CLAIMS

1. A method for preparing an enriched and expanded cell population of tumour reactive T-cells for use in cancer therapy comprising identifying and/or obtaining a cell population expressing CD150/SLAM/SLAMF1 and expanding the cell population.

2. A method according to Claim 1, in which the T-cells expressing CD150/SLAM/SLAMF1 are T-cells selected from cells originating from a subject.

3. A method according to Claim 1 or 2, in which selecting the T-cells expressing CD150/SLAM/SLAMF1 comprises one or more of (i) flow cytometry, (ii) antibody panning, (iii) magnetic selection and (iv) biomarker targeted cell enrichment.

4. A method according to Claim 1 or 2, in which selecting the T-cells comprises contacting the cell population with an anti-CD150/SLAM/SLAMF1 antibody.

5. A method according to any preceding claim, in which the expanding comprises:

(a) irradiating feeder cells and co-stimulating with an anti-CD150/SLAM/SLAMF1 antibody and optionally one or more cytokines;

(b) stimulating or activating CD150/SLAM/SLAMF1; or

(c) rapid expansion protocol (REP) in which cells are mixed with irradiated feeder cells and one or more cytokines until at least $1x10^9$ or at least $5x10^9$ or at least $1x10^{10}$ cells are obtained.

6. A method according to any preceding claim, in which the cell population is:

(a) a population of tumour infiltrating lymphocytes (TILs) from a tumour biopsy, lymph node or ascites;

(b) a population of T-cells engineered to express a CAR and/or a TCR; and/or

(c) a population of T-cells isolated from blood.

7. A method according to any preceding claim, in which the cancer is a melanoma, lung cancer, squamous cell cancer, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer including gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial cancer or uterine carcinoma, salivary gland

carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, head cancer or neck cancer.

8. A method according to any preceding claim, in which the cancer therapy is adoptive cell therapy.

9. A method according to any preceding claim, in which the method further comprises exposing the T-cells to a modulator that increases SLAM production.

10. A method according to Claim 9, in which the modulator comprises:

(I) a cytokine, optionally in which the cytokine is IL-2, IL-15, IL-18, IL-12, IL-23, IL-27, IL-35, IL-39, IL-18, IL-36, IL-37, IL-38, IFN-alpha, IFN-beta, IFN-gamma or a combination thereof; or

(II) a cytokine combination of IL-7+ IL-15, IL-2 + IL-7 + IL-15, IL-2 + IL-12, IL-2 + IL-18, IL-2 + IL-12 + IL-7 + IL-15, IL- 2 + IL-12 + IL-7 + IL-15 + IL-6, IL-2 + IL-12 + IL-7 + IL-15 + IL-21, IL-2 + IL-12 + IL- 7 + IL-15 + IL-6 + IL-21, IL-7 + IL-15 + IL-6, IL-7 + IL-15 + IL-21, IL-7 + IL-15 + IL-6 + IL-21, IL-2 + IL-12 + IL-6, IL-2 + IL-12 + IL-21, or IL-2 + IL-12 + IL-6 + IL-21.

11. A method according to Claim 9 or 10, in which the modulator further comprises a Th2 blocking agent, optionally in which the Th2 blocking agent is an antibody selected from:

(I) anti-IL-4 (aIL4), anti-IL-4R (aIL4R), anti-IL-5R (aIL5R), anti-IL-5 (aIL5), anti-IL13R (aIL13R) and anti-IL13 (aIL13); or

(II) Mepolizumab, Resilizumab, Benralizumab, Tralokinumab, Lebrikizumab and Dupilumab.

12. A method according to Claim 11, in which:

(I) the modulator comprises IL-2 + aIL4;

(II) the modulator comprises IL-2 + IL-12 + aIL4; or

(III) the modulator comprises IL-2+ IL-12 + IL-7 + IL-15 + aIL4.

13. A method according to Claim 10, 11 or 12, in which IL-12 is briefly added for 1-96 h at 1- 150 ng/ml at the expanding step and subsequently replaced with another cytokine.

14. A method according to any of Claims 10 to 13, in which the cytokine is produced by an artificial antigen presenting cell and the tumour reactive T cells are co-cultured with the antigen presenting cell.

15. A method according to any preceding claim, in which the cell population is isolated and cultured with a modulator that increases CD150/SLAM/SLAMF1 production and in which the cultured cells are separated from unselected cells.

16. A method according to any preceding claim, in which the T cells are engineered to express a cytokine receptor which provides cytokine signalling upon engagement of another drug or cytokine.

17. A method according to any preceding claim, in which the T cell is a CD4+ or a CD8+ T cell.

18. A population of cells obtained according to a method according to any preceding claim.

19. A population of cells according to Claim 18 for use in the treatment of cancer.

20. An enriched and expanded cell population of tumour reactive T-cells expressing CD150/SLAM/SLAMF1 for use in the treatment of cancer.

21. A population of cells according to Claim 18, 19 or 20, in which the population comprises T-cells and in which >25%, >30% or >40% of the T-cells express CD150/SLAM/SLAMF1.

22. A population of cells according to any of Claims 18 to 21, in which the cells are TILs.

23. Use of a population of cells according to any of Claims 18 to 22 in the preparation of a medicament for adoptive cell therapy, in which the population of cells is to be administered to a subject, in which the T-cells are autologous or allogenic.

24. Use of a population of cells according to any of Claims 18 to 22 in the preparation of a medicament for the treatment of a cancer in a subject, in which the population of cells is to be administered to the subject.

25. A pharmaceutical composition comprising a population of cells according to any of Claims 18 to 22.

26. A pharmaceutical composition according to Claim 25 for use in the treatment of cancer.

27. A method for assessing the tumour reactivity of a cell population which method comprises quantifying the proportion of T-cells expressing SLAM/SLAMF1/CD150 in the cell population.

28. A method according to Claim 27, in which the cell population is (i) TILs from a patient and the T-cells expressing SLAM/SLAMF1/CD150 are quantified pre-REP and/or post-REP; or (ii) a population of T-cells engineered to express an exogenous CAR and/or a TCR.

29. A method according to Claim 27 or 28, in which the proportion of T-cells expressing SLAM/SLAMF1/CD150 being at least 25% of the cell population indicates that the cell population is tumour reactive.

30. A method for identifying an agent for increasing SLAM/SLAMF1/CD150 expression in isolated ex vivo expansion of T cells for use in adoptive cell therapy, optionally, in which the T-cell is a CD4+ or a CD8+ T-cell, comprising

(a) contacting tumour infiltrating lymphocytes with a candidate modulator that upregulates the expression of SLAM in T cells;

(b) screening the effect of the modulator on the expression of SLAM in the cells; and

(c) identifying a modulator that increases the expression of SLAM in the cells.

31. Use of at least one biological marker in preparation of an agent for use in an *in vitro* method for the prognosis of patients who may receive tumour infiltrating lymphocyte (TIL) therapy for cancer, the method comprising:

(a) quantifying in a sample of tumour digest, TIL material during the manufacturing process or TIL product, from the patient, at least one biological marker on the TIL; and

(b) comparing the value obtained at step (a) for the at least one biological marker with a predetermined reference value for the same biological marker; which predetermined reference value is correlated with a specific prognosis of progression of the cancer.

32. Use according to Claim 31, in which the at least one biological marker is SLAM/SLAMF1/CD150.

33. Use of a cell population expressing CD150/SLAM/SLAMF1 in the preparation of a medicament for the treatment of cancer, the use comprising preparing an enriched and

expanded cell population of tumour reactive T-cells comprising identifying and/or obtaining a cell population expressing CD150/SLAM/SLAMF1, expanding the cell population, and administering to a cancer patient in need thereof cells from the cell population.

34. Use according to Claim 33, in which the T-cells expressing CD150/SLAM/SLAMF1 are T-cells selected from cells originating from a subject.

35. Use according to Claim 33 or 34, in which:

(I) selecting the T-cells expressing CD150/SLAM/SLAMF1 comprises one or more of (a) flow cytometry, (b) antibody panning, (c) magnetic selection and (d) biomarker targeted cell enrichment; or

(II) selecting the T-cells comprises contacting the cell population with an anti-CD150/SLAM/SLAMF1 antibody.

36. T Use according to Claim 33, 34 or 35, in which the expanding comprises:

(a) irradiating feeder cells and co-stimulating with an anti-CD150/SLAM/SLAMF1 antibody and optionally one or more cytokines;

(b) stimulating or activating CD150/SLAM/SLAMF1; or

(c) rapid expansion protocol (REP) in which cells are mixed with irradiated feeder cells and one or more cytokines until at least $1x10^9$ or at least $5x10^9$ or at least $1x10^{10}$ cells are obtained.

37. Use according to any of Claims 33 to 36, in which the cell population is:

(a) a population of tumour infiltrating lymphocytes (TILs) from a tumour biopsy, lymph node or ascites;

(b) a population of T-cells engineered to express a CAR and/or a TCR; and/or

(c) a population of T-cells isolated from blood.

38. Use according to any of Claims 33 to 37, in which the cancer is a melanoma, lung cancer or ovarian cancer.

39. Use according to any of Claims 33 to 38, in which the cancer therapy is adoptive cell therapy.

40. Use according to any of Claims 33 to 39, in which the method further comprises exposing the T-cells to a modulator that increases SLAM production.

41. Use according to Claim 40, in which the modulator comprises:

(I) a cytokine, optionally in which the cytokine is IL-2, IL-15, IL-18, IL-12, IL-23, IL-27, IL-35, IL-39, IL-18, IL-36, IL-37, IL-38, ILN-alpha, ILN-beta, ILN-gamma or a combination thereof; or

(II) a cytokine combination of IL-7+ IL-15, IL-2 + IL-7 + IL-15, IL-2 + IL-12, IL-2 + IL-18, IL-2 + IL-12 + IL-7 + IL-15, IL- 2 + IL-12 + IL-7 + IL-15 + IL-6, IL-2 + IL-12 + IL-7 + IL-15 + IL-21, IL-2 + IL-12 + IL- 7 + IL-15 + IL-6 + IL-21, IL-7 + IL-15 + IL-6, IL-7 + IL-15 + IL-21, IL-7 + IL-15 + IL-6 + IL-21, IL-2 + IL-12 + IL-6, IL-2 + IL-12 + IL-21, or IL-2 + IL-12 + IL-6 + IL-21.

42. Use according to Claim 40 or 41, in which the modulator further comprises a Th2 blocking agent, optionally in which the Th2 blocking agent is an antibody selected from:

(I) anti-IL-4 (aIL4), anti-IL-4R (aIL4R), anti-IL-5R (aIL5R), anti-IL-5 (aIL5), anti-IL13R (aIL13R) and anti-IL13 (aIL13); or

(II) Mepolizumab, Resilizumab, Benralizumab, Tralokinumab, Lebrikizumab or Dupilumab.

43. Use according to Claim 42, in which the modulator comprises:

(I) IL-2 + aIL4;

(II) IL-2 + IL-12 + aIL4; or

(III) IL-2+ IL-12 + IL-7 + IL-15 + aIL4.

44. Use according to Claim 41, 42 or 43, in which IL-12 is briefly added for 1-96 h at 1-150 ng/ml at the expanding step and subsequently replaced with another cytokine.

45. Use according to any of Claims 40 to 44, in which the modulator is produced by an artificial antigen presenting cell and the tumour reactive T cells are co-cultured with the antigen presenting cell.

46. Use according to any of Claims 33 to 45, in which the cell population is isolated, cultured with a modulator that increases CD150/SLAM/SLAMF1 production and in which the cultured cells are separated from unselected cells.

47. Use according to any of Claims 33 to 46, in which the T cells are engineered to express a cytokine receptor which provides cytokine signalling upon engagement of another drug or cytokine.

48. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer, comprising administering to a cancer patient in need thereof cells from a cell population, in which the cell population is prepared by a method comprising identifying and/or obtaining a cell population expressing CD150/SLAM/SLAMF1 and expanding the cell population.

49. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to Claim 48, in which the T-cells expressing CD150/SLAM/SLAMF1 are T-cells selected from cells originating from a subject.

50. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to Claim 48 or 49, in which:

(I) selecting the T-cells expressing CD150/SLAM/SLAMF1 comprises one or more of (a) flow cytometry, (b) antibody panning, (c) magnetic selection and (d) biomarker targeted cell enrichment; or

(II) selecting the T-cells comprises contacting the cell population with an anti-CD150/SLAM/SLAMF1 antibody.

51. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to Claim 48, 49 or 50, in which the expanding comprises:

(a) irradiating feeder cells and co-stimulating with an anti- CD150/SLAM/SLAMF1 antibody and optionally one or more cytokines;

(b) stimulating or activating CD150/SLAM/SLAMF1; or

(c) rapid expansion protocol (REP) in which cells are mixed with irradiated feeder cells and one or more cytokines until at least $1x10^9$ or at least $5x10^9$ or at least $1x10^{10}$ cells are obtained.

52. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to any of Claims 48 to 51, in which the cell population is:

(a) a population of tumour infiltrating lymphocytes (TILs) from a tumour biopsy, lymph node or ascites;

(b) a population of T-cells engineered to express a CAR and/or a TCR; and/or

(c) a population of T-cells isolated from blood.

53. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to any of Claims 48 to 52, in which the cancer is a melanoma, lung cancer, squamous cell cancer, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer including gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial cancer or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, head cancer or neck cancer.

54. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to any of Claims 48 to 53, in which the cancer treatment is adoptive cell therapy.

55. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to any of Claims 48 to 54, in which the method further comprises exposing the T-cells to a modulator that increases SLAM production.

56. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to Claim 55, in which the modulator comprises:

(I) a cytokine, optionally in which the cytokine is IL-2, IL-15, IL-18, IL-12, IL-23, IL-27, IL-35, IL-39, IL-18, IL-36, IL-37, IL-38, IFN-alpha, IFN-beta, IFN-gamma or a combination thereof; or

(II) in which the modulator is a cytokine combination of IL-7+ IL-15, IL-2 + IL-7 + IL-15, IL-2 + IL-12, IL-2 + IL-18, IL-2 + IL-12 + IL-7 + IL-15, IL-2 + IL-12 + IL-7 + IL-15 + IL-6, IL-2 + IL-12 + IL-7 + IL-15 + IL-21, IL-2 + IL-12 + IL-7 + IL-15 + IL-6 + IL-21, IL-7 + IL-15 + IL-6, IL-7 + IL-15 + IL-21, IL-7 + IL-15 + IL-6 + IL-21, IL-2 + IL-12 + IL-6, IL-2 + IL-12 + IL-21, or IL-2 + IL-12 + IL-6 + IL-21.

57. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to any of Claims 55 or 56, in which the modulator further comprises a Th2 blocking agent, optionally in which the Th2 blocking agent is an antibody selected from:

(I) anti-IL-4 (aIL4), anti-IL-4R (aIL4R), anti-IL-5R (aIL5R), anti-IL-5 (aIL5), anti-IL13R (aIL13R) and anti-IL13 (aIL13); or

(II) Mepolizumab, Resilizumab, Benralizumab, Tralokinumab, Lebrikizumab and Dupilumab.

58. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to Claim 57, in which the modulator comprises:

(I) IL-2 + aIL4;

(II) IL-2 + IL-12 + aIL4; or

(III) IL-2+ IL-12 + IL-7 + IL- 15 + aIL4.

59. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to Claim 56, 57 or 58, in which IL-12 is briefly added for 1-96 h at 1-150 ng/ml at the expanding step and subsequently replaced with another cytokine.

60. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to any of Claims 48 to 59, in which the modulator is produced by an artificial antigen presenting cell and the tumour reactive T cells are co-cultured with the antigen presenting cell.

61. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to any of Claims 48 to 60, in which the cell population is isolated and cultured with a modulator that increases CD150/SLAM/SLAMF1 production and in which the cultured cells are separated from unselected cells.

62. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to any of Claims 48 to 61, in which the T cells are engineered to express a cytokine receptor which provides cytokine signalling upon engagement of another drug or cytokine

63. An enriched and expanded cell population of tumour reactive T-cells for use in the treatment of cancer according to any of Claims 48 to 62, in which the T cell is a CD4+ or a CD 8+ T cell.

64. Use of a cytokine in increasing expression of CD150/SLAM/SLAMF1 in a method for preparing an enriched and expanded cell population of tumour reactive T-cells for use in cancer therapy comprising exposing the T cells to a cytokine.

65. Use according to Claim 64, in which the cytokine is used in combination with a Th2 blocking agent.

66. A method for increasing expression of CD150/SLAM/SLAMF1 in tumour reactive T-cells for use in cancer therapy, comprising identifying and/or obtaining a cell population expressing CD150/SLAM/SLAMF1 and expanding the cell population in the presence of a cytokine that increases expression of CD150/SLAM/SLAMF1.

67. A method according to Claim 66, in which the cytokine is used in combination with a Th2 blocking agent.