

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 responsiveness of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg, 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 and integrin alphaE, and the biological sample is a blood sample or a sample from gastrointestinal tract, (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 likely respond to the therapy when the baseline level of mRNA expression has been measured as elevated compared to the reference level. In one aspect, the present invention refers to a method of predicting responsiveness of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg, the method comprising: (a) measuring the baseline mRNA expression level of CD3epsilon in a biological sample obtained from the patient prior to the therapy, and the biological sample is a sample from gastrointestinal tract, (b) comparing the baseline mRNA expression level detected in the biological sample to a reference level that is obtained from a population of human subjects, and (c) predicting that the patient will likely respond to the therapy when the baseline level of mRNA expression has been measured as elevated 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] Disclosed is 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. 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] Disclosed is 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. 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 an antigen-binding 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 a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg, the at least one gene is selected from integrin beta7 and integrin alphaE, and the biological sample is a blood sample or a sample from gastrointestinal tract; (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. In one aspect, the present invention refers to use of an anti-beta7 antibody or an antigen-binding 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 CD3epsilon in a biological sample obtained from the patient prior to administration of a medicament comprising a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg, and the biological sample is a sample from gastrointestinal tract; (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. 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) $\text{MCS} \leq 2$ with no individual subscore > 1 .

[0025] In still yet another aspect, the present invention refers to a method of predicting the responsiveness of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 50 and 450 mg, 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, and the biological sample is a blood sample or a sample from gastrointestinal tract, (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 likely 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. 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] Disclosed is 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. 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] Disclosed is 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. 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 an antigen-binding 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 a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 50 and 450 mg, and the biological sample is a blood sample or a sample from gastrointestinal tract;

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 an antigen-binding fragment thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder in a patient who has been identified to express an elevated mRNA expression levels of at least one gene selected from integrin beta7 and integrin alphaE 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, wherein the biological sample is a blood sample or a sample from gastrointestinal tract, and the medicament comprises a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg. In yet another aspect, the present invention refers to use of an anti-beta7 antibody or an antigen-binding fragment thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder in a patient who has been identified to express an elevated mRNA expression levels of CD3 epsilon 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, wherein the biological sample is a sample from gastrointestinal tract, and the medicament comprises a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg.

[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 responsiveness of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg, 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 and integrin alphaE, and the biological sample is a blood sample or a sample from gastrointestinal tract,
 - (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 likely respond to the therapy when the baseline level of mRNA expression has been measured as elevated compared to the reference level.
2. A method of predicting responsiveness of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg, the method comprising:
 - (a) measuring the baseline mRNA expression level of CD3epsilon in a biological sample obtained from the patient prior to the therapy, and the biological sample is a sample from gastrointestinal tract,
 - (b) comparing the baseline mRNA expression level detected in the biological sample to a reference level that is obtained from a population of human subjects, and
 - (c) predicting that the patient will likely respond to the therapy when the baseline level of mRNA expression has been measured as elevated compared to the reference level.
3. The method of claim 1 or 2, further comprising (d) predicting that the patient will not likely respond to the therapy when the baseline level of mRNA expression has been measured as not elevated compared to the reference level.
4. Use of an anti-beta7 antibody or an antigen-binding 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 a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg, the at least one gene is selected from integrin beta7 and integrin alphaE, and the biological sample is a blood sample or a sample from gastrointestinal tract;
- (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. Use of an anti-beta7 antibody or an antigen-binding 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 CD3epsilon in a biological sample obtained from the patient prior to administration of a medicament comprising a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg, and the biological sample is a sample from gastrointestinal tract;

(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.6. The method of any one of claims 1-3 or use of claim 4 or 5, wherein about 50 mg, about 100 mg, about 150 mg, or about 200 mg of the anti-beta7 antibody or antigen-binding fragment thereof is to be administered subcutaneously to the patient.

7. The method of any one of claims 1-3 and 6 or use of any one of claims 4-6, wherein about 100 mg of the anti-beta7 antibody or antigen-binding 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 6-7 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 6-9 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 6-12 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 6-13 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 6-15 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 6-16 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 an antigen-binding fragment thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder in a patient who has been identified to express an elevated mRNA expression levels of at least one gene selected from integrin beta7 and integrin alphaE 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, wherein the biological sample is a blood sample or a sample from gastrointestinal tract, and the medicament comprises a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg.
19. Use of an anti-beta7 antibody or an antigen-binding fragment thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder in a patient who has been identified to express an elevated mRNA expression levels of CD3 epsilon 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, wherein the biological sample is a sample from gastrointestinal tract, and the medicament comprises a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 100 mg and 220 mg.
20. The use of claim 18 or 19, wherein about 100 mg of the anti-beta7 antibody or antigen-binding fragment thereof is to be administered subcutaneously once every four weeks to the patient.
21. The use of any one of claims 18-20, wherein the patient is a human.
22. The use of claim 21, wherein the patient is a TNF inadequate responder (TNF-IR).
23. The use of any one of claims 18-22, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease.
24. The use of claim 23, wherein the inflammatory bowel disease is ulcerative colitis or Crohn's disease.
25. The use of any one of claims 18-24, wherein the biological sample is selected from intestinal biopsy and peripheral whole blood.
26. The use of any one of claims 18-25, wherein the baseline mRNA expression level is measured by a PCR method.

27. The use of claim 26, wherein the PCR method comprises qPCR.
28. A method of predicting the responsiveness of a patient suffering from a gastrointestinal inflammatory disorder to a therapy comprising a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 50 and 450 mg, 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, and the biological sample is a blood sample or a sample from gastrointestinal tract,
 - (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 likely 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.
29. The method of claim 28, further comprising (d) predicting that the patient will not likely respond to the therapy when the baseline number of integrin alphaE-expressing cells has been measured as not elevated compared to the reference number of integrin alphaE-expressing cells.

30. Use of an anti-beta7 antibody or an antigen-binding 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 a flat dose of an anti-beta7 antibody or an antigen-binding fragment thereof, wherein the flat dose is between about 50 and 450 mg, and the biological sample is a blood sample or a sample from gastrointestinal tract;
- (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 claim 28 or 29 or use of claim 30, wherein the anti-beta7 antibody or antigen-binding fragment thereof is to be administered subcutaneously to the patient.

32. The method of any one of claims 28-29 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 antigen-binding fragment thereof is to be administered subcutaneously to the patient.

33. The method of any one of claims 28-29 and 31-32 or use of any one of claims 30-32, wherein about 100 mg of the anti-beta7 antibody or antigen-binding fragment thereof is to be administered subcutaneously once every four weeks to the patient.

34. The method of any one of claims 28-29 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 28-29 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 28-29 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 28-29 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 28-29 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 28-29 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 28-29 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 28-29 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 antigen-binding 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, 6-17, 28-29 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, 6-17, 28-29 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, 6-17, 28-29, and 31-47 or use of any one of claims 4-26 and 30-47, wherein the anti-beta7 antibody or antigen-binding fragment thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

- (i) the HVR-L1 comprises the amino acid sequence set forth in SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:9;
- (ii) the HVR-L2 comprises the amino acid sequence set forth in SEQ ID NO:2;
- (iii) the HVR-L3 comprises the amino acid sequence set forth in SEQ ID NO:3;
- (iv) the HVR-H1 comprises the amino acid sequence set forth in SEQ ID NO:4;
- (v) the HVR-H2 comprises the amino acid sequence set forth in SEQ ID NO:5; and
- (vi) the HVR-H3 comprises the amino acid sequence set forth in SEQ ID NO:6 or SEQ ID NO:16 or SEQ ID NO:17 or SEQ ID NO:19.

49. The method or use of claim 48, wherein the anti-beta7 antibody or antigen-binding fragment thereof comprises:

- (i) a HVR-L1 comprising the amino acid sequence set forth in SEQ ID NO:9;
- (ii) a HVR-L2 comprising the amino acid sequence set forth in SEQ ID NO:2;
- (iii) a HVR-L3 comprising the amino acid sequence set forth in SEQ ID NO:3;
- (iv) a HVR-H1 comprising the amino acid sequence set forth in SEQ ID NO:4;
- (v) a HVR-H2 comprising the amino acid sequence set forth in SEQ ID NO:5; and
- (vi) a HVR-H3 comprising the amino acid sequence set forth in SEQ ID NO:19.

50. The method or use of claim 48, wherein the anti-beta7 antibody or antigen-binding fragment thereof comprises:

- (i) a HVR-L1 comprising the amino acid sequence set forth in SEQ ID NO:9;
- (ii) a HVR-L2 comprising the amino acid sequence set forth in SEQ ID NO:2;
- (iii) a HVR-L3 comprising the amino acid sequence set forth in SEQ ID NO:3;
- (iv) a HVR-H1 comprising the amino acid sequence set forth in SEQ ID NO:4;
- (v) a HVR-H2 comprising the amino acid sequence set forth in SEQ ID NO:5; and
- (vi) a HVR-H3 comprising the amino acid sequence set forth in SEQ ID NO:17.

51. The method or use of any one of claims 48-50, wherein the anti-beta7 antibody or antigen-binding 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.

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

53. The method of any one of claims 1-3, 6-17, 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.

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