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 comprises the three complementarity determining regions (CDRs) of SEQ ID NO:5; and

(II) said CD3-specific VH domain comprises the three complementarity determining regions (CDRs) of SEQ ID NO:7, modified to comprise one or more amino acid substitutions selected from the group consisting of:

(i) I51T;

(ii) S52aN;

(iii) Y52cA;

(iv) N54S;

(v) A56T;

(vi) Y58E;

(vii) D61A; and

(viii) D65G;

wherein said numbering is according to the Kabat numbering scheme.

Claim 2. The CD3-binding molecule of claim 2, wherein said CD3-specific VL domain is selected from the group consisting of h-mab2 VL-4 (SEQ ID NO:22), h-mab2 VL-6 (SEQ ID NO:26), h-mab2 VL-7 (SEQ ID NO:28), h-mab2 VL-8 (SEQ ID NO:30), h-mab2 VL-9 (SEQ ID NO:32), and h-mab2 VL-10 (SEQ ID NO:34).

Claim 3. The CD3-binding molecule of any one of claims 1-2, wherein said CD3-specific VH domain is selected from the group consisting of h-mab2 VH-6L (SEQ ID NO:54), h-mab2 VH-8L (SEQ ID NO:55), h-mab2 VH-8 di-1 (SEQ ID NO:56), h-mab2 VH-8 di-2 (SEQ ID NO:57), h-mab2 VH-6M (SEQ ID NO:72), h-mab2

VH-8M (SEQ ID NO:74), h-mab2 VH-2k (SEQ ID NO:87), and h-mab2 VH-5k (SEQ ID NO:88).

Claim 4. The CD3-binding molecule of any one of claims 1-2, wherein said CD3-specific VH domain comprises an amino acid sequence that differs, by comprising said amino acid substitution, from the amino acid sequence of h-mab2 VH-1 (SEQ ID NO:36), h-mab2 VH-2 (SEQ ID NO:38), h-mab2 VH-3 (SEQ ID NO:40), h-mab2 VH-4 (SEQ ID NO:42), h-mab2 VH-5 (SEQ ID NO:44), h-mab2 VH-6 (SEQ ID NO:46), h-mab2 VH-7 (SEQ ID NO:48), and h-mab2 VH-8 (SEQ ID NO:50).

Claim 5. The CD3-binding molecule of any one of claims 1-4, wherein said CD3-binding molecule is an antibody.

Claim 6. The CD3-binding molecule of claim 5, 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 7. The CD3-binding molecule of any one of claims 1-4, wherein said CD3-binding 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 (N-) terminus and a carboxy (C-) 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 (N-) terminus and a carboxy (C-) 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); and

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

Claim 8. The CD3-binding diabody of claim 7, wherein said second epitope is not an epitope of CD3.

Claim 9. The CD3-binding diabody of claim 7, 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).

Claim 10. The CD3-binding molecule of any one of claims 1-9, which is humanized.

Claim 11. The CD3-binding molecule of any one of claims 1-4, 7, 8 or 10, which is a bispecific molecule capable of immunospecifically binding to CD3 and to fluorescein.

Claim 12. The CD3-binding molecule of any one of claims 1-4, 7, 8 or 10, which is a bispecific molecule 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 13. The CD3-binding molecule of claim 12, wherein said CD3-binding molecule is capable of immunospecifically binding to CD3 and to a tumor antigen expressed on a tumor cell, wherein said tumor cell is 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 14. The CD3-binding molecule of claim 12, wherein said CD3-binding 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, EGFR, A33, or Ep-CAM.

Claim 15. The CD3-binding molecule of claim 12, wherein said CD3-binding 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 a molecule involved in a T cell – B cell association, wherein 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 16. The CD3-binding molecule of any one of claims 7-9, 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 17. The CD3-binding diabody of any one of claims 7-9, 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 18. The CD3-binding diabody of any one of claims 7-17, wherein said CD3-specific VL domain is h-mab2 VL-6 (SEQ ID NO:26).

Claim 19. The CD3-binding molecule of any one of claims 1-18, wherein said CD3-binding molecule comprises an Fc domain or portion thereof.

Claim 20. The CD3-binding molecule of any one of claims 7-9 or 16-19, wherein:

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

(B) said first polypeptide chain additionally comprises a K coil sequence and said second polypeptide chain 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 21. A pharmaceutical composition comprising the CD3-binding molecule of any one of claims 1-20, and a pharmaceutically acceptable carrier, excipient or diluent.

Claim 22. Use of the CD3-binding molecule of any one of claims 1-20, or of the pharmaceutical composition of claim 21, in the manufacture of a medicament for the treatment of cancer or an autoimmune or inflammatory disease.

Claim 23. The use of claim 22, wherein said 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, and graft vs. host disease (GVHD).

Claim 24. The use of claim 23, wherein said autoimmune or inflammatory disease is type I insulin-dependent diabetes.