example of the disclosure, at least one epitope binding site of the diabody or diabody molecule is specific for an activating Fc receptor and at least one other site is specific for an inhibitory Fc receptor. In certain examples the activating Fc receptor is CD32A and the inhibitory Fc receptor is CD32B. In other examples the activating Fc receptor is BCR and the inhibitory Fc receptor is CD32B. In still other examples, the activating Fc receptor is IgERI and the inhibitory Fc receptor is CD32B.

[0031a] In another aspect, there is provided a diabody molecule comprising a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, wherein:

said first polypeptide chain comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD32B, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for CD79b, and (iii) a third domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;

said second polypeptide chain comprises: (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD79b, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD32B, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;

wherein said cysteine residue of said third and sixth domains form a disulfide bond between said first and second polypeptide chains;

wherein when said first polypeptide chain comprises said E-coil separator, said second polypeptide chain comprises said K-coil separator; and when said first polypeptide chain comprises said K-coil separator, said second polypeptide chain comprises said E-coil separator;

wherein the first domain and the fifth domain associate to form a first binding site (VL1)(VH1) that binds CD32B;

wherein the second domain and the fourth domain associate to form a second binding site (VL2)(VH2) that binds CD79b.

[0031b] In another aspect, there is provided a diabody that is a dimer of two diabody molecules, wherein:

(A) the first of said two diabody molecules comprises a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain of said first diabody molecule are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, and wherein:

said first polypeptide chain of said first diabody molecule comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD32B, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for CD79b, and (iii) a third domain comprising at least one cysteine residue, an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), and a CH2 domain and a CH3 domain;

which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;
said second polypeptide chain of said first diabody molecule comprises: (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD79b, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD32B, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;
wherein when said first polypeptide chain of said first diabody molecule comprises said E-oil separator, said second polypeptide chain of said first diabody molecule comprises said K-coil separator; and when said first polypeptide chain of said first diabody molecule comprises said K-coil separator, said second polypeptide chain of said first diabody molecule comprises said E-coil separator;
wherein said cysteine residue of said third and sixth domains of said first diabody molecule form a disulfide bond between said first and second polypeptide chains of said first diabody molecule;
wherein the first domain and the fifth domain of said first diabody molecule associate to form a first binding site (VL1)(VH1) that binds CD32B;
wherein the second domain and the fourth domain of said first diabody molecule associate to form a second binding site (VL2)(VH2) that binds CD79b; and
(B) the second of said two diabody molecules comprises a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain of said second diabody molecule are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, and wherein:
said first polypeptide chain of said second diabody molecule comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD32B, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for CD79b, and (iii) a third domain comprising at least one cysteine residue, an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), and a CH2 domain and a CH3 domain; which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;
said second polypeptide chain of said second diabody molecule comprises (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD79b, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD32B, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;
wherein when said first polypeptide chain of said second diabody molecule comprises said E-coil separator, said second polypeptide chain of said second diabody molecule comprises said K-coil separator; and when said first polypeptide chain of said second diabody molecule comprises said K-coil separator, said second polypeptide chain of said second diabody molecule comprises said E-coil separator;
wherein said cysteine residue of said third and sixth domains of said second diabody molecule form a disulfide bond between said first and second polypeptide chains of said second diabody molecule;

wherein the first domain and the fifth domain of said second diabody molecule associate to form a first binding site (VL1)(VH1) that binds CD32B;
wherein the second domain and the fourth domain of said second diabody molecule associate to form a second binding site (VL2)(VH2) that binds CD79b;
wherein said CH2 domain and CH3 domain of said first polypeptide chain of said first diabody molecule associates with said CH2 domain and CH3 domain of said first polypeptide chain of said second diabody molecule to form an Fc region.

[0031c] In another aspect, there is provided a diabody that is a dimer of two diabody molecules, wherein:

(A) the first of said two diabody molecules comprises a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain of said first diabody molecule are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, and wherein:
said first polypeptide chain of said first diabody molecule comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD79b, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for CD32B, and (iii) a third domain comprising at least one cysteine residue, an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), and a CH2 domain and a CH3 domain; which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;
said second polypeptide chain of said first diabody molecule comprises: (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD32B, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD79b, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;
wherein when said first polypeptide chain of said first diabody molecule comprises said E-coil separator, said second polypeptide chain of said first diabody molecule comprises said K-coil separator; and when said first polypeptide chain of said first diabody molecule comprises said K-coil separator, said second polypeptide chain of said first diabody molecule comprises said E-coil separator;
wherein said cysteine residue of said third and sixth domains of said first diabody molecule form a disulfide bond between said first and second polypeptide chains of said first diabody molecule;
wherein the first domain and the fifth domain of said first diabody molecule associate to form a first binding site (VL1)(VH1) that binds CD79b;
wherein the second domain and the fourth domain of said first diabody molecule associate to form a second binding site (VL2)(VH2) that binds CD32B; and

(B) the second of said two diabody molecules comprises a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain of said second diabody molecule are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, and wherein:
said first polypeptide chain of said second diabody molecule comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD79b, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for

CD32B, and (iii) a third domain comprising at least one cysteine residue, an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), and a CH2 domain and a CH3 domain; which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;

said second polypeptide chain of said second diabody molecule comprises: (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD32B, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD79b, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;

wherein when said first polypeptide chain of said second diabody molecule comprises said E-coil separator, said second polypeptide chain of said second diabody molecule comprises said K-coil separator; and when said first polypeptide chain of said second diabody molecule comprises said K-coil separator, said second polypeptide chain of said second diabody molecule comprises said E-coil separator;

wherein said cysteine residue of said third and sixth domains of said second diabody molecule form a disulfide bond between said first and second polypeptide chains of said second diabody molecule;

wherein the first domain and the fifth domain of said second diabody molecule associate to form a first binding site (VL1)(VH1) that binds CD79b;

wherein the second domain and the fourth domain of said second diabody molecule associate to form a second binding site (VL2)(VH2) that binds CD32B;

wherein said CH2 domain and CH3 domain of said first polypeptide chain of said first diabody molecule associates with said CH2 domain and CH3 domain of said first polypeptide chain of said second diabody molecule to form an Fc region.

[0032] In cases where one epitope binding site is specific for CD16A, the VL and VH domains can be the same as or similar to the VL and VH domains of the mouse antibody 3G8, the sequence of which has been cloned and is set forth herein. In other cases where one epitope binding site is specific for CD32A, the VL and VH domains can be the same as or similar to the VL and VH domains of the mouse antibody IV.3. In yet other cases where one epitope binding site is specific for CD32B, the VL and VH domains can be the same as or similar to the VL and VH domains of the mouse antibody 2B6, the sequence of which has been cloned and is set forth herein. It is to be understood that any of the VL or VH domains of the 3G8, 2B6 and IV.3 antibodies can be used in any combination. The present disclosure is also directed to a bispecific diabody or diabody molecule wherein the first epitope is specific for CD32B, and the second epitope is specific for CD16A.

[0033] In other examples, an epitope binding site can be specific for a pathogenic antigen. As used herein, a pathogenic antigen is an antigen involved in a specific pathogenic disease, including cancer, infection and autoimmune disease. Thus, the pathogenic antigen can be a tumor antigen, a bacterial antigen, a viral antigen, or an autoimmune antigen. Exemplary pathogenic antigens include, but are not limited to lipopolysaccharide, viral

WHAT IS CLAIMED IS

Claim 1. A diabody molecule comprising a first polypeptide chain and a second polypeptide chain, said polypeptide chains being covalently bonded to one another, wherein:

I. said first polypeptide chain comprises, in the N-terminal to C-terminal direction: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for an epitope (1); (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for an epitope (2); and (iii) a positively or negatively charged polypeptide domain that spontaneously assumes a helical conformation, wherein said negatively charged polypeptide domain is an E-coil separator (SEQ ID NO: 299) and said positively charged polypeptide domain is a K-coil separator (SEQ ID NO: 300);

which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form said epitope (1) binding site or said epitope (2) binding site;

II. said second polypeptide chain comprises, in the N-terminal to C-terminal direction: (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for said epitope (2); (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for said epitope (1); (iii) a positively or negatively charged polypeptide domain that spontaneously assumes a helical conformation linked to said fifth domain, wherein said negatively charged polypeptide domain is an E-coil separator (SEQ ID NO: 299) and said positively charged polypeptide domain is a K-coil separator (SEQ ID NO: 300), wherein when said first polypeptide chain comprises said E-coil separator, said second polypeptide chain comprises said K-coil separator, and when said first polypeptide chain comprises said K-coil separator, said second polypeptide chain comprises said E-coil separator;

which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form said epitope (1) binding site or said epitope (2) binding site;

wherein the first domain and the fifth domain associate to form a binding site (VL1)(VH1) that binds said epitope (1);

wherein the second domain and the fourth domain associate to form a binding site (VL2)(VH2) that binds said epitope (2).

Claim 2. The diabody molecule of claim 1, wherein said first polypeptide chain additionally comprises a third domain, said third domain being separated from said second domain by said charged polypeptide domain, wherein said third domain is an Fc domain, a heavy chain constant region 2 (CH2) and/or a heavy chain constant region 3 (CH3).

Claim 3. The diabody molecule of any one of claims 1-2, wherein said second polypeptide chain additionally comprises a sixth domain, said sixth domain being separated from said fifth domain by said charged polypeptide domain, wherein said sixth domain is an Fc domain, a heavy chain constant region 2 (CH2) and/or a heavy chain constant region 3 (CH3).

Claim 4. The diabody molecule of any one of claims 1-2, wherein said diabody additionally comprises a third polypeptide chain and a fourth polypeptide chain, said third and fourth polypeptide chains being covalently bonded to one another, wherein:

III. said third polypeptide chain comprises, in the N-terminal to C-terminal direction: (i) a seventh domain comprising a binding region of a light chain variable domain of a third immunoglobulin (VL3) specific for an epitope (3), (ii) an eighth domain comprising a binding region of a heavy chain variable domain of a fourth immunoglobulin (VH4) specific for an epitope (4), (iii) a positively or negatively charged polypeptide domain that spontaneously assumes a helical conformation, wherein said negatively charged polypeptide domain is an E-coil separator (SEQ ID

NO: 299) and said positively charged polypeptide domain is a K-coil separator (SEQ ID NO: 300), and (iv) a ninth domain, wherein said ninth domain is an Fc domain, a heavy chain constant region 2 (CH2) and/or a heavy chain constant region 3 (CH3) domain;

which seventh domain and eighth domain are covalently linked such that the seventh domain and eighth domain do not associate together to form said epitope (3) binding site or said epitope (4) binding site;

IV. said fourth polypeptide chain comprises, in the N-terminal to C-terminal direction: (i) a tenth domain comprising a binding region of a light chain variable domain of the fourth immunoglobulin (VL4) specific for said epitope (4), (ii) an eleventh domain comprising a binding region of a heavy chain variable domain of the third immunoglobulin (VH3) specific for said epitope (3), (iii) a positively or negatively charged polypeptide domain that spontaneously assumes a helical conformation linked to said eleventh domain, wherein said negatively charged polypeptide domain is an E-coil separator (SEQ ID NO: 299) and said positively charged polypeptide domain is a K-coil separator (SEQ ID NO: 300), wherein when said third polypeptide chain comprises said E-coil separator, said fourth polypeptide chain comprises said K-coil separator, and when said third polypeptide chain comprises said K-coil separator, said fourth polypeptide chain comprises said E-coil separator;

which tenth domain and eleventh domain are covalently linked such that the tenth domain and eleventh domain do not associate together to form said epitope (3) binding site or said epitope (4) binding site;

wherein the seventh domain and the eleventh domain associate together to form a binding site (VL3)(VH3) that binds said epitope (3);

wherein the eighth domain and the tenth domain associate together to form a binding site (VL4)(VH4) that binds said epitope (4).

Claim 5. The diabody molecule of claim 1, wherein said first polypeptide chain additionally comprises a polypeptide portion of a protein that binds to a serum protein, said polypeptide portion being capable of binding to said serum protein.

Claim 6. The diabody molecule of claim 5, wherein said second polypeptide chain additionally comprises a polypeptide portion of a protein that binds to a serum protein, said polypeptide portion being capable of binding to said serum protein.

Claim 7. The diabody molecule of claim 5 or 6, wherein said protein that binds to a serum protein is an albumin binding protein.

Claim 8. The diabody molecule of claim 7, wherein said albumin binding protein is streptococcal protein G and said polypeptide portion is an albumin-binding domain (ABD) of said streptococcal protein G.

Claim 9. The diabody molecule of claim 8, wherein said albumin-binding domain (ABD) of said streptococcal protein G is albumin-binding domain 3 (ABD3) of protein G of Streptococcus strain G148.

Claim 10. The diabody molecule of any one of claims 5-9, wherein said diabody molecule exhibits an in vivo serum half-life of greater than 2 hours.

Claim 11. The diabody molecule of claim 10, wherein said diabody molecule exhibits an in vivo serum half-life of greater than 10 hours.

Claim 12. The diabody molecule of claim 11, wherein said diabody exhibits an in vivo serum half-life greater than 20 hours.

Claim 13. The diabody molecule of any one of claims 1-12, wherein said diabody molecule binds an epitope of CD32B and an epitope of CD16.

Claim 14. The diabody molecule of any of claims 1-12, wherein said diabody molecule binds to the Natural Killer Group 2D (NKG2D) receptor.

Claim 15. The diabody molecule of any one of claims 1-12, wherein said diabody molecule binds to the T-cell receptor (TCR).

Claim 16. The diabody molecule of any one of claims 1-12, 14 and 15, wherein said diabody molecule binds to a tumor-associated antigen.

Claim 17. The diabody molecule of claim 16, wherein said tumor-associated antigen is a breast cancer antigen, an ovarian cancer antigen, a prostate cancer antigen, a cervical cancer antigen, a pancreatic carcinoma antigen, a lung cancer antigen, a bladder cancer antigen, a colon cancer antigen, a testicular cancer antigen, a glioblastoma cancer antigen, an antigen associated with a B cell malignancy, an antigen associated with multiple myeloma, an antigen associated with non-Hodgkin's lymphoma, or an antigen associated with chronic lymphocytic leukemia.

Claim 18. The diabody molecule of claim 16, wherein said tumor-associated antigen is A33; ADAM-9; ALCAM; B1; BAGE; beta-catenin; CA125; Carboxypeptidase M; CD5; CD19; CD20; CD22; CD23; CD25; CD27; CD28; CD32B; CD36; CD40; CD45; CD46; CD56; CD79a; CD79b; CD103; CD154; CDK4; CEA; CTLA4; Cytokeratin 8; EGF-R; an Ephrin receptor; ErbB1; ErbB3; ErbB4; GAGE-1; GAGE-2; GD2; GD3; GM2; gp100; HER-2/neu; human papillomavirus-E6; human papillomavirus-E7; Integrin Alpha-V-Beta-6; JAM-3; KID3; KID31; KSA; LUCA-2; MAGE-1; MAGE-3; MART; MUC-1; MUM-1; N-acetylglucosaminyltransferase; Oncostatin M; p15; PIPA; PSA; PSMA; RAAG10; ROR1; SART; sTn; TES7; the TNF-α receptor; the TNF-ß receptor; the TNF-γ receptor; the Transferrin Receptor or the VEGF receptor.

Claim 19. The diabody molecule of claim 18, wherein said tumor-associated antigen is HER-2/neu.

Claim 20. A diabody molecule comprising a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, wherein:

said first polypeptide chain comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD32B, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for CD79b, and (iii) a third domain

comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;

said second polypeptide chain comprises: (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD79b, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD32B, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;

wherein said cysteine residue of said third and sixth domains form a disulfide bond between said first and second polypeptide chains;

wherein when said first polypeptide chain comprises said E-coil separator, said second polypeptide chain comprises said K-coil separator; and when said first polypeptide chain comprises said K-coil separator, said second polypeptide chain comprises said E-coil separator;

wherein the first domain and the fifth domain associate to form a first binding site (VL1)(VH1) that binds CD32B;

wherein the second domain and the fourth domain associate to form a second binding site (VL2)(VH2) that binds CD79b.

Claim 21. The diabody molecule of claim 20, wherein said first polypeptide chain or said second polypeptide chain further comprises an Fc domain, a heavy chain constant region 2 (CH2) and/or a heavy chain constant region 3 (CH3).

Claim 22. The diabody molecule of claim 21, wherein said Fc domain, said CH2 and/or said CH3 is linked to said E-coil separator or said K-coil separator.

Claim 23. The diabody molecule of claim 21, wherein said Fc domain, said CH2 and/or said CH3 is linked to the N-terminus of said first domain or said fourth domain.

Claim 24. A diabody that is a dimer of two diabody molecules, wherein:

(A) the first of said two diabody molecules comprises a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain of said first diabody molecule are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, and wherein:

said first polypeptide chain of said first diabody molecule comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD32B, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for CD79b, and (iii) a third domain comprising at least one cysteine residue, an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), and a CH2 domain and a CH3 domain; which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;

said second polypeptide chain of said first diabody molecule comprises: (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD79b, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD32B, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;

wherein when said first polypeptide chain of said first diabody molecule comprises said E-coil separator, said second polypeptide chain of said first diabody molecule comprises said K-coil separator; and when said first polypeptide chain of said first diabody molecule comprises said K-coil separator, said second polypeptide chain of said first diabody molecule comprises said E-coil separator;

wherein said cysteine residue of said third and sixth domains of said first diabody molecule form a disulfide bond between said first and second polypeptide chains of said first diabody molecule;

wherein the first domain and the fifth domain of said first diabody molecule associate to form a first binding site (VL1)(VH1) that binds CD32B;

wherein the second domain and the fourth domain of said first diabody molecule associate to form a second binding site (VL2)(VH2) that binds CD79b; and

(B) the second of said two diabody molecules comprises a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain of said second diabody molecule are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, and wherein:

said first polypeptide chain of said second diabody molecule comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD32B, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for CD79b, and (iii) a third domain comprising at least one cysteine residue, an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), and a CH2 domain and a CH3 domain; which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;

said second polypeptide chain of said second diabody molecule comprises (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD79b, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD32B, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;

wherein when said first polypeptide chain of said second diabody molecule comprises said E-coil separator, said second polypeptide chain of said second diabody molecule comprises said K-coil separator; and when said first polypeptide chain of said second diabody molecule comprises said K-coil separator, said second polypeptide chain of said second diabody molecule comprises said E-coil separator;

wherein said cysteine residue of said third and sixth domains of said second diabody molecule form a disulfide bond between said first and second polypeptide chains of said second diabody molecule;

wherein the first domain and the fifth domain of said second diabody molecule associate to form a first binding site (VL1)(VH1) that binds CD32B;

wherein the second domain and the fourth domain of said second diabody molecule associate to form a second binding site (VL2)(VH2) that binds CD79b;

wherein said CH2 domain and CH3 domain of said first polypeptide chain of said first diabody molecule associates with said CH2 domain and CH3 domain of said first polypeptide chain of said second diabody molecule to form an Fc region.

Claim 25. A diabody that is a dimer of two diabody molecules, wherein:

(A) the first of said two diabody molecules comprises a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain of said first diabody molecule are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, and wherein:

said first polypeptide chain of said first diabody molecule comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD79b, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for CD32B, and (iii) a third domain comprising at least one cysteine residue, an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), and a CH2 domain and a CH3 domain; which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;

said second polypeptide chain of said first diabody molecule comprises: (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD32B, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD79b, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;

wherein when said first polypeptide chain of said first diabody molecule comprises said E-coil separator, said second polypeptide chain of said first diabody molecule comprises said K-coil separator; and when said first polypeptide chain of said first diabody molecule comprises said K-coil separator, said second polypeptide chain of said first diabody molecule comprises said E-coil separator;

wherein said cysteine residue of said third and sixth domains of said first diabody molecule form a disulfide bond between said first and second polypeptide chains of said first diabody molecule;

wherein the first domain and the fifth domain of said first diabody molecule associate to form a first binding site (VL1)(VH1) that binds CD79b;

wherein the second domain and the fourth domain of said first diabody molecule associate to form a second binding site (VL2)(VH2) that binds CD32B; and

(B) the second of said two diabody molecules comprises a first polypeptide chain and a second polypeptide chain, wherein said first polypeptide chain and said second polypeptide chain of said second diabody molecule are covalently linked to one another, with the proviso that the covalent link is not a peptide bond, and wherein:

said first polypeptide chain of said second diabody molecule comprises: (i) a first domain comprising a binding region of a light chain variable domain of a first immunoglobulin (VL1) specific for CD79b, (ii) a second domain comprising a binding region of a heavy chain variable domain of a second immunoglobulin

(VH2) specific for CD32B, and (iii) a third domain comprising at least one cysteine residue, an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), and a CH2 domain and a CH3 domain; which first domain and second domain are covalently linked such that the first domain and second domain do not associate to form an epitope binding site;

said second polypeptide chain of said second diabody molecule comprises: (i) a fourth domain comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for CD32B, (ii) a fifth domain comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) specific for CD79b, and (iii) a sixth domain comprising at least one cysteine residue, and an E-coil separator (SEQ ID NO:299) or a K-coil separator (SEQ ID NO:300), which fourth domain and fifth domain are covalently linked such that the fourth domain and fifth domain do not associate to form an epitope binding site;

wherein when said first polypeptide chain of said second diabody molecule comprises said E-coil separator, said second polypeptide chain of said second diabody molecule comprises said K-coil separator; and when said first polypeptide chain of said second diabody molecule comprises said K-coil separator, said second polypeptide chain of said second diabody molecule comprises said E-coil separator;

wherein said cysteine residue of said third and sixth domains of said second diabody molecule form a disulfide bond between said first and second polypeptide chains of said second diabody molecule;

wherein the first domain and the fifth domain of said second diabody molecule associate to form a first binding site (VL1)(VH1) that binds CD79b;

wherein the second domain and the fourth domain of said second diabody molecule associate to form a second binding site (VL2)(VH2) that binds CD32B;

wherein said CH2 domain and CH3 domain of said first polypeptide chain of said first diabody molecule associates with said CH2 domain and CH3 domain of said first polypeptide chain of said second diabody molecule to form an Fc region.

Claim 26. The diabody molecule of claim 20, wherein both said E-coil separator and said K-coil separator are linked to an Fc domain, a heavy chain constant region 2 (CH2) and/or a heavy chain constant region 3 (CH3).

Claim 27. The diabody molecule of claim 20, wherein said E-coil separator or said K-coil separator is linked to a polypeptide portion of a serum-binding protein, said polypeptide portion being capable of binding to said serum-binding protein.

Claim 28. The diabody molecule of claim 27, wherein said serum-binding protein is an albumin binding protein.

Claim 29. The diabody molecule of claim 28, wherein said albumin binding protein is streptococcal protein G and said polypeptide portion is an albumin-binding domain (ABD) of said streptococcal protein G.

Claim 30. The diabody molecule of claim 29, wherein said albumin-binding domain (ABD) of said streptococcal protein G is albumin-binding domain 3 (ABD3) of protein G of Streptococcus strain G148.

Claim 31. The diabody molecule of claim 27, wherein said diabody molecule exhibits an in vivo serum half-life greater than 2 hours.

Claim 32. The diabody molecule of claim 31, wherein said diabody molecule exhibits an in vivo serum half-life greater than 10 hours.

Claim 33. The diabody molecule of claim 32, wherein said diabody molecule exhibits an in vivo serum half-life greater than 20 hours.

Claim 34. The diabody molecule of any one of claims 20-24 and 26-33, wherein:

(A) said first polypeptide chain comprises the light chain variable domain, the intervening GGGSGGGG linker (SEQ ID NO:10) and the heavy chain variable domain of SEQ ID NO:252; and

(B) said second polypeptide chain comprises:

(i) the light chain variable domain, the intervening GGGSGGGG linker (SEQ ID NO:10) and the heavy chain variable domain of SEQ ID NO:254; or

(ii) the light chain variable domain, the intervening GGGSGGGG linker (SEQ ID NO:10) and the heavy chain variable domain of SEQ ID NO:256.

Claim 35. The diabody molecule of claim 34, wherein said second polypeptide chain comprises said light chain variable domain, said intervening GGGSGGGG linker (SEQ ID NO:10) and said heavy chain variable domain of SEQ ID NO:254.

Claim 36. The diabody molecule of claim 34, wherein said second polypeptide chain comprises said light chain variable domain, said intervening GGGSGGGG linker (SEQ ID NO:10) and said heavy chain variable domain of SEQ ID NO:256.

Claim 37. The diabody molecule of claim 25, wherein:

(A) said first polypeptide chain comprises:

(i) the light chain variable domain, the intervening GGGSGGGG linker (SEQ ID NO:10) and the heavy chain variable domain of SEQ ID NO:254; or

(ii) the light chain variable domain, the intervening GGGSGGGG linker (SEQ ID NO:10) and the heavy chain variable domain of SEQ ID NO:256; and

(B) said second polypeptide chain comprises the light chain variable domain, the intervening GGGSGGGG linker (SEQ ID NO:10) and the heavy chain variable domain of SEQ ID NO:252.

Claim 38. The diabody molecule of claim 37, wherein said first polypeptide chain comprises said light chain variable domain, said intervening GGGSGGGG linker (SEQ ID NO:10) and said heavy chain variable domain of SEQ ID NO:254.

Claim 39. The diabody molecule of claim 37, wherein said first polypeptide chain comprises said light chain variable domain, said intervening GGGSGGGG linker (SEQ ID NO:10) and said heavy chain variable domain of SEQ ID NO:256.

Claim 40. A pharmaceutical composition comprising the diabody molecule of any one of claims 1-39 and a pharmaceutically acceptable carrier.

Claim 41. Use of the diabody molecule of any one of claims 20-39 or the pharmaceutical composition of claim 40 for the manufacture of a medicament for inhibiting B-cell proliferation.

Claim 42. Use of the diabody molecule of any one of claims 20-39 or the pharmaceutical composition of claim 40 for the manufacture of a medicament for inhibiting B-cell activation.

Claim 43. Use of the diabody molecule of any one of claims 20-39 or the pharmaceutical composition of claim 40 for the manufacture of a medicament for the treatment of an autoimmune disorder.