

CLAIMS

What is Claimed is:

1. A method for treating psoriasis in a subject, the method comprising:
measuring a level of at least one biomarker in a biological sample of uninvolved skin isolated from the subject prior to treatment with an anti-tumor necrosis factor (anti-TNF) agent, wherein the at least one biomarker is
 - (a) ubiquitin specific protease 18 (USP18) and the level of USP18 is increased relative to a control level;
 - (b) keratin, type II cytoskeletal 2 epidermal (KRT2) and the level of KRT2 is decreased relative to a control level;
 - (c) interleukin 4 receptor (IL4R) and the level of IL4R is increased relative to a control level;
 - (d) sex-determining region Y-box transcription factor 5 (SOX5), and the level of SOX5 is decreased relative to a control level;
 - (e) interferon induced with helicase C domain 1 (IFIH1), and the level of IFIH1 is increased relative to a control level; or
 - (f) a combination of biomarkers of any two or more of (a)-(e),wherein the increased or decreased level of the biomarker in the subject relative to the control level predicts that the subject will be responsive to treatment with the anti-TNF agent, and
wherein the control level is the mean level of the biomarker in uninvolved skin in a population of subjects suffering from psoriasis prior to treatment with the anti-TNF agent; and
administering an effective amount of an anti-TNF agent to the subject predicted to be responsive to treatment.
2. The method of claim 1, wherein the at least one biomarker is USP18.
3. The method of claim 1, wherein the at least one biomarker is KRT2.
4. The method of claim 1, wherein the at least one biomarker is IL4R.
5. The method of claim 1, wherein the at least one biomarker is SOX5.
6. The method of claim 1, wherein the at least one biomarker is IFIH1.

7. The method of claim 1, wherein the at least one biomarker is a combination of any two or more of USP18, KRT2, IL4R, SOX5, or IFIH1.
8. The method of claim 1, wherein the at least one biomarker is a combination of any two or more of USP18, KRT2, IL4R, SOX5, or IFIH1 as set out in any of the combinations in Table 1.
9. The method of claim 1 or 2, wherein the level of USP18 is increased by at least about 86% or more relative to the control level.
10. The method of claim 1 or 3, wherein the level of KRT2 is decreased by at least about 99% or more relative to the control level.
11. The method of claim 1 or 4, wherein the level of IL4R is increased by at least about 36% or more relative to the control level.
12. The method of claim 1 or 5, wherein the level of SOX5 is decreased by at least about 89% or more relative to the control level.
13. The method of claim 1 or 6, wherein the level of IFIH1 is increased by at least about 49% or more relative to the control level.
14. The method of any one of claims 1-13, wherein the level is a measure of the level of a nucleic acid or protein present in the biological sample.
15. The method of claim 14, wherein the nucleic acid is deoxyribonucleic acid.
16. The method of claim 14, wherein the nucleic acid is ribonucleic acid.
17. The method of any one of claims 1-16, wherein the anti-TNF agent is etanercept, infliximab, adalimumab, certolizumab pegot, or golimumab.
18. The method of any one of claims 1-16, wherein the anti-TNF agent is thalidomide, lenalidomide, pomalidomide, a xanthine derivative, or bupropion.
19. The method of any one of claims 1-18, wherein the psoriasis is plaque psoriasis, guttate psoriasis, inverse psoriasis, intertriginous psoriasis, pustular psoriasis, erythrodermic psoriasis, or psoriatic arthritis.
20. The method of any one of claims 1-19, further comprising administering to the subject at least one additional treatment or medication for psoriasis.
21. The method of any one of claims 1-20, wherein the subject is a human subject.

22. The method of any one of claims 1-21, wherein the level of the biomarker is measured with an immunoassay, Northern blot analysis, reverse transcription quantitative polymerase chain reaction, RNA sequencing, or high-throughput sequencing.

23. The method of any one of claims 1-22, wherein the subject treated with the anti-TNF agent shows PASI improvement by about 12 weeks of treatment.

24. The method of claim 23, wherein the PASI improvement is at least about 10% of PASI improvement.

25. A method for prognosing responsiveness to an anti-TNF agent in treatment of psoriasis in a subject, the method comprising:

measuring a level of at least one biomarker in a biological sample of uninvolved skin isolated from the subject prior to treatment with an anti-tumor necrosis factor (anti-TNF) agent, wherein the at least one biomarker is

- (a) ubiquitin specific protease 18 (USP18);
- (b) keratin, type II cytoskeletal 2 epidermal (KRT2);
- (c) interleukin 4 receptor (IL4R);
- (d) sex-determining region Y-box transcription factor 5 (SOX5);
- (e) interferon induced with helicase C domain 1 (IFIH1); or
- (f) a combination of biomarkers of any two or more of (a)-(e), and

comparing the level with a control level, wherein the control level is the mean level of the biomarker in uninvolved skin in a population of subjects suffering from psoriasis prior to treatment with the anti-TNF agent,

wherein when the level of USP18, ILR4, and/or IFIH1 in the subject is increased relative to the control level of the biomarker, the subject is predicted to be responsive to treatment with the anti-TNF agent;

wherein when the level of KRT2 and/or SOX5 in the subject is decreased relative to the control level of the biomarker, the subject is predicted to be responsive to treatment with the anti-TNF agent;

wherein when the level of USP18, ILR4, and/or IFIH1 in the subject is not increased relative to the control level of the biomarker, the subject is predicted to be non-responsive to treatment with the anti-TNF agent; and/or

wherein when the level of KRT2 and/or SOX5 in the subject is not decreased relative to the control level of the biomarker, the subject is predicted to be non-responsive to treatment with the anti-TNF agent.

26. The method of claim 25 further comprising administering an effective amount of the anti-TNF agent to treat the subject predicted to be responsive to treatment with the anti-TNF agent.

27. The method of claim 25 or 26, wherein the at least one biomarker is USP18.

28. The method of claim 25 or 26, wherein the at least one biomarker is KRT2.

29. The method of claim 25 or 26, wherein the at least one biomarker is IL4R.

30. The method of claim 25 or 26, wherein the at least one biomarker is SOX5.

31. The method of claim 25 or 26, wherein the at least one biomarker is IFIH1.

32. The method of claim 25 or 26, wherein the at least one biomarker is a combination of any two or more of USP18, KRT2, IL4R, SOX5, and IFIH1.

33. The method of claim 25 or 26, wherein the at least one biomarker is a combination of any two or more of USP18, KRT2, IL4R, SOX5, and IFIH1 as set out in any of the combinations in Table 1.

34. The method of claim 25, 26, or 27, wherein the level of USP18 is increased by at least about 86% or more relative to the control level.

35. The method of claim 25, 26, or 28, wherein the level of KRT2 is decreased by at least about 99% or more relative to the control level.

36. The method of claim 25, 26, or 29, wherein the level of IL4R is increased by at least about 36% or more relative to the control level.

37. The method of claim 25, 26, or 30, wherein the level of SOX5 is decreased by at least about 89% or more relative to the control level.

38. The method of claim 25, 26, or 30, wherein the level of IFIH1 is increased by at least about 49% or more relative to the control level.

39. The method of any one of claims 25-28, wherein the level is a measure of the level of a nucleic acid or protein present in the biological sample.

40. The method of claim 39, wherein the nucleic acid is deoxyribonucleic acid.

41. The method of claim 39, wherein the nucleic acid is ribonucleic acid.

42. The method of any one of claims 25-41, wherein the anti-TNF agent is etanercept, infliximab, adalimumab, certolizumab pegot, or golimumab.
43. The method of any one of claims 25-41, wherein the anti-TNF agent is thalidomide, lenalidomide, pomalidomide, a xanthine derivative, or bupropion.
44. The method of any one of claims 25-43, wherein the psoriasis is plaque psoriasis, guttate psoriasis, inverse psoriasis, intertriginous psoriasis, pustular psoriasis, erythrodermic psoriasis, or psoriatic arthritis.
45. The method of any one of claims 25-44, further comprising administering to the subject at least one additional treatment or medication for psoriasis.
46. The method of any one of claims 25-45, wherein the subject is a human subject.
47. The method of any one of claims 25-46, wherein the level of the biomarker is measured with an immunoassay, Northern blot analysis, reverse transcription quantitative polymerase chain reaction, RNA sequencing, or high-throughput sequencing.
48. The method of any one of claims 25-47, wherein the subject predicted to be responsive to treatment with the anti-TNF agent is expected to show PASI improvement by about 12 weeks of treatment.
49. The method of claim 48, wherein the PASI improvement is expected to be at least about 10% of PASI improvement.
50. A kit comprising reagents for measuring a level of at least one biomarker in a biological sample of uninvolved skin isolated from a subject suffering from psoriasis prior to treatment with an anti-tumor necrosis factor (anti-TNF) agent, wherein the at least one biomarker is
- (a) ubiquitin specific protease 18 (USP18);
 - (b) keratin, type II cytoskeletal 2 epidermal (KRT2);
 - (c) interleukin 4 receptor (IL4R);
 - (d) sex-determining region Y-box transcription factor 5 (SOX5);
 - (e) interferon induced with helicase C domain 1 (IFIH1); or
 - (f) a combination of biomarkers of any two or more of (a)-(e), and
- wherein the level is the level of nucleic acid or protein of the biomarker in the biological sample.

51. The kit of claim 50, further comprising a means for comparing the level of the nucleic acid or protein of the biomarker in the biological sample with a control level, wherein the control level is the mean level of the biomarker in uninvolved skin in a population of subjects suffering from psoriasis prior to treatment with the anti-TNF agent.

52. The kit of claim 50 or 51, wherein the biological sample is obtained from a biopsy of uninvolved skin from a subject suffering from psoriasis.

53. Use of measurement of an increased or decreased level of at least one biomarker in a biological sample of uninvolved skin from a subject suffering from psoriasis in comparison to measurement of a control level, wherein the control level is the mean level of the biomarker in uninvolved skin in a population of subjects suffering from psoriasis prior to treatment with the anti-TNF agent, for prognosing responsiveness of the subject to treatment with an anti-tumor necrosis factor (anti-TNF) agent, wherein the at least one biomarker is

- (a) ubiquitin specific protease 18 (USP18);
- (b) keratin, type II cytoskeletal 2 epidermal (KRT2);
- (c) interleukin 4 receptor (IL4R);
- (d) sex-determining region Y-box transcription factor 5 (SOX5);
- (e) interferon induced with helicase C domain 1 (IFIH1); or
- (f) a combination of biomarkers of any two or more of (a)-(e), and

wherein when the level of USP18, ILR4, and/or IFIH1 in the subject is increased relative to the control level of the biomarker, the subject is predicted to be responsive to treatment with the anti-TNF agent;

wherein when the level of KRT2 and/or SOX5 in the subject is decreased relative to the control level of the biomarker, the subject is predicted to be responsive to treatment with the anti-TNF agent;

wherein when the level of USP18, ILR4, and/or IFIH1 in the subject is not increased relative to the control level of the biomarker, the subject is predicted to be non-responsive to treatment with the anti-TNF agent; and/or

wherein when the level of KRT2 and/or SOX5 in the subject is not decreased relative to the control level of the biomarker, the subject is predicted to be non-responsive to treatment with the anti-TNF agent.

54. The use of claim 53, wherein the at least one biomarker is USP18.

55. The use of claim 53, wherein the at least one biomarker is KRT2.

56. The use of claim 53, wherein the at least one biomarker is IL4R.
57. The use of claim 53, wherein the at least one biomarker is SOX5.
58. The use of claim 53, wherein the at least one biomarker is IFIH1.
59. The use of claim 53, wherein the at least one biomarker is a combination of any two or more of USP18, KRT2, IL4R, SOX5, or IFIH1.
60. The use of claim 53, wherein the at least one biomarker is a combination of any two or more of USP18, KRT2, IL4R, SOX5, or IFIH1 as set out in any of the combinations in Table 1.
61. The use of claim 53 or 54, wherein the level of USP18 is increased by at least about 86% or more relative to the control level.
62. The use of claim 53 or 55, wherein the level of KRT2 is decreased by at least about 99% or more relative to the control level.
63. The use of claim 53 or 56, wherein the level of IL4R is increased by at least about 36% or more relative to the control level.
64. The use of claim 53 or 57, wherein the level of SOX5 is decreased by at least about 89% or more relative to the control level.
65. The use of claim 53 or 58, wherein the level of IFIH1 is increased by at least about 49% or more relative to the control level.
66. The use of any one of claims 53-65, wherein the level is a measure of the level of a nucleic acid or protein present in the biological sample.
67. The use of claim 66, wherein the nucleic acid is deoxyribonucleic acid.
68. The use of claim 66, wherein the nucleic acid is ribonucleic acid.
69. The use of any one of claims 53-68, wherein the anti-TNF agent is etanercept, infliximab, adalimumab, certolizumab pegot, or golimumab.
70. The use of any one of claims 53-68, wherein the anti-TNF agent is thalidomide, lenalidomide, pomalidomide, a xanthine derivative, or bupropion.
71. The use of any one of claims 53-70, wherein the psoriasis is plaque psoriasis, guttate psoriasis, inverse psoriasis, intertriginous psoriasis, pustular psoriasis, erythrodermic psoriasis, or psoriatic arthritis.
72. The use of any one of claims 53-71, wherein the subject is a human subject.

73. The use of any one of claims 53-72, wherein the level of the biomarker is measured with an immunoassay, Northern blot analysis, reverse transcription quantitative polymerase chain reaction, RNA sequencing, or high-throughput sequencing.

74. The use of any one of claims 53-73, wherein the subject predicted to be responsive to treatment with the anti-TNF agent is expected to show PASI improvement by about 12 weeks of treatment.

75. The use of claim 74, wherein the PASI improvement is expected to be at least about 10% of PASI improvement.