(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.

In some aspects, the disclosure provides a use of an anti-TNF agent, wherein the anti-TNF agent is etanercept, infliximab, adalimumab, certolizumab pegol, or golimumab, in the manufacture of a medicament for treating psoriasis in a subject, wherein the use comprises:

measuring a level of a combination of any two or more biomarkers in a biological sample of uninvolved skin isolated from the subject prior to treatment with the anti-tumor necrosis factor (anti-TNF) agent, wherein the any two or more biomarkers are selected from

(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; and

(e) interferon induced with helicase C domain 1 (IFIH1), and the level of IFIH1 is increased relative to a control level

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

wherein an effective amount of the anti-TNF agent is to be administered to the subject predicted to be responsive to treatment.

[0009] In some examples, the at least one biomarker is USP18. In some examples, the at least one biomarker is KRT2. In some examples, the at least one biomarker is IL4R. In some examples, the at least one biomarker is SOX5. In some examples, the at least one biomarker is IFIH1. In some examples, the at least one biomarker is a combination of any two or more of USP18, KRT2, IL4R, SOX5, and IFIH1. In some examples, 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.

[0010] In some examples, the level of USP18 is increased by at least about 86% or more relative to the control level. In some examples, the level of KRT2 is decreased by at least about 99% or more relative to the control level. In some examples, the level of IL4R is increased by at least about 36% or more relative to the control level. In some examples, the level of SOX5 is decreased by at least about 89% or more relative to the control level. In some examples, the level of IFIH1 is increased by at least about 49% or more relative to the control level.

[0011] In some examples, the level is a measure of the level of a nucleic acid or protein present in the biological sample. In some examples, the nucleic acid is deoxyribonucleic acid. In some examples, the nucleic acid is ribonucleic acid.

[0012] In some examples, the anti-TNF agent is etanercept, infliximab, adalimumab, certolizumab pegot, or golimumab or a biosimilar thereof. In some examples, the anti-TNF agent is thalidomide, lenalidomide, pomalidomide, a xanthine derivative, or bupropion.

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. In some aspects, the disclosure provides an *in vitro* method for prognosing responsiveness to an anti-TNF agent, wherein the anti-TNF agent is etanercept, infliximab, adalimumab, certolizumab pegol, or golimumab, in treatment of psoriasis in a subject, wherein the method comprises

measuring a level of a combination of any two or more biomarkers 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 any two or more biomarkers are selected from

(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); and

(e) interferon induced with helicase C domain 1 (IFIH1);

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;

[0024] In some examples, the psoriasis is plaque psoriasis, guttate psoriasis, inverse psoriasis, intertriginous psoriasis, pustular psoriasis, erythrodermic psoriasis, or psoriatic arthritis.

[0025] In some examples, the method further comprises administering to the subject at least one additional treatment or medication for psoriasis.

[0026] In some examples, the subject is a human subject.

[0027] In some examples, 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.

[0028] In some examples, the subject treated with the anti-TNF agent shows PASI improvement by about 12 weeks of treatment. In some examples, PASI improvement is observed earlier than 12 weeks after treatment. In some examples, the PASI improvement is at least about 10% of PASI improvement.

[0029] In some aspects, the disclosure provides a kit comprising reagents for measuring a level of a nucleic acid or protein of a combination of any two or more biomarkers 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 combination of any two or more biomarkers are selected from

(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); and

(e) interferon induced with helicase C domain 1 (IFIH1).

[0030] In some examples, the kit further comprises 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. In some examples, the biological sample is obtained from a biopsy of uninvolved skin from a subject suffering from psoriasis. In some examples, the biological sample is obtained from a

Claims

What is Claimed is:

1. Use of an anti-TNF agent, wherein the anti-TNF agent is etanercept, infliximab, adalimumab, certolizumab pegol, or golimumab, in the manufacture of a medicament for treating psoriasis in a subject, wherein the use comprises:

measuring a level of a combination of any two or more biomarkers in a biological sample of uninvolved skin isolated from the subject prior to treatment with the anti-tumor necrosis factor (anti-TNF) agent, wherein the any two or more biomarkers are selected from

(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; and

(e) interferon induced with helicase C domain 1 (IFIH1), and the level of IFIH1 is increased relative to a control level;

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

wherein an effective amount of the anti-TNF agent is to be administered to the subject predicted to be responsive to treatment.

2. The use of claim 1, wherein the combination of any two or more of USP18, KRT2, IL4R, SOX5, and IFIH1 is a combination as set out in any of the combinations of two or more of USP18, KRT2, IL4R, SOX5, and IFIH1 in Table 1.

3. The use of claim 1, wherein the level of USP18 is increased by at least 86% relative to the control level.

4. The use of claim 1, wherein the level of KRT2 is decreased by at least 99% relative to the control level.

5. The use of claim 1, wherein the level of IL4R is increased by at least 36% relative to the control level.

6. The use of claim 1, wherein the level of SOX5 is decreased by at least 89% relative to the control level.

7. The use of claim 1, wherein the level of IFIH1 is increased by at least 49% relative to the control level.

8. The use of any one of claims 1-7, wherein the level is a measure of the level of a nucleic acid or protein present in the biological sample.

9. The use of claim 8, wherein the nucleic acid is deoxyribonucleic acid.

10. The use of claim 8, wherein the nucleic acid is ribonucleic acid.

11. The use of any one of claims 1-10, wherein the anti-TNF agent is etanercept.

12. The use of any one of claims 1-11, wherein the psoriasis is plaque psoriasis, guttate psoriasis, inverse psoriasis, intertriginous psoriasis, pustular psoriasis, erythrodermic psoriasis, or psoriatic arthritis.

13. The use of any one of claims 1-12, wherein the subject is to be further administered with at least one additional treatment or medication for psoriasis.

14. The use of any one of claims 1-13, wherein the subject is a human subject.

15. The use of any one of claims 1-14, 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.

16. The use of any one of claims 1-15, wherein the subject treated with the anti-TNF agent shows PASI improvement by about 12 weeks after treatment with the anti-TNF agent.

17. The use of claim 16, wherein the PASI improvement is at least 10% of PASI improvement.

18. An *in vitro* method for prognosing responsiveness to an anti-TNF agent, wherein the anti-TNF agent is etanercept, infliximab, adalimumab, certolizumab pegol, or golimumab, in treatment of psoriasis in a subject, wherein the method comprises:

measuring a level of a combination of any two or more biomarkers 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 any two or more biomarkers are selected from

(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); and

(e) interferon induced with helicase C domain 1 (IFIH1);

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.

19. The method of claim 18, wherein the combination of any two or more biomarkers is a combination of any two of USP18, KRT2, IL4R, SOX5, and IFIH1 as set out in any of the combinations of two or more of USP18, KRT2, IL4R, SOX5, and IFIH1 in Table 1.

20. The method of claim 18, wherein the level of USP18 is increased by at least 86% relative to the control level.

21. The method of claim 18, wherein the level of KRT2 is decreased by at least 99% relative to the control level.

22. The method of claim 18, wherein the level of IL4R is increased by at least 36% relative to the control level.

23. The method of claim 18, wherein the level of SOX5 is decreased by at least 89% relative to the control level.

24. The method of claim 18, wherein the level of IFIH1 is increased by at least 49% relative to the control level.

25. The method of any one of claims 18-24, wherein the level is a measure of the level of a nucleic acid or protein present in the biological sample.

26. The method of claim 25, wherein the nucleic acid is deoxyribonucleic acid.

27. The method of claim 25, wherein the nucleic acid is ribonucleic acid.

28. The method of any one of claims 18-27, wherein the anti-TNF agent is etanercept.

29. The method of any one of claims 18-28, wherein the psoriasis is plaque psoriasis, guttate psoriasis, inverse psoriasis, intertriginous psoriasis, pustular psoriasis, erythrodermic psoriasis, or psoriatic arthritis.

30. The method of any one of claims 18-29, wherein the subject is a human subject.

31. The method of any one of claims 18-30, 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.

32. The method of any one of claims 18-31, wherein the subject predicted to be responsive to treatment with the anti-TNF agent shows PASI improvement by about 12 weeks after treatment with the anti-TNF agent.

33. The method of claim 32, wherein the PASI improvement is at least 10% of PASI improvement.

34. A kit comprising reagents for measuring a level of a nucleic acid or protein of a combination of any two or more biomarkers 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 combination of any two or more biomarkers are selected from

(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); and

(e) interferon induced with helicase C domain 1 (IFIH1).

35. The kit of claim 34, wherein the biological sample is a biopsy of uninvolved skin from a subject suffering from psoriasis.