from the group consisting of CD19, CD20, CD22, CD23, CD27, CD32B, CD38, CD40, CD79a, CD79b, CD80, CD86, LFA-I, LFA-3 and CFA-I.

[0027] In a second aspect, there is provided a pharmaceutical composition comprising any of the CD3-binding molecules as described herein, ~~any of the antibodies or diabodies as described herein,~~ and a pharmaceutically acceptable carrier, excipient or diluent.

[0028] In a third aspect, there is provided the pharmaceutical composition as described herein, for use in the treatment of cancer or an autoimmune or inflammatory disease.

[0029] The disclosure further concerns the above-described pharmaceutical composition for use in the treatment of an autoimmune or inflammatory disease selected from the group consisting of: type I insulin-dependent diabetes, rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, inflammatory bowel disease, myasthenia gravis, celiac's disease, Sjogren's syndrome, Grave's disease, Crohn's disease, autoimmune hepatitis, psoriasis, psoriatic arthritis, asthma, allergic rhinitis, effects from organ transplantation, or graft vs. host disease (GVHD). The disclosure further concerns the above-described pharmaceutical composition for use in the treatment of type I insulin-dependent diabetes.

Brief Description of the Drawings:

[0030] **Figures 1A-1B** show the results of a capture ELISA in which the ability of anti-CD3 antibody mAB1 (**Figure 1A**) or a chimeric derivative of antibody mAB1 (ch-mAb1) (**Figure 1B**) was assessed using human soluble CD3 ("shCD3").

[0031] **Figures 2A-2B** show the results of a capture ELISA in which the ability of anti-CD3 antibody mAB2 (**Figure 2A**) or a chimeric derivative of antibody mAB2 (ch-mAb2) (**Figure 2B**) was assessed using human soluble CD3 ("shCD3") or soluble cynomolgus monkey CD3 ("scCD3").

[0032] **Figure 3** show the results of analyses to determine the effect of variations in Kabat numbered framework residues 41-46 of the light chain of mAb2.

What Is Claimed Is:

Claim 1. A CD3-binding molecule comprising an antigen-binding fragment of an antibody, wherein said antigen-binding fragment comprises an antibody CD3-specific VL domain and an antibody CD3-specific VH domain, wherein said CD3-specific VL domain and said CD3-specific VH domain form an antigen-binding domain capable of immunospecifically binding to both an epitope of human CD3 and to an epitope of the CD3 of a non-human mammal, wherein:

(I) said CD3-specific VL domain is selected from the group consisting of h-mab1 VL-1 (**SEQ ID NO:10**) and h-mab1 VL-2 (**SEQ ID NO:12**), and

(II) said CD3-specific VH domain is h-mab1 VH (**SEQ ID NO:14**).

Claim 2. The CD3-binding molecule of claim 1, wherein said CD3-specific VL domain is h-mab1 VL-1 (**SEQ ID NO:10**).

Claim 3. The CD3-binding molecule of claim 1, wherein said CD3-specific VL domain is h-mab1 VH-2 (**SEQ ID NO:12**).

Claim 4. The CD3-binding molecule of any one of claims 1-3, wherein said molecule is an antibody.

Claim 5. The CD3-binding antibody of claim 4, wherein said antibody:

(A) lacks an Fc region;

or

(B) comprises an Fc region that:

(i) lacks effector function; or

(ii) has reduced effector function; or

(iii) impairs the ability of the Fc region of said antibody to bind to an Fc receptor;

wherein said lack of effector function, said reduction in effector function, and said impairment of binding ability is relative to that of a wild-type Fc receptor.

Claim 6. The CD3-binding molecule of any of claims 1-3, wherein said molecule is a CD3-binding diabody that comprises a first polypeptide chain and a second polypeptide chain, said chains being covalently bonded to one another, wherein:

(I) said first polypeptide chain comprises an amino terminus and a carboxy terminus and from N-terminus to C-terminus:

(i) a domain (A) comprising said CD3-specific VL domain;

(ii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2); and

(iii) a domain (C);

wherein said domains (A) and (B) do not associate with one another to form an epitope binding site;

and

(II) said second polypeptide chain comprises an amino terminus and a carboxy terminus and from N-terminus to C-terminus:

(i) a domain (D) comprising a binding region of a light chain variable domain of said second immunoglobulin (VL2);

(ii) a domain (E) comprising said CD3-specific VH domain;

and

(iii) a domain (F);

wherein said domains (D) and (E) do not associate with one another to form an epitope binding site; and

wherein:

(1) said domains (A) and (E) associate to form said antigen-binding domain that is capable of immunospecifically binding to both human CD3 and to the CD3 of a non-human mammal;

(2) said domains (B) and (D) associate to form a binding site that immunospecifically binds to a second epitope, wherein said second epitope is an epitope of CD3 that is different from the CD3 epitope bound by the antigen-binding domain formed from said association of said domains (A) and (E); and

(3) said domains (C) and (F) are covalently associated together.

Claim 7. The CD3-binding molecule of any one of claims 1-3, wherein said molecule is a CD3-binding diabody that comprises a first polypeptide chain and a second polypeptide chain, said chains being covalently bonded to one another, wherein:

(I) said first polypeptide chain comprises an amino terminus and a carboxy terminus and from N-terminus to C-terminus:

(i) a domain (A) comprising said CD3-specific VL domain;

(ii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2); and

(iii) a domain (C);

wherein said domains (A) and (B) do not associate with one another to form an epitope binding site;

and

(II) said second polypeptide chain comprises an amino terminus and a carboxy terminus and from N-terminus to C-terminus:

(i) a domain (D) comprising a binding region of a light chain variable domain of said second immunoglobulin (VL2);

(ii) a domain (E) comprising said CD3-specific VH domain;

and

(iii) a domain (F);

wherein said domains (D) and (E) do not associate with one another to form an epitope binding site; and

wherein:

(1) said domains (A) and (E) associate to form said antigen-binding domain that is capable of immunospecifically binding to both human CD3 and to the CD3 of a non-human mammal;

(2) said domains (B) and (D) associate to form a binding site that immunospecifically binds to a second epitope, said second epitope being different from the CD3 epitope bound by the antigen-binding domain formed from said association of said domains (A) and (E), wherein said second epitope is an epitope of: (a) a tumor antigen, (b) a cell surface antigen, receptor or receptor ligand, or (c) a detectable label;

and

(3) said domains (C) and (F) are covalently associated together.

Claim 8. The CD3-binding molecule of any one of claims **1-7** which is humanized.

Claim 9. The CD3-binding molecule of any one of claims **1-3 or 6-8**, which is capable of immunospecifically binding to CD3 and to fluorescein.

Claim 10. The CD3-binding molecule of any one of claims **1-3 or 6-8**, which is capable of immunospecifically binding to both: (i) CD3 and (ii)(a) a tumor antigen, or (ii)(b) a cell surface antigen, receptor or receptor ligand.

Claim 11. The CD3-binding molecule of claim 10, wherein said molecule is capable of immunospecifically binding to CD3 and to a tumor antigen expressed on a tumor cell, wherein said tumor cell is a tumor cell from a cancer selected from the group consisting of: breast cancer, prostate cancer, gastric cancer, lung cancer, stomach cancer, colon cancer, rectal cancer, pancreatic cancer, liver cancer, ovarian cancer, oral cavity cancer, pharyngeal cancer, esophageal cancer, laryngeal cancer, bone cancer, skin cancer, melanoma, uterine cancer, testicular cancer, bladder cancer, kidney cancer, brain cancer, glioblastoma, thyroid cancer, lymphoma, myeloma, and leukemia.

Claim 12. The CD3-binding molecule of claim 10, wherein said molecule is capable of immunospecifically binding to CD3 and to a cell surface antigen, receptor or receptor ligand, wherein said cell surface antigen, receptor or receptor ligand is HER2/neu, B7-H3, CD20, PSMA, IGF-1R., Ep-CAM, or is a molecule involved in a T cell – B cell association that leads to T cell or B cell activation in an adaptive immune response.

Claim 13. The CD3-binding molecule of claim 12, wherein said molecule is capable of immunospecifically binding to CD3 and to a molecule involved in said T cell – B cell association and said molecule involved in said T cell – B cell association is selected from the group consisting of CD19, CD20, CD22, CD23, CD27, CD32B, CD38, CD40, CD79a, CD79b, CD80, CD86, LFA-I, LFA-3 and CFA-I.

Claim 14. The CD3-binding molecule of any one of claims 6-8 and 10-12, wherein:

(A) said domain (B) comprises amino acid residues 119-238 of **SEQ ID NO: 65**; and

(B) said domain (D) comprises amino acid residues 1-107 of **SEQ ID NO: 64**.

Claim 15. The CD3-binding molecule of any one of claims 6-8 and 10-12, wherein:

(A) said domain (B) comprises amino acid residues 119-240 of **SEQ ID NO: 67**; and

(B) said domain (D) comprises amino acid residues 1-107 of **SEQ ID NO: 66**.

Claim 16. The CD3-binding molecule of any one of claims 6-15, wherein said CD3-binding diabody comprises an Fc domain or portion thereof.

Claim 17. The CD3-binding diabody of any one of claims 6-16 wherein:

(A) said polypeptide chain I additionally comprises an E coil sequence and said polypeptide chain II additionally comprises a K coil sequence; or

(B) said polypeptide chain I additionally comprises a K coil sequence and said polypeptide chain II additionally comprises an E coil sequence;

wherein said E coil sequence is amino acid residues 244-271 of SEQ ID NO: 62, and said K coil sequence is residues 247-274 of SEQ ID NO: 63.

Claim **18.** A pharmaceutical composition comprising the CD3-binding molecule of any one of claims 1-**17** and a pharmaceutically acceptable carrier, excipient or diluent.

Claim **19.** The pharmaceutical composition of claim **18**, for use in the treatment of cancer or an autoimmune or inflammatory disease.

Claim **20.** The pharmaceutical composition of claim **19**, for use in the treatment of an autoimmune or inflammatory disease **is** selected from the group consisting of: type I insulin-dependent diabetes, rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, inflammatory bowel disease, myasthenia gravis, celiac's disease, Sjogren's syndrome, Grave's disease, Crohn's disease, autoimmune hepatitis, psoriasis, psoriatic arthritis, asthma, allergic rhinitis, effects from organ transplantation, or graft vs. host disease (GVHD).

Claim **21**. The pharmaceutical composition of claim **20**, for use in the treatment of type I insulin-dependent diabetes.

What Is Claimed Is:

Claim 1. A CD3-binding molecule comprising an antigen-binding fragment of an antibody, wherein said antigen-binding fragment comprises an antibody CD3-specific VL domain and an antibody CD3-specific VH domain, wherein said CD3-specific VL domain and said CD3-specific VH domain form an antigen-binding domain capable of immunospecifically binding to both an epitope of human CD3 and to an epitope of the CD3 of a non-human mammal, wherein:

(I) said CD3-specific VL domain is selected from the group consisting of h-mab1 VL-1 (**SEQ ID NO:10**) and h-mab1 VL-2 (**SEQ ID NO:12**),and

(II) said CD3-specific VH domain is h-mab1 VH (**SEQ ID NO:14**).

Claim 2. The CD3-binding molecule of claim 1, wherein said CD3-specific VL domain is h-mab1 VL-1 (**SEQ ID NO:10**).

Claim 3. The CD3-binding molecule of any of claim 1, wherein said CD3-specific VL domain is h-mab1 VH-2 (**SEQ ID NO:12**).

Claim 4. The CD3-binding molecule of any one of claims 1-3, wherein said molecule is an antibody.

Claim 5. The CD3-binding antibody of claim 4, wherein said antibody:

(A) lacks an Fc region;

or

(B) comprises an Fc region that:

(i) lacks effector function; or

(ii) has reduced effector function; or

(iii) impairs the ability of the Fc region of said antibody to bind to an Fc receptor;

wherein said lack of effector function, said reduction in effector function, and said impairment of binding ability is relative to that of a wild-type Fc receptor.

Claim 6. The CD3-binding molecule of any of claims 1-3, wherein said molecule is a CD3-binding diabody that comprises a first polypeptide chain and a second polypeptide chain, said chains being covalently bonded to one another, wherein:

(I) said first polypeptide chain comprises an amino terminus and a carboxy terminus and from N-terminus to C-terminus:

(i) a domain (A) comprising said CD3-specific VL domain;

(ii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2); and

(iii) a domain (C);

wherein said domains (A) and (B) do not associate with one another to form an epitope binding site;

and

(II) said second polypeptide chain comprises an amino terminus and a carboxy terminus and from N-terminus to C-terminus:

(i) a domain (D) comprising a binding region of a light chain variable domain of said second immunoglobulin (VL2);

(ii) a domain (E) comprising said CD3-specific VH domain;

and

(iii) a domain (F);

wherein said domains (D) and (E) do not associate with one another to form an epitope binding site; and

wherein:

(1) said domains (A) and (E) associate to form said antigen-binding domain that is capable of immunospecifically binding to both human CD3 and to the CD3 of a non-human mammal;

(2) said domains (B) and (D) associate to form a binding site that immunospecifically binds to a second epitope, wherein said second epitope is an epitope of CD3 that is different from the CD3 epitope bound by the antigen-binding domain formed from said association of said domains (A) and (E); and

(3) said domains (C) and (F) are covalently associated together.

Claim 7. The CD3-binding molecule of any one of claims 1-3, wherein said molecule is a CD3-binding diabody that comprises a first polypeptide chain and a second polypeptide chain, said chains being covalently bonded to one another, wherein:

(I) said first polypeptide chain comprises an amino terminus and a carboxy terminus and from N-terminus to C-terminus:

(i) a domain (A) comprising said CD3-specific VL domain;

(ii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2); and

(iii) a domain (C);

wherein said domains (A) and (B) do not associate with one another to form an epitope binding site;

and

(II) said second polypeptide chain comprises an amino terminus and a carboxy terminus and from N-terminus to C-terminus:

(i) a domain (D) comprising a binding region of a light chain variable domain of said second immunoglobulin (VL2);

(ii) a domain (E) comprising said CD3-specific VH domain;

and

(iii) a domain (F);

wherein said domains (D) and (E) do not associate with one another to form an epitope binding site; and

wherein:

(1) said domains (A) and (E) associate to form said antigen-binding domain that is capable of immunospecifically binding to both human CD3 and to the CD3 of a non-human mammal;

(2) said domains (B) and (D) associate to form a binding site that immunospecifically binds to a second epitope, said second epitope being different from the CD3 epitope bound by the antigen-binding domain formed from said association of said domains (A) and (E), wherein said second epitope is an epitope of: (a) a tumor antigen, (b) a cell surface antigen, receptor or receptor ligand, or (c) a detectable label;

and

(3) said domains (C) and (F) are covalently associated together.

Claim 8. The CD3-binding molecule of any one of claims 1-3, the antibody of any one of claims 4-5, or the diabody of any one of claims 6-7 which is humanized.

Claim 9. The CD3-binding molecule of any one of claims 1-3 or 8, or the diabody of any one of claims 7-8, which is capable of immunospecifically binding to CD3 and to fluorescein.

Claim 10. The CD3-binding molecule of any one of claims 1-3 or 8, or the diabody of any one of claims 7-8, which is capable of immunospecifically binding to both: (i) CD3 and (ii)(a) a tumor antigen, or (ii)(b) a cell surface antigen, receptor or receptor ligand.

Claim 11. The CD3-binding molecule or diabody of claim 10, wherein said molecule or diabody is capable of immunospecifically binding to CD3 and to a tumor antigen expressed on a tumor cell, wherein said tumor cell is a tumor cell from a cancer selected from the group consisting of: breast cancer, prostate cancer, gastric cancer, lung cancer, stomach cancer, colon cancer, rectal cancer, pancreatic cancer, liver cancer, ovarian cancer, oral cavity cancer, pharyngeal cancer, esophageal cancer, laryngeal cancer, bone cancer, skin cancer, melanoma, uterine cancer, testicular cancer, bladder cancer, kidney cancer, brain cancer, glioblastoma, thyroid cancer, lymphoma, myeloma, and leukemia.

Claim 12. The CD3-binding molecule or diabody of claim 10, wherein said molecule or diabody is capable of immunospecifically binding to CD3 and to a cell surface antigen, receptor or receptor ligand, wherein said cell surface antigen, receptor or receptor ligand is HER2/neu, B7-H3, CD20, PSMA, IGF-1R., Ep-CAM, or is a molecule involved in a T cell – B cell association that leads to T cell or B cell activation in an adaptive immune response.

Claim 13. The CD3-binding molecule or diabody of claim 12, wherein said molecule or diabody is capable of immunospecifically binding to CD3 and to a molecule involved in said T cell – B cell association and said molecule involved in said T cell – B cell association is selected from the group consisting of CD19, CD20, CD22, CD23, CD27, CD32B, CD38, CD40, CD79a, CD79b, CD80, CD86, LFA-I, LFA-3 and CFA-I.

Claim 14. A pharmaceutical composition comprising the CD3-binding molecule of any one of claims 1-3 or 8-13, the antibody of any one of claims 4-5, or the diabody of any one of claims 6-13, and a pharmaceutically acceptable carrier, excipient or diluent.

Claim 15. The pharmaceutical composition of claim 14, for use in the treatment of cancer or an autoimmune or inflammatory disease.

Claim 16. The pharmaceutical composition of claim 15, for use in the treatment of an autoimmune or inflammatory disease selected from the group consisting of: type I insulin-dependent diabetes, rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, inflammatory bowel disease, myasthenia gravis, celiac's disease, Sjogren's syndrome, Grave's disease, Crohn's disease, autoimmune hepatitis, psoriasis, psoriatic arthritis, asthma, allergic rhinitis, effects from organ transplantation, or graft vs. host disease (GVHD).

Claim 17. The pharmaceutical composition of claim 16, for use in the treatment of type I insulin-dependent diabetes.