CLAIMS

1. An isolated antibody which binds to the same epitope on variants 1 and 2 of human CD74 as at least one antibody selected from

(a) an antibody comprising a VH region comprising the sequence of SEQ ID NO:19 and a VL region comprising the sequence of SEQ ID NO:26 **[011];**

(b) an antibody comprising a VH region comprising the sequence of SEQ ID NO:7 and a VL region comprising the sequence of SEQ ID NO:23 **[005]**;

(c) an antibody comprising a VH region comprising the sequence of SEQ ID NO:11 and a VL region comprising the sequence of SEQ ID NO:26 **[006]**; and

(d) an antibody comprising a VH region comprising the sequence of SEQ ID NO:15 and a VL region comprising the sequence of SEQ ID NO:26 **[008]**.

2. An antibody which binds to CD74 variants 1 and 2 and comprises a V_H CDR3 region selected from the group consisting of SEQ ID NOS: 22, 10, 14, or 18.

3. The antibody of any one of the preceding claims, which

(a) binds to the extracellular domain of CD74 variant 1 with an EC_{50} of less than about 500 ng/mL, less than about 400 ng/mL, less than about 350 ng/mL, or less than about 330 ng/mL;

(b) binds to the extracellular domain of CD74 variant 2 with an EC_{50} of less than about 400 ng/mL, less than about 300 ng/mL, less than about 250 ng/mL, or less than about 220 ng/mL; or

(c) both of (a) and (b),

when determined as described in Example 11.

4. The antibody of any one of the preceding claims, which binds to CD74 on Raji cells with an EC_{50} of less than about 400 ng/mL, less than about 300 ng/mL, less than about 250 ng/mL, or less than about 200 ng/mL, when determined as described in Example 11.

5. The antibody of any one of the preceding claims, which binds to cynomolgous CD74.

6. The antibody of any one of the preceding claims, which is internalized after binding to CD74 expressed on the surface of a cell.

7. The antibody of claim 6, wherein the cell is a Raji cell.

8. The antibody of any one of the preceding claims, which has an EC_{50} of less than about 60 ng/mL, less than about 40 ng/mL, less than about 30 ng/mL, or about 25 ng/mL or less in inducing killing of Raji cells in an anti-kappa ETA' assay, when determined as described in Example 14.

9. The antibody of any one of the preceding claims, which has an off-rate at 0°C of 0.02 to 1.0 min^{-1}, 0.03 to about 0.30 min^{-1}, 0.04 to 0.10 or 0.15 to 0.30 min^{-1}.

10. The antibody of any one of the preceding claims, which comprises a V_L region comprising the CDR1, 2 and 3 sequences of SEQ ID NO:24, AAS and SEQ ID NO:25, and

a) a V_H region comprising the CDR1, 2 and 3 sequences of SEQ ID NO: 20, 21 and 22 (**011**);
b) a V_H region comprising the CDR1, 2 and 3 sequences of SEQ ID NOS: 8, 9 and 10 (**005**);
c) a V_H region comprising the CDR1, 2 and 3 sequences of SEQ ID NO: 12, 13 and 14 (**006**);
d) a V_H region comprising the CDR1, 2 and 3 sequences of SEQ ID NO: 16, 17 and 18 (**008**); or
e) a variant of any of said antibodies, which variant preferably has at most one, two or three amino acid modifications in the V_H and/or V_L region, more preferably amino acid substitutions, such as conservative amino acid substitutions in said sequences.

11. The antibody according to any of the preceding claims, comprising a V_H region having

a) at least 80% identity, such as at least 90%, at least 95%, or at least 98% or 100% identity to a V_H region sequence selected from the group consisting of SEQ ID NOS: 7, 11, 15 and 19, or
b) at most 20, such as 15, or 10, or 5, 4, 3, 2 or 1 amino acid modifications, more preferably amino acid substitutions, such as conservative amino acid substitutions as compared to a V_H region sequence selected from the group consisting of: SEQ ID NOS: 7, 11, 15 and 19.

12. The antibody according to any of the preceding claims comprising a V_L having

a) at least 80% identity, such as at least 90%, at least 95%, or at least 98% or 100% identity to a V_L region sequence selected from the group consisting of: SEQ ID NOS: 23 and 26; or
b) at most 20, such as 15, or 10, or 5, 4, 3, 2 or 1 amino acid modifications, more preferably amino acid substitutions, such as conservative amino acid substitutions as

compared to a V_H region sequence selected from the group consisting of: SEQ ID NOS: 23 and 26.

13. An antibody which binds to CD74 variants 1 and 2 and comprises:

(a) a V_H region comprising the sequence of SEQ ID NO: 19 and a V_L region comprising the sequence of SEQ ID NO: 26 **[011]**;

(b) a V_H region comprising the sequence of SEQ ID NO: 7 and a V_L region comprising the sequence of SEQ ID NO: 26 [**005/011**]

(c) a V_H region comprising the sequence of SEQ ID NO: 7 and a V_L region comprising the sequence of SEQ ID NO: 23 [**005**];

(d) a V_H region comprising the sequence of SEQ ID NO: 11 and a V_L region comprising the sequence of SEQ ID NO: 26 **[006]**; or

(d) a V_H region comprising the sequence of SEQ ID NO: 15 and a V_L region comprising the sequence of SEQ ID NO: 26 **[008]**.

14. The antibody of any one of the preceding claims, which is a human monoclonal antibody.

15. The antibody of any one of the preceding claims, which has an isotype selected from IgG1 and IgG4.

16. An antibody of any one of the preceding claims, which is conjugated to a therapeutic moiety.

17. The antibody of claim 16, which is conjugated to the therapeutic moiety via a linker attached to sulphydryl residues in the antibody, obtained by at least partial reduction of the antibody.

18. The antibody of any one of claims 16 and 17, wherein the therapeutic moiety is a cytotoxic moiety, a radioisotope, a chemotherapeutic agent, a lytic peptide or a cytokine.

19. The antibody of claim 18, which is conjugated to a cytotoxic moiety.

20. The antibody of claim 19, wherein the cytotoxic moiety is selected from the group consisting of taxol; cytochalasin B; gramicidin D; ethidium bromide; emetine; mitomycin; etoposide; tenoposide; vincristine; vinblastine; colchicin; doxorubicin; daunorubicin; dihydroxy anthracin dione; maytansine or an analog or derivative thereof; an auristatin or a functional peptide analog or derivative thereof such as monomethyl auristatin E (MMAE) or

F (MMAF); dolastatin 10 or 15 or an analogue thereof; irinotecan or an analogue thereof; mitoxantrone; mithramycin; actinomycin D; 1–dehydrotestosterone; a glucocorticoid; procaine; tetracaine; lidocaine; propranolol; puromycin; calicheamicin or an analog or derivative thereof; an antimetabolite such as methotrexate, 6 mercaptopurine, 6 thioguanine, cytarabine, fludarabin, 5 fluorouracil, decarbazine, hydroxyurea, asparaginase, gemcitabine, or cladribine; an alkylating agent such as mechlorethamine, thioepa, chlorambucil, melphalan, carmustine (BSNU), lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, dacarbazine (DTIC), procarbazine, mitomycin C; a platinum derivative such as cisplatin or carboplatin; duocarmycin A, duocarmycin SA, rachelmycin (CC-1065), or an analog or derivative thereof; an antibiotic such as dactinomycin, bleomycin, daunorubicin, doxorubicin, idarubicin, mithramycin, mitomycin, mitoxantrone, plicamycin, anthramycin (AMC)); pyrrolo[2,1-c][1,4]-benzodiazepines (PDB); diphtheria toxin and related molecules such as diphtheria A chain and active fragments thereof and hybrid molecules, ricin toxin such as ricin A or a deglycosylated ricin A chain toxin, cholera toxin, a Shiga-like toxin such as SLT I, SLT II, SLT IIV, LT toxin, C3 toxin, Shiga toxin, pertussis toxin, tetanus toxin, soybean Bowman-Birk protease inhibitor, Pseudomonas exotoxin, alorin, saporin, modeccin, gelanin, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolacca americana proteins such as PAPI, PAPII, and PAP-S, momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, and enomycin toxins; ribonuclease (RNase); DNase I, Staphylococcal enterotoxin A; pokeweed antiviral protein; diphtherin toxin; and Pseudomonas endotoxin.

21. The antibody of claim 19, which is conjugated to a cytotoxic moiety selected from the group consisting of an anthracycline, a pyrrolo[2,1-c][1,4]-benzodiazepine, maytansine, calicheamicin, duocarmycin, rachelmycin (CC-1065), dolastatin 10 or 15, irinotecan, monomethyl auristatin E and monomethyl auristatin F, or from an analog, derivative, or prodrug of any thereof.

22. The antibody of claim 19, wherein the cytotoxic moiety is an auristatin or a functional peptide analog or derivate thereof, optionally conjugated to the antibody via a linker attached to one or more cysteine residues in the antibody.

23. The antibody of claim 19, which is conjugated to MMAE (formula I).

24. The antibody of claim 19 which is conjugated to vcMMAE (formula IV).

25. The antibody of claim 19, which is conjugated to MMAF (formula II).

26. The antibody of claim 19, which is conjugated to vcMMAF (formula III) or mcMMAF (formula V).

27. The antibody of any one of claims 16 to 26, which has an IC_{50} of less than about 0.5 μg/mL, less than about 0.3 μg/mL, less than about 0.2 μg/mL, or less than about 0.1 μg/mL in inducing killing of Raji, Daudi or M4A4 cells, when determined as described in Example 18.

28. The antibody of claim 18, which is conjugated to a cytokine selected from the group consisting of IL-2, IL-4, IL-6, IL-7, IL-10, IL-12, IL-13, IL-15, IL-18, IL-23, IL-24, IL-27, IL-28a, IL-28b, IL-29, KGF, IFNα, IFNβ, IFNγ, GM-CSF, CD40L, Flt3 ligand, stem cell factor, ancestim, and TNFα.

29. The antibody of any preceding claim, which is a multispecific antibody, comprising a first antigen-binding region of an antibody as defined in any one of the preceding claims, and at least one second antigen-binding region having a different binding specificity.

30. The antibody of claim 29, which is a bispecific antibody, optionally wherein the second antigen-binding region has binding specificity for an antigen on a human effector cell, such as a human T cell.

31. The antibody of any one of claims 29 and 30, which is a bispecific antibody wherein

the first antigen-binding region is linked to a first Fc-region having an amino acid substitution at a position selected from the group consisting of 366, 368, 370, 399, 405, 407 and 409, and the second antigen-binding region is linked to a second Fc-region having an amino acid substitution at a position selected from the group consisting of 366, 368, 370, 399, 405, 407 and 409, and

the first and second Fc-regions are not substituted in the same positions.

32. An anti-idiotypic antibody against the antibody of any preceding claim, optionally against an antibody according to claim 13.

33. An expression vector comprising a nucleotide sequence encoding one or more of the amino acid sequences selected from the group consisting of SEQ ID NOS: 7, 11, 15, 19, 23 and 26, or any combination thereof.

34. An expression vector according to claim 34, further comprising a nucleotide sequence encoding the constant region of a human antibody light chain, of a human antibody heavy chain, or both.

35. A recombinant eukaryotic or prokaryotic host cell which produces the antibody of any one of claims 1 to 16 or 18 to 32.

36. A pharmaceutical composition comprising the antibody of any one of claims 1 to 32 and a pharmaceutically acceptable carrier.

37. The antibody of any one of claims 1 to 32 for use as a medicament.

38. The antibody of any one of claims 1 to 32 for use in the treatment of cancer.

39. The antibody of any one of claims 1 to 32 for use in cancer prophylaxis.

40. The antibody for the use of claim 39, wherein the cancer prophylaxis comprises one or more of reducing the risk for developing cancer, reducing the risk for cancer progression, and/or reducing the risk of recurrence of a cancer in remission.

41. The antibody for the use of any one of claims 37 to 40, wherein the cancer is selected from the group consisting of breast cancer, colorectal cancer, endometrial/cervical cancer, gastric cancer, head and neck cancer, lung cancer, malignant glioma, malignant melanoma, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, liver cancer, thymus cancer, malignant fibrous histiosarcoma, acoustic schwannoma, pituitary adenoma, and an adenoma.

42. The antibody for the use of any one of claims 37 to 40, wherein the cancer is selected from the group consisting of malignant lymphoma, B cell chronic lymphocytic leukemia (B-CLL), chronic myeloid leukemia (CML) in blast phase, non-Hodgkin's lymphoma (NHL), multiple myeloma (MM), monocytiod B cell lymphoma (MBCL), hairy-cell leukemia (HCL), and T cell lymphoma.

43. The antibody for the use of claim 42, wherein the cancer is NHL.

44. The antibody for the use of claim 42, wherein the cancer is MM.

45. The antibody for the use of claim 41, wherein the cancer is ovarian cancer.

46. The antibody for the use of claim 41, wherein the cancer is breast cancer.

47. The antibody for the use of claim 41, wherein the cancer is pancreatic cancer.

48. The antibody for the use of claim 41, wherein the cancer is selected from prostate cancer, gastric cancer, and colorectal cancer.

49. The antibody for the use of claim 37, for use in the treatment of an autoimmune disease.

50. The antibody for the use of any one of claims 37 to 49 in combination with at least one further therapeutic agent.

51. The antibody for the use of claim 50, wherein at least one further therapeutic agent is selected from a second antibody or ADC; a chemotherapeutic agent; an inhibitor of angiogenesis, neovascularization, and/or other vascularization; an anti-cancer immunogen; a cytokine or chemokine; a cell cycle control or apoptosis regulator; a hormonal regulating agent; an anti-anergic agent; a tumor suppressor gene-containing nucleic acid or vector; an anti-cancer nucleic acid; a virus or viral proteins; immune system cells; a differentiation inducing agent; a CD74 up-regulating agent; and an anti-inflammatory, immunosuppressive and/or immunomodulatory agent; or a combination of any thereof.

52. The antibody for the use of claim 51, wherein at least one therapeutic agent is selected from a CD20-specific antibody, a CD138-specific antibody, a CD38-specific antibody, an anti-VEGF-A antibody, melphalanan, lenalidomide, bortezomib, fluorouracil, gemticabine, irinotecan, cisplatin, or a derivative or analog thereof.

53. Use of an antibody of any one of the claims 1-32 for the manufacture of a medicament for treatment of cancer.

54. The use of claim 53, comprising the further features of any of claims 36 to 52.

55. A method for inducing cell death, inhibiting growth, and/or inhibiting proliferation of a cell expressing CD74, comprising administering the antibody of any of claims 16 to 29.

56. A method for treating a disease of any one of claims 37 to 52 by administering, to an individual in need thereof, an effective amount of an antibody of any one of claims 1-32, optionally in combination with a further therapeutic agent of any one of claims 51 and 52.

What is claimed is:

1. An invention not claimed in any divisional application.