epsilon protein and detecting the amount of complex formed, and thereby measuring the number of protein-expressing cells.
38. The use of claim 28, wherein the number of expressing cells in the sample is divided by the total number of cells in the sample.
39. The use of claim 28, wherein the number of expressing cells in a high power field under a light microscope is determined.
40. The use of claim 28, wherein the reference level is a median value.
41. The use of claim 5 or claim 29, wherein the integrin beta7 antagonist is to be administered results in one or more of the following: (1) a 3-point decrease and 30% reduction from baseline in MCS and ≥ 1 -point decrease in rectal bleeding subscore or absolute rectal bleeding score of 0 or 1, (2) an endoscopic subscore of 0 or 1, (3) MCS ≤ 2 with no individual subscore > 1 .
42. The method of any one of claims 1-3 or 25-27, or the use of any one of claims 4-24 or 28-41, wherein the integrin beta7 antagonist is a monoclonal anti-beta7 antibody.
43. The method or use of claim 42, wherein the anti-beta7 antibody is selected from a chimeric antibody, a human antibody, and a humanized antibody.
44. The method or use of claim 43, wherein the anti-beta7 antibody is an antibody fragment.
45. The method or use of claim 43, wherein the anti-beta7 antibody comprises six hypervariable regions (HVRs), wherein:
- (i) HVR-L1 comprises amino acid sequence A1-A11, wherein A1-A11 is RASESVDTYLH (SEQ ID NO:1); RASESVDSLH (SEQ ID NO:7), RASESVDTLH (SEQ ID NO:8), or RASESVDDLH (SEQ ID NO:9) or a variant of SEQ ID NOs:1, 7, 8 or 9 (SEQ ID NO:26) wherein amino acid A2 is selected from the group consisting of A, G, S,

T, and V and/or amino acid A3 is selected from the group consisting of S, G, I, K, N, P, Q, R, and T, and/or A4 is selected from the group consisting of E, V, Q, A, D, G, H, I, K, L, N, and R, and/or amino acid A5 is selected from the group consisting of S, Y, A, D, G, H, I, K, N, P, R, T, and V, and/or amino acid A6 is selected from the group consisting of V, R, I, A, G, K, L, M, and Q, and/or amino acid A7 is selected from the group consisting of D, V, S, A, E, G, H, I, K, L, N, P, S, and T, and/or amino acid A8 is selected from the group consisting of D, G, N, E, T, P and S, and/or amino acid A9 is selected from the group consisting of L, Y, I and M, and/or amino acid A10 is selected from the group consisting of L, A, I, M, and V and/or amino acid A11 is selected from the group consisting of H, Y, F, and S;

(ii) HVR-L2 comprises amino acid sequence B1-B8, wherein B1-B8 is KYASQSSIS (SEQ ID NO:2), RYASQSSIS (SEQ ID NO:20), or XaaYASQSSIS (SEQ ID NO:21, where Xaa represents any amino acid) or a variant of SEQ ID NOs:2, 20 or 21 (SEQ ID NO:27) wherein amino acid B1 is selected from the group consisting of K, R, N, V, A, F, Q, H, P, I, L, Y and Xaa (where Xaa represents any amino acid), and/or amino acid B4 is selected from the group consisting of S and D, and/or amino acid B5 is selected from the group consisting of Q and S, and/or amino acid B6 is selected from the group consisting of S, D, L, and R, and/or amino acid B7 is selected from the group consisting of I, V, E, and K;

(iii) HVR-L3 comprises amino acid sequence C1-C9, wherein C1-C9 is QQGNLSPNT (SEQ ID NO:3) or a variant of SEQ ID NO:3 (SEQ ID NO:28) wherein amino acid C8 is selected from the group consisting of N, V, W, Y, R, S, T, A, F, H, I L, and M;

(iv) HVR-H1 comprises amino acid sequence D1-D10 wherein D1-D10 is GFFITNNYWG (SEQ ID NO:4);

(v) HVR-H2 comprises amino acid sequence E1-E17 wherein E1-E17 is GYISYSGSTSYNPSLKS (SEQ ID NO:5), or a variant of SEQ ID NO:5 (SEQ ID NO:29) wherein amino acid E2 is selected from the group consisting of Y, F, V, and D, and/or amino acid E6 is selected from the group consisting of S and G, and/or amino acid E10 is selected from the group consisting of S and Y, and/or amino acid E12 is selected from the group consisting of N, T, A, and D, and/or amino acid 13 is selected from the group consisting of P, H, D, and A, and/or amino acid E15 is selected from the group consisting of L and V, and/or amino acid E17 is selected from the group consisting of S and G; and

(vi) HVR-H3 comprises amino acid sequence F2-F11 wherein F2 -F11 is MTGSSGYFDF (SEQ ID NO:6) or RTGSSGYFDF (SEQ ID NO:19); or comprises amino acid sequence F1-F11, wherein F1-F11 is AMTGSSGYFDF (SEQ ID NO:16),

ARTGSSSGYFDF (SEQ ID NO:17), or AQTGSSSGYFDF (SEQ ID NO:18), or a variant of SEQ ID NOs:6, 16, 17, 18, or 19 (SEQ ID NO:30) wherein amino acid F2 is R, M, A, E, G, Q, S, and/or amino acid F11 is selected from the group consisting of F and Y.

46. The method or use of claim 45, wherein the anti-beta7 antibody comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:9;

(ii) HVR-L2 comprises SEQ ID NO:2;

(iii) HVR-L3 comprises SEQ ID NO:3;

(iv) HVR-H1 comprises SEQ ID NO:4;

(v) HVR-H2 comprises SEQ ID NO:5; and

(vi) HVR-H3 comprises SEQ ID NO:6 or SEQ ID NO:16 or SEQ ID NO:17 or SEQ ID NO:19.

47. The method or use of claim 46, wherein the anti-beta7 antibody comprises a variable light chain comprising the amino acid sequence of SEQ ID NO:24 and a variable heavy chain comprising the amino acid sequence of SEQ ID NO:31.

48. The method or use of claim 47, wherein the anti-beta7 antibody is etrolizumab.

49. The method of any one of claims 1-3 or 25-27, or the use of any one of claims 4-24 or 28-41, wherein the integrin beta7 antagonist is a monoclonal anti-alpha4/beta7 antibody.

50. The method or use of claim 49, wherein the anti-alpha4/beta7 antibody is selected from vedolizumab and AMG 181.